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DEVELOPMENT OF AN ELECTRONIC LUNG AIRWAY ATLAS

by

Jacob Nickel

A thesis submitted in partial fulfillment of the
requirements for the Master of Science
degree in Electrical and Computer Engineering
in the Graduate College of
The University of Iowa

May 2008

Thesis Supervisor: Associate Professor Gary E. Christensen

Graduate College
The University of Iowa
Iowa City, Iowa

CERTIFICATE OF APPROVAL

MASTER'S THESIS

This is to certify that the Master's thesis of

Jacob Nickel

has been approved by the Examining Committee for the thesis requirement for the Master of Science degree in Electrical and Computer Engineering at the May 2008 graduation.

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To my late grandma Gloria and grandpa Rolex.
May your souls rest together in eternal peace.

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CHAPTER 1 INTRODUCTION

1.1 Motivation and Background

In its most traditional sense, a road atlas is a book that displays towns, cities, counties, states, and the highways and interstates that travel through and across them. In addition to providing the location of these places, the atlas may also provide some more detailed information as to the location of parks, lakes, or other landmarks that may be of interest to travelers.

An anatomical book atlas serves a similar purpose by presenting the anatomy of a species. Pictures are displayed in order for the reader to get a better idea as to the shape and size of body parts and where they are located relative to one another. These images can either be artist renderings or actual snapshots of a specimen. Text is added which provides the reader with names of specific body parts being displayed. Often, due to dense anatomical locations and limited page size, this text is placed outside the image area with straight lines drawn from the text to the body part it describes. Figure 1.1 shows an example from one of Netter's anatomical book atlases[19].

According to MacKenzie-Graham et al.[15], "Atlases incorporate three critical elements: (1) graphical reconstructions highlighting important anatomical detail; (2) nomenclature and description of anatomical structures; and (3) a three-dimensional (3D) coordinate system." Talairach and Tournoux developed an anatomical book atlas[27] which introduced a new coordinate system for the human brain. This

approach references locations in the brain with respect to the anterior commissure and posterior commissure, which are aligned to lie on a straight line. These three-dimensional locations with respect to the commissures in the brain are commonly called Talairach coordinates but are sometimes referred to as stereotaxic coordinates[32]. The original Talairach atlas has been enhanced and extended into an electronic version which is available in CD-ROM form for various applications [22, 21, 23, 24, 20].

While a book atlas is adequate for learning the fundamental aspects of a species, it fails to offer some important features such as three dimensional display and user interaction that would significantly increase its usefulness. Additionally, researchers use atlases in order to determine average shape and size. To do this, it is necessary to collect many measurements of the anatomical structure. This allows for researchers to perform statistical calculations on these measurements in order to define what is normal and the variation of normality. Manually performing these anatomical measurements in order to be included in a book atlas is very tedious and time consuming. Computers can perform the same measurements automatically in a fraction of the time and in a consistent manner which eliminates human error. Comparing these measurements is also much better suited for electronic atlases once this data is included for a large number of subjects, especially since the number of measurements recorded continually increases. It is then easy to more specifically determine average size and shape for certain populations based on demographics such as age, sex, and race using an electronic atlas. For these reasons and more, medical researchers all over the world have realized the enormous potential for electronic

anatomical atlases (herein simply referred to as an “atlas”).

Atlases have historically been used to serve a wide variety of purposes, including automatic segmentation of anatomical structures[9] and mapping brain function[4, 6, 3]. They are also commonly used as a teaching tool[9, 2, 1, 25, 8]. One such tool is the National Library of Medicine’s Visible Human Project[®][2, 1, 25]. In this project, computed tomography (CT), magnetic resonance (MR), and cryosection images of both male and female cadavers were acquired. The male cadavers were sliced at one millimeter intervals while the female cadavers were sliced at one-third of a millimeter in order to depict normal representations of the male and female bodies[14].

A lot of work has been done the last few decades to create atlases of the brain[15, 3, 17, 18, 29, 28, 7, 5] for humans and other species such as mice and rats. Mazziotta et al. have focused on developing probabilistic atlases of the human brain [17, 18] in up to four dimensions which help to determine normal brain size and shape. Meanwhile, Thompson and Toga et al. have focused on detecting abnormalities in the brain using probabilistic methods[29, 28].

While a lot of work has been done to create atlases of the brain, much less attention has been focused on other body sites such as the lungs. As alluded to above, electronic atlases can be used to compare normal versus abnormal shape in subjects by removing individual variations and providing a common reference frame for reporting and comparing results. These comparisons could eventually be performed in four dimensions in order to track normal versus abnormal breathing motion, something that would be extremely difficult to do in a book atlas. Thus, development of an

electronic lung atlas is crucial to understanding lung disease, early detection of lung disease, and evaluating treatment of lung disease.

The goal of this project was to develop an atlas for researching both human and rat lungs. The atlas was intended to be general purpose so that additional species can be studied in the future using the same tool. An incremental software engineering model was incorporated which allows for multiple versions of the atlas to be released as successive improvements and modifications are made. This thesis encompasses the initial version of the developed software application.

1.2 Thesis Outline

The structure of this thesis is as follows. Chapter 2 will introduce previous atlas work performed by other groups. This was researched in order to capture a feel for the current state of anatomical atlases in the medical imaging arena. The pros and cons of each atlas researched were noted in order to get an idea of those characteristics that are either expected or desired and those that are not necessary.

Chapter 3 details the tools and technologies used to develop the atlas. Section 3.1 covers those used to create the atlas' graphical user interface. Section 3.2 describes the development of the database that interacts with the graphical user interface in order for population statistics to be presented to the user.

Chapter 4 encompasses the implementation of the atlas. The reader will be introduced to the files comprising the application, what they do, and how they work together. Chapter 5 shows the current status of the atlas and more specifically introduces the atlas from an operational perspective. Common user interaction will

be covered as well as the differences between the rat and human atlases. Screenshot images are provided for clarity purposes.

Chapter 6 will objectively discuss the pros and cons of the project as well as propose improvements and extensions that can be made to the atlas in the future to make it a more powerful tool. The thesis will end with a conclusion in Chapter 7.

Lungs In Situ: Anterior View

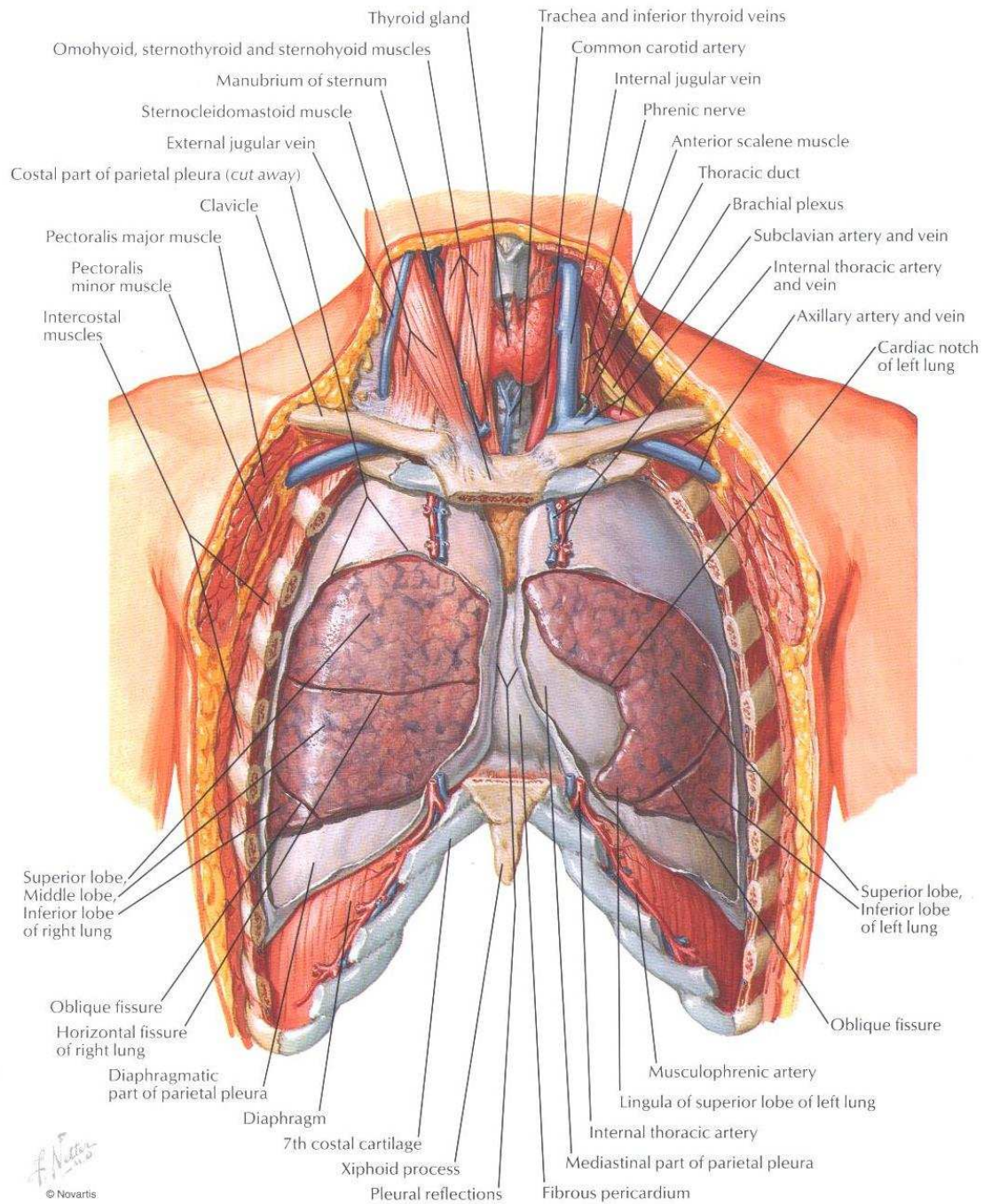


Figure 1.1: An illustration of the anterior view of lungs in situ from an anatomical book atlas[19].

CHAPTER 2 RELATED WORK

The first step taken in developing the atlas was deciding what features to incorporate. In order to get an idea as to what the medical imaging community was already doing, research was done in September 2006 to investigate the current status of atlases at that time. After a very short time searching the internet, a few glaring weaknesses stood out in the atlases found. First, there was a desperate need for improving the user interfaces. Next, there was a severe lack of 3D interaction. All of the atlases found incorporated some sort of 2D image viewer but very few offered any sort of volume viewer allowing for user rotation. These observations showed that a standalone application would much better suit an atlas than a web-based approach. The final trait that stood out after internet research was the fact that the majority of existing atlases were for the brain, while none of those found involved lungs.

While the overall glaring weaknesses of the atlases found through internet search are given above, many desired characteristics were found. In order to further investigate the pros and cons of the current atlases, three were selected for a more in-depth analysis. Namely, those are the UCLA Laboratory of Neuro Imaging (LONI) Rat Atlas[30], the Michigan State University (MSU) Navigable Atlas of the Human Brain[26], and the Biomedical Informatics Research Network (BIRN) Mouse MRI Volume Atlas[16]. It is important to note that all of the websites hosting these atlases have been updated since this research was performed. Therefore, some of the following content could have been changed.

2.1 LONI Rat Atlas

The UCLA Laboratory of Neuro Imaging Rat Atlas came closest to creating a user interface resembling a standalone application, even though it was entirely web-based. It incorporated a windowed look-and-feel with different panels contained within. The main panel contained a black and white image corresponding to a cross-sectional image of a rat brain. A box-shaped scale was provided around the main image in order to provide a reference as to the size of the brain and its components. An option gave users the ability to change modality from an artist rendering to cryosections of an actual rat brain. The top-left panel allowed users to choose either the coronal, sagittal, or transverse orientation for the picture shown in the main panel. In order to give the user an idea where the displayed 2D slice was located within the brain, the LONI Rat Atlas also showed a picture of a real rat brain with a red line transposed over the image in its corresponding location. A screenshot of the UCLA Laboratory of Neuro Imaging Rat Atlas can be seen in Figure 2.1.

2.2 MSU Navigable Atlas of the Human Brain

The Michigan State University Navigable Atlas of the Human Brain was also developed strictly for web-based use, therefore its developers were probably not worried about creating a user interface with look-and-feel of a standalone application. Upon accessing the atlas, the very first page required the user to choose between a coronal, horizontal, or sagittal “montage”, a brain stem atlas, and what the group deemed external views (coronal, horizontal, and sagittal) of the brain. The montages simply consisted of a page full of many cross-sectional pictures of the brain in the ori-

entation selected by the user. The brain stem atlas and the three external views were all very similar but for different views and sections of the brain. All of these options depicted a 2D image of the brain with lines transposed over it which were essentially links to another page which displays a cross-sectional picture corresponding to that location.

This atlas incorporated MRI images of a living subject as well as pictures of cadavers that were sliced and stained in order to show either cell bodies or nerve fibers and then placed between two glass panes. One greatly desired characteristic of the Michigan State atlas was the ability to turn labels of anatomical names on and off anywhere they were displayed. This allowed the user to better see small details in certain areas that would not be possible if the labels were permanently fixed to the images. A portion of the home page of the Navigable Atlas of the Human Brain can be seen in Figure 2.2.

2.3 BIRN Mouse MRI Volume Atlas

The Biomedical Informatics Research Network Mouse MRI Volume Atlas offered a rotatable 3D visualization of a data set. The panel allowing for rotation was surrounded by three other panels which contained orthogonal images of the three corresponding orientations. One nice feature included in the BIRN atlas besides the 3D visualization was the colored segmentation of the brain dataset. However, the most desired characteristic of the BIRN atlas was the interaction between the four panels. Clicking on the 3D image would update the other three panels by changing their slices to the appropriate location and render cross-hairs over the images in order

to show the exact point selected. Similarly, clicking in one of the orthogonal panels would change the images displayed in the other orthogonal panels. The only downfall to this interaction was that the user was unable to change the orthogonal slice of a particular orientation by directly interacting with its corresponding panel. For instance, in order to change the orthogonal slice shown in the coronal view panel the user had to click on the 3D volume or on either the sagittal or transverse view panels rather than interacting with the coronal image panel itself. A screenshot of the BIRN mouse atlas can be seen in Figure 2.3.

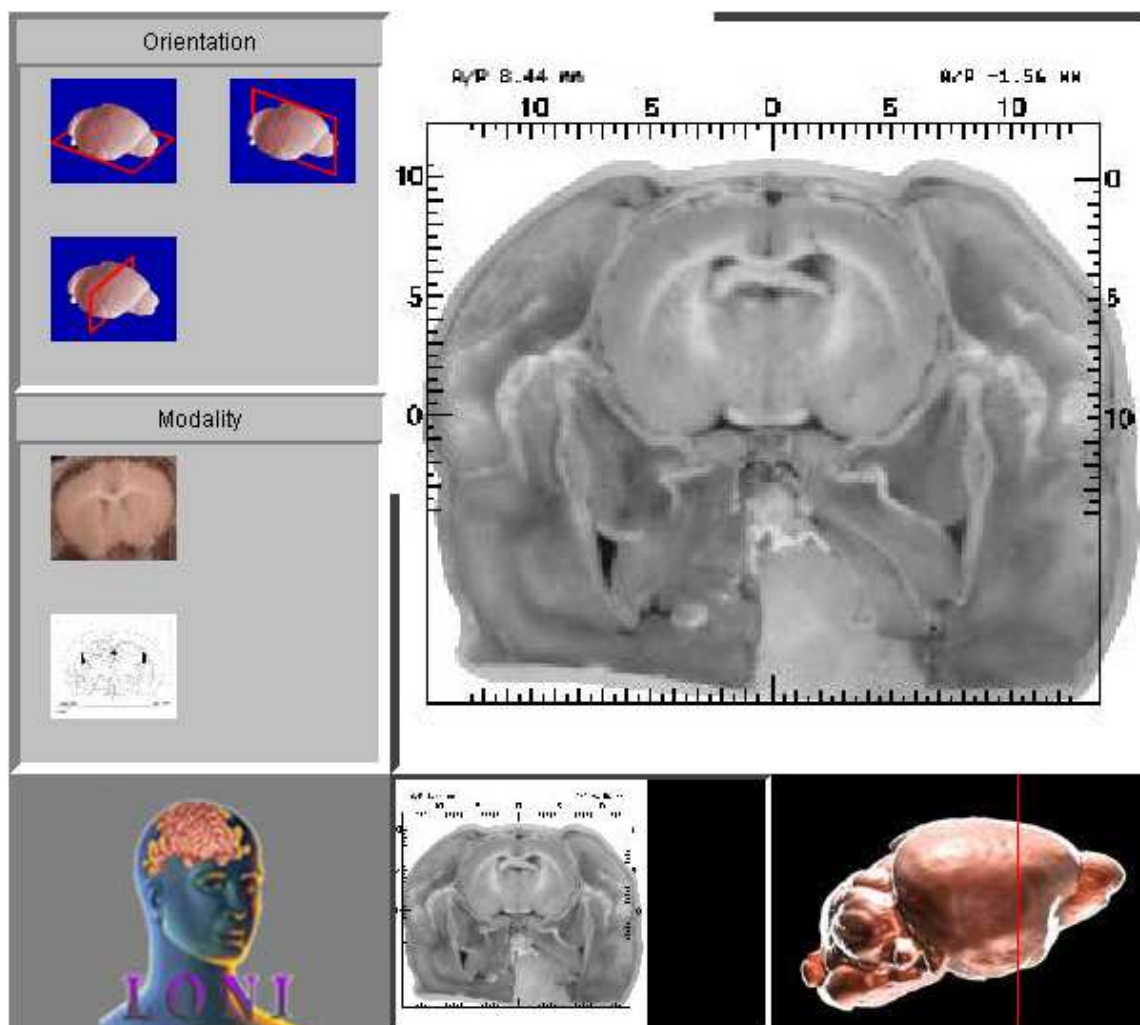


Figure 2.1: A screenshot of the UCLA Laboratory of Neuro Imaging Rat Atlas.

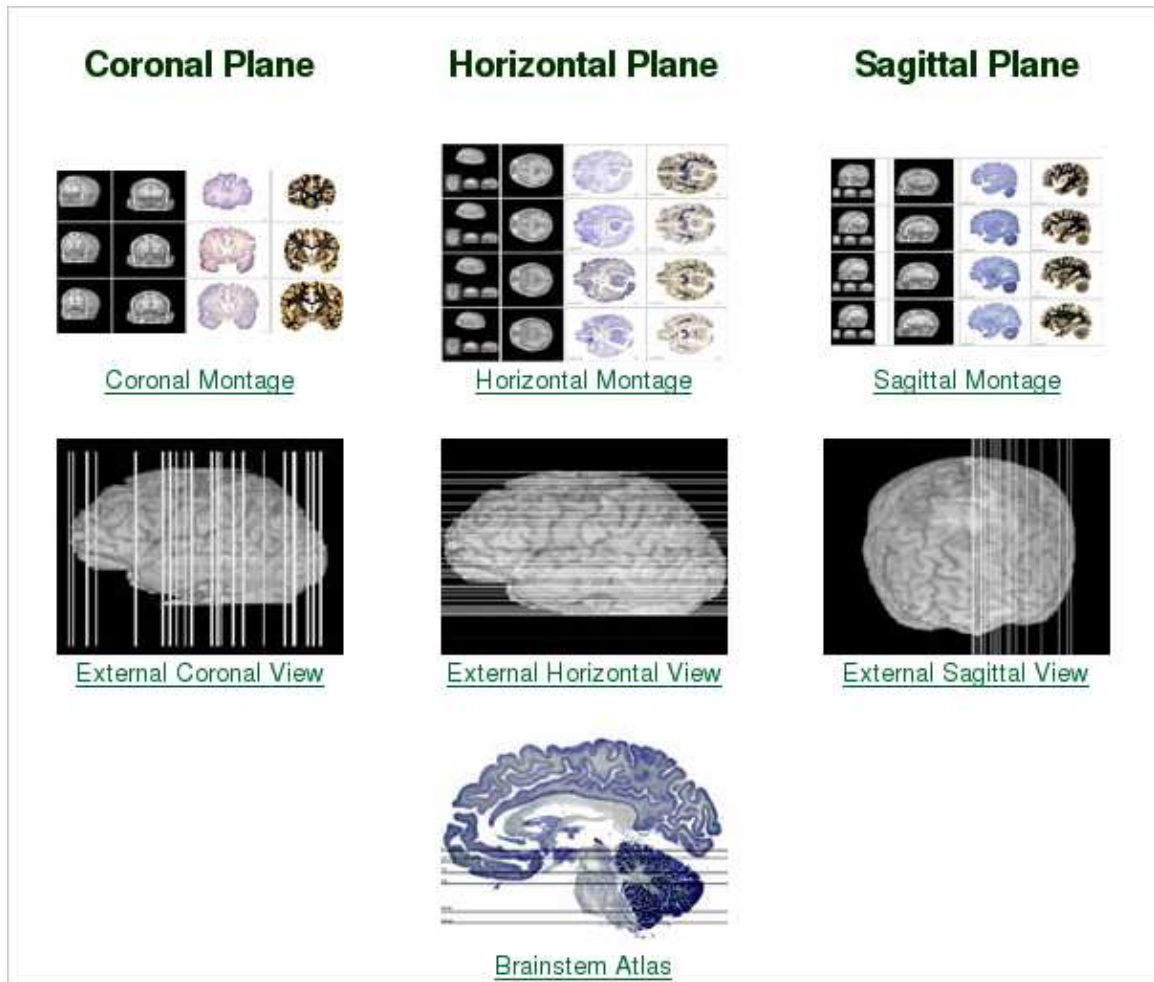


Figure 2.2: A screenshot of the Michigan State University Navigable Atlas of the Human Brain. Reproduced with permission from <http://www.msu.edu/~brains/brains/human/index.html>. The U.S. National Science Foundation supports this website.

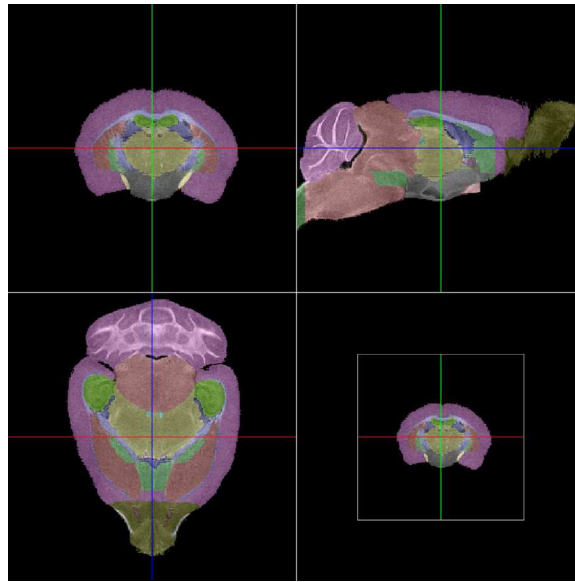


Figure 2.3: A screenshot of the Biomedical Informatics Research Network Mouse MRI Volume Atlas. Reproduced with permission from Primary Investigator Arthur Toga and Project Manager Jyl Boline.

CHAPTER 3 METHODS

3.1 Graphical User Interface

The graphical user interface (GUI) of the atlas was developed using C++, ITK, VTK, and KWWidgets. An explanation of each of these technologies follows. C++ is a very well known and widely used programming language that was originally developed as an enhancement to the original C programming language. “It is a statically typed, free-form, multi-paradigm, usually compiled language supporting procedural programming, data abstraction, object-oriented programming, and generic programming[31].”

ITK, VTK, and KWWidgets are all cross-platform, open-source toolkits developed by Kitware, Inc., a small software company founded in 1998 that specializes in 3D graphics and medical image analysis and visualization[10]. Each of these toolkits has a very active user community that includes an electronic mailing list where users can send any questions, comments, or requests. This proved to be an invaluable asset over the course of the project.

ITK is short for the National Library of Medicine Insight Segmentation and Registration Toolkit[11]. As its name suggests, ITK is primarily used for two main components of medical image processing known as image segmentation and image registration. Image segmentation is the process of separating part of an image from the rest of its pixels (in 2D) or voxels (in 3 or more dimensions). This is done in order to focus attention on a specific portion of the data and reduce necessary computing

time and power. For instance, image segmentation could be performed on a 3D computed tomography (CT) image in order to extract the lung airway tree from the bones, lung lobes, blood vessels, and other anatomy present in the dataset. Image registration is the process of using mathematical formulas to match two or more images to one another in order to determine the similarities and differences between them.

VTK stands for the Visualization Toolkit[13]. This toolkit focuses on the rendering and display of both two-dimensional and three-dimensional images. Many computer graphics techniques are incorporated into the toolkit in order to be very powerful and versatile.

KWWidgets is a toolkit built atop VTK that aids in the rapid development of graphical user interfaces[12]. It provides containers for VTK objects to be included in separate frames within a window while also implementing everyday user interface components such as checkboxes, drop-down menus, and pushbuttons.

3.2 Database

In order to study characteristics of the lung airways displayed by the atlas GUI, users are able to query statistics stored in a MySQL database. According to Wikipedia, MySQL is a multithreaded, multi-user SQL database management system (DBMS) which has more than 11 million installations[33]. Currently, the database is being hosted from a local machine for development purposes. However, in order to release the atlas application to potential users, the database will need to be moved to a publicly accessible server unless another option is chosen for database services.

Communication between the atlas GUI and the database is accomplished through a separate interface developed using KWidgets and C++, which will be referred to as the database window.

CHAPTER 4 IMPLEMENTATION

In all, sixteen original C++ classes were written to create the atlas. Thirteen of these are subclasses of either a VTK or KWWidgets class and therefore follow the same naming convention. That is, any class inheriting directly from KWWidgets has a name containing the prefix “vtkKW” and any class inheriting directly from VTK has a name starting with just “vtk”. A list of the classes inheriting from either VTK or KWWidgets is given in Table 4.1 along with the name of their direct superclass. Note that file suffixes (such as .h and .cxx) have been omitted.

The layout of the devised atlas GUI can be seen in Figure 4.1. As alluded to above, not all of the classes created are direct subclasses of either VTK or KWWidgets. For that matter, not all of the files that comprise the atlas are classes. Figure 4.2 shows all of the atlas files and how they interact in order to create the atlas. Once again, file suffixes have been omitted. All of the double-arrows represent a one-to-one relationship unless specifically noted otherwise on the figure. Herein, the “vtk” or “vtkKW” may be dropped from class names in order to save space and improve readability.

As shown, LungAtlas is the top-most file where everything begins. This file contains the special “main” function where C++ programs begin execution. In main, a library is created consisting of all atlas files that use C++ methods as callbacks. These files are then wrapped in a scripting language used by KWWidgets called Tcl before being placed in the library. Next, a KWWidgets application is created. After

Table 4.1: Atlas Classes and their Superclasses

Atlas Class	Superclass
vtkAtlasGenericXMLParser	vtkAtlasXMLParser
vtkAtlasXMLDataParser	vtkAtlasXMLParser
vtkAtlasXMLLabelParser	vtkAtlasXMLParser
vtkAtlasXMLParser	vtkXMLParser
vtkBead	vtkObject
vtkBeadHandler	vtkObject
vtkInteractorStyleCursorLinkAtlas	vtkInteractorStyle
vtkInteractorStyleCursorLinkOrtho	vtkInteractorStyle
vtkKWAtlasDataBase	vtkKWWindow
vtkKWAtlasRenderWidget	vtkKWRenderWidget
vtkKWAtlasWelcome	vtkKWWindowBase
vtkKWAtlasWindow	vtkKWWindow
vtkKWOrthogonalRenderWidget	vtkKWRenderWidget

this has been done, a splash screen is displayed by LungAtlas until control is passed to the AtlasWelcome class.

The AtlasWelcome class is a simple class that displays a dialog allowing the user to select between the human atlas and rat atlas by clicking a push button. Upon doing so, this dialog is withdrawn and the appropriate splash screen is displayed until the AtlasWindow class has loaded and is ready to be displayed.

As its name suggests, the AtlasWindow class is a window that serves as the main graphical user interface. It maintains control of many other classes that are “plugged in” to the window as well as some that are behind the scenes. The classes that are controlled directly by AtlasWindow are AtlasRenderWidget, DataHandler, and KWAtlasDataBase. As shown in Figure 4.2, each AtlasWindow has 2 instances of the AtlasRenderWidget class, which each maintain 3 instances of the OrthogonalRenderWidget class. This leads to the AtlasWindow containing 6 OrthogonalRen-

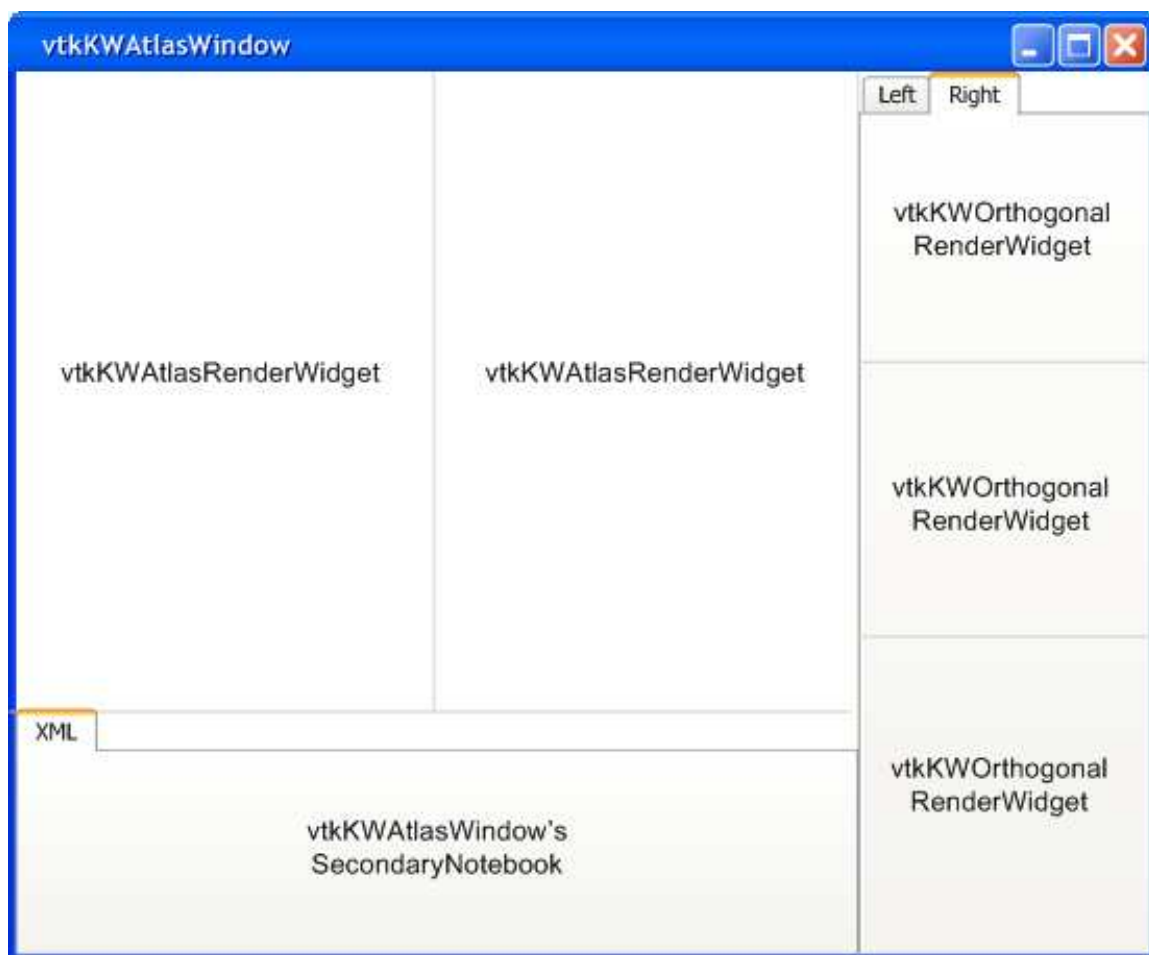


Figure 4.1: The layout of the atlas GUI and its encapsulated widgets.

derWidgets in total. Each of these classes will be described in more detail later.

The DataHandler class was created before a database was incorporated into the project. Its purpose is to keep track of such things as file names and locations of images to be displayed in the GUI. This class was created in order to serve as a compromise between hard-coding and dynamic data retrieval. It uses the AtlasXML-DataParser to parse an XML file that stores names and attributes of images to be

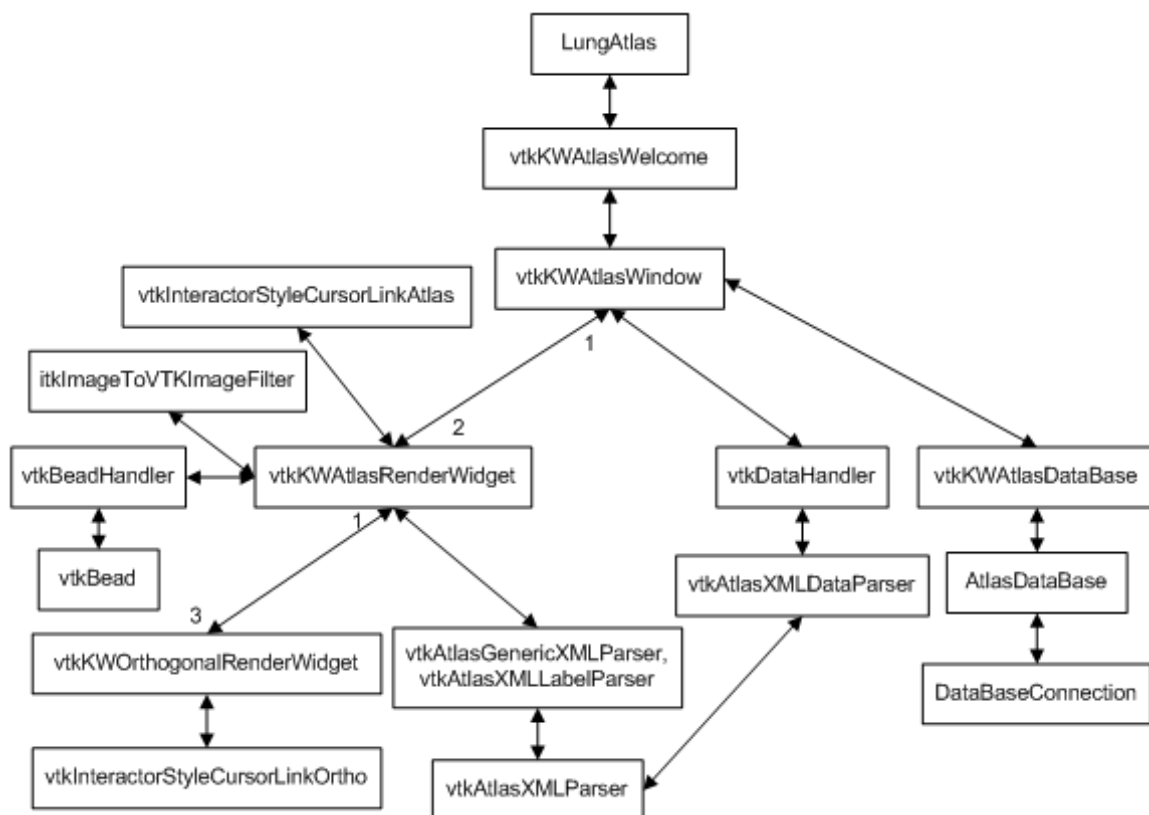


Figure 4.2: The interaction of C++ files comprising the atlas.

displayed by the atlas. This allows for additional images to be provided to the atlas user without needing to re-compile the application. Thus, for small incremental changes in the size of the database population, little work is required on the developer's side. However, as the number of subjects in the database grows more rapidly, it will be convenient to adapt the application to read all of this information directly from the database.

The user is able to launch the KWAtlasDataBase class from the AtlasWindow by clicking on a push button located near the bottom of the GUI. This class creates

and displays a `vtkKWWindow`, just like the GUI itself. Therefore, rather than the `KWAtlasDataBase` being encapsulated by the `AtlasWindow`, they can be thought of as being on the same level even though there is an obvious parent-child relationship that exists. The `AtlasRenderWidget` and `OrthogonalRenderWidget` classes can communicate with the `KWAtlasDataBase` class if it has been opened by the user, but this interaction must go through the `AtlasWindow`. In order to connect to the database and retrieve information from it, `KWAtlasDataBase` uses two other classes, `AtlasDataBase` and `DataBaseConnection`.

The majority of the atlas GUI consists of multiple instances of two classes mentioned earlier, `AtlasRenderWidget` and `OrthogonalRenderWidget`. When the atlas GUI is loaded, two `AtlasRenderWidget`s are created. Initially, the left `AtlasRenderWidget` displays a 2D artist rendering of the lung airway and the right `AtlasRenderWidget` displays a 3D lung airway surface. Each of these `AtlasRenderWidget`s is able to switch back and forth between 2D and 3D views. Whenever an `AtlasRenderWidget` is created, 3 instances of the `OrthogonalRenderWidget` class are created as well. This class consists of an image canvas that displays an orthogonal slice of the 3D airway rendered in the `AtlasRenderWidget` and a slider that allows the user to traverse through the slices. The `OrthogonalRenderWidget`s are displayed in a tabbed frame on the right side of the atlas GUI, with only three of them viewable at a time to save screen space. Thus, the three orthogonal slices of a 3D surface being displayed in either the left or right `AtlasRenderWidget` can be viewed, but not all six simultaneously.

The `AtlasRenderWindow` and `OrthogonalRenderWindow` classes each have a class which deals with all user interaction within the specific widget. These classes are, respectively, `InteractorStyleCursorLinkAtlas` and `InteractorStyleCursorLinkOrtho`. When an `AtlasRenderWindow` is double clicked, `InteractorStyleCursorLinkAtlas` takes care of such things as displaying a sphere on the 3D surface, changing the orthogonal image slices, and displaying cross-hairs in each `OrthogonalRenderWindow`. `InteractorStyleCursorLinkOrtho` handles tasks such as updating slices and cross-hairs of all three `OrthogonalRenderWidgets` when an airway is selected in one of the orthogonal views.

In order to open the 3D images displayed by the `AtlasRenderWidgets` and `OrthogonalRenderWidgets`, a class named `itkImageToVTKImageFilter` was used. This class was not originally developed as part of the atlas project but was rather created by an ITK developer. It was included in the class hierarchy diagram in order to show how ITK was incorporated into the project, as loading the 3D image is the only task performed by ITK in the project. This class was used because the 3D images displayed within the atlas GUI are in the Mayo Clinic's Analyze software version 7.5 file format. VTK does not yet have a class that reads these files, whereas ITK does. Therefore, this class opens the images in ITK and converts them to a format that is understandable to VTK so that they can be rendered within the atlas GUI.

The `BeadHandler` class allows for spheres, or "beads", to be rendered in a 3D `AtlasRenderWindow` view. These beads are pre-computed using a separate software program implementing what is known in the medical imaging world as a snake.

This snake program traverses down the centerline of an airway and selects three-dimensional bead locations of equidistant intervals. This program is only partially automatic, as the user must provide some starting points for the program to consider as well as the number of locations to divide each airway segment. Thus, the spacing of the beads depends on the total length of the airway segment traversed and the number of beads desired for that segment. The `BeadHandler` class uses the `Bead` class for each sphere that is rendered, which for the most part simply holds the (x, y, z)-location of the bead.

The `AtlasXMLLabelParser` class, which is a subclass of the `AtlasXMLParser` class, allows for labels to be automatically loaded into an `AtlasRenderWidget`. This class reads XML files that describe each label's text, color, size, location, and other attributes that determine the style of the label. The `AtlasGenericXMLParser` class is another subclass of `AtlasXMLParser`. Its job is to parse XML files associated to the 3D images displayed within the GUI and maintain a pointer to this data. Then, upon user interaction with these images, relevant data is retrieved and populated within the `AtlasWindow`'s `SecondaryNotebook` that is shown in Figure 4.1.

When the `AtlasWindow` is closed, the `AtlasWelcome` dialog returns. This allows a user to go from the human atlas to the rat atlas and vice versa as many times as they wish. However, due to the withdrawing of the `AtlasWelcome` dialog after one of its push buttons is clicked, it is not possible to open the human atlas and rat atlas at the same time. Nor is it possible to display multiple instances of either the human atlas or rat atlas simultaneously, in order to avoid any memory issues that

may arise from attempting to load too many of the large 3D images. Once the user is done using the atlas application and closes the AtlasWelcome dialog, the LungAtlas file takes control once again, frees up memory, and exits.

CHAPTER 5 RESULTS

Upon launching the atlas program, a splash screen shown in Figure 5.1 is displayed for a brief period of time while the application initializes. A simple dialog shown in Figure 5.2 is then displayed which allows the user to open either the human atlas or the rat atlas by pressing the appropriate push button. After making this selection, another splash screen corresponding to either the human atlas or rat atlas (depending on the user's choice) is displayed while the graphical user interface loads. Splash screens for both the human and rat atlas can be seen in Figure 5.3.



Figure 5.1: Splash screen displayed upon launching the atlas.

Once the graphical user interface has loaded it is displayed and the atlas-specific splash screen is withdrawn. The atlas GUI consists of three main panels containing many different image canvases, as shown for the human atlas in Figure 5.4. These three main panels are organized horizontally from left to right. The first

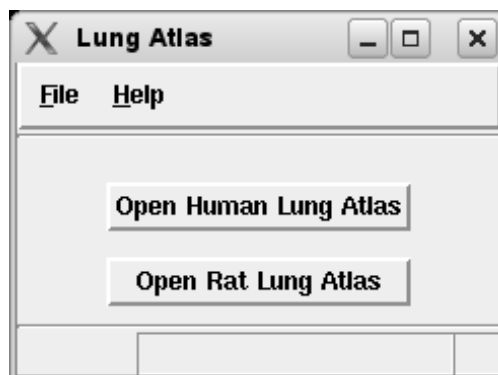


Figure 5.2: A screenshot of the lung atlas welcome dialog.



Figure 5.3: Splash screens for the human and rat atlas.

panel initially displays an artist's drawing of the lung airway tree. The second image panel initially contains a 3D surface that is created from a segmented lung airway dataset. The third and right-most image panel simultaneously contains three separate canvases displaying the different orthogonal cross-sections of the same dataset used for the 3D surface. These orthogonal cross-sections, or slices, are laid out in a vertical manner. The top orthogonal image canvas contains transverse (X-Y plane) slices of the dataset, the middle orthogonal image canvas contains sagittal (Y-Z plane) slices

of the dataset, and the bottom orthogonal image canvas contains coronal (X-Z plane) slices of the dataset.

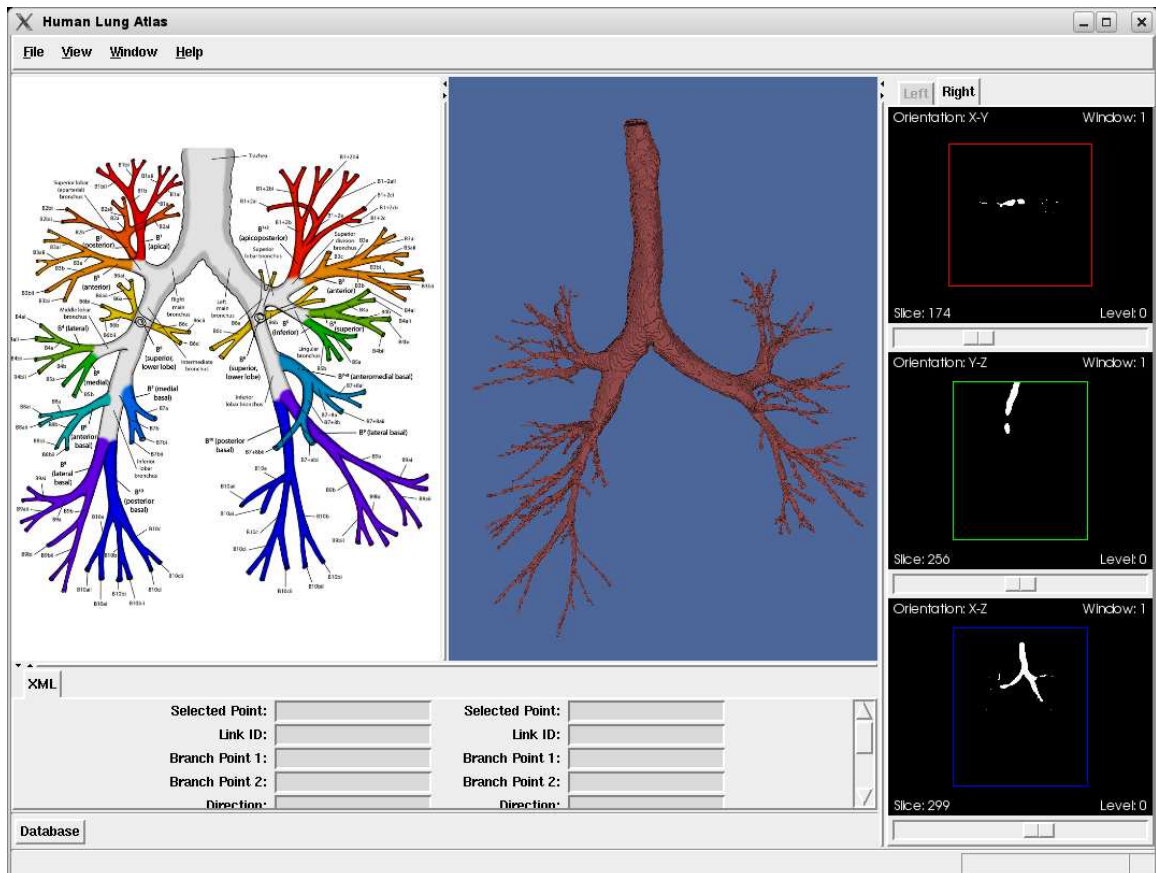


Figure 5.4: Graphical user interface for the human lung atlas.

The left and center image panels can be changed from 2D to 3D views and vice versa. This allows the user to open two different three-dimensional dataset surfaces simultaneously in order to view their similarities and differences. When two surfaces are displayed simultaneously, the orthogonal slices of each can be viewed in

the right-most image panel. This panel contains two tabbed frames, with the left tab corresponding to the surface being displayed in the left image panel and the right tab corresponding to the surface being displayed in the center image panel of the GUI. When a 2D artist drawing is being displayed in either the left or center image panels, the corresponding tab in the right image panel becomes inactive. This can be seen in Figure 5.4, as the left tab of the right image panel is inactive since the 2D artist drawing is being displayed in the left image panel.

The 2D image canvas basically serves the same purpose as a traditional book atlas, by showing a picture that portrays the basic structure of the lung airway. In order to further emulate a traditional book atlas, labels are displayed on the image in order to inform the user of airway names and their relative location. However, in dense locations these labels can become rather crowded. This is one small example of the advantage electronic atlases hold over traditional book atlases, as simply right-clicking on the 2D image canvas provides an option to turn the labeling of the airways on and off. The user can also zoom in or out on the 2D image by scrolling the middle mouse button up (to zoom in) or down (to zoom out) while the cursor is within the bounds of the 2D image canvas.

The 3D segmented image rendering of a real lung airway tree helps users to get a much better feel for the true size and shape of airways relative to one another than is possible with a two-dimensional, artist rendered image. The 3D image canvas further separates the electronic atlas from the traditional book atlas by providing for user interaction to rotate, translate, and zoom in or out on the 3D lung airway

surface. As in the 2D case, the 3D surface also provides an option for airway labels to be displayed. This can be done by simply right-clicking on the image canvas and selecting the desired labels from a pop-up menu. A screenshot of the human atlas after rendering labels on the 3D surface can be seen in Figure 5.5.

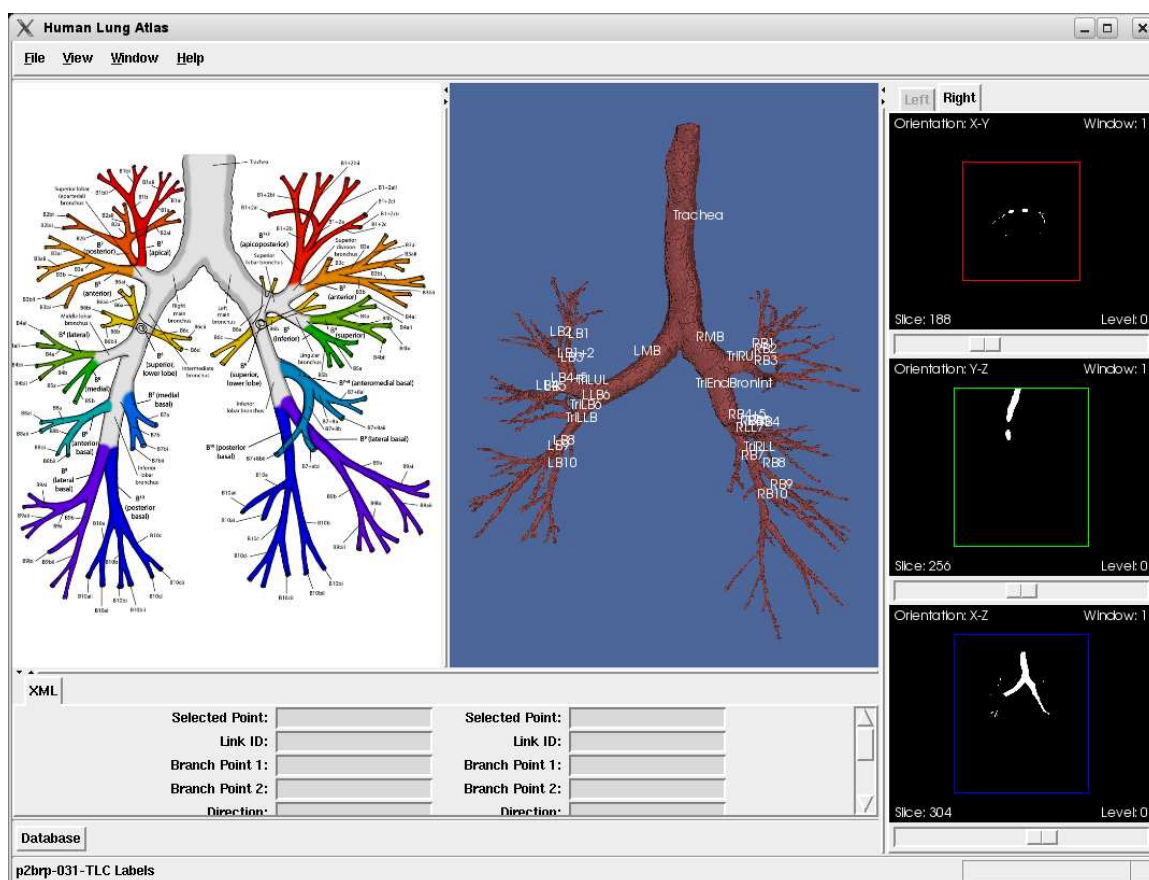


Figure 5.5: Human atlas with labels rendered on the 3D surface.

Rotating the 3D surface is accomplished by holding down the left mouse button and dragging the mouse while the cursor is inside the 3D image canvas. This is

done using what is known in computer graphics as a trackball camera, which is very intuitive and takes little time to grasp. Translating the surface involves the same user interaction as rotation but with the middle mouse button rather than the left. Zooming in and out on the 3D surface can be done by scrolling the mouse wheel in an identical fashion as the 2D case. Right-clicking the mouse while the cursor is within the 3D image canvas bounds causes the aforementioned pop-up menu to open, giving the user options including turning the airway rendering on and off and switching the panel to a 2D view.

The 3D surface also interacts with all of the orthogonal slices, as these are simply different views of the same image. Double-clicking on the 3D surface with the left mouse button causes a chain of events to occur. First, a sphere is rendered on the surface where the user double-clicked. Next, if an airway branch segmented image is used to create the surface, the branch containing the selected voxel is rendered in red. An airway branch segmented image is one whose voxels belonging to the same airway branch all have an identical value unique from that of all other airway branches. For instance, all voxels corresponding to the subject's trachea could have a value of '1', while another airway branch may have a value of '2', and so on.

After the sphere is rendered and the selected airway segment is possibly highlighted, the transverse orthogonal image canvas updates to the correct slice within the image. It then renders cross-hairs atop the image so that the user-selected point becomes obvious. The sagittal and coronal orthogonal image canvases then follow suit, completing the waterfall of events caused by double-clicking on the 3D surface.

Identical events occur when the user left clicks in any of the three orthogonal image canvases, but in a different order that depends on which specific image canvas witnessed the event.

Aside from the generic functionality detailed above which is independent of the atlas that was chosen, the human and rat atlases have some differences that will be outlined below along with some project-specific details that are worth mentioning.

5.1 Human Atlas

One goal of this project is to determine differences across and similarities within different demographic categories of humans such as age, sex, race, and ethnicity while classifying subjects as “normal” for healthy patients or “diseased” for individuals with asthma, emphysema, or other pulmonary illnesses. In order to do so, it was necessary to incorporate a database into the project to maintain airway statistics that can be used to compare various groups of the population. Hundreds of human subjects, which are all intended to one day be included in the population of the atlas, have already been scanned by the Radiology department at the University of Iowa. However, in order to keep things simple for the first version of the atlas and allow for more concentration on the development of the atlas GUI, the current population of the database was kept small. Currently there are three males and three females deemed to be “normal” by an expert within the University of Iowa Radiology department. In addition, three asthmatic subjects have been added to the human atlas population in order to develop a framework for comparing healthy versus diseased patients. The 3D images displayed in the atlas GUI for these patients are all airway

branch segmented images. A screenshot of the human atlas that helps to portray the use of an airway branch segmented image is shown in Figure 5.6. The number of subjects included in the atlas population will incrementally grow in the future to provide a more accurate representation of humans from all walks of life.

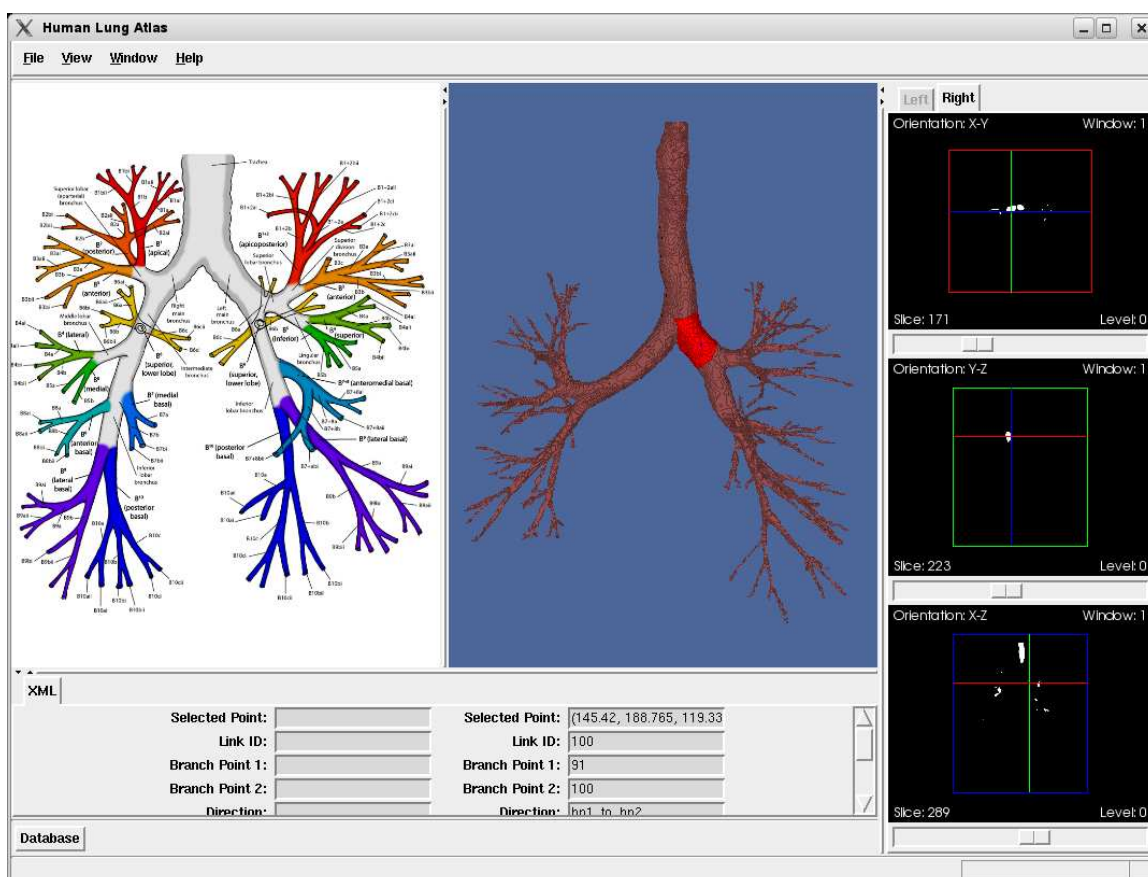


Figure 5.6: A screenshot of the human atlas after double-clicking the 3D image.

Statistics of the lung airway scans used in the atlas population were calculated by Pulmonary Workstation, a software program developed by Vida Diagnostics, Inc.

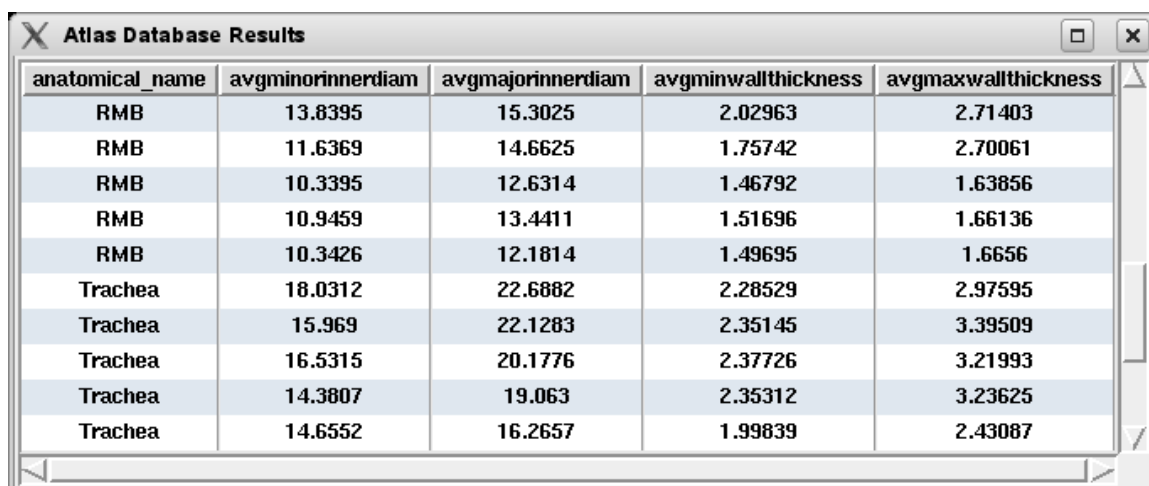
Examples of the many statistics calculated by this program include diameters and wall thicknesses for each airway segment. These statistics were calculated and can be retrieved at both Functional Residual Capacity (FRC) and Total Lung Capacity (TLC) for all nine human subjects in the database. Additionally, the user is able to select whether to display an FRC or TLC image within the GUI itself. In order to initiate communication with the database, the user must click on the “Database” button that is located at the bottom of the atlas GUI. This displays the database window that can be seen in Figure 5.7.

The database window gives the user the ability to query the database for any of the statistics calculated and stored by Pulmonary Workstation. The left panel of the database window allows the user to narrow the scope of their query by specifying the desired demographics of subjects in the database such as age, sex, and race. Additionally, the user can return statistics corresponding to normal subjects, diseased subjects, or both. The top-middle panel of the database window allows users to choose airway branches of interest to be queried. The top-right panel of the database window currently does not contribute at all to the actual query that is submitted, as the database currently contains nothing but airway measurements stored in textual format. However, in future versions of the atlas, the database will be expanded to hold a wider range of data including different types of images that users will be able to request using this top-right panel. Thus, this panel has been added to the database window for subsequent revisions of the atlas when the database is more completely populated. The bottom panel of the database window allows the user to select the

The screenshot shows the 'Query Atlas Database' interface. It features several input sections: 'Subject Demographics' (Age: 0-100, Gender/Sex, Ethnicity), 'Racial Categories' (American Indian/Alaska, Asian, etc.), 'Cohort' (Normal/Diseased checkboxes, Diseases list), 'Branches by generation: 4' (Trachea, RMB, LMB, etc.), 'Audio' (Biomagnetic imaging, etc.), and 'Diameter', 'Wall Thickness', 'Area', 'Operations' (avgminorinnerdiam, etc.). There are also checkboxes for 'Centerline', 'FRC', 'TLC', and 'Residual Volume'. The interface includes 'Select All' and 'Deselect All' buttons for the lists, and 'Submit Query' and 'Reset Form' buttons at the bottom.

Figure 5.7: A screenshot of the database window.

actual airway measurements they would like returned from the database. Once the user has selected the desired demographics, airways, and statistics, they can click the “Submit Query” button in order to retrieve the data. An example of results returned from the query can be seen in Figure 5.8.



anatomical_name	avgminorinnerdiam	avgmajorinnerdiam	avgminwallthickness	avgmaxwallthickness
RMB	13.8395	15.3025	2.02963	2.71403
RMB	11.6369	14.6625	1.75742	2.70061
RMB	10.3395	12.6314	1.46792	1.63856
RMB	10.9459	13.4411	1.51696	1.66136
RMB	10.3426	12.1814	1.49695	1.6656
Trachea	18.0312	22.6882	2.28529	2.97595
Trachea	15.969	22.1283	2.35145	3.39509
Trachea	16.5315	20.1776	2.37726	3.21993
Trachea	14.3807	19.063	2.35312	3.23625
Trachea	14.6552	16.2657	1.99839	2.43087

Figure 5.8: Example results returned from querying the atlas database.

5.2 Rat Atlas

One challenge with the Rat Atlas involved communicating lung airway names between the involved researchers. Prior to this project, no knowledge of a standard rat lung airway nomenclature existed. It is believed that rats and other similar species possess an airway tree structure consisting of solely bifurcations, and thus no trifurcations. That is, it is believed that each airway segment splits into no more than two child segments. Therefore, an original attempt at naming the rat lung airway consisted of a binary naming scheme. In this scheme, the top-most airway branch in the tree structure (what is known as the Trachea in humans) was assigned a name of '1'. From there, each branch was assigned a name consisting of its parent's name with a zero or one appended to the end. Therefore, the two children of the top-most branch would have names of '10' and '11'. Whether a zero or one was appended to

the end was determined by the airway branch diameters. A zero was appended for each “major” branch (that with the larger diameter) and a one was appended for the “minor” branches. A manually segmented rat airway showing the first generations of such a binary naming scheme can be seen in Figure 5.9.

While binary naming schemes are convenient for computers, they fail to be intuitive for person-to-person communication. Additionally, it is common to see rat airways with over 500 of these bifurcations. For these reasons the group decided to devise a naming scheme that would allow for meaningful human interaction and avoid discussing branches with names such as “1001010”. A scheme developed by Charles Plopper et al. at the University of California-Davis was adopted. Rather than divide the airway tree into short branches that stop once a bifurcation is encountered, the tree is divided into airways that are logically related with respect to location and orientation within the lung. To date, fifteen airways have been named. The current nomenclature can be seen in Figure 5.10.

As in a human, the “root” of the tree structure is called the Trachea (T). The bifurcation at the end of the Trachea results in the Left Main Airway (L) and the Right Main Airway (R). As the Left Main Airway is contained solely within the Left Lobe, its children consist of the segments Left Airway A (LA) through Left Airway E (LE). The right side of the rat lung is more involved as it consists of four total lobes. Three of them, the Right Cranial Lobe, Right Middle Lobe, and Accessory Lobe, each contain one main airway which borrows its name from the parent lobe (RCr, RM, Acc). The fourth lobe on the right side of the rat lung is the Right Caudal

Lobe, which has four children whose names are Right Caudal A (RCdA) through Right Caudal D (RCdD). While it may not be obvious from the figure, the Left Main Airway and Right Main Airway extend all the way from the end of the trachea down to the smallest generations. This is the vast difference between the adopted naming scheme and the originally proposed binary scheme, as the airway segments are not forced to stop as soon as a bifurcation is encountered.

A screenshot of the rat atlas taken directly after its opening can be seen in Figure 5.11. The current population included in the rat atlas consists of six subjects scanned and segmented by researchers at Pacific Northwest National Laboratory in Richland, WA. In contrast to the human atlas, a database has not yet been created in order to allow the user to query calculated airway measurements.

Users of the rat atlas can also render center line beads for any of the six rat airways in a 3D image panel. The location of these beads were pre-computed by a separate software program which implements a “snake” that traverses the center line of the airway and determines (x, y, z) -locations at relative intervals, as described in Chapter 4. A screenshot of the rat atlas with beads rendered on the 3D surface can be seen in Figure 5.12. More than one set of beads can be rendered at a time and beads corresponding to a different airway than that being displayed in the 3D image panel can be rendered so that differences between the airways become apparent. These beads help to create correspondences between the six airway trees that will be used when it comes time to register the images.

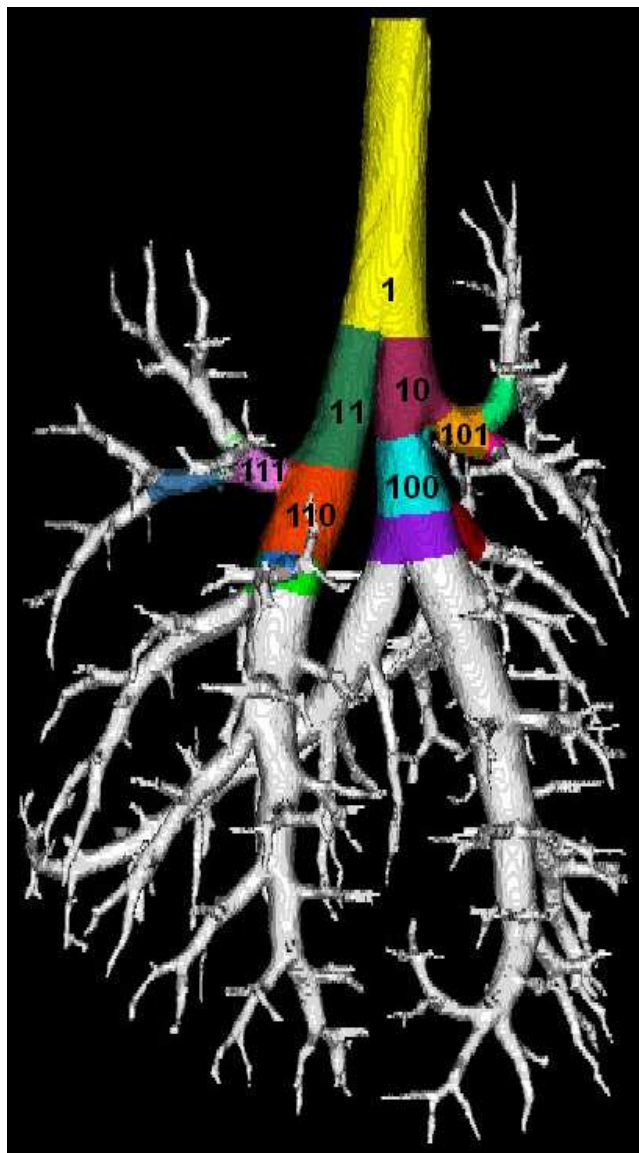


Figure 5.9: A manually segmented rat lung airway with its first generations labeled using a binary naming scheme.

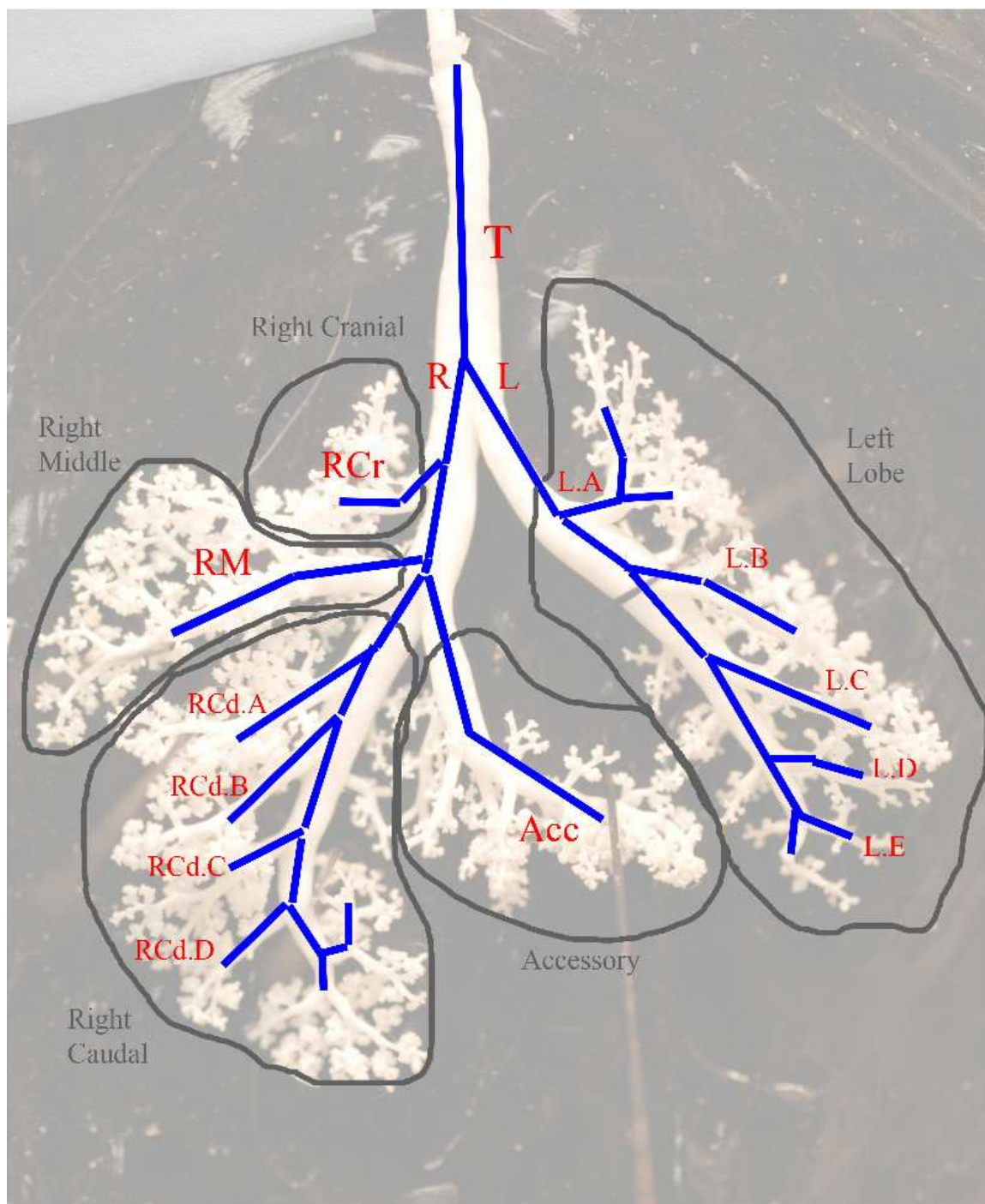


Figure 5.10: A depiction of the rat lung airway naming scheme devised by Plopper et al. at the University of California-Davis.

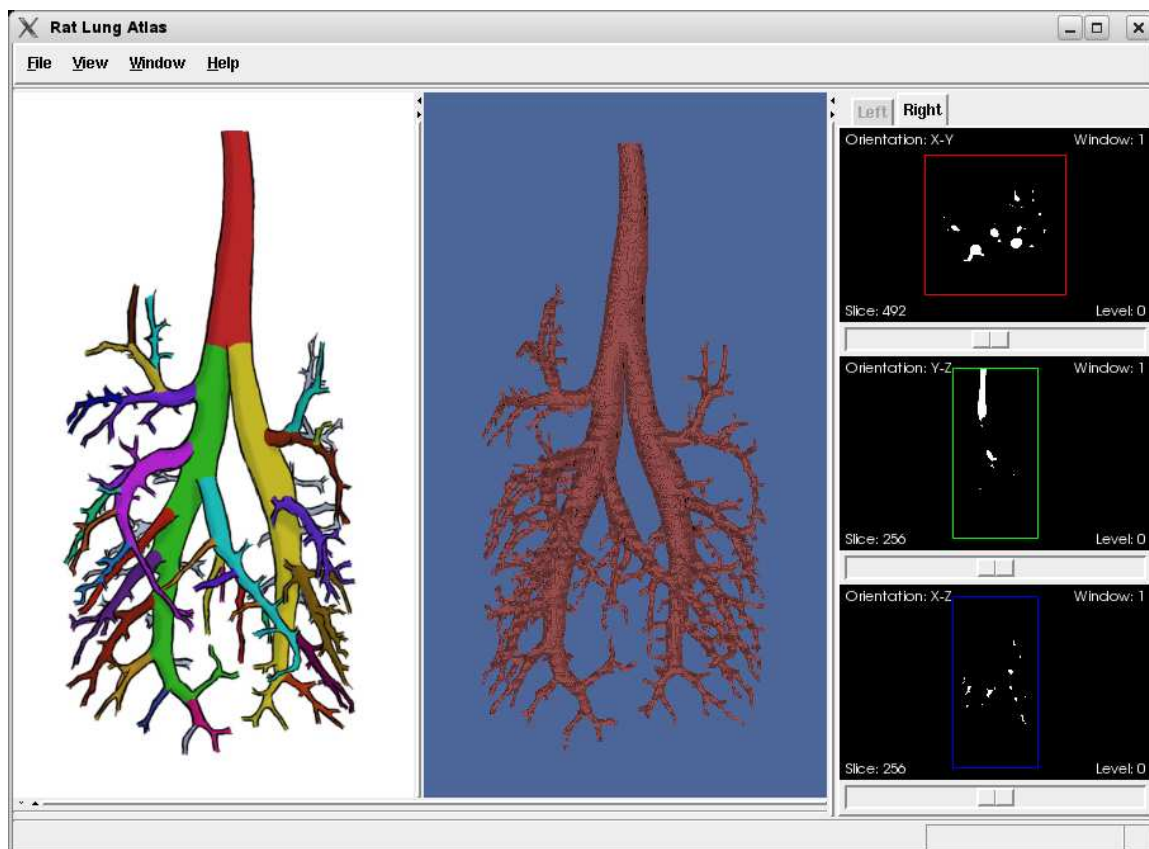


Figure 5.11: A screenshot of the rat atlas.

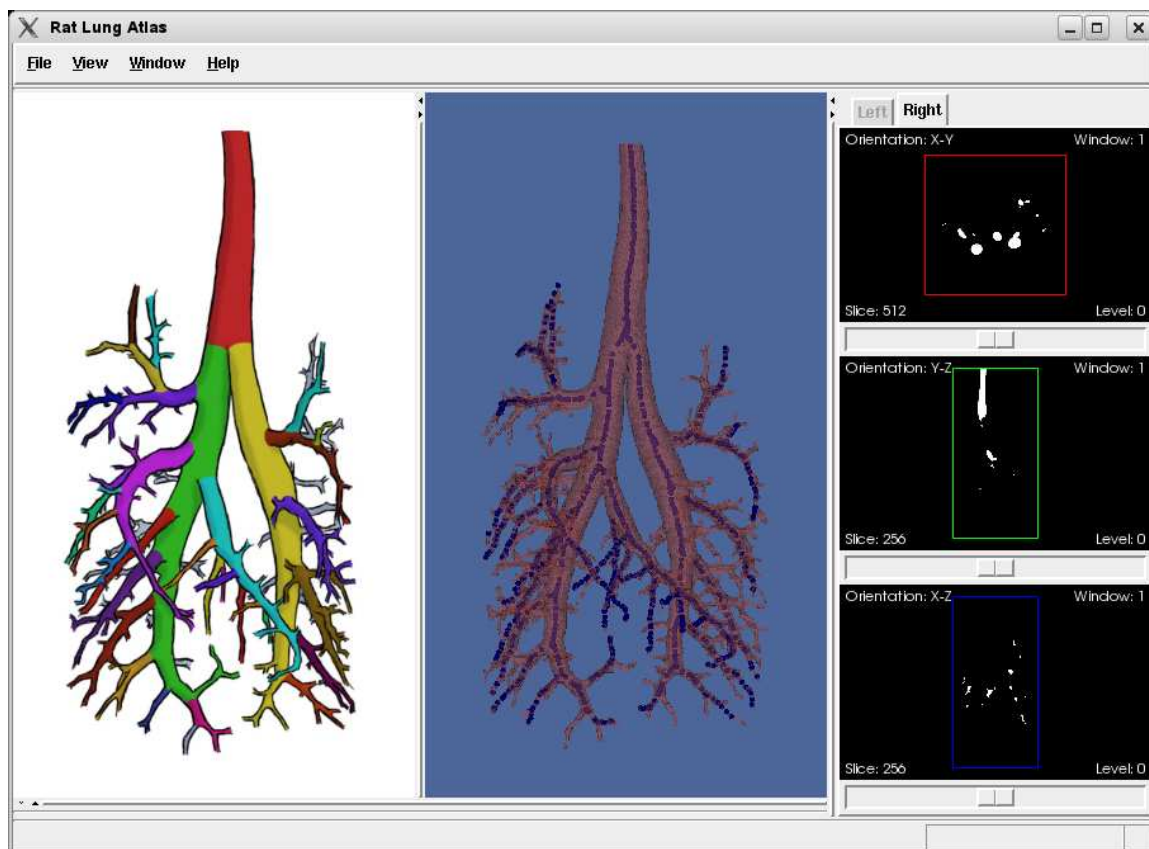


Figure 5.12: Rat atlas with beads rendered in the 3D image panel.

CHAPTER 6 DISCUSSION

This initial version of the atlas suffices as a proof of concept. However, in order to make it a viable commodity that will be accepted and used by the medical imaging community, some significant improvements must be made. Many of these improvements were touched upon in previous chapters.

One weakness of the application is the lack of database interaction for the rat atlas. While the user is able to visualize all six of the subjects currently included in the population, their experience would greatly benefit from incorporating data about the subjects being visualized. This data would allow for much easier comparisons and contrasts of a subject against the entire population. There exists an obvious codependence between visualizing a subject's airway and retrieving data related to the subject. Without one of these important features, usability of the system decreases. Another added benefit would be to fill the database with images of different modalities so that functionality can be added to the associated panel in the database window.

While incorporating a database of the 15 named airways of the rat would be an improvement, being able to address every airway segment in the image would be of even greater significance. In order to do so, a general naming scheme should be devised for smaller generations branching off of the major airways that have already been named. For example, the human naming scheme used in this project appends a's and b's to the end of the major airway names, depending on the locations of the segments following the bifurcation.

Obviously, accessing unreliable data is equally sufficed to accessing no data at all. Therefore, adding subjects to the population for both the human and rat atlas would make statistics calculated from values found in the database much more stable, as a greater sample size would reduce the effect of any outliers that may exist. As mentioned previously, the population size was kept small in order to focus more heavily on the development of the graphical user interface and will grow more rapidly with future versions of the atlas.

Using three-dimensional airway branch segmented images rather than alternative image types allows for more flexibility in the visualization, as previously described. Such an image provides the user with visual feedback to assure that they selected the desired airway and clearly portrays where the airway segment starts and stops. It also allows for more additional features to be added to the application. One such feature could highlight the entire path from the selected airway segment all the way up to the Trachea rather than just highlighting the selected airway segment itself.

Much improvement can be made to the atlas graphical user interface. The main downfall of the current GUI is the rather dated look-and-feel provided by KWWidgets. Identical and even extended functionality can be facilitated by other frameworks that are better established, such as wxWidgets, which also has the added benefits of a more modern look-and-feel and provides for interfaces to be developed more rapidly.

To this point the atlas has barely begun to scratch the surface of possibilities that can be accomplished. The incremental software development cycle easily accom-

modates the addition of new features as well as the improvement of existing tools. Adding more tools to the atlas will only help to strengthen its usefulness and increase its chance of sustaining existence for years to come.

With the vast technological strides that are constantly made by computer manufacturers, it is easy for programmers to forget about possible memory implications. However, with the improving technology of the computers and workstations comes the improvement of scanner technology which captures the 3D images to be displayed by these machines. Micro-CT is becoming more and more prevalent, which means that the resolution of these images will continue to improve. Thus, it is important that the developers of this atlas and other applications in the medical imaging arena are aware of memory implications and work toward achieving better response times and more rapid rendering of 3D images.

CHAPTER 7 CONCLUSION

This thesis has shown that electronic anatomical atlases are able to extend beyond the capabilities of traditional anatomical book atlases. By giving a user more options, flexibility, and intuitive interaction, electronic atlases are able to better serve the medical research and learning community. User interaction is the most obvious advantage that an electronic atlas holds over a book atlas. Allowing a user to view the anatomy from all possible angles and positions gives them a better grasp of the size and structure of objects located in the subject's body.

The developed software application allows users to study human and rat lung airways. It has been created in a way that easily allows for additional species to be added in the future. In order to numerically compare and contrast human lung airways, a database has been incorporated into the project which stores measurements that can be queried by the user. A framework has been developed which allows for users to compare different demographic groups such as males versus females or normal patients versus asthmatics.

While this project has made significant improvements to a traditional book atlas, it has only begun to scratch the surface of possible functionality that can be incorporated into an electronic atlas. Improving current performance, incorporating new functionality, and using new and improved tools and technologies will deliver an extremely powerful product that will solidify the electronic atlas' place in the medical imaging arena for years and years to come.

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