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Development of A Computer-Aided Detection (CAD) Tool For Contrast Micro Computed

Tomography Imaging In Diagnosing Liver Metastases

Anderson Steadham Peck

A Thesis Submitted to the Graduate Faculty of

## GRAND VALLEY STATE UNIVERSITY

In

Partial Fulfillment of the Requirements

For the Degree of

Master of Science in Engineering

Padnos College of Engineering

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#### Abstract

High morbidity of metastatic tumors in the liver has been observed in several different types of cancers. Liver failure from metastases is one of the primary causes of death in these patients. Effective treatments for liver metastases do not currently exist. However, new pharmaceutical treatments are being explored in a preclinical setting where the cancer and its treatments are designed in vitro and then studied in vivo in mice. Therefore, effective and accurate techniques for non-invasive imaging and analysis of liver metastases in mice are critical to the development of new treatments.

In-vivo micro CT imaging is not only one of the most commonly used imaging technologies in pre-clinical oncology study, but also highly translational. However, it is difficult to apply this technology to studies related to liver metastases due to poor inherent soft tissue contrast and the need for highly technical, manual analysis of the data. The evidence from our research has shown that Kupffer cells (macrophages in the liver) will concentrate among the liver metastases and allow the delivery of macrophage-specific contrast agents for the detection of small metastatic lesions. Using this new contrast enhancement method, CAD software was developed to enable automated detection of liver lesions. Software is able to assess disease stage based on these contrast patterns and compare them over successive weekly scans. The combination of the new imaging and analysis method enables automated detection and evaluation of liver metastases 1 mm or smaller from as early as 1 week. The CAD software allows for better visualization and quantification, but also for large scale longitudinal studies of liver disease and potential treatments. Moreover, it provides new insight into macrophage motility within the liver.

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#### **1. Introduction**

#### **1.1 Preclinical Imaging**

Preclinical imaging is an integral component of truly translational cancer research. While advances in biomedical science often occur first in the petri dish, there is a long and complex road to making those discoveries a part of medical treatments. This is referred to as the gap between the bench-top and the bed-side. Filling this void is a long and expensive process which usually includes extensive animal testing. This animal testing involves costly regulatory approval processes that create a tremendous challenge for even the most promising new treatments. An efficient way to reduce costs and the regulatory burden is to find a way to do a study with fewer animals and to show that the results from the animal study can have a direct correlation to humans. Preclinical imaging provides these advantages by reducing the number of animals required for a study by an order of magnitude and by utilizing the same techniques for analysis that are used in the clinic.

Preclinical imaging consists of a range of imaging modalities that function similarly to a radiology department in a hospital. Common scanners used in a human clinic for diagnosis and disease monitoring like MRI, CT, PET and Ultrasound are also used in the preclinical setting to image small animals. These preclinical imaging modalities produce medical images as effectively and with the same high quality as those developed for human subjects. This allows results from animal studies to be more easily correlated to human data, providing easily translated results. Historically in the research field, studies consisted of hundreds of animals and, at various time-points, a predetermined number were euthanized and examined. This

method carries significant expense as well as limiting the results to be based on averages among groups of animals. In an imaging study, the same animal can be evaluated throughout a study without need for sacrifices. This allows the animal to serve as its own control and makes the results definitive rather than relying on statistical response generalized from a group. As more research efforts shift towards the use of preclinical imaging, some obstacles have prevented large-scale adoption. In a hospital radiology department, a radiologist is responsible for interpreting the images for each patient. In a preclinical imaging facility it isn't feasible to have a veterinary radiologist on staff to interpret the images from each scan. For a busy imaging laboratory, over 100 scans per day are generated and it often takes more time to analyze the images than it does to complete the scans. For certain types of research, the volume of data that would be produced in an imaging study is so enormous that it is simply impossible to take on the problems with the current tools on hand. The need for complex image analysis limits the flexibility in study design by creating excessive costs. In addition, there is a need to standardize results for reproducibility which is not always possible when relying solely on human subjective analysis. To address all these issues, there is a push to develop user-friendly software tools that can assist and speed up preclinical image analysis thus making it possible to study even the most challenging aspects of animal pathophysiology.

#### 1.2 Focus: Pancreatic Cancer Liver Metastasis

Pancreatic cancer is one of the more deadly forms of cancer. It typically does not present symptoms that result in a diagnosis until it is well established and in advanced stages. Once it is developed, it quickly metastasizes throughout the body, predominantly in the liver. To a large extent, the high morbidity rate associated with pancreatic cancer is due to its spread to the liver causing liver failure. Few treatments for liver metastasis currently exist. The most common

prescription is for resection of the affected parts of the liver, leaving the patient with a fraction of their needed liver function. Liver resection is only intended to prolong life, however, and is not a cure. For an effective treatment of liver metastasis to be developed, the research community needs a model with which to test new drugs.

The development of mouse models for liver metastasis is still a challenge. Not only does the mouse need to present the disease in a similar fashion to the human counterpart, there also need to be ways to monitor the mouse as it receives treatments. Blood samples, biopsies, and CT scans are the standard for human disease monitoring and the same tools are used on mice. Of these, only CT scans can give accurate information on the status of the disease, such as tumor size and number of lesions. This information is critical when deciding when to administer treatments and to evaluate their efficacy. However, the mouse liver presents a challenge. Obtaining precise anatomical information about the liver is difficult using common CT scanners because the liver soft tissue is of similar density to other internal organs in close proximity. Novel contrast agents have been created for computed tomography that now make finding the livers borders with automated image analyses possible. This can facilitate the large scale study of drug treatments for liver metastasis in the mouse model of pancreatic cancer.

#### **1.3 Summary**

The study of treatments for liver metastasis of pancreatic cancer has been thwarted by the lack of reliable, repeatable and low cost methods for monitoring the disease in mice. While imaging methods existed for visualizing the liver, the data that was generated was very time-consuming to analyze and required expert interpretation. With the latest molecular contrast on the market and the application of complex image processing techniques, large-scale, longitudinal studies of the liver are now possible.

#### 2. Literature Review

#### 2.1 Micro Computed Tomography

Micro computed tomography (microCT) provides a method to capture and analyze the anatomical structures of mice in an identical manner to the common CT scanners used on humans. Micro CT relies on the attenuation of X-rays taken from regular angular intervals around a subject which are reconstructed mathematically to create a 3 dimensional volumetric image.<sup>1</sup> X-ray attenuation is directly related to the density of the object the X-ray passes through so that the captured image gives a view in the variation of density within a subject. This means that bone will show up well differentiated from soft tissue, soft tissue from fluid, and fluid from air as they all have significant variation in density.<sup>2</sup> Historically microCT technology has had wide use in the study of bone and lung disease because of the ease with which they can be visualized using microCT.

#### 2.2 CT Contrast

Soft tissue visualization using microCT has come to rely on the use of an injectable form of contrast enhancement.<sup>3</sup> The soft tissues do not naturally display a visible variation in contrast in a microCT scan because of the organs proximity to one another and their similar densities. Injectable contrast agents that target a specific organ and have an inherently high attenuation coefficient can provide significant improvement in soft tissue visualization.<sup>4</sup> Contrast agents typically consist of an alkaline earth metal element in a custom designed delivery vehicle such as a liposome or specialized polymer coating.<sup>3</sup> Contrast designed for humans is commonly based on a water soluble iodine preparation. However, due to the rapid clearance of water soluble compounds and the extended scan time of microCT compared to CT, a specialized coating is required to facilitate the effective contrast of a target organ throughout a microCT scan.<sup>1</sup>

Liver visualization in mice requires contrast enhancement to differentiate it from the nearby heart, stomach, kidneys, spleen, and intestines.<sup>5</sup> Contrast agents targeting the liver have been developed based on both liposome and polymer coatings with varied results.<sup>1,3,4</sup> Fenestra LC, introduced and described in the early 90's, is an effective liver contrast based on a lipophilic core. It clears slowly from the vascular pool (~2-3 hours) and is only retained in the liver for 4-6 hours until it is excreted through the biliary system making injection timing and accuracy of utmost importance.<sup>1,6</sup> Exitron nano 6000 is a recently introduced liver contrast agent in mice. It is an alkaline earth-based nanoparticle sterically stabilized by a polymer coating with a mean hydrodynamic diameter of 110 nm. Upon i.v. injection it targets the cells of the reticuloendothelial system in particular the macrophage cells in the liver, Kupffer Cells.<sup>7</sup> Exitron nano 6000 can provide liver contrast for the entire usable lifespan of a research mouse from a single injection.<sup>3</sup>

#### 2.3 Other concerns for microCT study of livers in mice

In a microCT study of mice for the purpose of visualizing the liver there are a number of concerns related to the care and handling of the mice that may have significant impact on the results if not properly addressed. First, the treatments and surgical procedures that may be required can have effects on the physiologic functions of the mouse, potentially including the mechanisms of action for the selected contrast agent. Second, the availability of anesthetic and injection procedures varies among mice strains and could limit the delivery of certain agents.<sup>7</sup> Third, automated software analysis may depend on the repeatable positioning of the mouse on the scan bed, the inclusion of certain reference bones in the scans field of view, or the fasting of mice to eliminate excessive mineral content in the GI tract. Lastly, the livers proximity to the lungs introduces motion artifact from the constant respiratory movement which may be dealt

with using respiratory gating, single breath hold ventilation, or high frequency oscillatory ventilation.<sup>8</sup>

#### 2.4 Immunology and the role of Macrophage

Using mice for the study of cancer goes beyond tumor models and evaluation of tumor growth. It offers a platform for the study of the underlying physiologic processes that interact to maintain a healthy living system or send it into an uncontrollable downward spiral. One of the key players in a living system is the immune system and one of its key mechanisms of action is the macrophage. The liver is a primary filter for material entering the body and it utilizes its resident macrophage, Kupffer Cells, to destroy foreign and dangerous particles in the blood stream.<sup>9</sup> Beyond the use of Kupffer cells as an imaging target<sup>3</sup>, they are of interest for their role in the immune response to liver metastasis.<sup>7,10</sup> They have been pointed out as possible Tumor Associated Macrophages (TAMs)<sup>9,11</sup> which actually help cancer cells proliferate. This makes understanding Kupffer cell motility and efficacy in immune response an important area of research within itself.

#### 2.5 Image Processing – Liver Segmentation

The primary concern for software analysis of the liver is segmenting the liver from the surrounding soft tissue and bones. Several techniques have been put forward in the clinical research space for liver segmentation, though they do not all have direct relevance in the preclinical environment due to the differences in images produced by clinical versus preclinical scanners. Liver and brain segmentation are the most well established fields of research for soft tissue segmentation because they are the most difficult to process.<sup>12</sup> With both organs, the ability to measure variations in density is difficult because they do not have much variation. In the liver it is also a challenge because of the similar densities of nearby organs. The approaches

seen in the literature vary and include both automated and semi-automated algorithms as outlined below.

#### 2.5.1 Live Wire Segmentation

The live wire algorithms<sup>13</sup> are a class of algorithms that rely on user input and are thus "semiautomated". The method has a user steer<sup>14</sup> a wire around the item being segmented. Images are treated as weighted graphs with vertices corresponding to pixels. The connections all have an associated weight computed as a sum of various image features such as gradient value, gradient direction, Laplacian zero-crossing, or gray value. The user selects a starting point and then moves the cursor while the computer calculates the minimum-cost paths from that point to all other points in the image. As the cursor moves, the boundary behaves like a live wire as it constantly updates to the new minimum cost path. This process is repeated sequentially until the final contour is created.<sup>15</sup> This method allows the user to have complete control but speeds up the process by letting a computer do the heavy lifting. The major drawbacks to this approach are related to its premise. It relies on a user which means costs associated with technician time and the introduction of intra- and inter-operator variability.

#### 2.5.2 Gray-level based Segmentation

This method relies on the basic threshold function of image processing. By user prior knowledge about the livers density or a histological estimation method, a threshold is set to obtain a liver mask.<sup>16,17</sup> Usually an iterative thresholding process is implemented slice by slice and then slices are compared for similarity.<sup>15</sup> Additional morphological imaging is often required to remove other organs from within the segmented region. A disadvantage of any thresholding algorithm is that density variation will affect the outcome.<sup>15</sup>

#### 2.5.3 Neural network based Segmentation

This approach utilizes a learning database to obtain the pattern of the liver and its boundary. It can achieve course liver segmentation using a training set of images that have been established prior to analysis.<sup>18</sup> By comparing the structures in the training set of images together to find patterns, it can identify similar patterns or structures in future images.<sup>19</sup> Neural networks have problems handling variations in basic image characteristics and are not suitable to low or medium resolution mice images.<sup>15</sup>

#### 2.5.4 Model fitting Segmentation

Model fitting relies on 3D surface models that have been developed in advance. These models are then deformed to adapt them to the CT data. An energy function is used to measure the match between the direction of the image gradient and the unit surface normal of the deformable model.<sup>15</sup> The initial placement of the model has a dramatic effect on the results so it is sometimes done manually by a user.<sup>20</sup> Another difficulty is the need to create a surface model that accurately describes the object.<sup>21</sup>

#### 2.5.5 Probabilistic Atlas Segmentation

Atlas based segmentation relies on a set of training data that will be registered with the CT data manually or automatically.<sup>22</sup> The thin plate spline, together with mutual information, is used as a similarity measure and then the data is registered with the organ surfaces using a warping transform.<sup>23,24</sup> The region that maximizes the posterior probability of being the correct order is extracted with the iterative conditional mode algorithm.<sup>15</sup> The major obstacles with atlasing are the computational time for registering the data and the complexity of developing the code.

#### 2.5.6 Level Set Segmentation

The level-set approach utilizes a novel speed function to control front propagation of an implicitly defined surface.<sup>15</sup> This surface is moved towards the liver boundary by the algorithm which changes dynamically based on previous history.<sup>25</sup> The propagation is constrained by set anatomic information regarding distance of the liver to the skin. This approach is also useful as a final component of a more course set of algorithms.<sup>26</sup>

#### 2.6 Image Processing – Liver Internal Structure Analysis

Currently, the primary goal of liver analysis has been focused on finding volumes of medium to large tumors. The CT contrasts designed for humans have a well established and homogeneous uptake throughout the healthy liver tissues, with no uptake in liver tumor.<sup>27</sup> This allows simple threshold techniques to accurately segment and quantify the lesions within the liver. The same thresholding technique can be applied to the preclinical contrast Fenestra LC as it has the same uptake qualities as clinical contrast agents.<sup>5</sup> The dynamic physiologic qualities of Exitron Nano 6000 make it unique and there are no current equivalent algorithms in literature for the analysis of a motile contrast. Analysis of internal liver structures using Exitron will rely on a clear understanding of its mechanism of action and its underlying physiologic processes.

#### 3. Specific aims

The purpose of this thesis project is to develop a methodology for evaluating disease stage in a mouse liver. This will require the evaluation and characterization of a CT contrast agent to enable soft tissue visualization of low contrast microCT scans. A scanning protocol will need to be established that provides adequate images while reducing dose to the mice under study. Software will need to be written that facilitates the management and analysis of the image data. For the longitudinal study of liver disease, the software should be able to associate multiple scans of the same mouse together for evaluation and simultaneous display. Semi-automated software tools based on grey level based segmentation, splines, 3D similarity analyses, and morphological operations will help segment the liver and evaluate lesions.

#### 4. Methods

The software requirements for this study are unique to the specific imaging protocol being performed. The algorithms will depend on the behavior of the contrast media being used to label and track the Kupffer cells in the liver. Several aspects of this study make it unique when compared to the current scientific literature. The majority of the research in medical image processing is focused on clinical imaging. In some areas, the research is applicable to preclinical applications but there are some important limitations on the scope of its applicability. The imaging equipment used in hospitals cannot be used in a preclinical setting. Mouse organs vary between being 100 to 1000 times smaller than their human counterparts. For an effective translational study we will need a preclinical scanner to have an equivalent effective resolution to the human scanner. This implies that the small animal scanner must have 100 to 1000 times better resolution than the human scanner. Small animal scanners have achieved this but they sacrifice sensitivity and scan time. This has detrimental implications for our study as lack of sensitivity prohibits our use of established clinical algorithms and our requirement to limit dose means we must limit scan time leading to further sacrifices in sensitivity or resolution. Good sensitivity enables us to differentiate between objects of similar density. Small animal scanners are not capable of reproducing images with the same sensitivity as human scanners. Therefore, the soft tissues in the peritoneal cavity are not as easily discernible in the mouse. This makes differentiating the liver from the stomach, spleen, kidneys, and intestines more difficult and limits our ability to use many algorithms established for human liver image analysis. Scan time is a concern in these studies because of the ionizing radiation involved in the scans. Due to the small size of the animals, and the techniques used to achieve sub-millimeter resolution, the radiation dose for each scan can be physiologically significant. It has been

demonstrated that a high resolution scan requires radiation doses capable of significant DNA damage.<sup>28</sup> With these concerns, we must reduce scan time as much as reasonably possible, and thus reduce our sensitivity further. These steps remove many important corollaries to human medical imaging research and limit our use of more advanced algorithms, leaving grey level based segmentation and morphology as the primary means of processing.

The final problem with relying on the established research for image processing algorithms is the differences in mouse anatomy and human anatomy. Though the organ systems are quite similar, mice organs are less organized than human organs. They demonstrate considerable variability in size and location between strains and genders even in major organs like the liver. In addition, their bodies and rib cages are extremely flexible. Slight changes in posture can result in organs changing their relative locations dramatically. This lack of organization and high variability necessitates more complex algorithms and sometimes alternate algorithms for different scenarios.

The direct application of most well researched algorithms from human medical imaging will not be possible. Grey-level based segmentation will be the most useful approach for this study because our resolution is too poor compared to many of the other techniques. Additionally the contrast enhancement being used will only allow a threshold to effectively segment the liver at the early time points in the study. Since we know our liver contrast is a dynamic entity, it is not possible to segment the liver entirely based on late stage scans. For these scans in which the segmentation algorithm is ineffective, historical scans from the same mouse combined with user input will be used to achieve the best possible liver region of interest.

The image processing problem can be split into 2 components. The first problem is finding the liver. For this, an algorithm determines the 3 dimensional region of interest that follows the

contours of the liver to entirely separate it from the surrounding rib cage and other soft tissues. The second problem is processing the liver. A method and algorithm will evaluate the stage of disease based on the visualization of the contrast agent. Lastly the software will associate and display results for multiple image sets from a longitudinal study.

#### **4.1 Imaging Protocol**

Exitron Nano 6000 will be injected into the mice 1 day prior to the surgical implantation of cancer cells. The mice will then be scanned 1 day post implantation and weekly thereafter until they reach morbidity. The microCT scan settings will be for the shortest exposure time of 500 ms to try to reduce dose at the cost of sensitivity. The number of projections will be 360 and the x-ray tube voltage will be 45 kVp. The images are reconstructed using Filtered Backprojection with a Shepp-Logan filter.

#### 4.2 User Interface & Database

A new user interface is developed to allow for the storage, association, and display of longitudinal image data. The interface can display up to 8 separate images from the same mouse and allow the user to perform built in functions on all of the images simultaneously. The images are stored in a database as unsigned 8-bit integers in binary format retaining appropriate header data for exporting to other software platforms. Additional files created via the image processing functions are also stored in the database and are associated with the original files. The image processing functions are fully automated but they rely on the user to input two initial conditions. Using a built in feature, the user must find the slice that represents the last image of the lungs and heart before the liver and the last slice of the liver before the abdomen. This serves as a starting point for the image processing software and saves considerable processing time by allowing the software to ignore parts of the scan that do not contain liver.

#### **4.3 Defining Regions of Interest (ROI)**

The first step of analysis is the creation of a 3D Region of Interest (ROI) of the skeleton from the 3D image data. To complete this, a threshold is applied at 400 Hounsfield Units (HU) and 3D morphological operations are performed. 400 HU is twice the designated bone value of 200 HU. This ensures that only dense bone is selected and the skeleton ROI doesn't encroach on soft tissue that is in direct contact with the bone. The contrast agent is designed to show up on CT scans at the same density as bone so by using a higher threshold, the dense cores of the bones are found without also picking up the contrast. The output of a threshold operation is a binary image mask where a 1 represents areas that are kept and 0 are areas not selected.

Morphological operations are used to produce an accurate and complete skeleton ROI from the dense bone that was obtained from the threshold. The goal is to connect and fill in areas between adjacent bones to create a solid reference ROI. Variations of the image processing functions dilate and erode can be used to achieve the goal accurately. The basic ideas of dilation and erosion rely on a structuring element, an n x n array, that is probed across the image and analysis is performed at each location to determine the outcome for that location.

$$A \ominus B = \{z | (B_z \subseteq A)\}$$
  $B = \begin{bmatrix} 1 & 1 & 1 \\ 1 & 1 & 1 \\ 1 & 1 & 1 \end{bmatrix}$ 

The binary erosion or dilation of A (starting image) by B (structuring element) is the set of pixel locations z, where with the origin of B translated to z, it overlaps only with the foreground pixels in A. Dilation causes an object to grow equally in every direction and erosion causes the opposite. Dilation followed by erosion is referred to as a 'close' operation because the dilation will cause nearby items to attach, but the subsequent erosion does not cause them to detach. The

subsequent erosion also returns all other areas of the image to their previous state with only minor averaging of contours, provided a 3x3 structuring matrix is used. This method is a reliable way to create a solid skeleton ROI when applied iteratively in each of 3 dimensions. Using the 3D skeleton ROI as input, a 3D ROI of the torso is created by clamping the skeleton from 360 different directions every 1 degree around the image. Clamping is performed by simulating a number of equally spaced lines drawn across an image at the same angle. Software travels at equal speeds down each line until the first object is encountered. This point serves as the output point of that clamping operation. Using these clamping points as input to a bicubic spline creates a circular ROI that surrounds the ribcage and everything inside it. One source of error in this torso ROI is the arm and shoulder bones of the mice. These bones often extend down outside the ribcage and create error in the clamping points and subsequent ROI. To eliminate this, a 3D similarity check is performed. The check starts at the bottom of the ribcage (which is found based on the original user input) and works towards the top where it will encounter the arms. By subtracting each ROI of the next slice from the current slice, the software determines whether there is too much slice-to-slice variability, indicating an arm bone. Excessive variability is evaluated by taking the subtracted image and eroding it twice using a 3x3 structuring element. Normal variation should result in a very thin line in a circle where the two ROIs differed, so eroding once will delete them and twice will make certain. Abnormal variation from an arm or shoulder blade will create a difference image with a large mass sticking off the side. Masses erode much more slowly using a 3x3 structuring element so they will be left behind. The test for too much variability is checking to see if there is anything left in the subtracted and eroded image.

In the case where too much variability is found, the next ROI is replaced with the current ROI. Because the ribcage gets smaller as the slices move towards the top, the current slice ROI will always contain the entire torso in the next slice ROI. Once the torso ROI is completed it can be used for future processing functions and can be used to refine the skeleton ROI to remove unwanted bones from images. Both of these ROIs are saved in the database so they can be loaded and displayed on the user interface or for future processing functions.

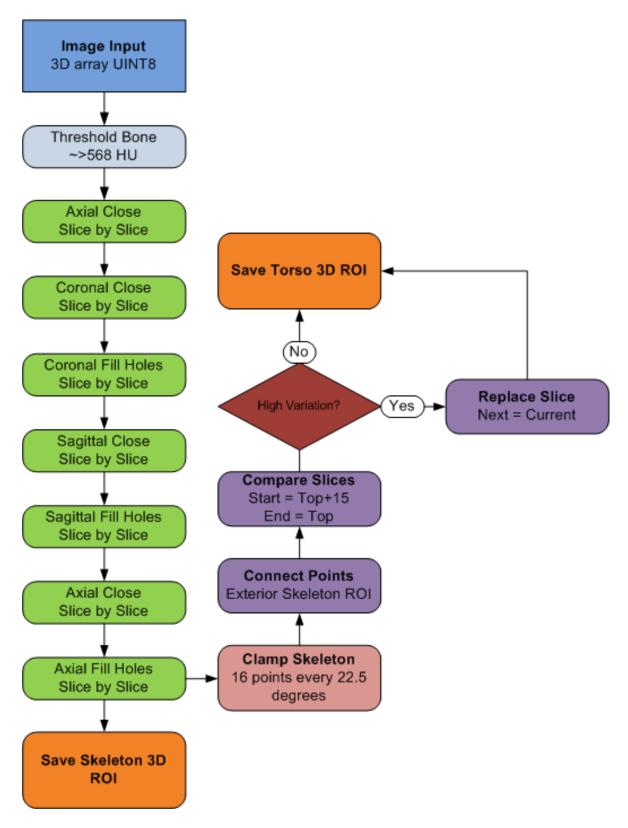


Figure 1: Software Flow Chart for Skeleton and Torso ROIs

#### 4.4 Segmenting the Liver

After skeleton and torso ROIs are completed, the next step of analysis is to segment the liver from the rest of the skeleton and abdomen. The liver soft tissue is contrast enhanced compared to the other soft tissues in the torso. This makes thresholding an effective method for separating the soft tissues. First, though, a series of masks is performed to remove the skeleton and the stomach contents from the image. Separating the liver from the ribs is complex because they are in direct contact and eliminating stomach contents can be difficult because the size and location of the stomach and its contents are dynamic and unpredictable. A robust algorithm is developed utilizing the skeleton and torso ROIs. 3D region growing is used to achieve a more precise ROI by using rib points from previous slices but masking off points that fall too far inside. Dilation of the torso ROI twice using a 3x3 structuring element can reliably move it to the inside of the ribcage. Using this new inside ribcage ROI and the original torso ROI and applying them both to the skeleton ROI will only keep the central points from each rib. These rib particles are treated as unique and their center of mass is recorded. With the location of each ribs center of mass, a new ROI is created using the points as input into a bicubic spline. This new ROI is used as the segmentation ROI to separate the soft tissue from bone. Because the surface of the liver is one of the points of high activity, and this surface is often in direct contact with bones, the region is intentionally slightly larger than the liver. This entails that some small parts of bones are still included in the image. They are eliminated by applying the original skeleton ROI as a mask to the image.

As the analysis propagates slice by slice through the liver, the point inputs into the spline from each ribs center of mass are carried over iteratively. This creates considerably more points for

the spline and thus the spline improves in its accuracy. Old points that move too far from the current slices actual edge are eliminated by the current slices inside ribcage ROI or torso ROI. The final threshold to obtain the liver ROI is a variable implementation. Due to the fluctuations in retained contrast in the liver, there is no standard threshold level that can be set and applied to all images. There is a default level set at 100 HU, there is a dynamic function that calculates the level based on each images histogram<sup>29</sup>, and there is a user controlled option that allows the user to adjust threshold in real time to find the optimum levels for each data set. The default value of 100 HU is effective at obtaining the liver but it also frequently includes parts of the stomach that should not be included. The histogram based function is not effective because the histogram contains no peaks and the ideal threshold level always turns out to be somewhere in the middle of a plateau. The user controlled option is the most reliable and the software is able to save the results of the user selection for future use.

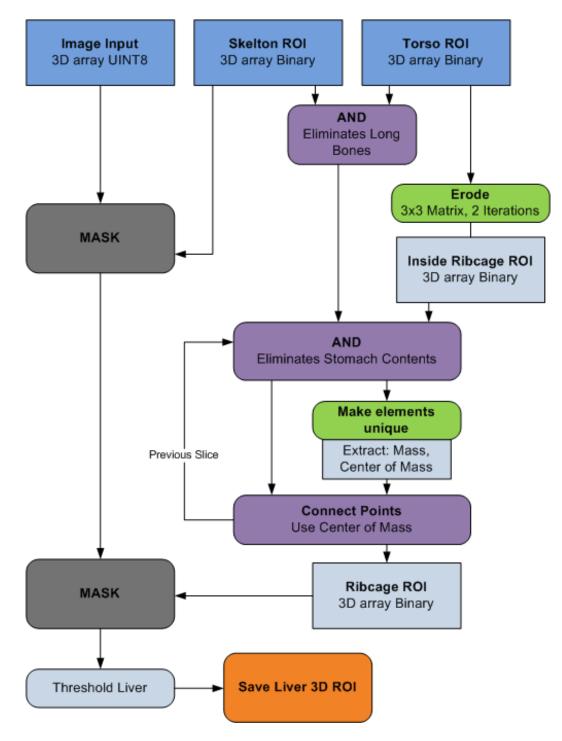


Figure 2: Software Flow Chart for Liver ROI

#### 4.5 Processing the Liver

Processing the liver can be achieved through thresholding and basic morphological operations provided the liver segmentation is accurate. There is no significant development of shapes at the early stage so the goal is to evaluate the distribution and density of contrast within the liver. An automated analysis process equalizes the image and thresholds based on user input. The function then outputs location, perimeter, and area information about each selected region of concentrated contrast. User controlled functionality allows further analysis as well as allowing exportation of final data to other visualization and analysis programs.

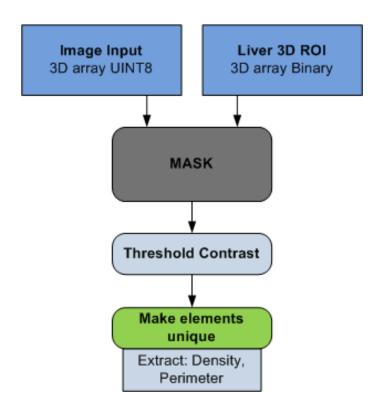


Figure 3: Software Flow Chart for Process Liver

#### **4.6 User Interaction**

The interface is designed to communicate information for large sets of data without significant user input. There are features allowing the user to assist the automation by correcting ROIs

within the user interface. Manual manipulation of ROIs, threshold levels, brightness and contrast levels, and 3D viewing is built in to assist the user.

#### 5. Results

#### **5.1 Finding the Skeleton**

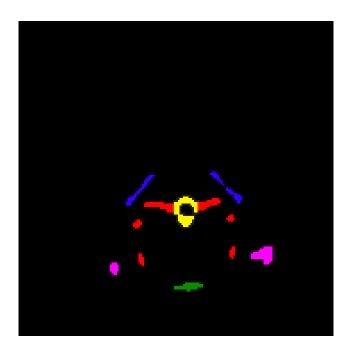


Figure 4 - An axial slice of the 3D CT volume thresholded to only display bone. Blue = Shoulder, Yellow = Spine, Red = Ribs, Pink = Front legs, Green = Sternum

Applying a threshold at 400 Hounsfield Units gives a view of the skeleton. Depending on which axial slice is selected, several bone groups may be displayed and require differentiation as seen in Figure 4. Prior to the automatic differentiation of the bone groups, the skeleton must be filled in 3 dimensions to ensure all bones are complete and continuous on every slice. The volume is filled sequentially in 3 dimensions as shown in figures 5-7.

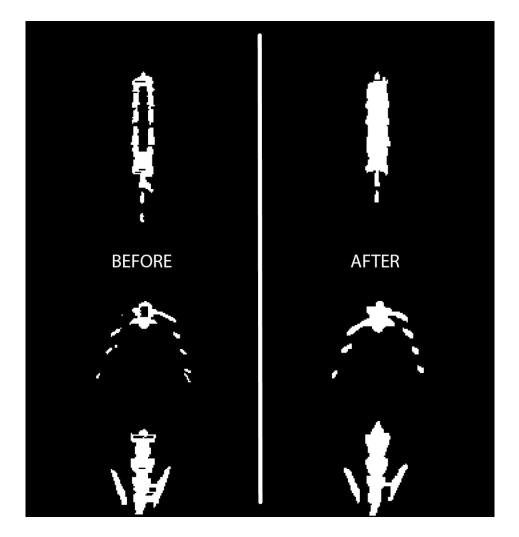


Figure 5 - Two coronal slices are shown before and after the morphological closing operation is performed. Top: Spine. Bottom: Ribs, Spine, Pelvis.

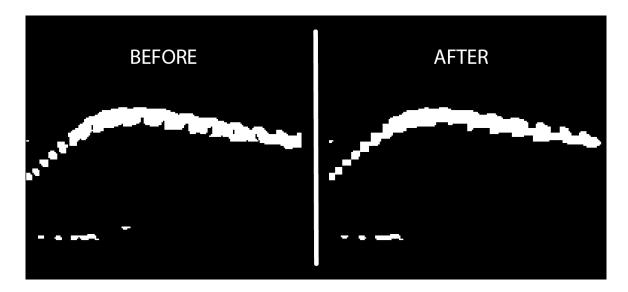


Figure 6 - A sagittal slice showing the spine and sternum is displayed before and after morphological closing is performed.

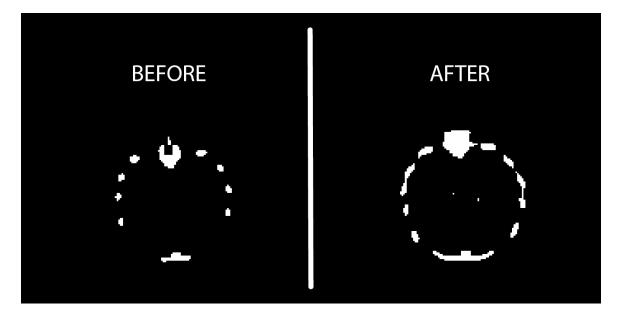


Figure 7 - The axial view of the ribcage is displayed before and after the 3D closing is performed.

After processing the skeleton to verify its completeness, the data can be processed to create masks. A torso mask that includes the ribcage and everything inside it is created from the skeleton using a clamping operation.

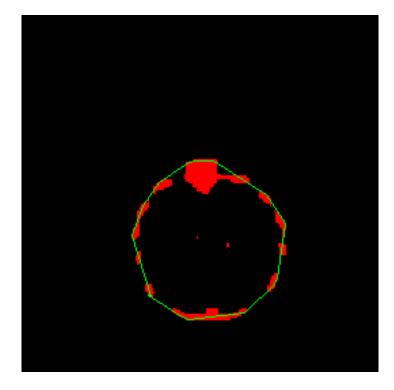


Figure 8 - The final skeleton, shown in red, is clamped from 360 degrees to obtain points that are fed to a bicubic spline algorithm creating the torso mask, shown in green.

The preliminary torso mask will contain errors where the legs, shoulders and pelvis are present in the skeleton image. These are eliminated by processing the skeleton for similarity, shown in Figure 9.

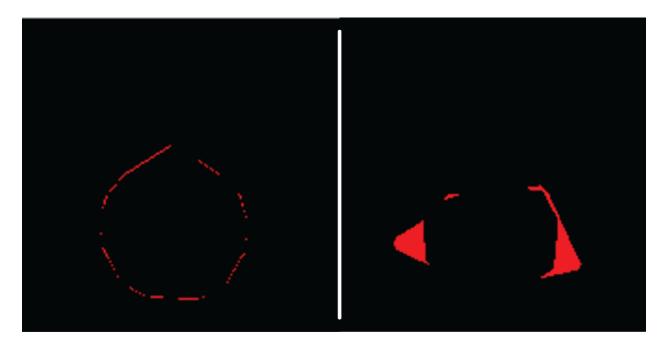


Figure 9 - The resulting image when two like images are subtracted, on the left, and the result from two different images on the right.

Similarity is assessed by subtracting consecutive slices from one another. The resultant image will have very little mass when two like images are subtracted and much more significant mass when two different images are subtracted. The larger mass is indicative of significant variation indicating the next slice contains regions outside the torso.

## **5.2 Finding the Liver**

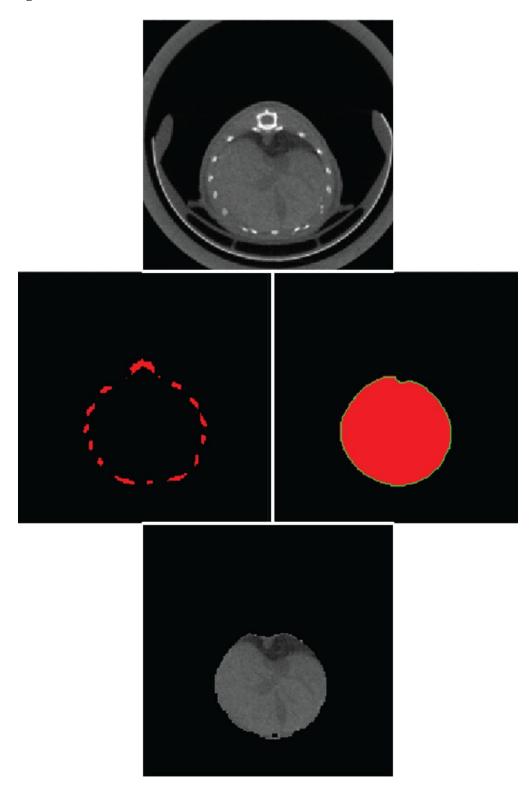


Figure 10 - Top: Axial slice of original image. Left: The skeleton mask produced from the original. Right: The torso mask produced from the original. Bottom: The remaining image after the skeleton and torso masks are applied.

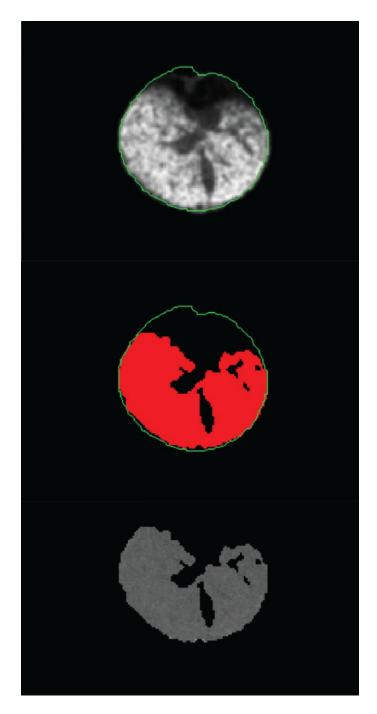


Figure 11 - Top: The bottom image from Figure 10 after an equalization makes the contrast enhanced liver stand out from the background. Middle: A threshold creates an ROI that only includes liver tissue. Bottom: The original data with the final liver ROI applied.

# **5.3 Processing the Liver**

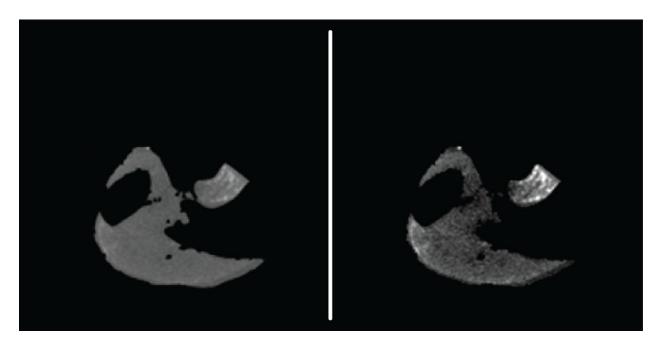


Figure 12 - Left: An original axial slice after the liver mask has been applied. Right: The same image after an equalization to highlight regions of the liver where concentrated contrast is located.

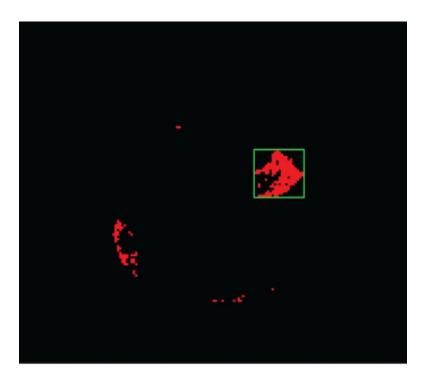


Figure 13 - A threshold extracts only the regions of concentrated contrast which can then be analyzed with particle analysis.

Table 1 - Statistics for Region 1 in Figure 13				
Object #	Center of Mass X	Center of Mass Y	Perimeter	Area
1	117.57368	92.57895	88.18362	67.61338

Figure 14 - The table shows some statistics that can be used to quantify and monitor regions of interest in an image.

#### 6. Discussion

Using a thresholding technique as described in Section 4.3 to develop a skeleton ROI is a reasonable first step but there are some issues that need to be resolved morphologically before it can be relied on for reference. A key to a robust algorithm is to have a repeatable anchor to give the software a point of reference. The spine is a good choice because it is constant and in a fairly fixed location. One issue is that the spine is not a continuous bone, but many bones separated by cartilage. This means that on different slices the spine may show up as a circle, two horizontal lines, or 3 unique bones. The diagram below shows three different slices from the same CT scan demonstrating the problem.



The solution to this problem is to use morphologic operations to connect and fill in the spine in 3 dimensions. The operations 'Close' and 'Fill Holes' can be applied in series on the Axial, Coronal, and Sagittal planes creating a cumulative effect giving a solid spine. This process is demonstrated in Figures 5-7.

A reliable ROI describing the torso is important to liver segmentation because it provides a way to eliminate extraneous bones and stomach contents that will skew further segmentation. By comparing the torso with the skeleton, the bones in the shoulders and legs can be removed. The torso ROI can also be morphologically eroded to create the ROI of the interior of the ribcage. The ribcage interior ROI can be used to determine an area appropriate to threshold for stomach contents, which is the same density as bone.

The product of masking the skeleton ROI with both the torso and ribcage interior ROIs is also useful. It gives very accurate rib locations for the center of mass measurement which is required to obtain the liver ROI. This ROI is based a region growing spline that propagates points from slice to slice. This gives considerably more points for a more accurate mask and old points that no longer apply are masked off by the ribcage interior ROI.

Processing the liver for lesions turned out to be a different task than originally anticipated. Historically liver contrast has been a stagnant entity remaining homogeneously distributed within the liver. This made the initial goal to process looking for lesions with necrotic centers that show up because of the dark color of the fluid center compared to the surrounding healthy tissue. This approach has a significant downside that necrotic centers do not develop until metastases are in late stages. If the goal is to evaluate new drug treatments then it becomes more important to estimate initial signs of the disease for early interventional treatments to succeed. An earlier detection method is sought and the contrast we have evaluated provides that.

Exitron Nano 6000 tags the macrophage of the liver, Kupffer Cells, which move and respond to disease as a primary defender for the immune system. By tagging and visualizing their movements, we can see metastatic processes developing before any significant lesions exist. Through histopathology we have determined that when the CT scans show the first movement of contrast, the metastic foci are still less than 1000 cells in size. This gives us the opportunity to correlate and quantify the amount of contrast movement to the stage of the disease. Instead of processing the liver and looking for large necrotic tumors, we are now processing to look for concentrations of contrast in the liver. These regions are not well organized so there are no actual volumes to measure. The goal is to find and label regions that have accumulated contrast, assess the approximate concentration of contrast in that area, and give a general size of the area. This information monitored longitudinally can give us insight into the development of metastases and its response to treatments.

#### 7. Conclusion

The new contrast enhanced imaging method developed here creates the possibility for more efficient analysis of liver lesions. The contrast moves and concentrates in areas of the liver that have cancer cells in the early stages of development. Software is able to take advantage of this new contrast enhanced micro CT imaging to provide a higher throughput analytic toolkit to the researcher. The ability to assess the liver at an early stage in metastatic formation is unparalleled in the research environment. Though it isn't possible to give specific sizes to specific lesions until late stage growth, it is still possible to quantify the stage of the metastases based on the movement and concentration of contrast. Basic statistics such as metastatic microenvironment size and perimeter can be tracked over time to give effective snapshots into the progression of disease.

There are still many obstacles in using this contrast for image processing. In high concentrations the contrast is the same density as bone, which makes it very difficult to differentiate from bone. Because it moves throughout a longitudinal study, it does not provide the ability to accurately segment the liver at late time-points in a study. Fortunately, by the late stages of the study, there are large enough lesions that they could be analyzed independently.

The software developed here and the methodology described enable automated detection and evaluation of liver metastases 1 mm or smaller from as early as 1 week. The CAD software allows not only better visualization and quantification, but also for the large scale longitudinal study of liver disease and potential treatments.

### 8. Future Work

The software can be refined in a number of ways to increase quality and throughput, by requiring less user intervention:

The 3D similarity method for evaluating the torso to remove the shoulders and legs could be applied to the final liver mask to help remove stomach contents.

The selection of the final threshold level for creating the liver mask is currently user controlled because the automated implementations weren't entirely effective. The software retains the user selected threshold for each histogram as well as the histogram in memory. In the future a neural network based threshold selection can be implemented using the historical user selection data by attempting to match new histograms to ones from the database.

An atlas based skeleton segmentation could eliminate the need for any user input.

The microCT scanners field of view is not uniform even for homogeneous samples so an evaluation and correction for this could make thresholding more effective.

A software model describing Kupffer Cell motility could assist in staging the disease with fewer time-points.

### 9. Bibliography

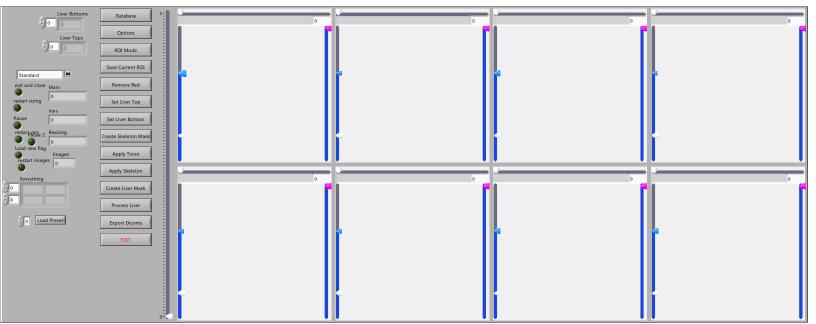
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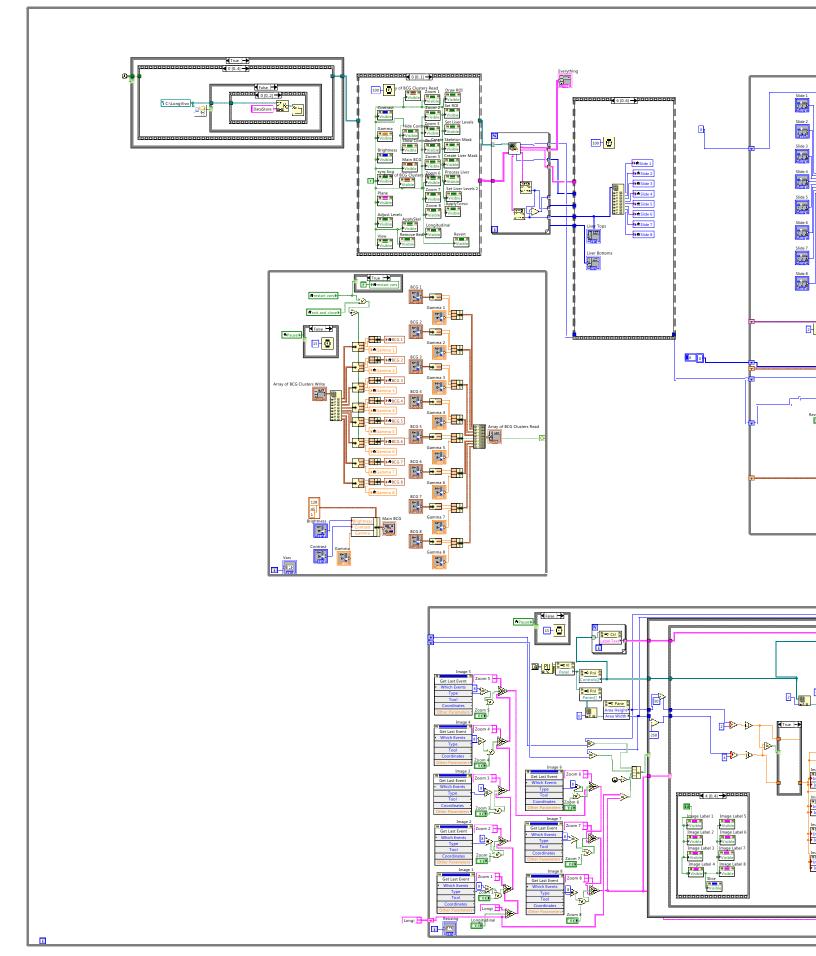
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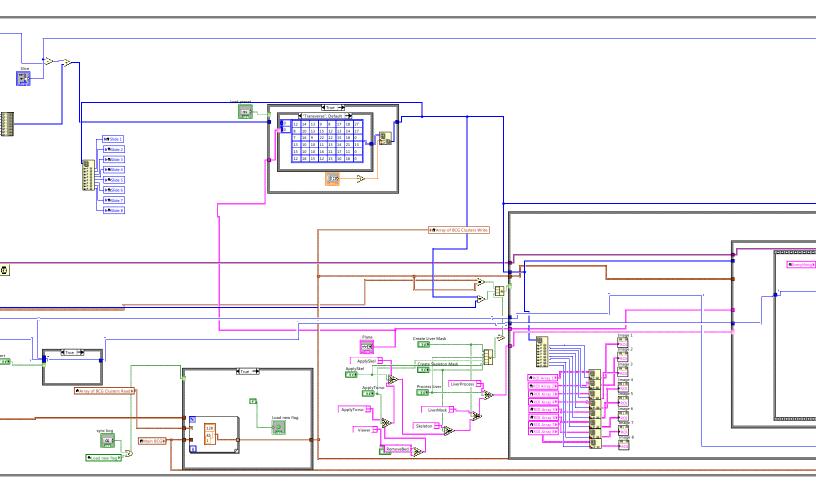
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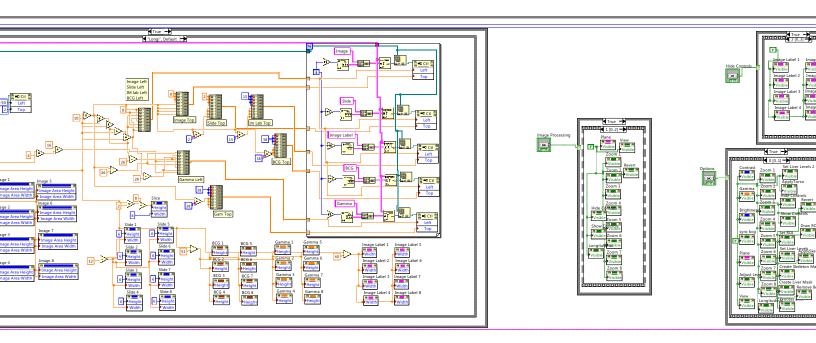
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Appendix 1 – Labview Software

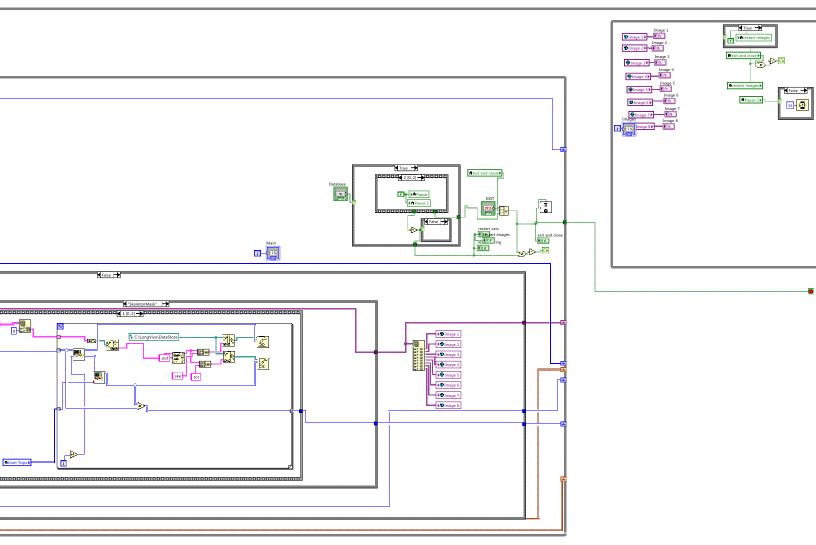


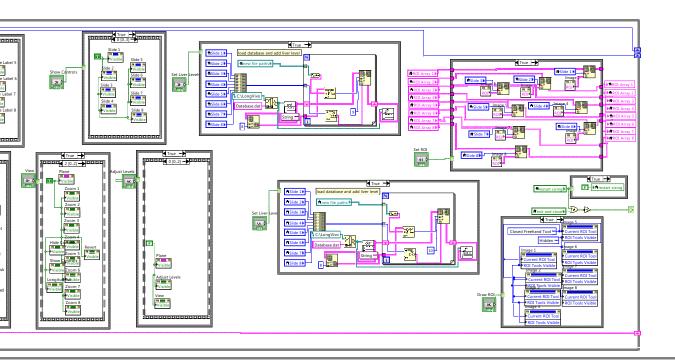






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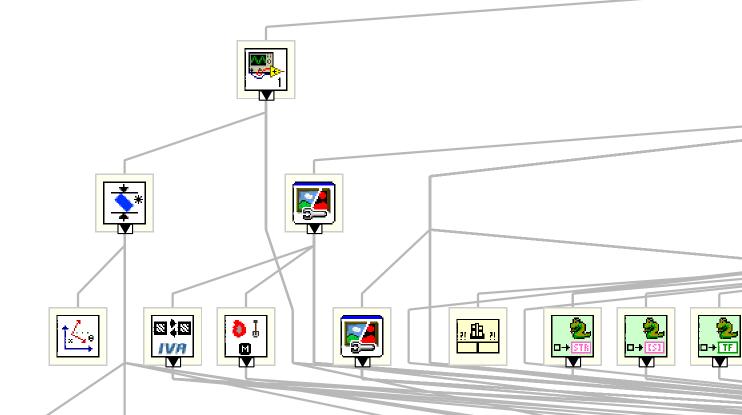
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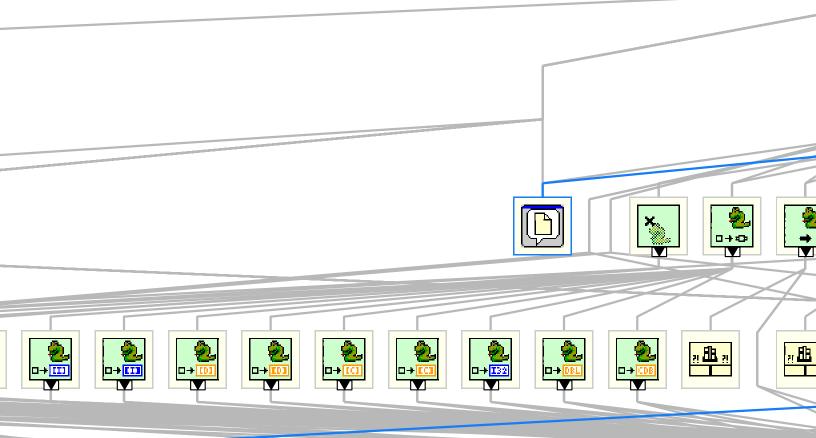
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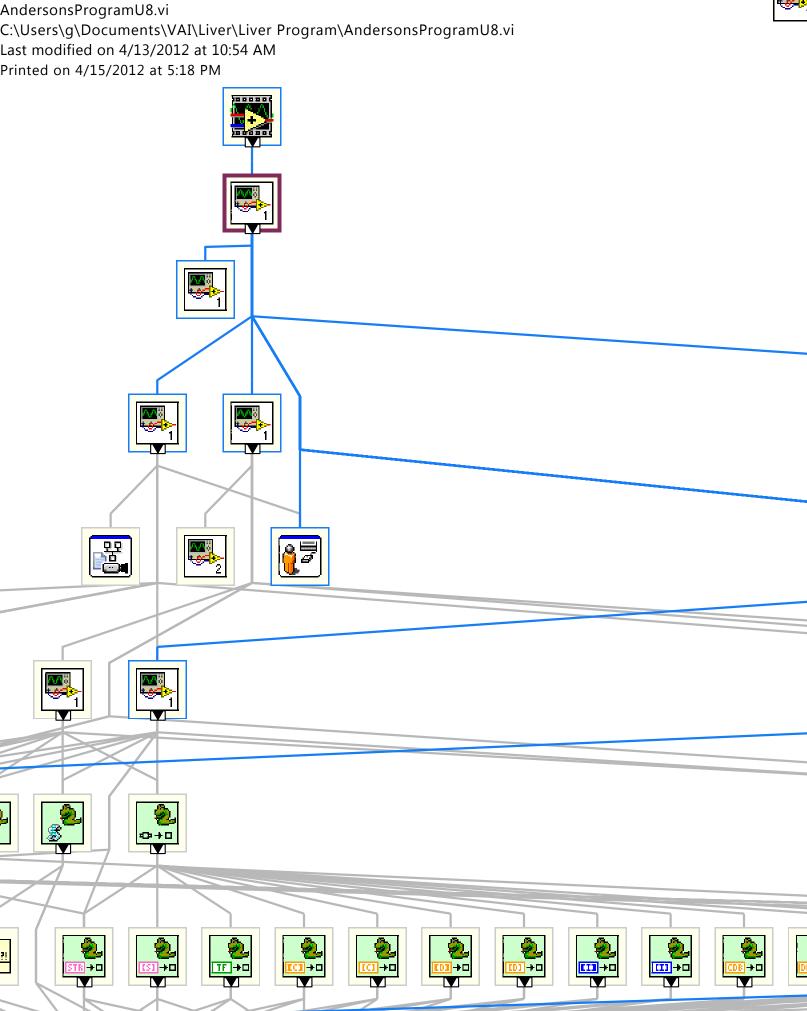
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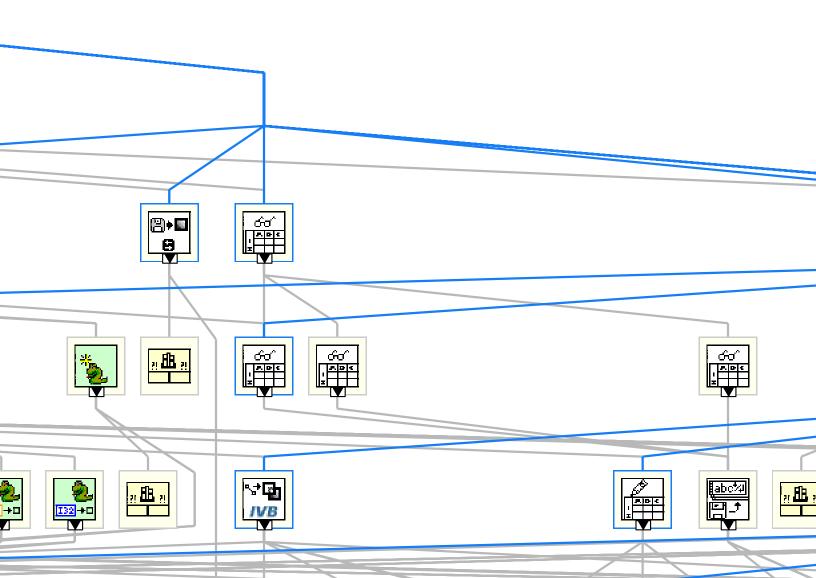




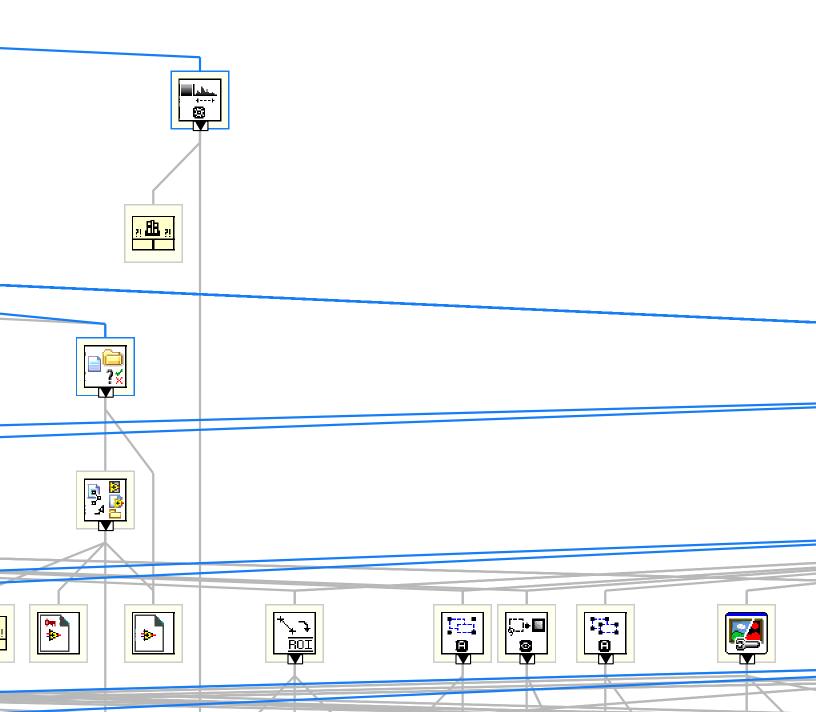


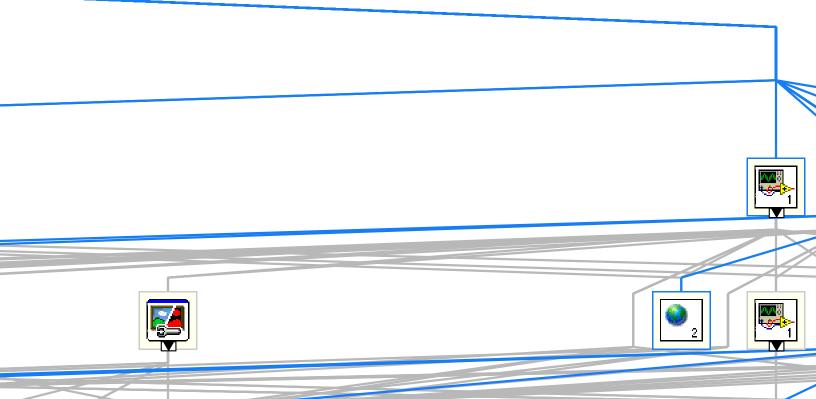
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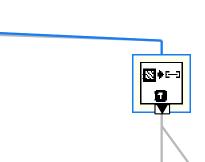


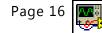






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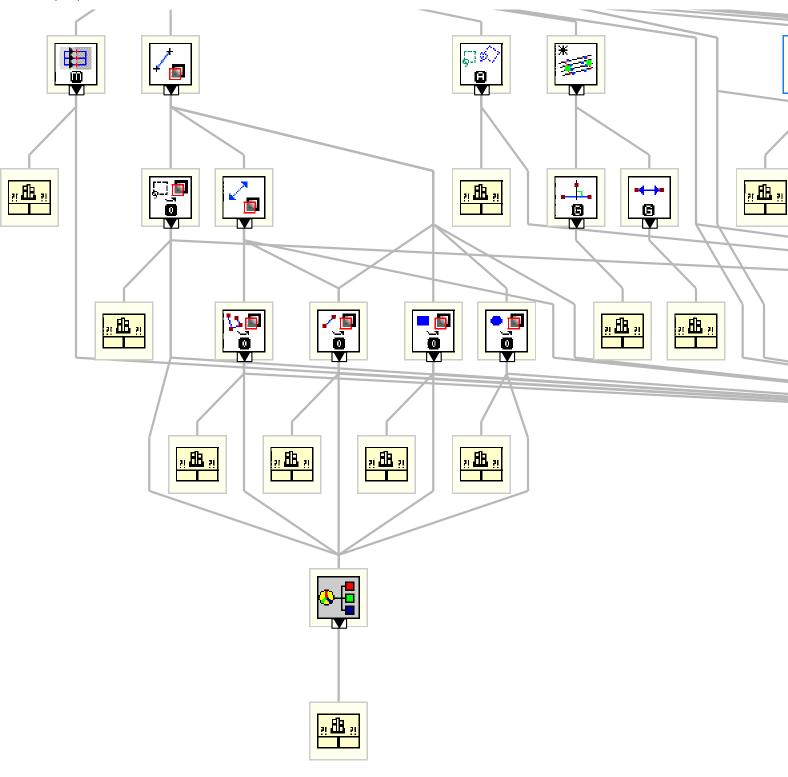




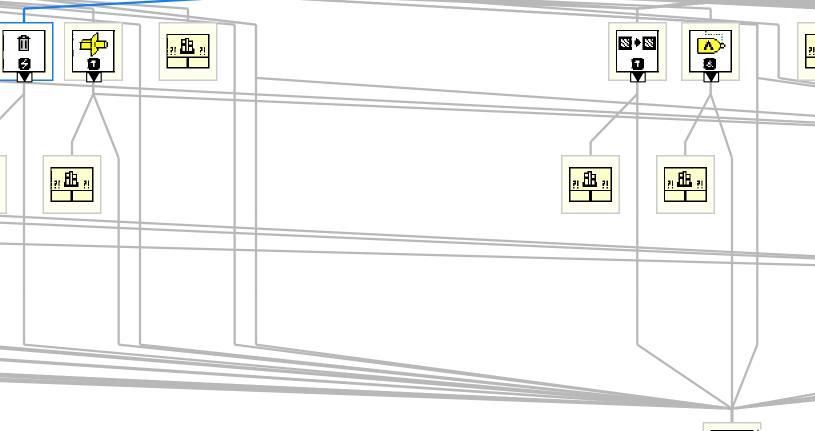
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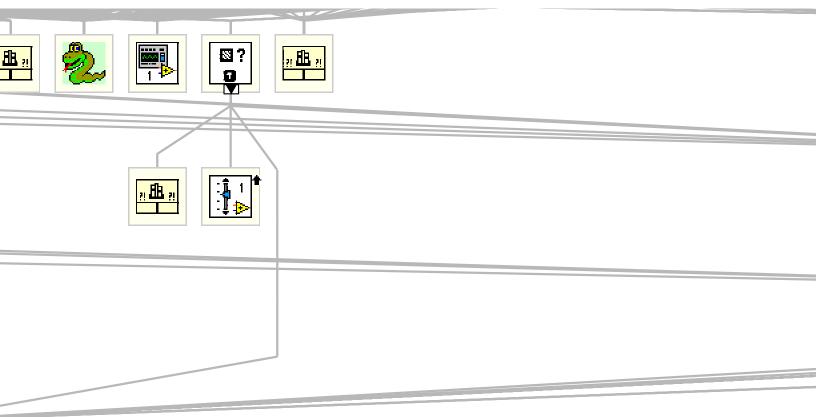




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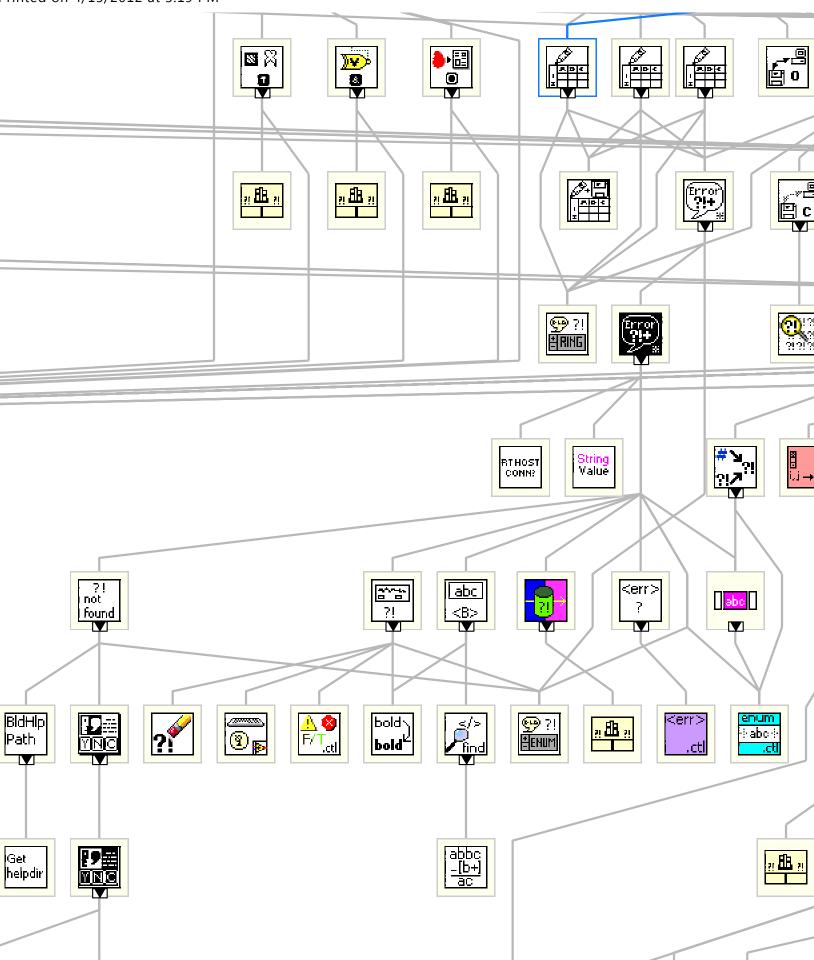


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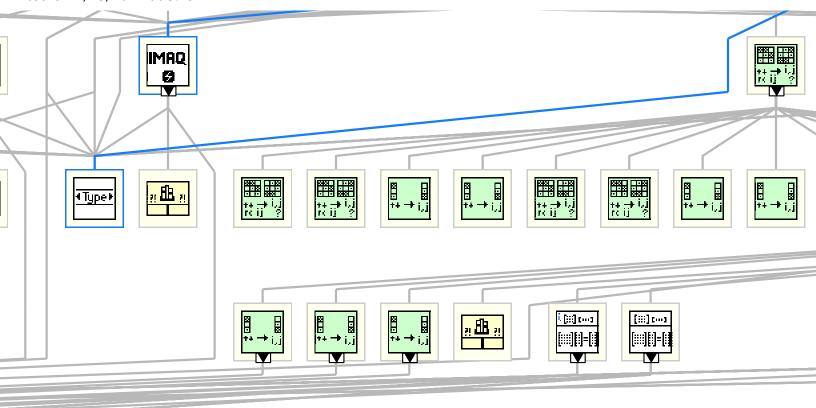
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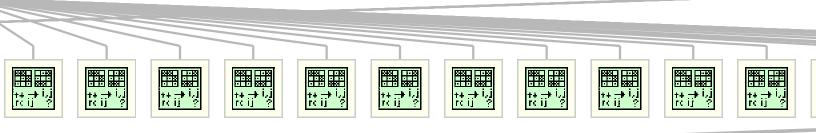


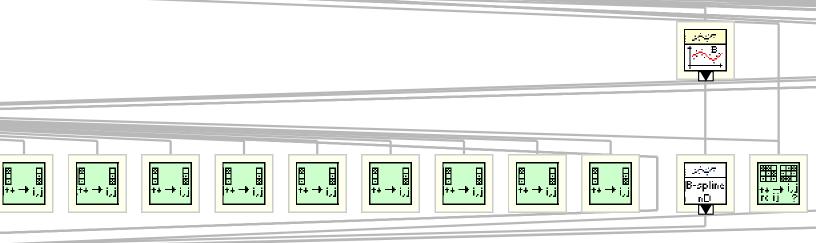
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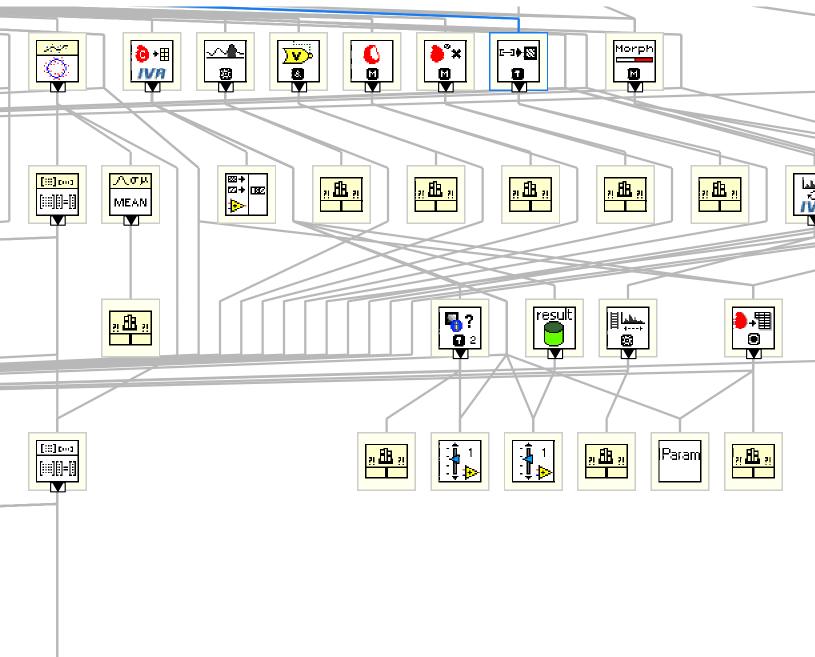
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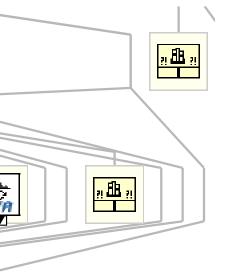
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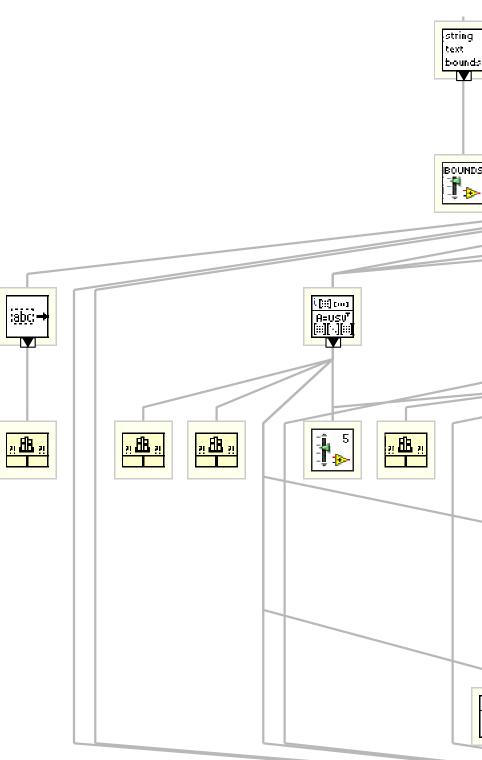


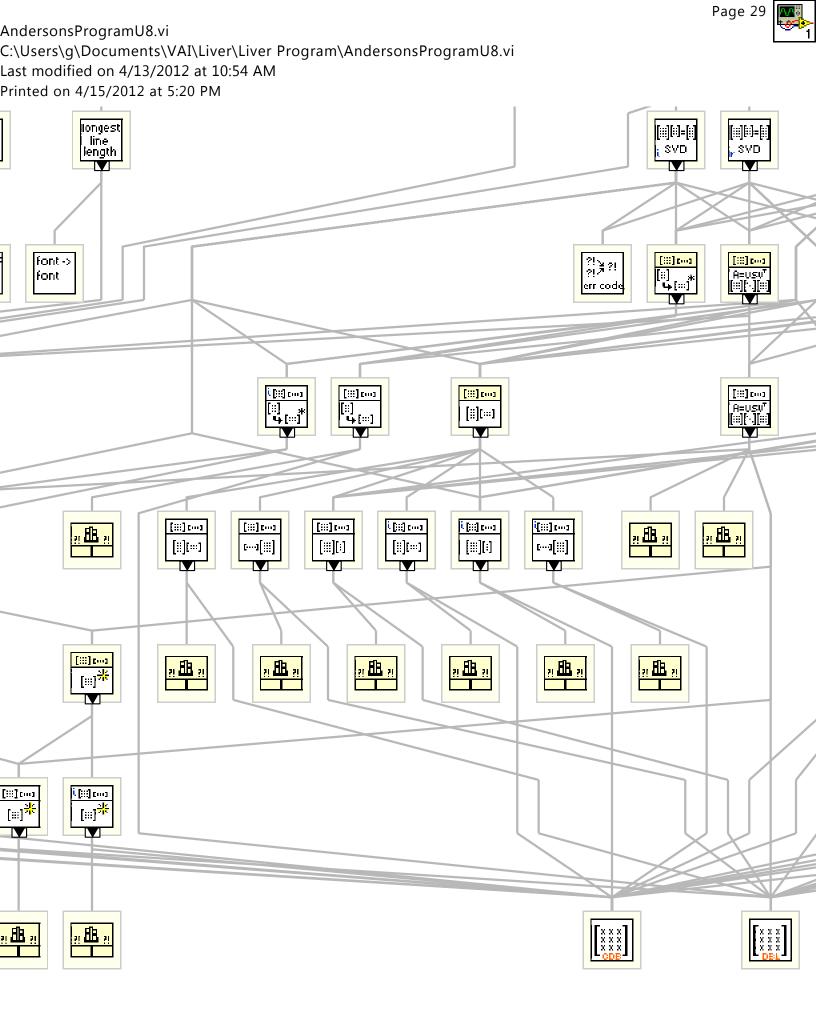
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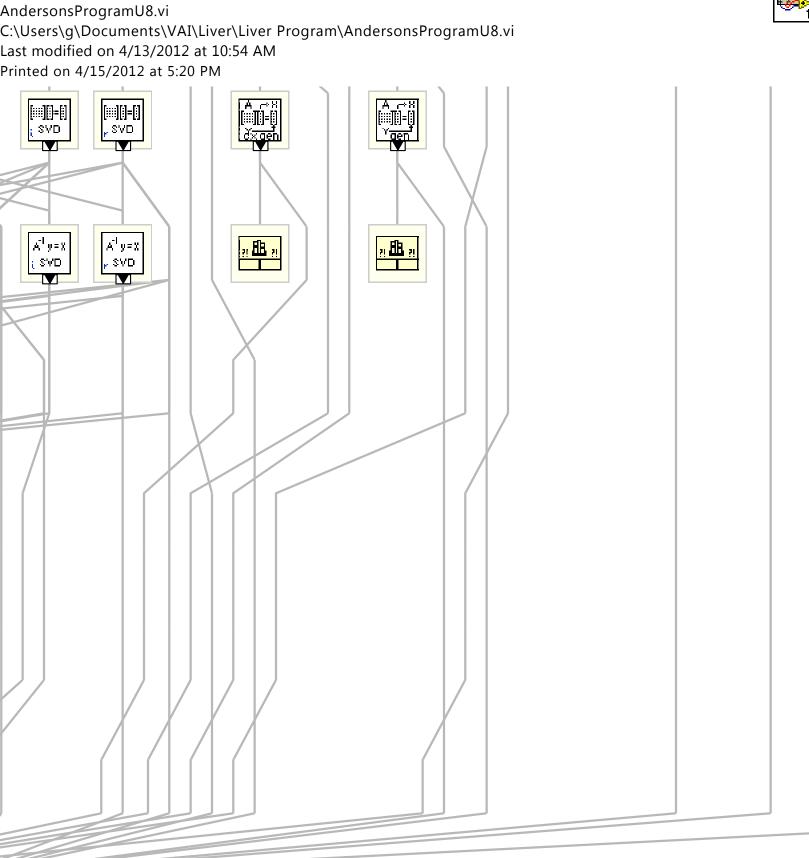
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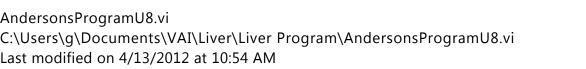




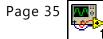


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Image.vi

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# **Imaq Dispose**

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# **IMAQ Create**

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### IMAQ ArrayToImage

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### IMAQ ImageToArray

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### IMAQ ReadFile C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Files.llb\IMAQ ReadFile



#### IVA Mask from Image File 2.vi C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Vision Assistant Utils.llb\IVA Mask from Image File 2.vi



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# ExportFilesPYTHONwithMeta.vi

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### Write To Spreadsheet File (string).vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Utility\file.llb\Write To Spreadsheet File (string).vi



### Write To Spreadsheet File.vi

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# **File Dialog**

File Dialog Displays a dialog box with which you can specify the path to a file or directory. \_\_\_\_\_

This Express VI is configured as follows:

Selection Mode: New or existing directory



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#### **Prompt User for Input** Prompt User for Input

Displays a standard dialog box that prompts users to enter information, such as a user name and password.

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This Express VI is configured as follows:

Message to Display to the User:Input a name to append to the file name The inputs are: Text Entry Box: Description



### Mask Liver MAIN.vi

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Evaluate Torso.vi

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### Read From Spreadsheet File.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Utility\file.llb\Read From Spreadsheet File.vi



### DatabaseNavi.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\DatabaseNavi.vi



### Check if File or Folder Exists.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Utility\libraryn.llb\Check if File or Folder Exists.vi



### Vision Assistant2

IPtesterOLD.vi

Vision Assistant Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



# ProcessLiverIntegrated.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\ProcessLiverIntegrated.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\IPtesterOLD.vi

AndersonsProgramU8.vi C:\Users\g\Documents\VAI\Liver\Liver Program\AndersonsProgramU8.vi Last modified on 4/13/2012 at 10:54 AM Printed on 4/15/2012 at 5:20 PM



# convertedIPtester.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\convertedIPtester.vi



# Main\_Skeleton.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\Main\_Skeleton.vi

	input cluster				
	255= Max 255= Cut	off			
	225- 225-		Original 10	Original 3	Original 4
	200- 200-				
	175- 175-				
	150- 150-				
	125- 125-				
	100- 100-				
	75- 75-				
	50- 50-		Y Y		
	25- 25-				
	0- 0-				
			176x176 1.5X 8-bit image 64 (14,80)	176x176 1.5X 8-bit image 0 (0,143)	176x176 1.5X 8-bit image 0
			Original 2	Original 5	Original 6
			Original 2		
	Skeleton Mask	Delay	· · · <b>/</b> · <b>. →</b> · · · ·		
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176x164 1.5X 8-bit image 0 (0,0)

176x164 1.5X 8-bit image 0 (0,0)

### Find Skeleton MAIN.vi C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Find Skeleton MAIN.vi Last modified on 4/15/2012 at 5:07 PM Printed on 4/15/2012 at 5:20 PM

1000-0-

input cluster

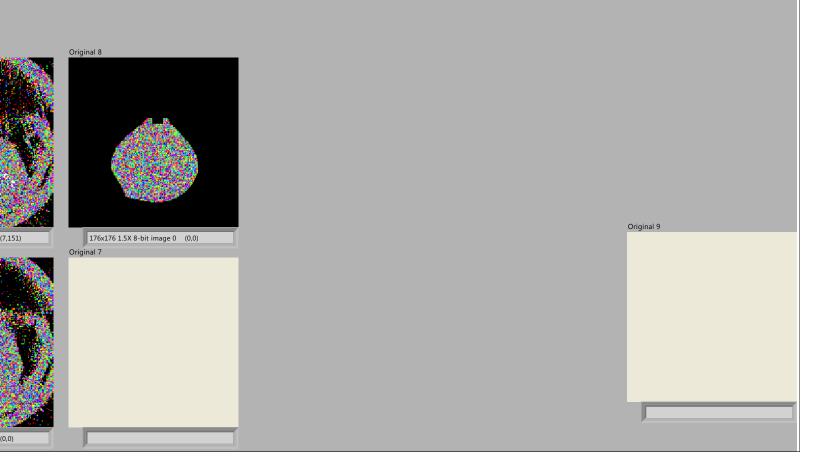
Everything

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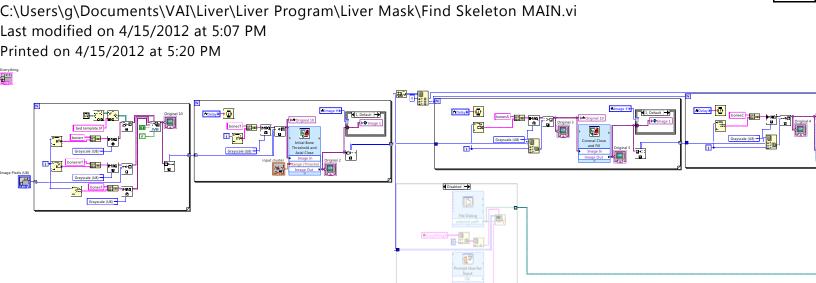


176x176 1.5X 8-bit image 0

1

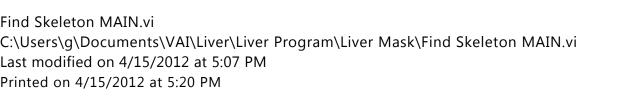


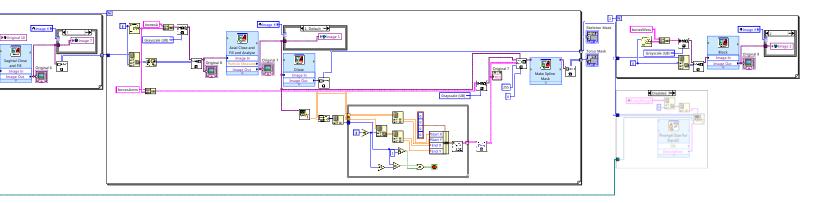


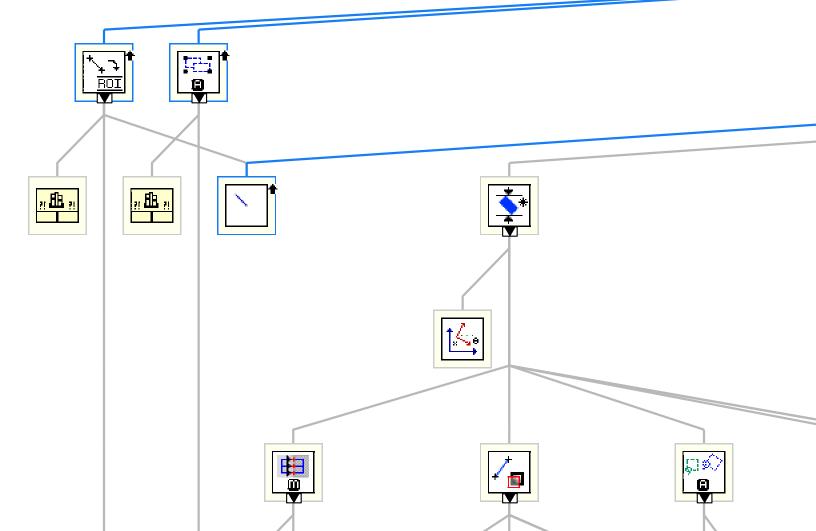


Find Skeleton MAIN.vi

Page 3

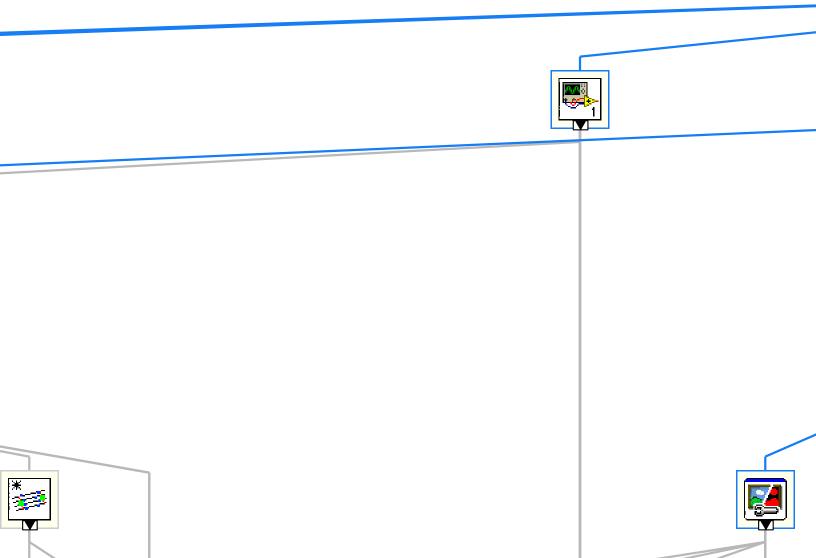


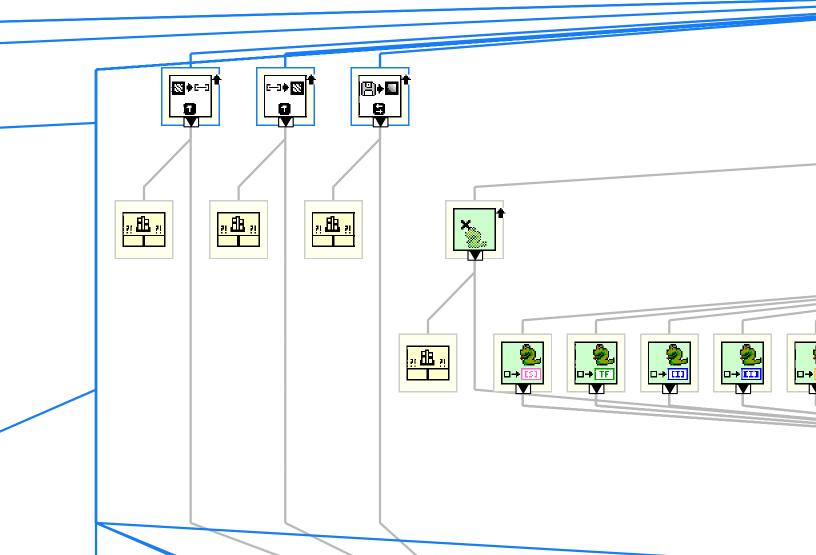




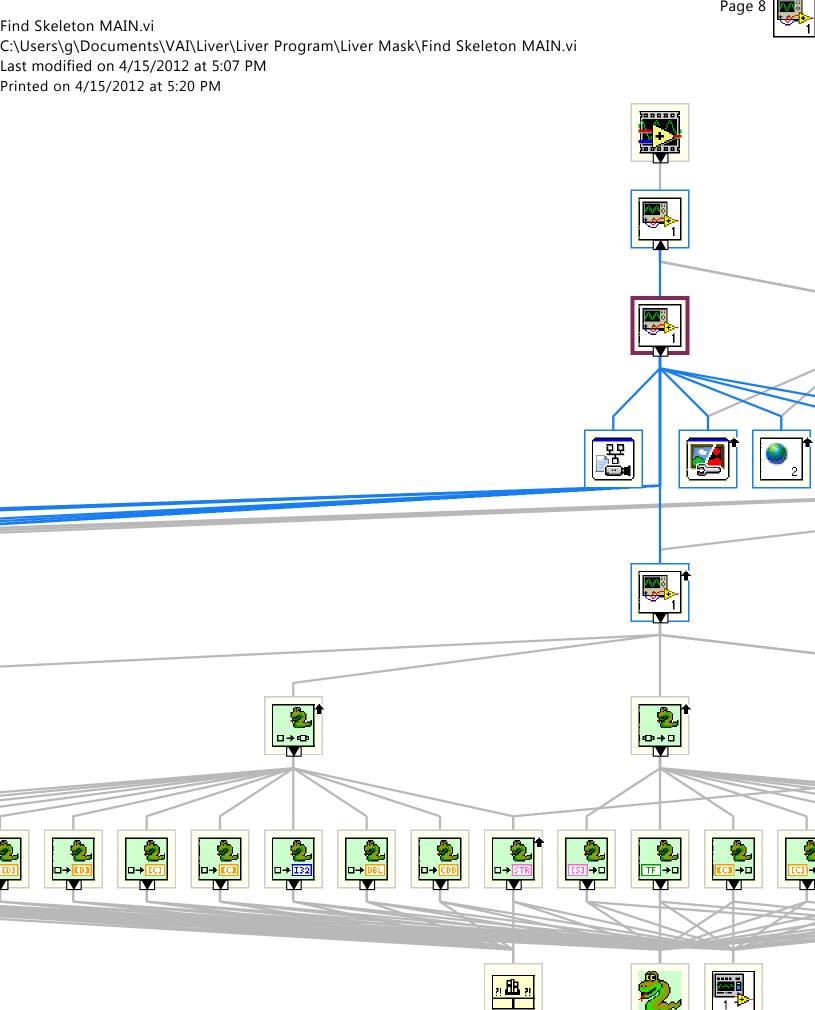




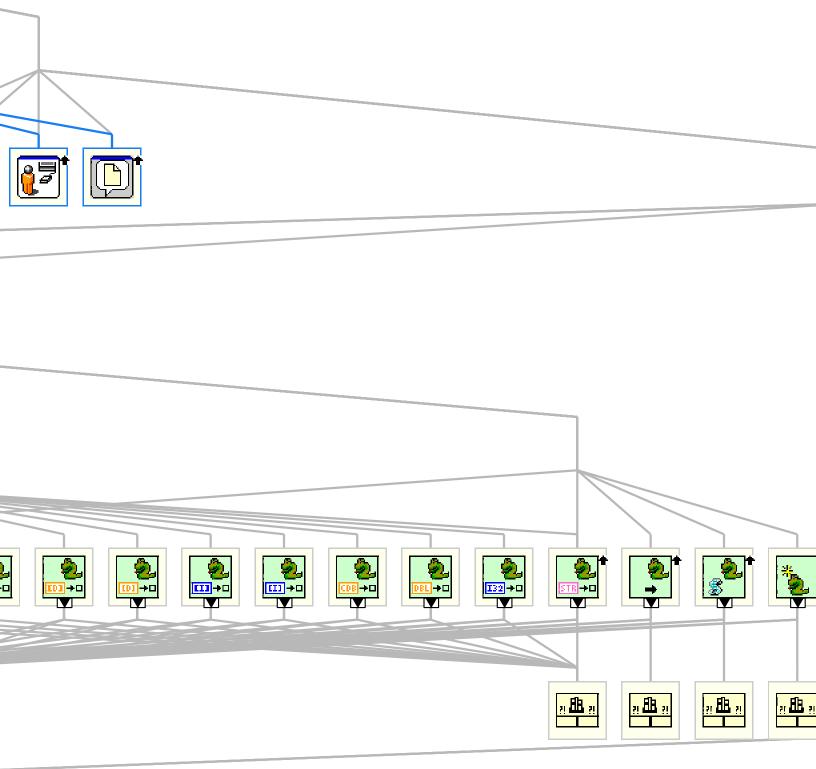




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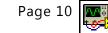










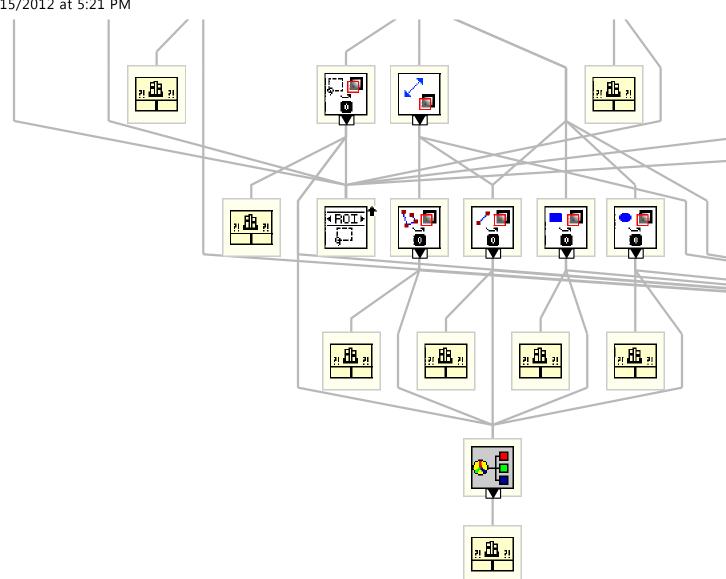


Find Skeleton MAIN.vi

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Last modified on 4/15/2012 at 5:07 PM

Printed on 4/15/2012 at 5:21 PM





### Black

Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



### IMAQ Create

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Basics.llb\IMAQ Create



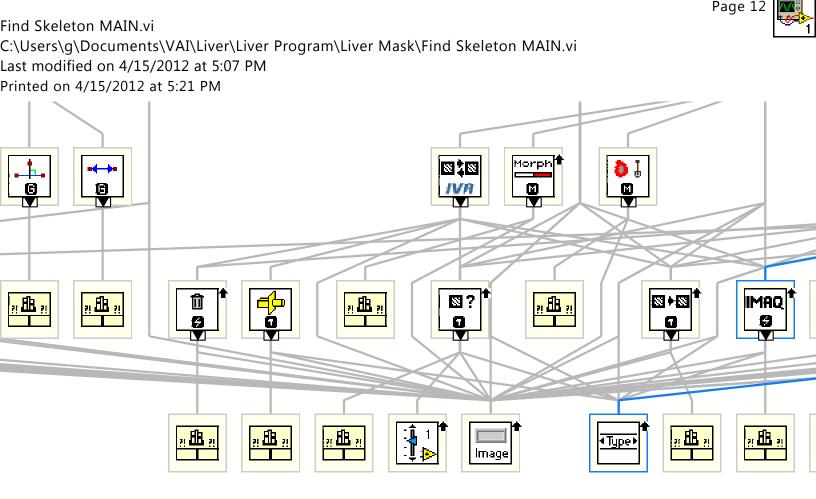
### Image Type

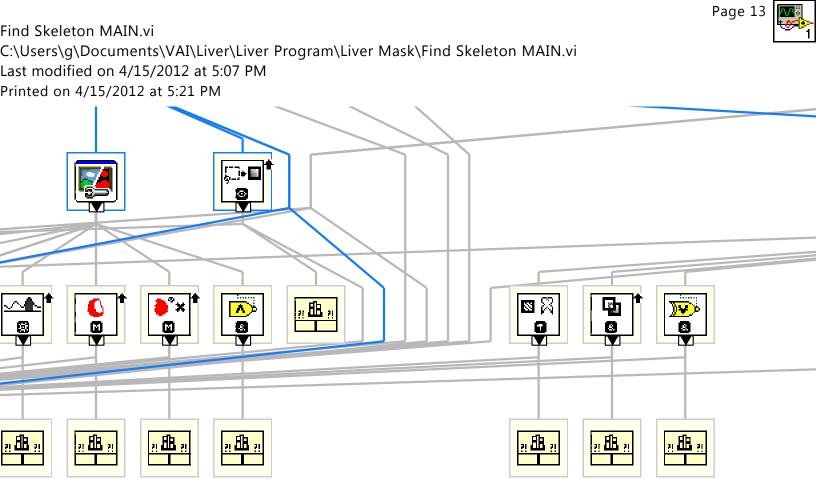
C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Image Controls.llb\Image Type



### IMAQ Convert Line to ROI

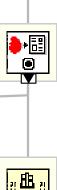
C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\ROI Conversion.llb\IMAQ Convert Line to ROI

















IMAQ Line

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Image Controls.llb\IMAQ Line



#### **Dilate** Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



### Make Spline Mask

### Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



### NI\_Vision\_Development\_Module.lvlib:IMAQ ROIToMask 2

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Vision\ROI Tools.llb\IMAQ ROIToMask 2



# IMAQ Group ROIs

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Vision\ROI Tools.llb\IMAQ Group ROIs

# 360clamp.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\360clamp.vi



# Axial Close and Fill and Analyze

Vision Assistant Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



### Sagittal Close and Fill

### Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



#### **Coronal Close and Fill** Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



### Image.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\Image.vi



### Initial Bone Threshold and Axial Close

#### Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



### IMAQ ImageToArray

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Vision\Basics.llb\IMAQ ImageToArray



### IVA Mask from Image File 2.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Vision Assistant Utils.llb\IVA Mask from Image File 2.vi



### IMAQ ArrayToImage

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Vision\Basics.llb\IMAQ ArrayToImage



### IMAQ ReadFile

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Files.llb\IMAQ ReadFile



### **Prompt User for Input2**

Prompt User for Input

Displays a standard dialog box that prompts users to enter information, such as a user name and password.

-----

This Express VI is configured as follows:

Message to Display to the User:Input a name to append to the file name The inputs are: Text Entry Box: Description



#### **Prompt User for Input** Prompt User for Input

Displays a standard dialog box that prompts users to enter information, such as a user name and password.

-----

This Express VI is configured as follows:

Message to Display to the User:Input a name to append to the file name The inputs are: Text Entry Box: Description



File Dialog

File Dialog Displays a dialog box with which you can specify the path to a file or directory.

This Express VI is configured as follows:

Selection Mode: New or existing directory



### ExportFilesPYTHONwithMeta.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\ExportFilesPYTHONwithMeta.vi



### Sagittal.vi

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#### Get Ribs2 Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



### Vision Acquisition

#### Vision Acquisition

Creates, and edits acquisitions using the NI Vision Acquisition Express VI.

The NI Vision Acquisition Wizard is launched by placing the Express VI on the block diagram. Select an acquisition source and configure an acquisition using NI-IMAQ, NI-IMAQdx, or simulate an acquisition by reading an AVI or image files from a folder. After an acquisition is configured, select controls and indicators to be able to programmatically set in LabVIEW. Double-click the Vision Acquisition Express VI to edit the acquisition.

Note: Any images created by the Express VI need to be disposed after use. Use the IMAQ Dispose.vi to cleanup the images output by the Express VI when they are no longer needed.

Find Skeleton MAIN.vi C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Find Skeleton MAIN.vi Last modified on 4/15/2012 at 5:07 PM

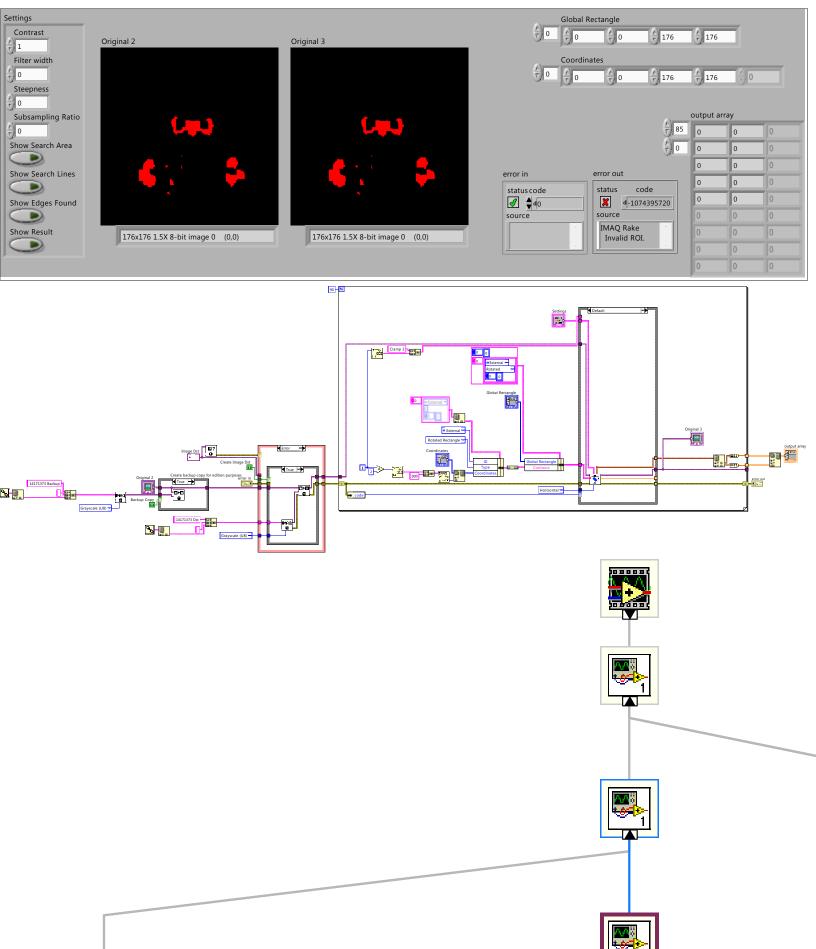
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# Initial Bone Threshold.vi

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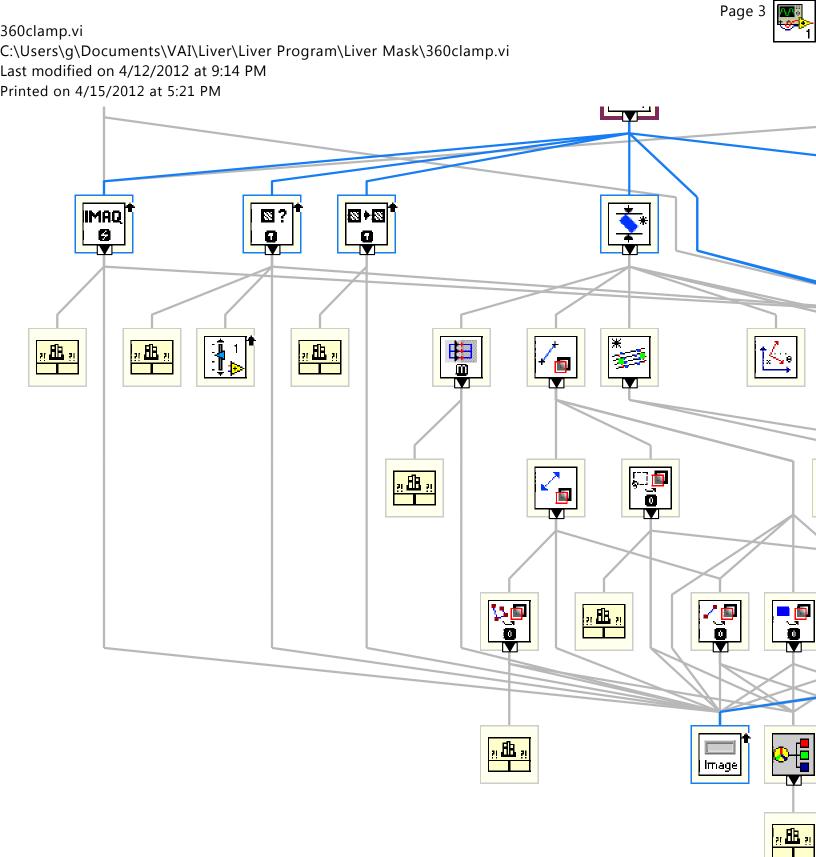
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### IMAQ Image.ctl

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#### Image Type

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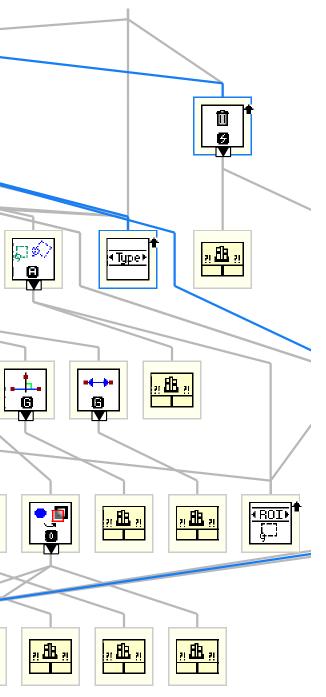
#### Imaq GetImageInfo

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Page 4 🌆

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360clamp.vi C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\360clamp.vi Last modified on 4/12/2012 at 9:14 PM Printed on 4/15/2012 at 5:21 PM



Page 5

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#### IMAQ Create

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#### IMAQ Copy

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#### IVA Gauge Algorithm Max.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Vision Assistant Utils.llb\IVA Gauge Algorithm Max.vi



#### Imaq Dispose

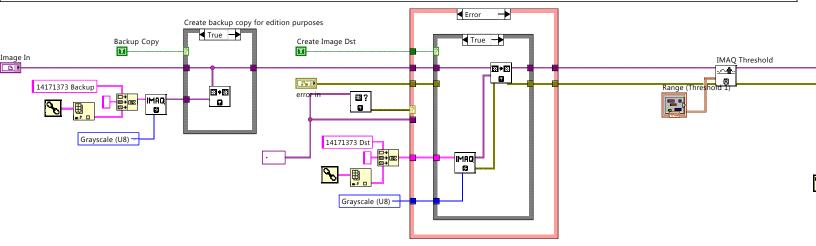
C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Basics.llb\Imaq Dispose

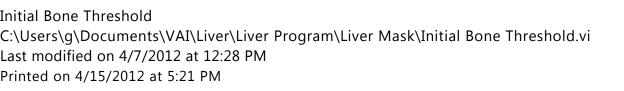
Initial Bone Threshold
C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Initial Bone Threshold.vi
Last modified on 4/7/2012 at 12:28 PM
Printed on 4/15/2012 at 5:21 PM

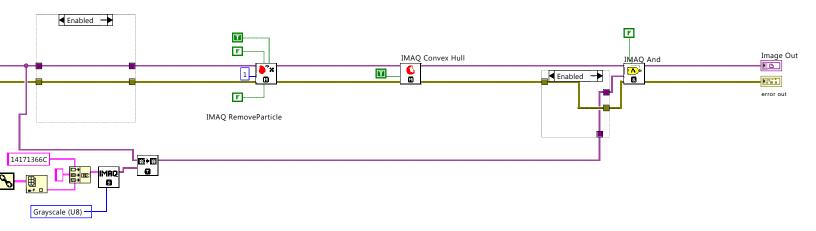
Image In	Image Out	
Range (Threshold 1)       Lower value       200       Upper value       255		
error in status code source		

error out

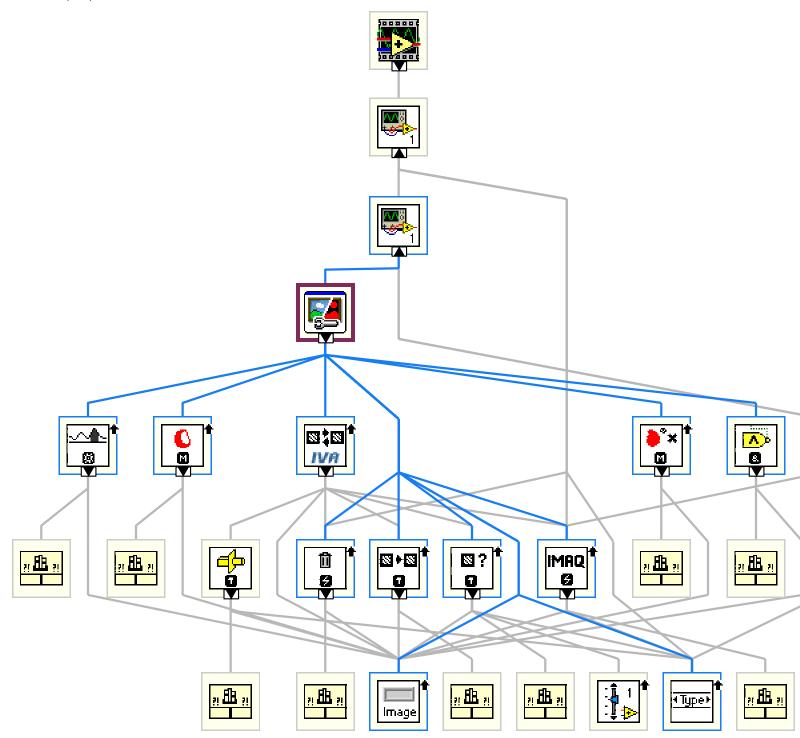








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#### IMAQ Image.ctl

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#### Image Type

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#### IMAQ Create

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Page 3

Initial Bone Threshold C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Initial Bone Threshold.vi Last modified on 4/7/2012 at 12:28 PM Printed on 4/15/2012 at 5:21 PM



Page 5

Initial Bone Threshold C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Initial Bone Threshold.vi Last modified on 4/7/2012 at 12:28 PM Printed on 4/15/2012 at 5:21 PM

NI\_Vision\_Development\_Module.lvlib:IMAQ Threshold

NI\_Vision\_Development\_Module.lvlib:IMAQ Convex Hull



C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Process.llb\IMAQ Threshold



NI\_Vision\_Development\_Module.lvlib:IMAQ RemoveParticle C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Morpho.llb\IMAQ RemoveParticle



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#### IMAQ Copy

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C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Morpho.llb\IMAQ Convex Hull



NI\_Vision\_Development\_Module.lvlib:IMAQ And C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Operator.llb\IMAQ And



#### Imaq Dispose

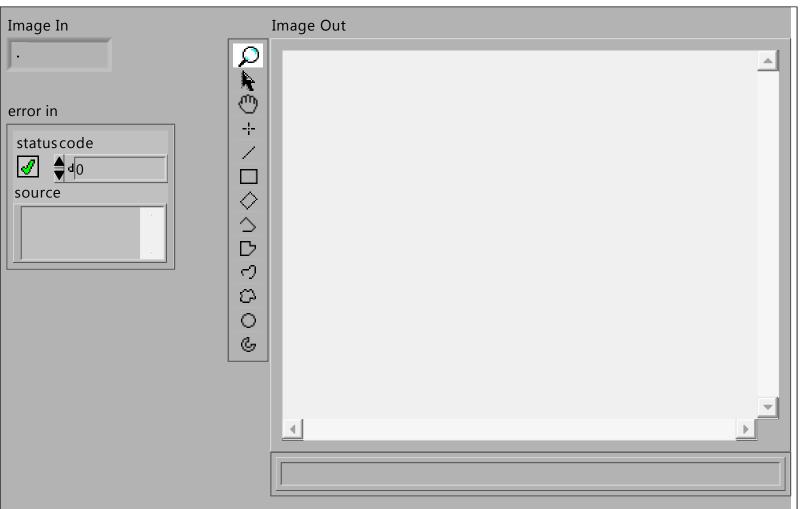
C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Basics.llb\Imaq Dispose



#### IVA Image Buffer.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Vision Assistant Utils.llb\IVA Image Buffer.vi

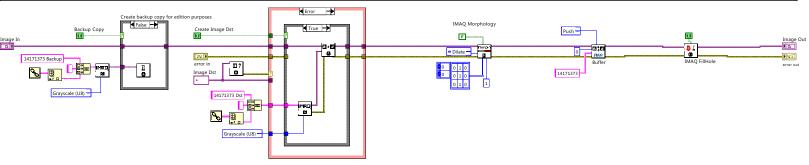
Sagittal C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Sagittal.vi Last modified on 4/7/2012 at 12:07 PM Printed on 4/15/2012 at 5:21 PM



#### error out

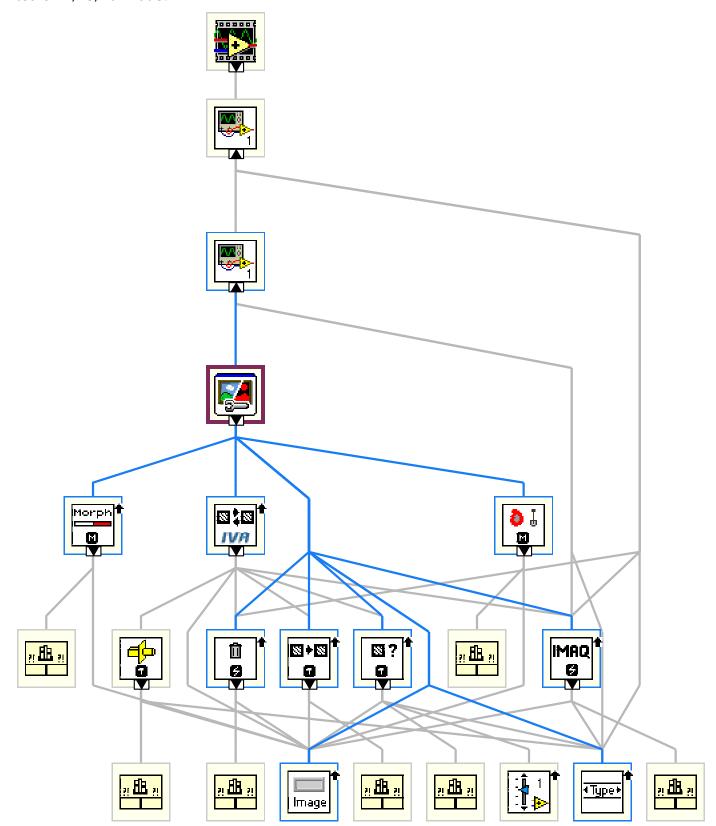


Page 1





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### Image C:\Program Files

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Image Type

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Sagittal

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#### Imag GetImageInfo

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### IMAQ Create

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Basics.llb\IMAQ Create



#### NI\_Vision\_Development\_Module.lvlib:IMAQ Morphology C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Morpho.llb\IMAQ Morphology



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### NI\_Vision\_Development\_Module.lvlib:IMAQ FillHole

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#### IMAQ Copy

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#### IVA Image Buffer.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Vision Assistant Utils.llb\IVA Image Buffer.vi

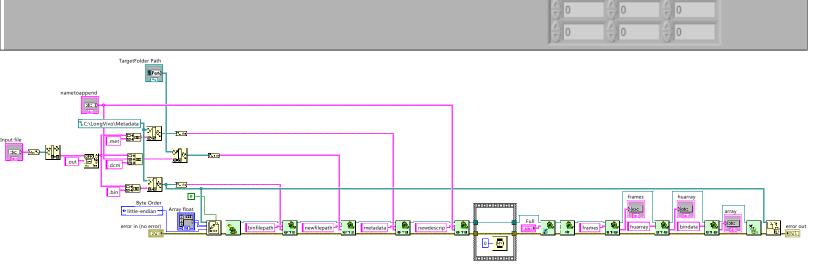


#### Imaq Dispose

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Basics.llb\Imaq Dispose

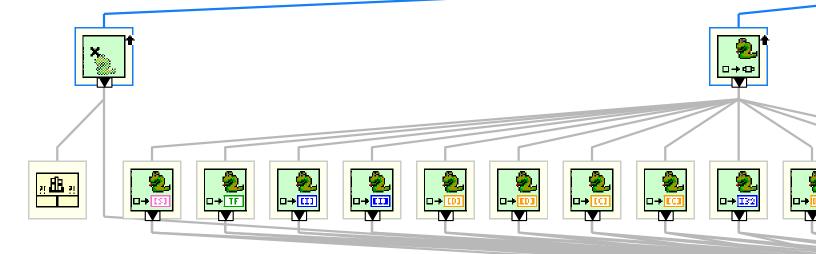


netoappend Input file	
C:\LongVivo\Database\20120305-120708-AP_Liver-Met	:s_DM576-1-00_Day-1.out
TargetFolder Path	
<pre>import dicom import numpy import sys import os.path  dcm = dicom.read_file(metadata) bindata = numpy.fromfile(binfilepath, dtype=numpy.uint8) frames = numpy.divide(numpy.divide(bindata.size,dcm.Rows),dcm.Columns)</pre>	frames 2 huarray 1 array
array = bindata.reshape(frames,dcm.Rows,dcm.Columns) huarray = numpy.array(array, dtype=numpy.float32) huarray = huarray/255.0*2000.0 huarray -= 1000.0 huarray = (huarray - dcm.RescaleIntercept)/dcm.RescaleSlope dcm.SeriesDescription = newdescrip dcm.NumberofFrames = frames dcm.PixelData = huarray.astype(numpy.uint16).tostring()	3 error out error in (no error) status code
dcm.save_as(newfilepath)	
	Array float $\overline{\tau}$ </td



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#### PYTHON Close Session\_\_ogtk.vi

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#### PYTHON Get String Data\_ogtk.vi

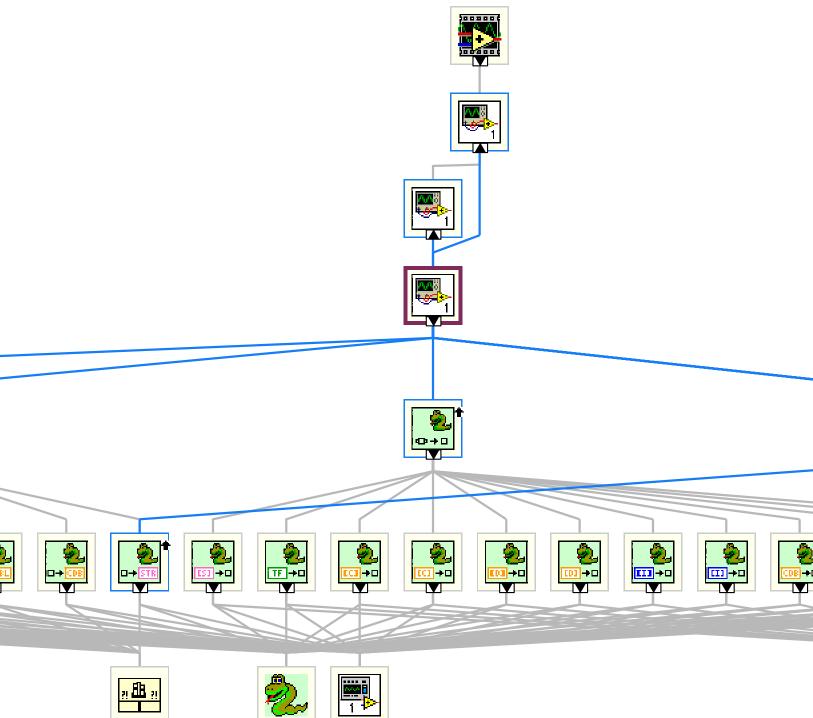
C:\Program Files\National Instruments\LabVIEW 2010\user.lib\\_OpenG.lib\labpython\labpython.llb\ PYTHON Get String Data\_\_ogtk.vi



#### PYTHON Get Data\_ogtk.vi

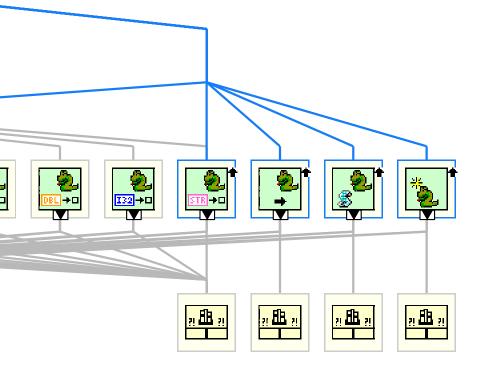
C:\Program Files\National Instruments\LabVIEW 2010\user.lib\\_OpenG.lib\labpython\labpython.llb\ PYTHON Get Data\_\_ogtk.vi





Page 3

1







#### **PYTHON Execute Script\_\_ogtk.vi**

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#### PYTHON Set Script Text\_ogtk.vi

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#### PYTHON Set String Data\_\_ogtk.vi

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#### PYTHON Set Data\_ogtk.vi

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#### PYTHON New Session\_\_ogtk.vi

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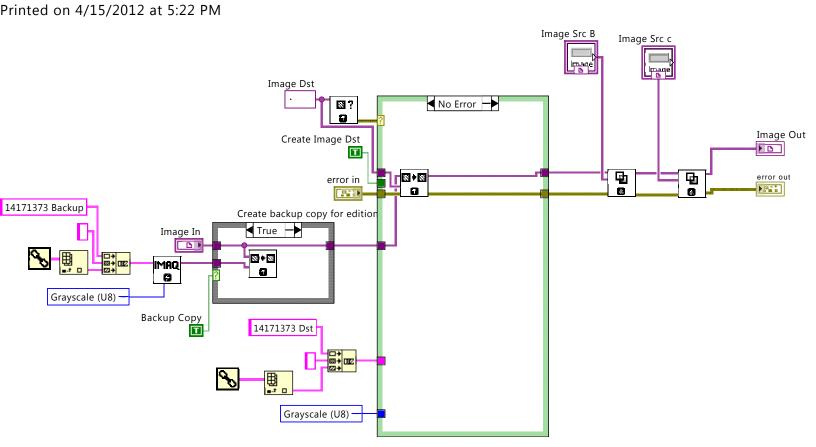


Apply Bone Mask C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Apply 2 Bone Mask.vi Last modified on 3/14/2012 at 11:50 AM Printed on 4/15/2012 at 5:22 PM Image Src B

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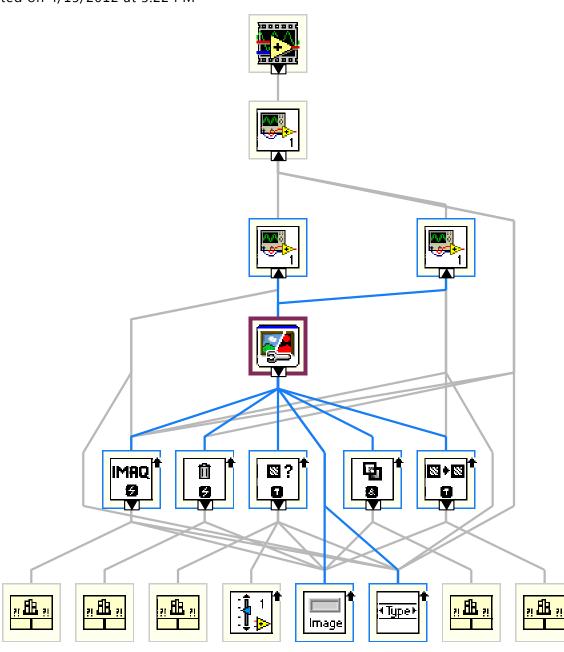
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#### IMAQ Image.ctl

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## <u> • Type</u>⊧

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Imaq GetImageInfo

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#### NI\_Vision\_Development\_Module.lvlib:IMAQ Mask

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#### IMAQ Copy

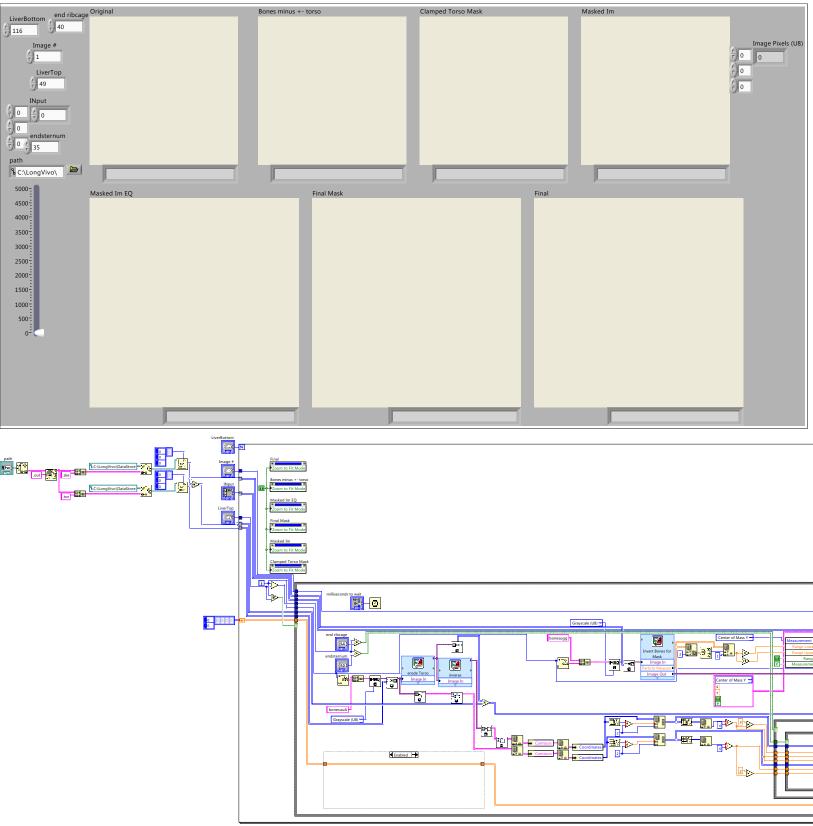
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Apply Bone Mask C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Apply 2 Bone Mask.vi Last modified on 3/14/2012 at 11:50 AM Printed on 4/15/2012 at 5:22 PM

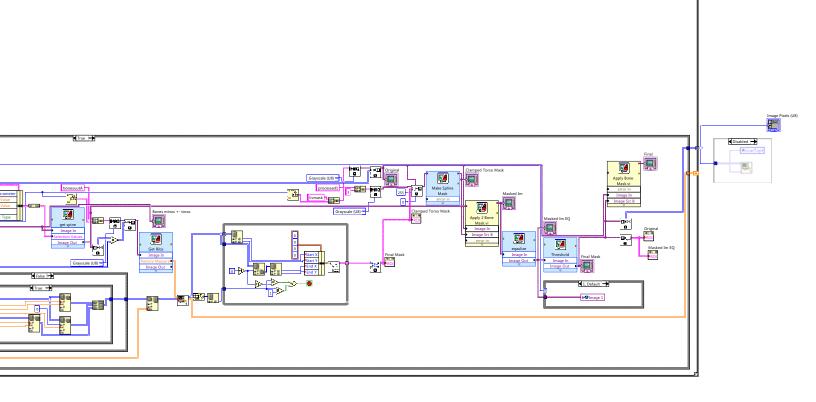


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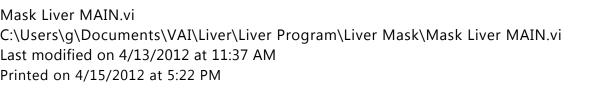
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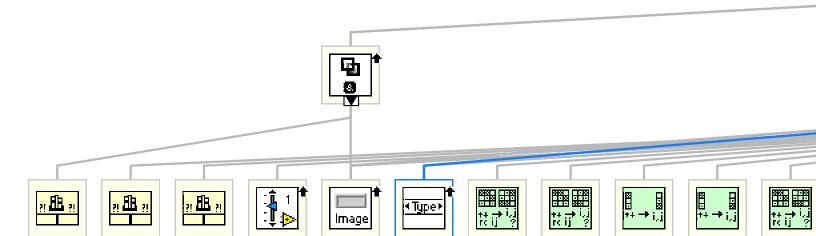


Page 1



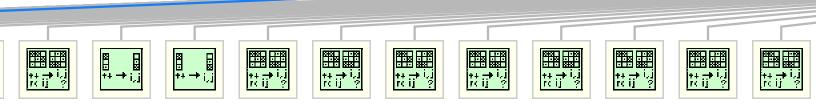




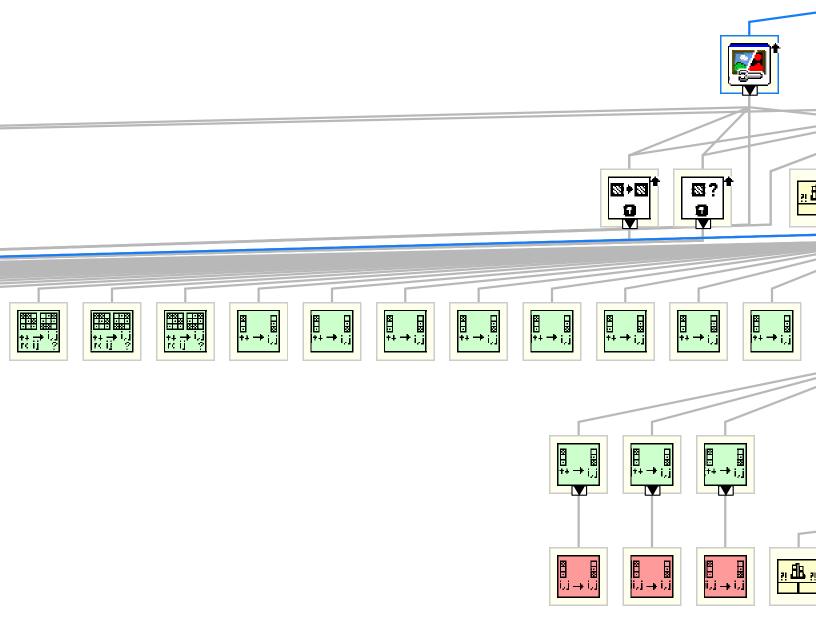




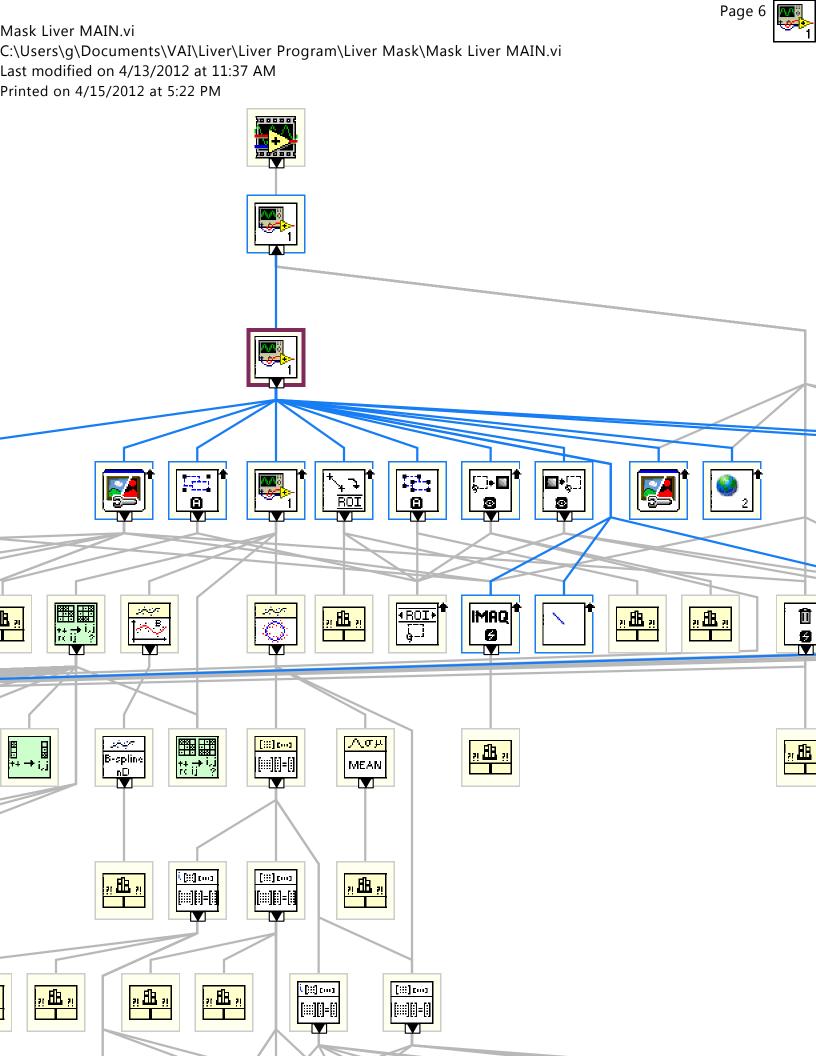




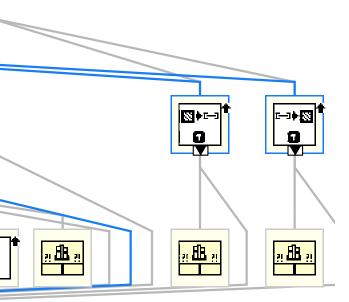






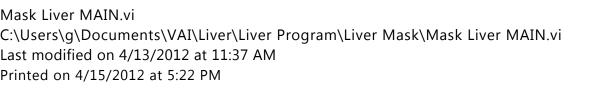




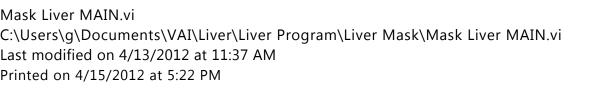






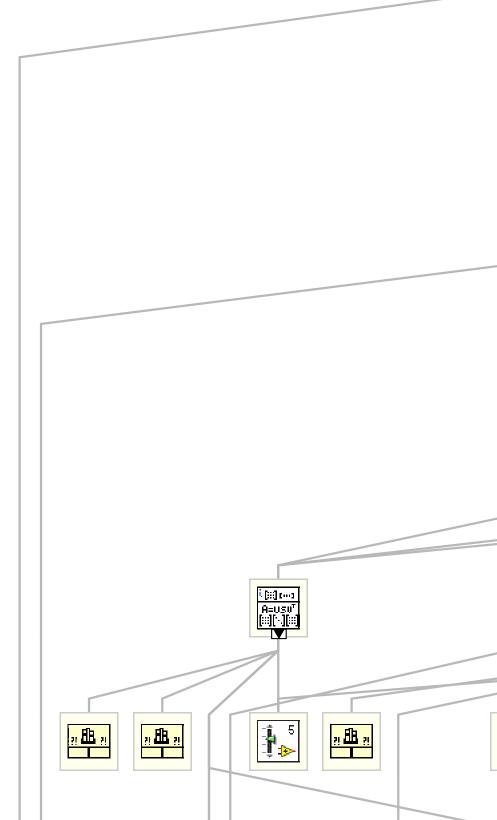


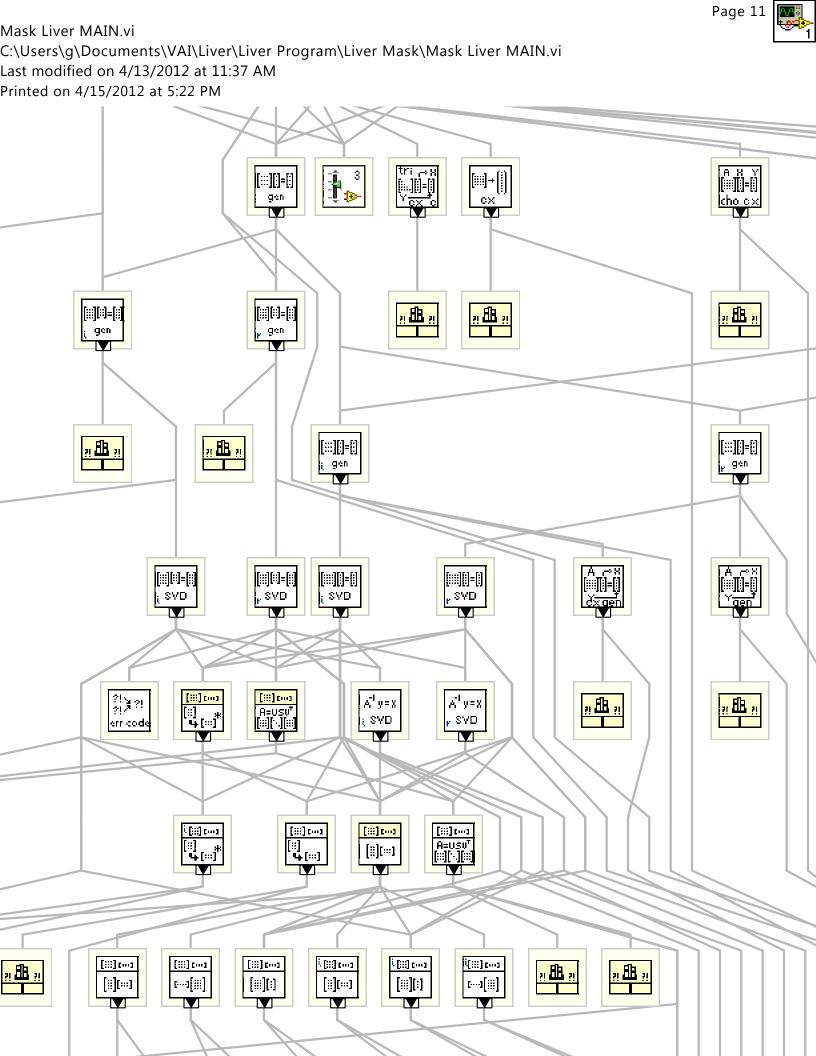


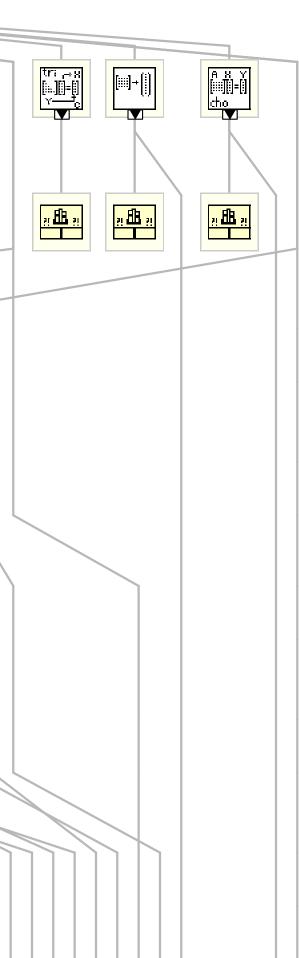


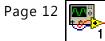
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#### IMAQ Create

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#### IMAQ ArrayToImage

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#### IMAQ ImageToArray

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#### IMAQ Group ROIs

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**NI\_Vision\_Development\_Module.lvlib:IMAQ ROIToMask 2** C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Vision\ROI Tools.llb\IMAQ ROIToMask 2



#### IMAQ Convert Line to ROI

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#### Image.vi

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#### Apply Bone Mask.vi

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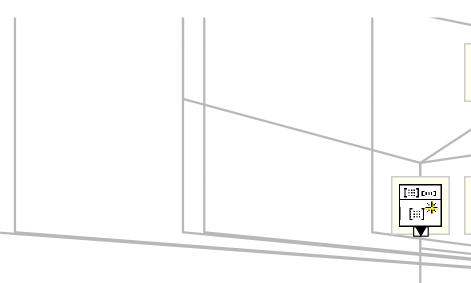


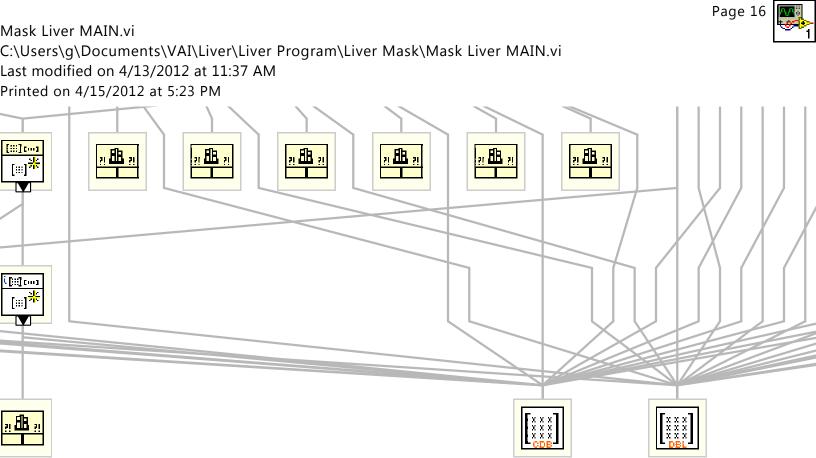


Page 15

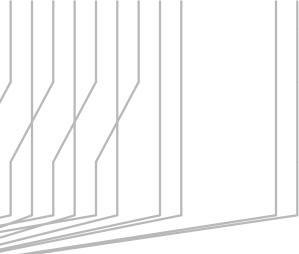
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Mask Liver MAIN.vi C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Mask Liver MAIN.vi Last modified on 4/13/2012 at 11:37 AM Printed on 4/15/2012 at 5:23 PM



#### Threshold Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



# eqaulize

Vision Assistant Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



## Apply 2 Bone Mask.vi

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# Make Spline Mask

## Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

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# Spline Spline fit.vi

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# Get Ribs

Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

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### inverse

Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



### **erode Torso** Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

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# IMAQ Ungroup ROIs

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## NI\_Vision\_Development\_Module.lvlib:IMAQ MaskToROI

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# get spine

Vision Assistant Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



# Invert Bones for Mask

Vision Assistant Creates, edits, and runs vision algorithms using NI Vision Assistant.

When you place this Express VI on the block diagram, NI Vision Assistant launches. Create an algorithm using the Vision Assistant processing functions. After you create an algorithm, you can select the controls and indicators that you want to be able to programmatically set in LabVIEW. Double-click the Vision Assistant Express VI to edit the algorithm.



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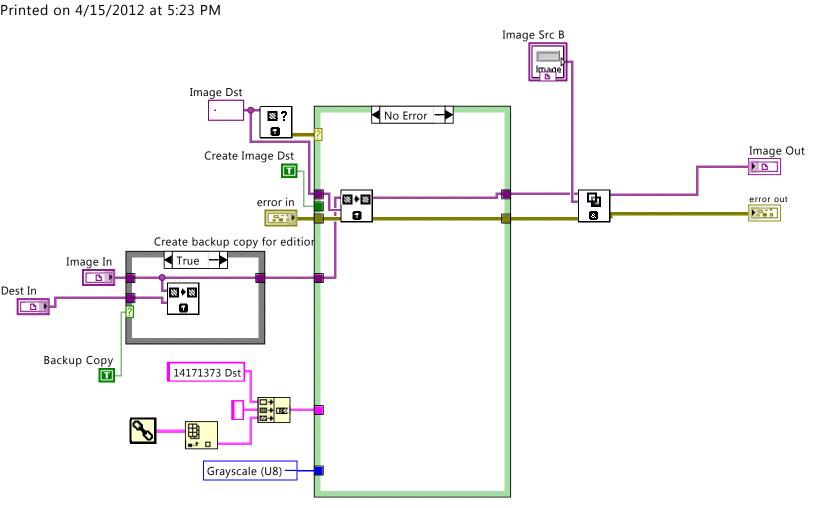
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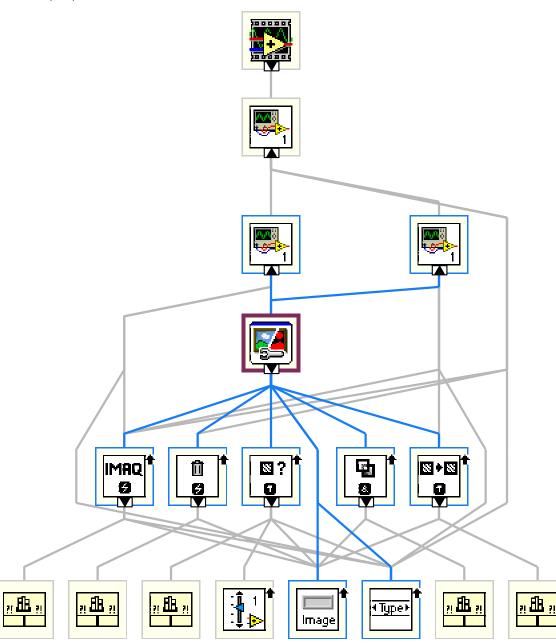


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# image

# IMAQ Image.ctl

Imaq GetImageInfo

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# <u> • Type</u>⊧

# Image Type

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IMAQ

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# NI\_Vision\_Development\_Module.lvlib:IMAQ Mask

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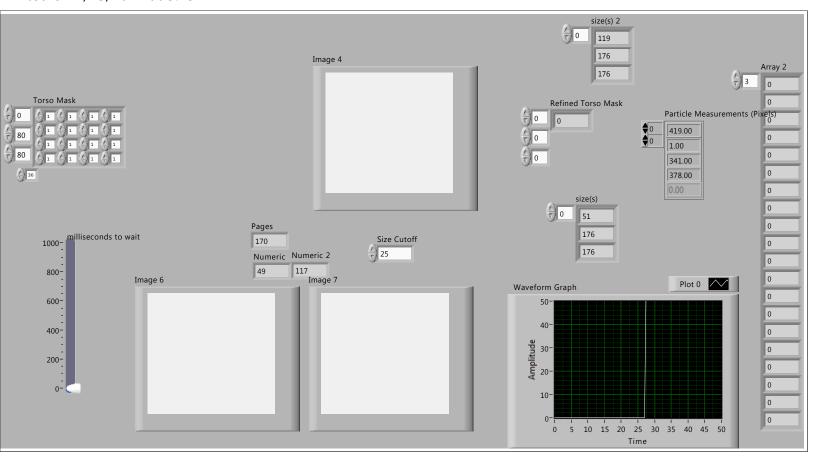
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# Imaq Dispose

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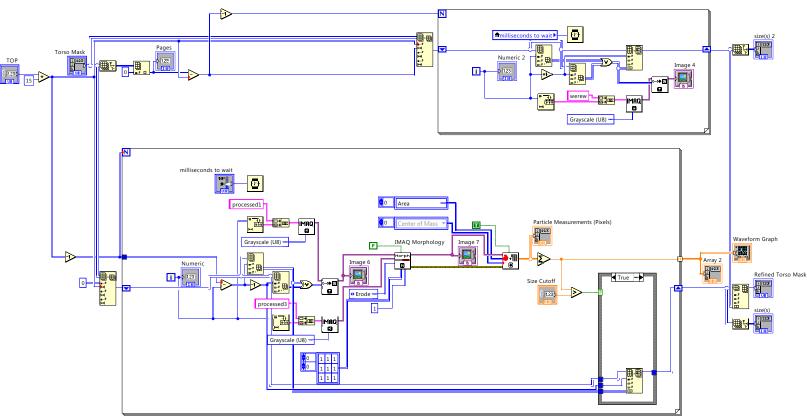
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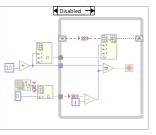
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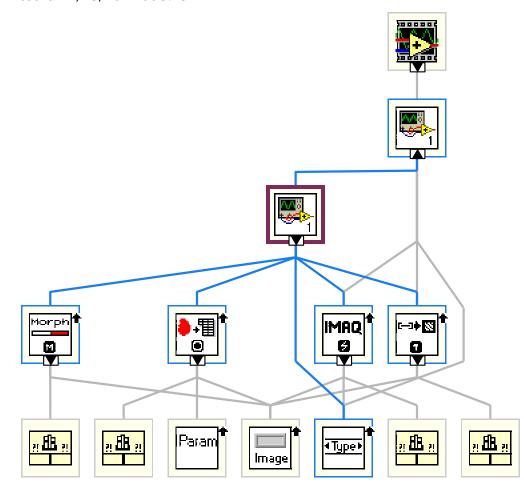
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Evaluate Torso.vi C:\Users\g\Documents\VAI\Liver\Liver Program\Liver Mask\Evaluate Torso.vi Last modified on 4/11/2012 at 11:45 PM Printed on 4/15/2012 at 5:23 PM





# Image Type

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IMAQ Create

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# IMAQ ArrayToImage

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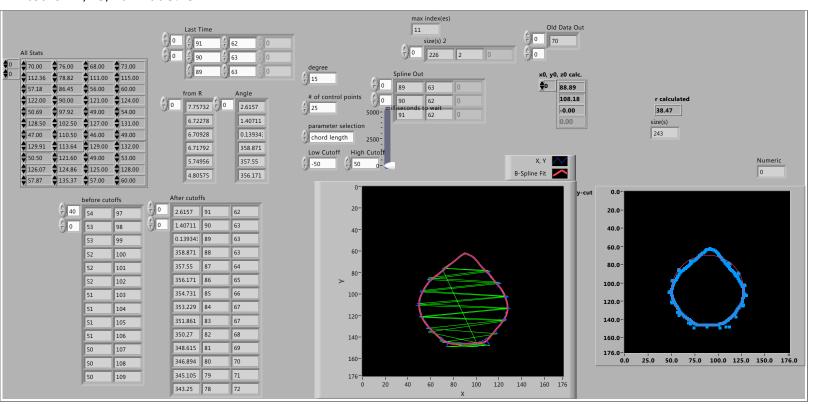
NI\_Vision\_Development\_Module.lvlib:IMAQ Morphology C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Morpho.llb\IMAQ Morphology

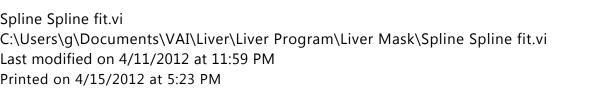


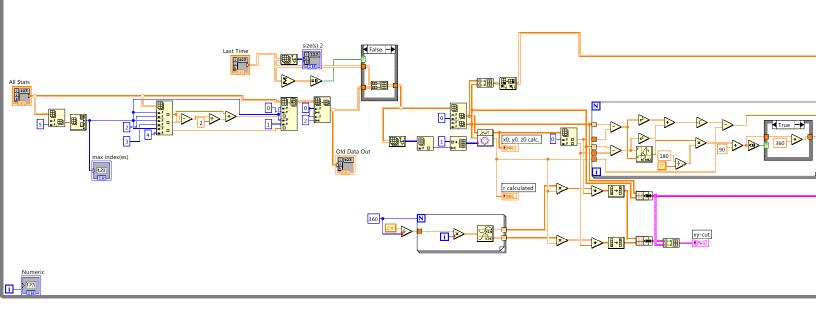


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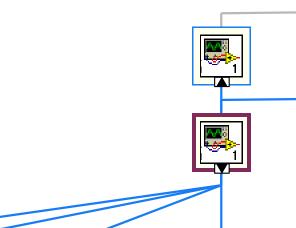


Last modified on 4/11/2012 at 11:59 PM Printed on 4/15/2012 at 5:23 PM Ν True 🗕 ₿.;₿ High Cutoff 0before cutoffs ( 1.23) DEL Low Cutoff After cutoff from R 1 123 E **::**(# 1D B-Spline Fit on Arbitrary Curve 3 ∎ tij V i. • ascending 8+ • column — E III 8. Spline Out Angle 0 **:**::: size(s) parameter selection - **123** milliseconds to wait degree # of control points 0 5 0 12 5 11 10 5 5 9 5 8 12 6 11 10 9 6 6 6 4 8 4 4 5 6 7 6 5 5 5 4 3 2 0

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Spline Spline fit.vi

Page 3

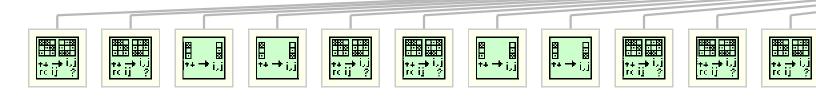




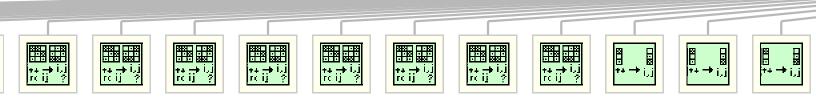


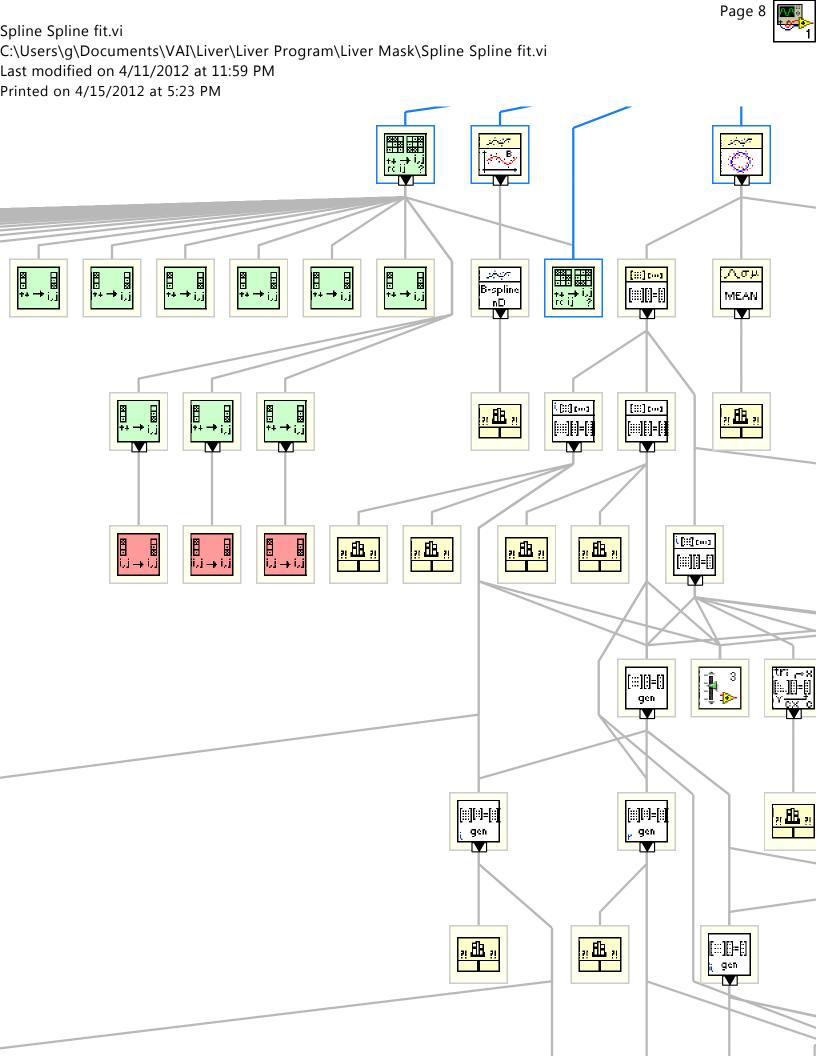


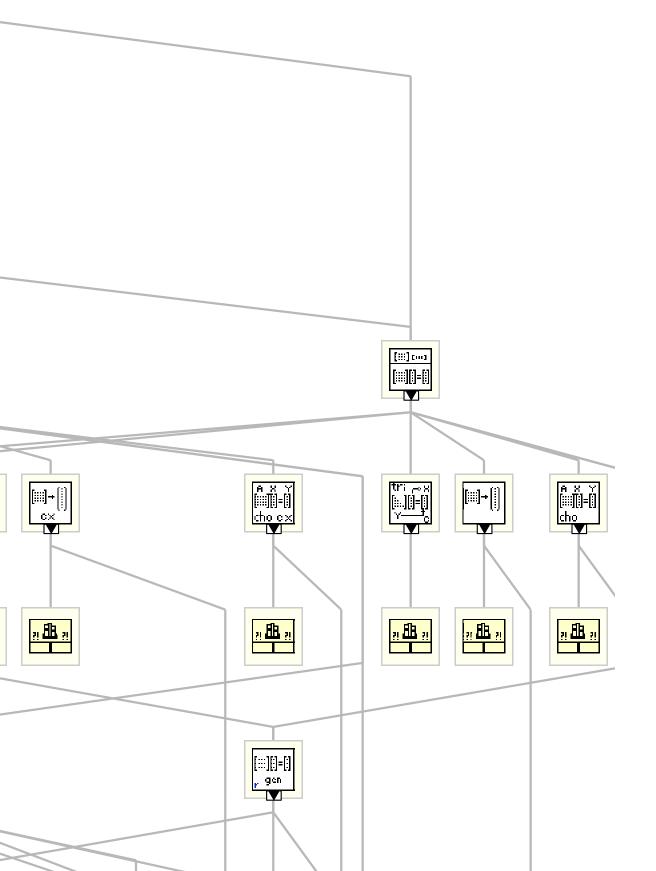




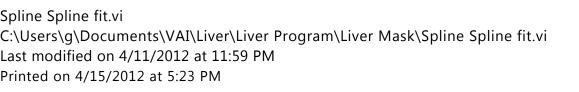












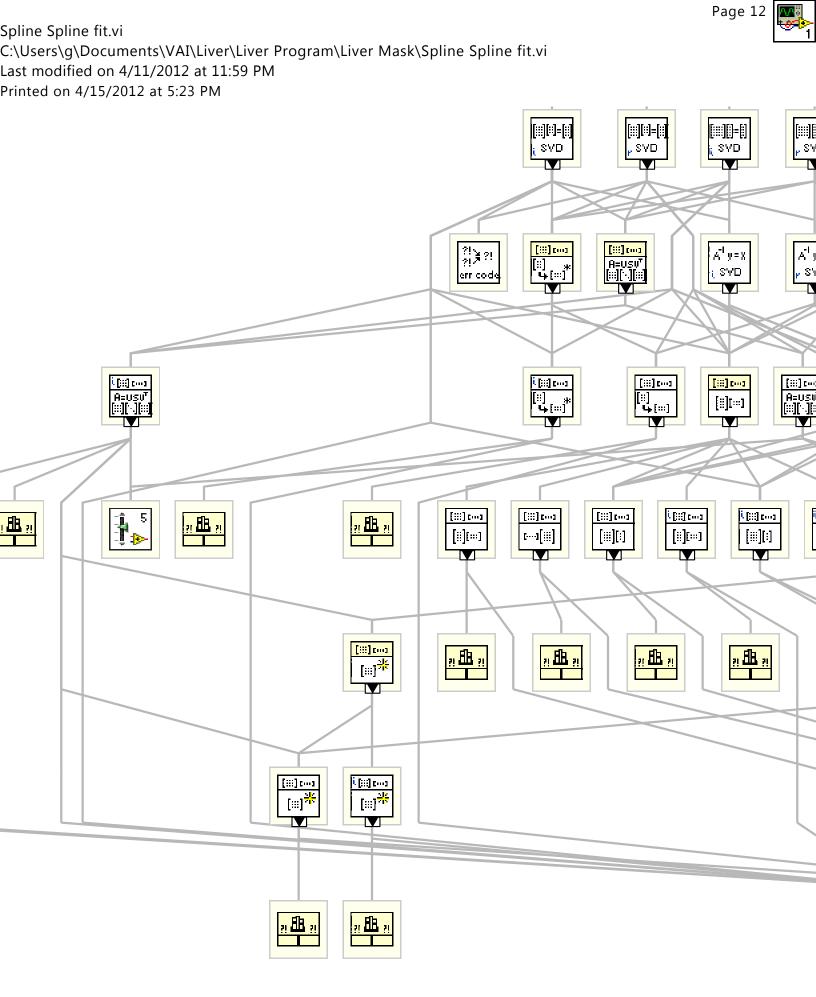






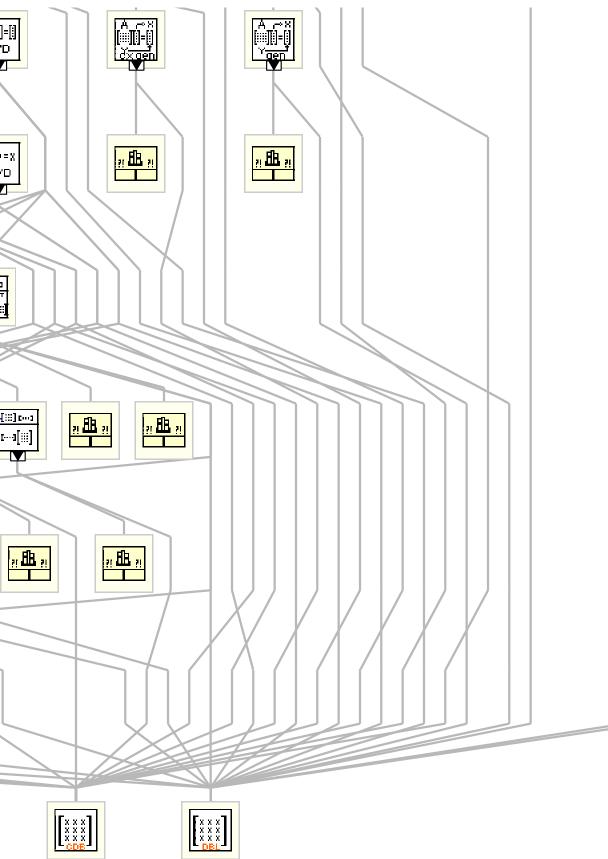


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# Sort 2D Array (DBL)\_\_ogtk.vi

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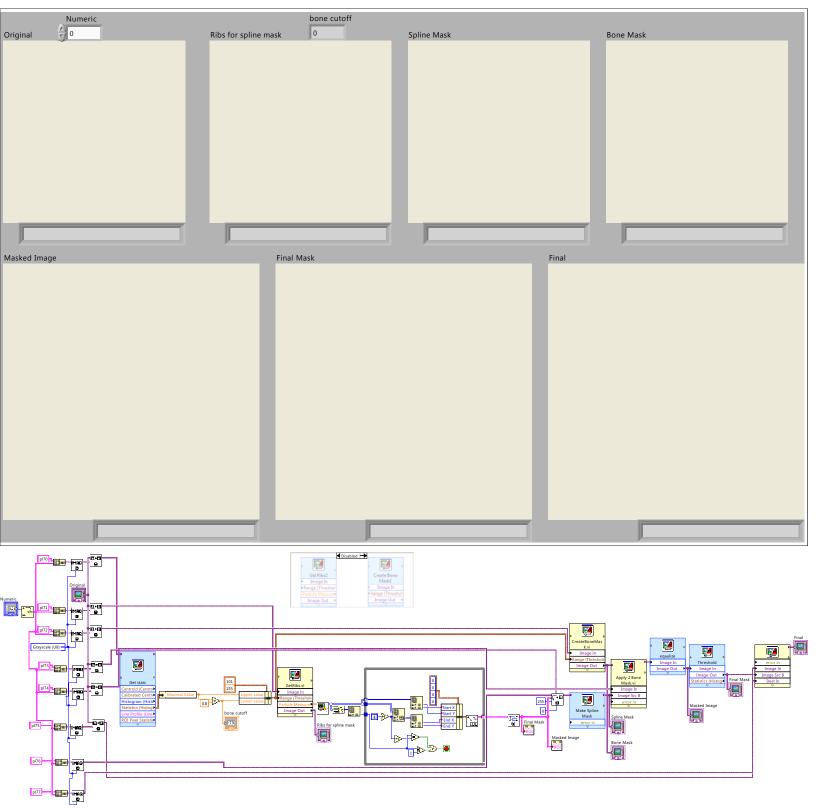
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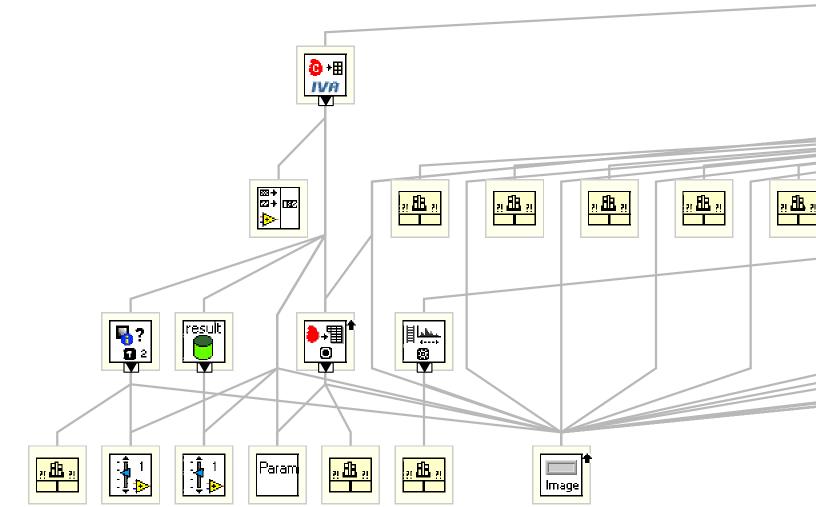
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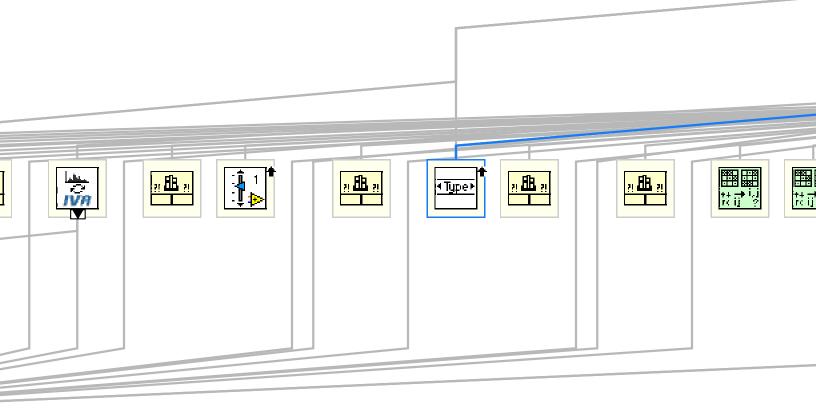
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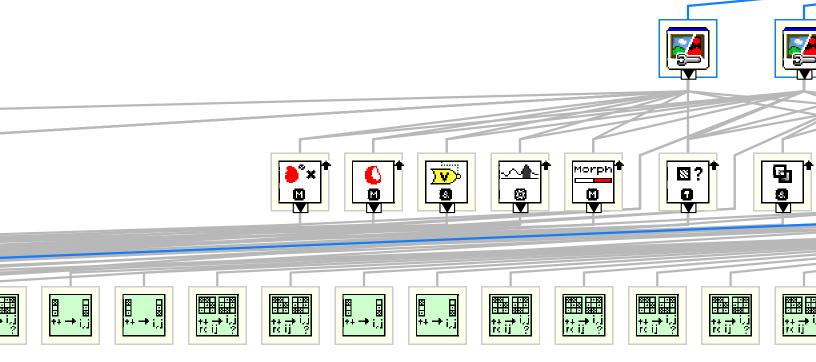




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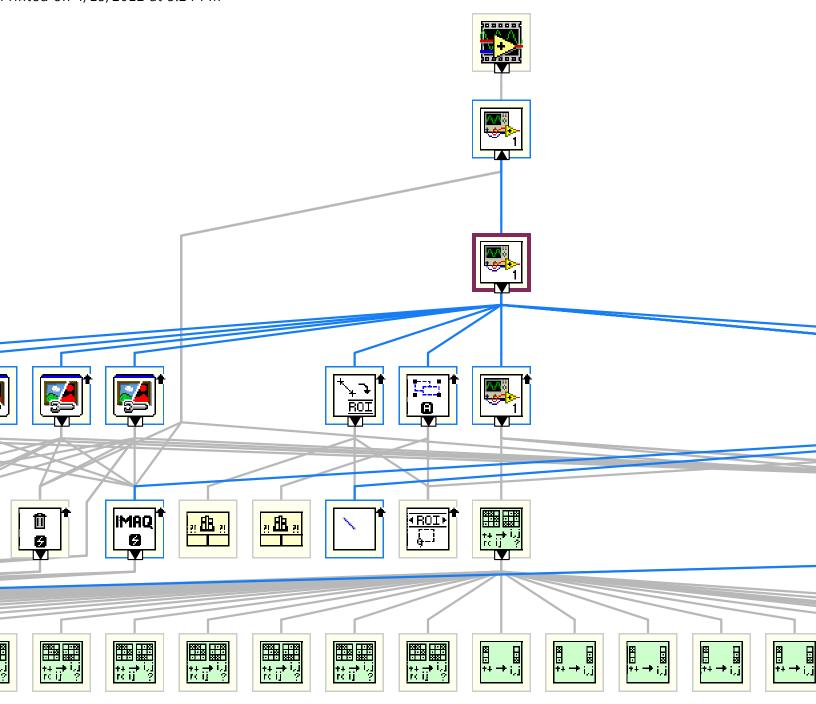






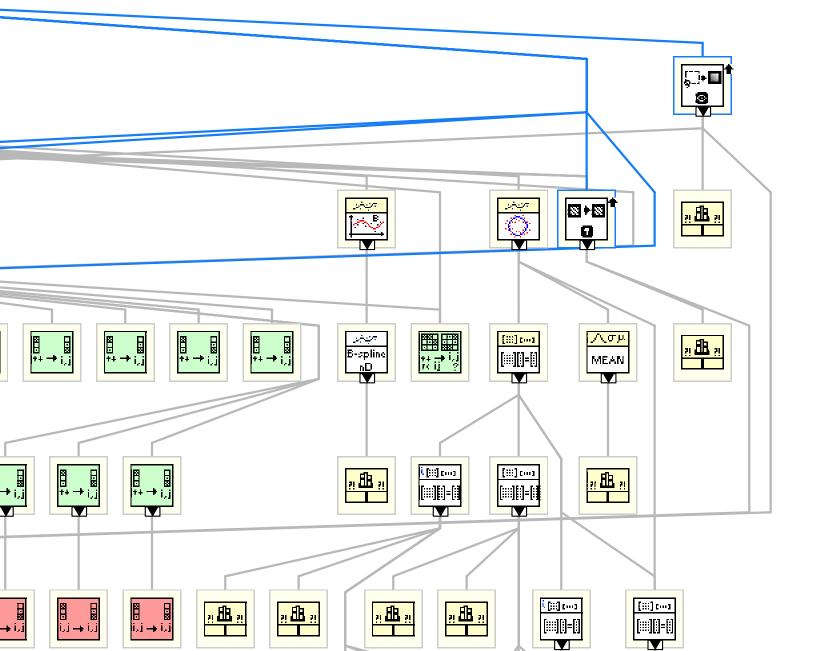
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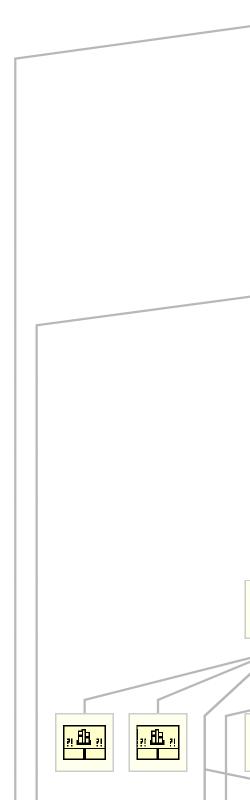




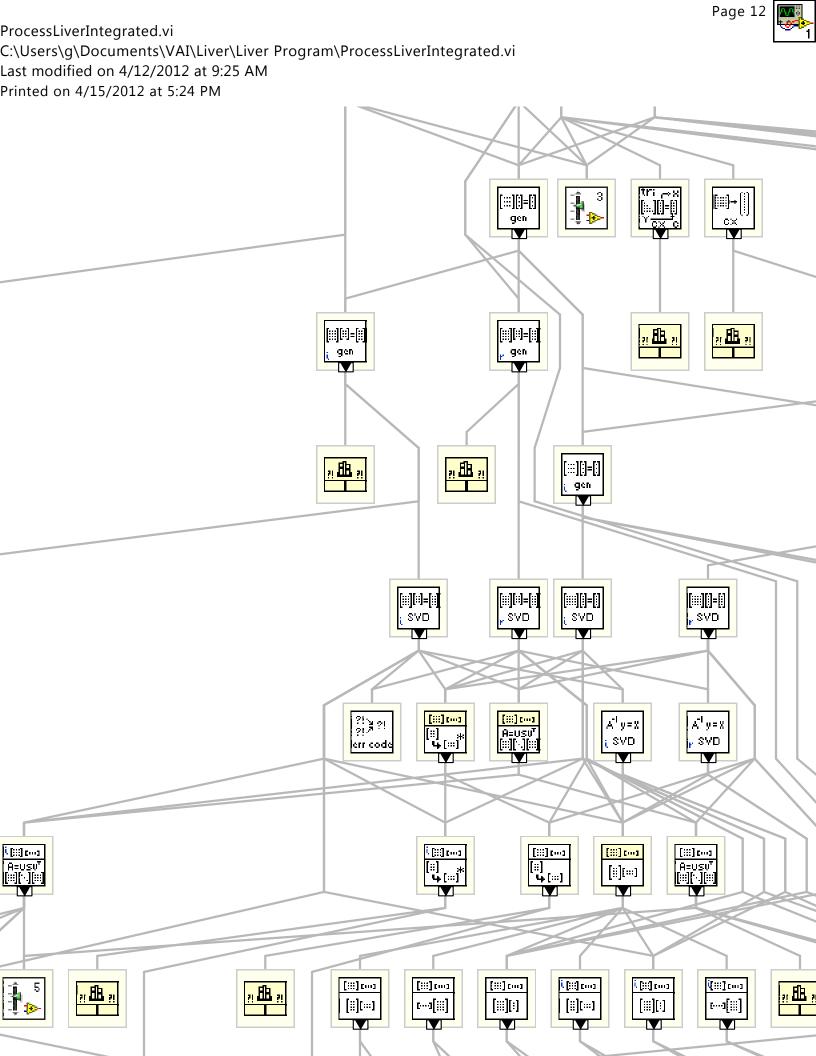




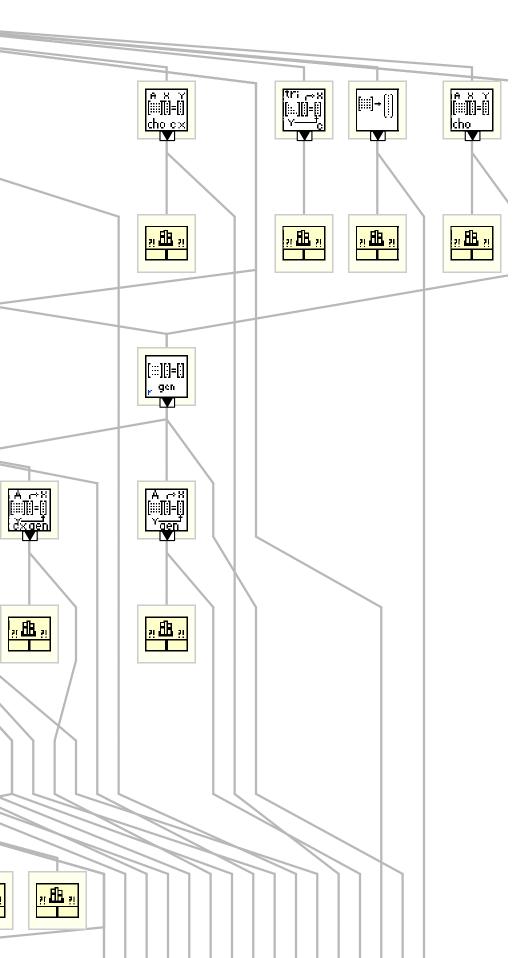
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Page 13



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#### Image Type

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#### **IMAQ** Line

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#### **IMAQ Copy**

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**IMAQ Group ROIs** C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Vision\ROI Tools.llb\IMAQ Group ROIs

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# Apply Bone Mask.vi

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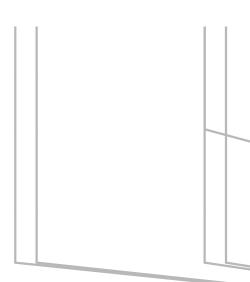
#### **IMAQ Convert Line to ROI**

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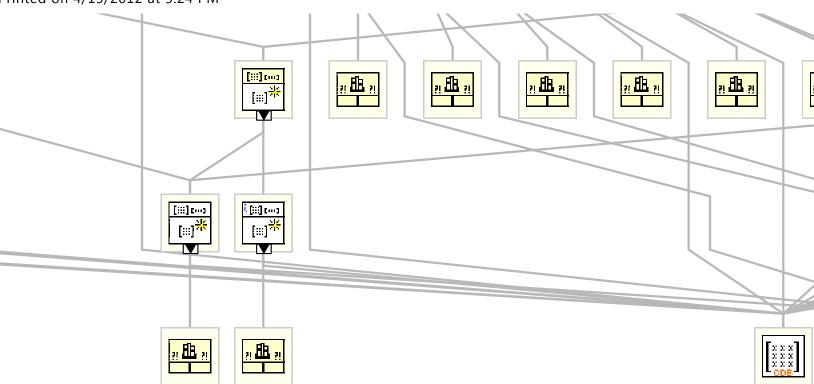




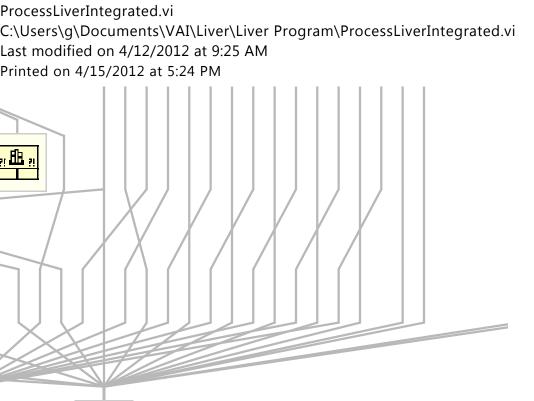
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Page 18







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#### Threshold Vision Assistant

Creates, edits, and runs vision algorithms using NI Vision Assistant.

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#### eqaulize

Vision Assistant Creates, edits, and runs vision algorithms using NI Vision Assistant.

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#### Make Spline Mask

Vision Assistant

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#### CreateBoneMask.vi

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#### Get stats Vision Assistant

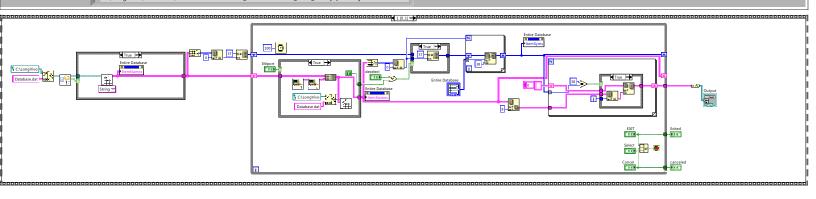
Creates, edits, and runs vision algorithms using NI Vision Assistant.

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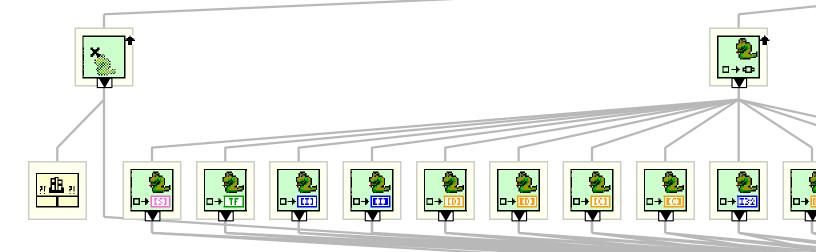
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Import files	ay-post-inj	06-14-2011	090023	RP	5-01_35d-post-inj	RP_nano6000-liver_5-01_35day-post-inj	C:\LongVivo\Database\	2 0			
	ay-post-inj	06-16-2011	102613	RP	5-01_37d-post-inj	RP_nano6000-liver_5-01_37day-post-inj	C:\LongVivo\Database\	2 0			Timepoint
		05-10-2011	104613	RP	7-01_1h-post-inj	RP_nano6000-liver_5-01-1hr	C:\LongVivo\Database\2	14			Scan Date
Cancel	y-post-inj	05-11-2011	105404	RP	7-01_2d-post-inj	RP_nano6000-liver_7-01_2day-post-inj	C:\LongVivo\Database\	2 0			Scan Time
	y-post-inj	05-17-2011 102907 RP 7-01_7d-post-inj		7-01_7d-post-inj	RP_nano6000-liver_7-01_7day-post-inj	C:\LongVivo\Database\	2 0			Scall Tille	
	ay-post-inj	05-24-2011	100848	JVO	7-01_14d-post-inj	JVO_nano6000-liver_7-01_14day-post-inj	C:\LongVivo\Database\2	0			Technician
EXIT	ay-post-inj	05-31-2011	102538	RP	7-01_21d-post-inj	RP_nano6000-liver_7-01_21day-post-inj	C:\LongVivo\Database\.	2 0			File Name
	ay-post-inj	06-07-2011	095920	RP	7-01_28d-post-inj	RP_nano6000-liver_7-01_28day-post-inj	C:\LongVivo\Database\	2 0			
	ay-post-inj	06-14-2011	091336	RP	7-01_35d-post-inj	RP_nano6000-liver_7-01_35day-post-inj	C:\LongVivo\Database\	2 0			File ID
DeSelect All		05-10-2011	113025	RP	7-03_1h-post-inj	RP_nano6000-liver_7-03-1hr	C:\LongVivo\Database\2	12			Database Address
	y-post-inj	05-11-2011	111545	RP	7-03_2d-post-inj	RP_nano6000-liver_7-03_2day-post-inj	C:\LongVivo\Database\.	2 18			Liver Top Level
	y-post-inj         05-17-2011         104240         RP         7-03_7d-post-inj           ay-post-inj         05-24-2011         102151         JVO         7-03_14d-post-inj           ay-post-inj         05-31-2011         103919         RP         7-03_21d-post-inj		RP_nano6000-liver_7-03_7day-post-inj	C:\LongVivo\Database\.	2 14			· · · · ·			
			JVO_nano6000-liver_7-03_14day-post-inj	C:\LongVivo\Database\2	12			Liver Bottom Lev			
			RP_nano6000-liver_7-03_21day-post-inj	C:\LongVivo\Database\.	2 15						
	ay-post-inj 06-07-2011 101			RP	7-03_28d-post-inj	RP_nano6000-liver_7-03_28day-post-inj	C:\LongVivo\Database\2 10			i	
	ay-post-inj	06-10-2011	101448	RP	7-03_31d-post-inj	RP_nano6000-liver_7.03_31day-post-inj	C:\LongVivo\Database\	2 17			
	y-post-inj	08-22-2011	184901	AP	AP_Exitron6000-Control_1_0-day-post-inj	AP_Monsma-liver_1_0day-post-inj	C:\LongVivo\Database\	2 0	0 🔻		
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	Output	canceled <sup>Exite</sup>	ed								
	© % C:\LongVivo\Database\20110510-113025-RP_nano6000-liver_7-03-1hr.out										
	S C:\Lo	ongVivo\Database\	20110511	-111545-RF	_nano6000-liver_7-03_2day-post-inj.out						
	S C:\Lo	ongVivo\Database\	20110517	-104240- R	P_nano6000-liver_7-03_7day-post-inj.out						
	S C:\Lo	ongVivo\Database\	20110524-	102151-JVC	_nano6000-liver_7-03_14day-post-inj.out						
	۲ C:\Lo	ongVivo\Database\	20110531	-103919-RF	_nano6000-liver_7-03_21day-post-inj.out						

C:\LongVivo\Database\20110607-101135-RP\_nano6000-liver\_7-03\_28day-post-inj.out

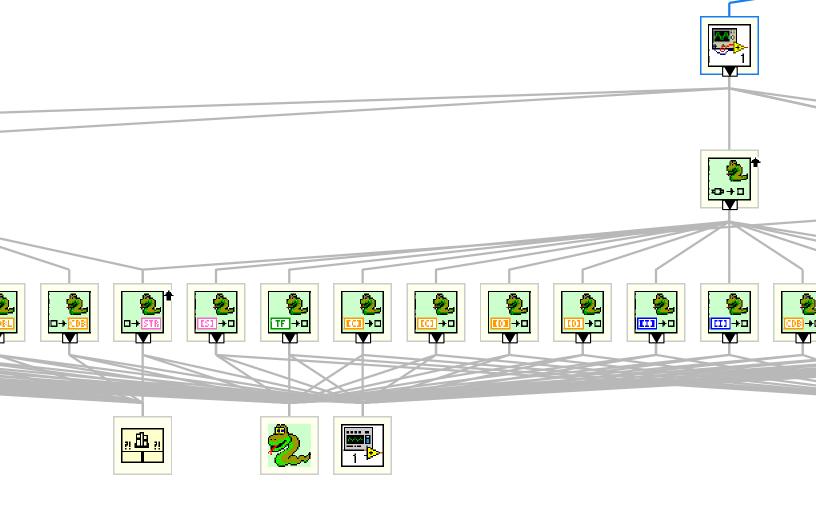




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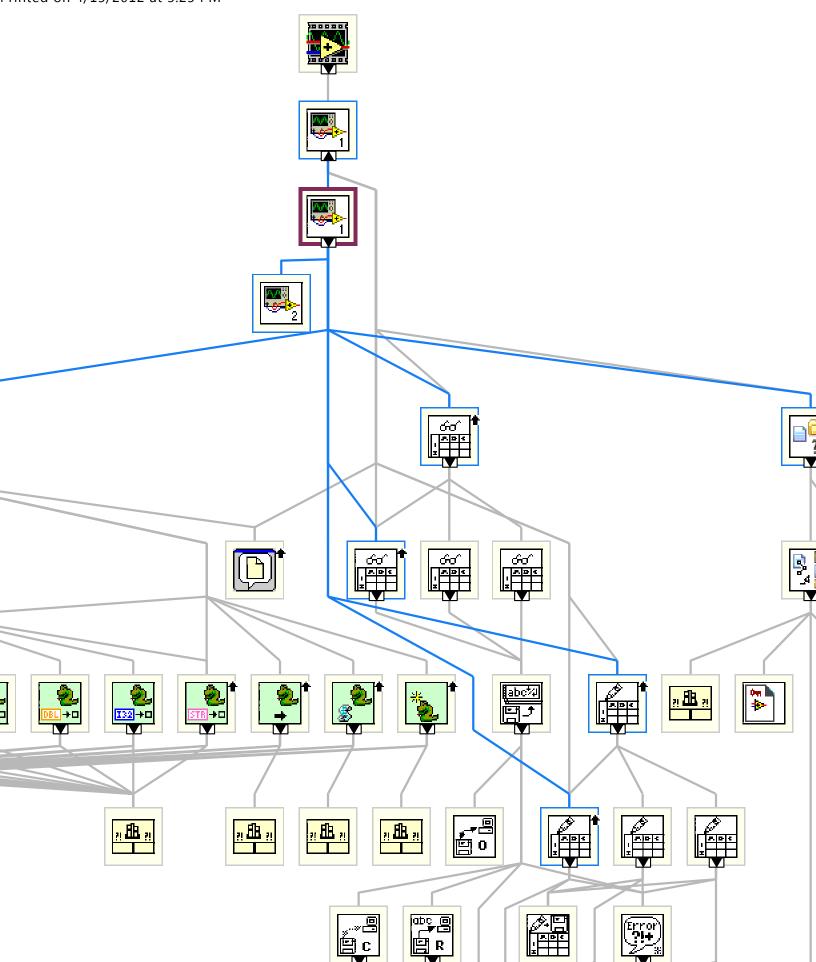


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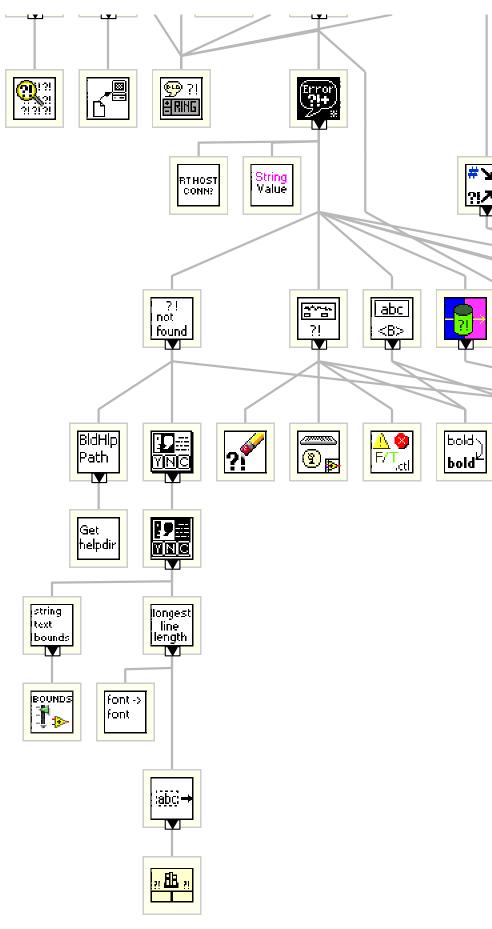
Page 5 🏧





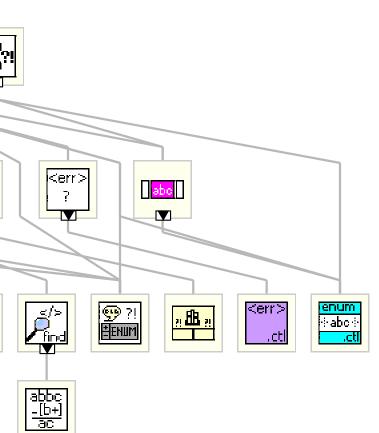


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DatabaseNavi.vi C:\Users\g\Documents\VAI\Liver\Liver Program\DatabaseNavi.vi Last modified on 4/9/2012 at 8:30 AM Printed on 4/15/2012 at 5:25 PM



#### Read From Spreadsheet File.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Utility\file.llb\Read From Spreadsheet File.vi



#### Read From Spreadsheet File (string).vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Utility\file.llb\Read From Spreadsheet File (string).vi



#### Write To Spreadsheet File.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Utility\file.llb\Write To Spreadsheet File.vi

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#### Write To Spreadsheet File (string).vi C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Utility\file.llb\Write To Spreadsheet File (string).vi



#### Parse database from import.vi

C:\Users\g\Documents\VAI\Liver\Liver Program\Parse database from import.vi



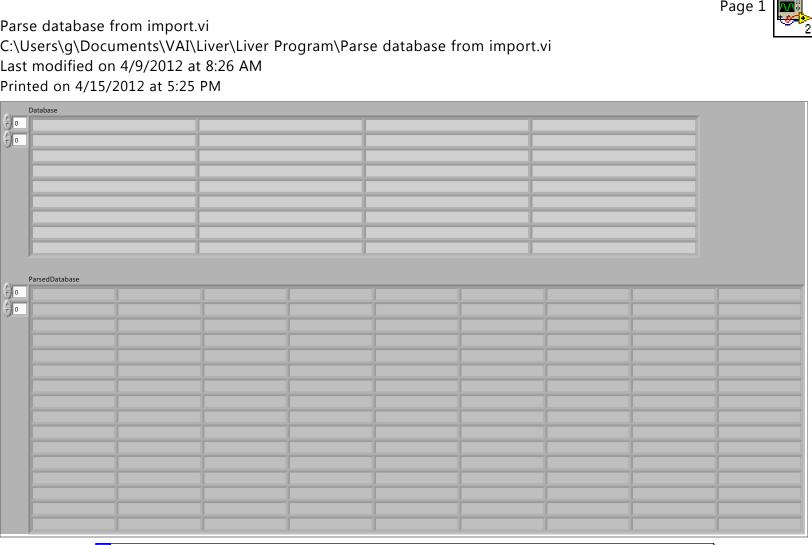
# ImportFilesPYTHONsaveMeta.vi

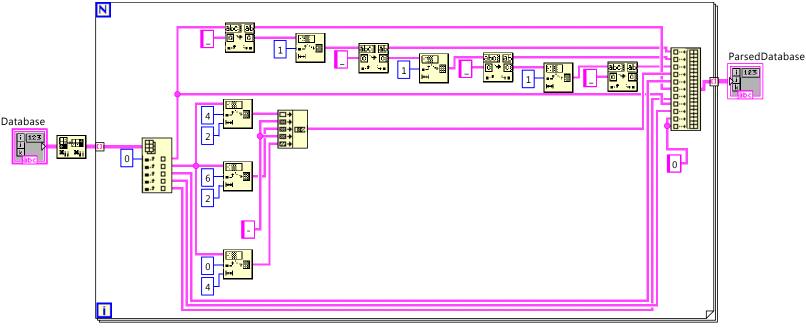
 $C:\Users\g\Documents\VAI\Liver\Program\ImportFiles\PYTHONsaveMeta.vi$ 



#### Check if File or Folder Exists.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\Utility\libraryn.llb\Check if File or Folder Exists.vi





Parse database from import.vi C:\Users\g\Documents\VAI\Liver\Liver Program\Parse database from import.vi Last modified on 4/9/2012 at 8:26 AM Printed on 4/15/2012 at 5:25 PM



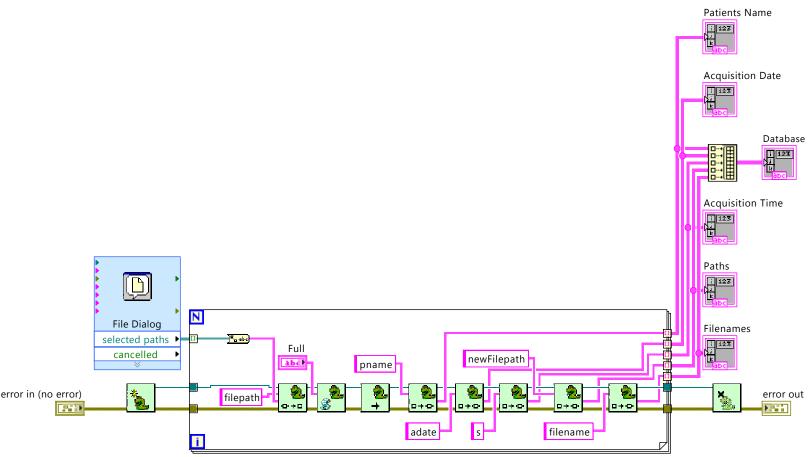




#### ImportFilesPYTHONsaveMeta.vi C:\Users\g\Documents\VAI\Liver\Liver Program\ImportFilesPYTHONsaveMeta.vi Last modified on 4/6/2012 at 8:46 PM Printed on 4/15/2012 at 5:25 PM

Р	atients Name		Acquisition Date	Acquisition Time	e Pa	ths			
	Full import dicom import numpy import sys import os.path dcm = dicom.read_file(filepath) ctField = numpy.array(dcm.pixel_array, dtype=numpy.float3; ctField = ctField * dcm.RescaleSlope + dcm.RescaleIntercept ctField(ctField.2000) = 2000 ctField = ctField/ctField.max()*255.0 dim = numpy.array(ctField.shack()*255.0 dim = numpy.argy(ctField.shack()*255.0 dim = numpy.argy(ctField.shack()*255.0	2)	Acquisition Date	0	Pa	ths Databa	Se	error out status source	error in (no error) status code source code a
	adate = dcm.AcquisitionDate atime = dcm.AcquisitionTime s, ms = atimes.plit(".") head = "C.\LongVivo\Database" tail = adate+'-'ss+'-'+pname+'.out' newFilepath = os.path.join(head, tail) dataToSave.tofile(newFilepath) headmeta = "C:\LongVivo\Metadata" tailmeta = adate+'-+s+'-'*pname+'.met' newFilepathmeta = os.path.join(headmeta, tailmeta) dcm.PixelData = dcm.pixel_array[0:1,::].tostring() dcm.NumberofFrames = 1 dcm.save_as(newFilepathmeta)								

ImportFilesPYTHONsaveMeta.vi C:\Users\g\Documents\VAI\Liver\Liver Program\ImportFilesPYTHONsaveMeta.vi Last modified on 4/6/2012 at 8:46 PM Printed on 4/15/2012 at 5:25 PM



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ImportFilesPYTHONsaveMeta.vi C:\Users\g\Documents\VAI\Liver\Liver Program\ImportFilesPYTHONsaveMeta.vi Last modified on 4/6/2012 at 8:46 PM Printed on 4/15/2012 at 5:25 PM



# **\* PY**

#### PYTHON New Session\_\_ogtk.vi

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#### PYTHON Close Session\_\_ogtk.vi

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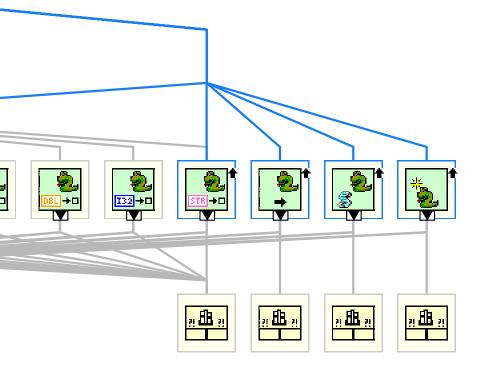
ImportFilesPYTHONsaveMeta.vi

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Page 4

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ImportFilesPYTHONsaveMeta.vi C:\Users\g\Documents\VAI\Liver\Liver Program\ImportFilesPYTHONsaveMeta.vi Last modified on 4/6/2012 at 8:46 PM Printed on 4/15/2012 at 5:25 PM





ImportFilesPYTHONsaveMeta.vi C:\Users\g\Documents\VAI\Liver\Liver Program\ImportFilesPYTHONsaveMeta.vi Last modified on 4/6/2012 at 8:46 PM Printed on 4/15/2012 at 5:25 PM



## PYTHON Set Data\_ogtk.vi

C:\Program Files\National Instruments\LabVIEW 2010\user.lib\\_OpenG.lib\labpython\labpython.llb\ PYTHON Set Data\_\_ogtk.vi



#### PYTHON Set String Data\_ogtk.vi

C:\Program Files\National Instruments\LabVIEW 2010\user.lib\\_OpenG.lib\labpython\labpython.llb\ PYTHON Set String Data\_\_ogtk.vi



#### PYTHON Set Script Text\_\_ogtk.vi

C:\Program Files\National Instruments\LabVIEW 2010\user.lib\\_OpenG.lib\labpython\labpython.llb\ PYTHON Set Script Text\_\_ogtk.vi



#### **PYTHON Execute Script\_ogtk.vi**

C:\Program Files\National Instruments\LabVIEW 2010\user.lib\\_OpenG.lib\labpython\labpython.llb\ PYTHON Execute Script\_\_ogtk.vi



#### PYTHON Get Data\_ogtk.vi

C:\Program Files\National Instruments\LabVIEW 2010\user.lib\\_OpenG.lib\labpython\labpython.llb\ PYTHON Get Data\_\_ogtk.vi



#### PYTHON Get String Data\_\_ogtk.vi

C:\Program Files\National Instruments\LabVIEW 2010\user.lib\\_OpenG.lib\labpython\labpython.llb\ PYTHON Get String Data\_\_ogtk.vi

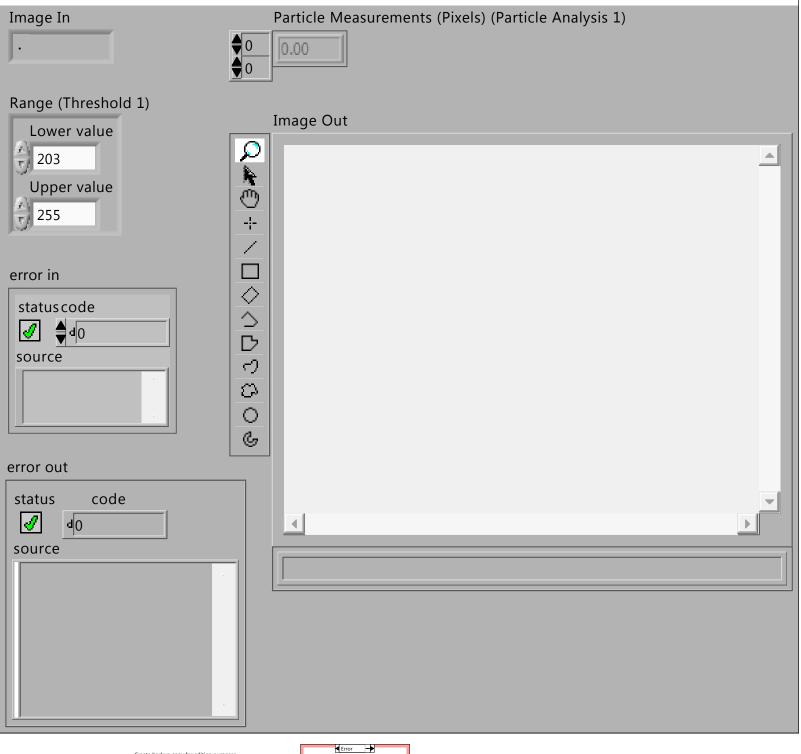


## File Dialog

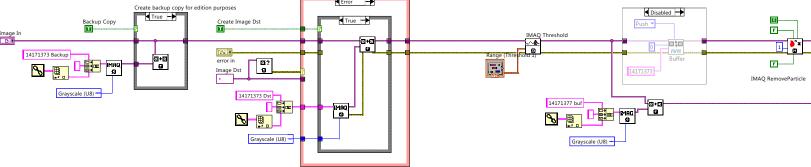
File Dialog Displays a dialog box with which you can specify the path to a file or directory.

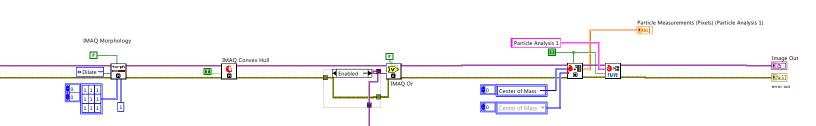
This Express VI is configured as follows:

Selection Mode: Multi-select

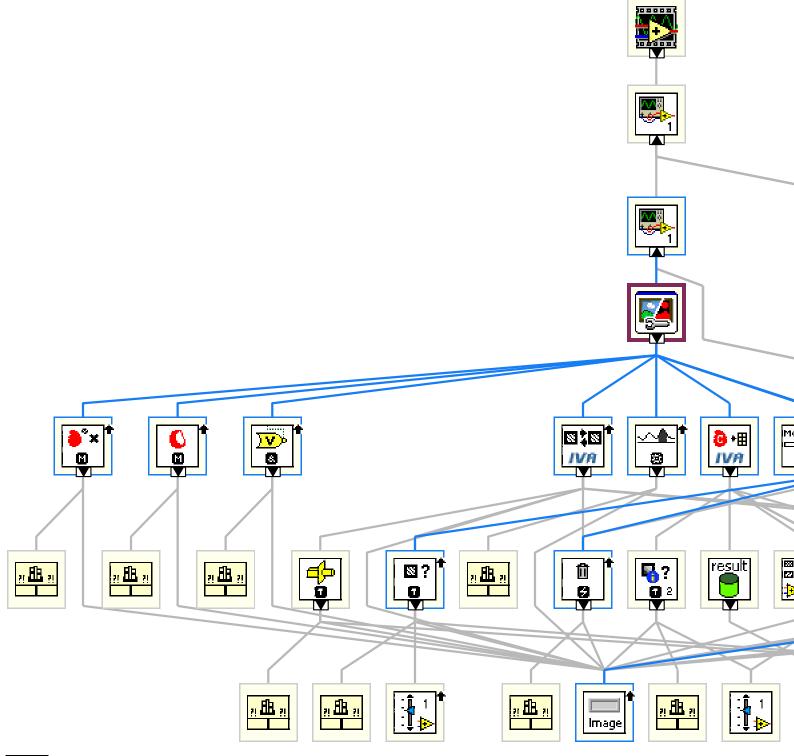


Page 1











#### IMAQ Image.ctl

Image Type

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Image Controls.llb\IMAQ Image.ctl

# • Type⊁

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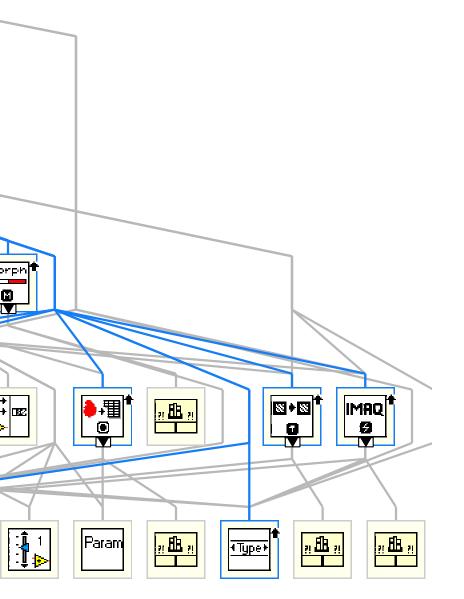
#### Imaq GetImageInfo

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Basics.llb\Imaq GetImageInfo

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Image Controls.llb\Image Type

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Get Ribs C:\Users\g\Documents\VAI\Liver\Liver Program\GetRibs.vi Last modified on 3/21/2012 at 1:06 PM Printed on 4/15/2012 at 5:25 PM





# IMAQ Create

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NI\_Vision\_Development\_Module.lvlib:IMAQ Threshold C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Process.llb\IMAQ Threshold



Morph

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NI\_Vision\_Development\_Module.lvlib:IMAQ Morphology C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Morpho.llb\IMAQ Morphology



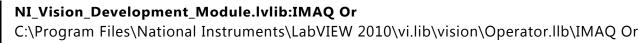
**NI\_Vision\_Development\_Module.lvlib:IMAQ Convex Hull** C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Morpho.llb\IMAQ Convex Hull



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IMAQ Copy C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Management.llb\IMAQ Copy





**NI\_Vision\_Development\_Module.lvlib:IMAQ Particle Analysis** C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Analysis.llb\IMAQ Particle Analysis



#### IVA Store Particles Results.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Vision Assistant Utils.llb\IVA Store Particles Results.vi



#### Imaq Dispose

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Basics.llb\Imaq Dispose



### IVA Image Buffer.vi

C:\Program Files\National Instruments\LabVIEW 2010\vi.lib\vision\Vision Assistant Utils.llb\IVA Image Buffer.vi

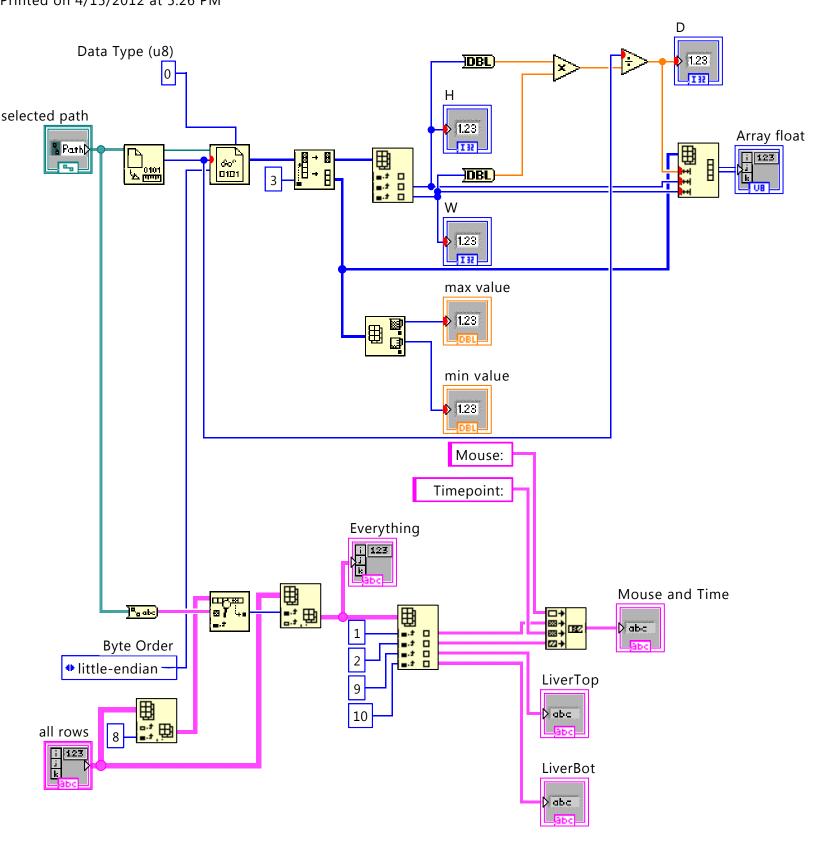


Binary txt to 3D array U8.vi C:\Users\g\Documents\VAI\Liver\Liver Program\Binary txt to 3D array U8.vi Last modified on 4/9/2012 at 11:56 PM Printed on 4/15/2012 at 5:26 PM

Array float												
	50	0	0	0	0	0	0	0	0	0	0	0
W	50	0	0	0	0	0	0	0	0	0	0	0
H	<u>6</u>	0	0	0	0	0	0	0	0	0	0	0
0		0	0	0	0	0	0	0	0	0	0	0
		0	0	0	0	0	0	0	0	0	0	0
D		0	0	0	0	0	0	0	0	0	0	0
selected path C:\Users\g\ VAI\Liver\D nano 6000 C AP_Exitron6 Control_1_0 inj_hu.out	ICOM\Exi Control St 000-	tron udy\	(T)	0	erything e and Ti			0	n value			
		LiverTop					erBot		[			



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