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基於深度學習之生醫影像分割暨分類

Biomedical Image Segmentation and Classification Using  
Deep Learning

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Biomedical Image Segmentation and Classification Using  
Deep Learning

本論文係彭強森君（學號 R03922147）在國立臺灣大學資訊工程學系完成之碩士學位論文，於民國 105 年 7 月 9 日承下列考試委員審查通過及口試及格，特此證明

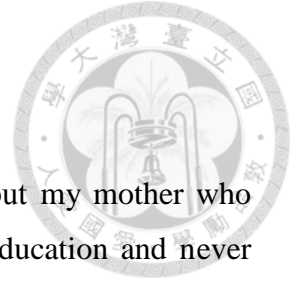
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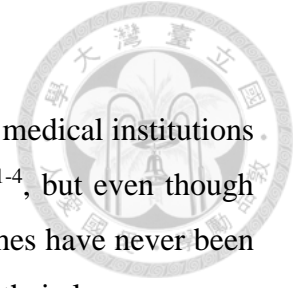
趙坤茂



### **Acknowledgement and Dedication**

The following Master's Thesis would have never been possible without my mother who went through so many hardships just to be able to give me a good education and never asked for anything in return.

I would also like to thank my advisor, Steven Liao, for his mentoring and tutoring in this period of my life.



## Abstract

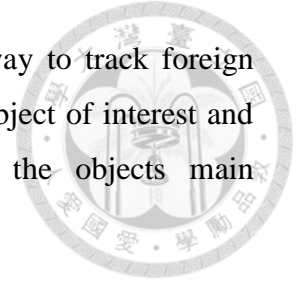
Processing of biomedical images is one of the most important tasks that medical institutions such as hospitals and research centers deal with in a day to day basis<sup>1-4</sup>, but even though this is such an important and basic task technology and current approaches have never been able to be successfully used in practical situations mainly because of their low accuracy, this has started to change in the beginning of 2012 with the use of convolutional neural networks and deep learning to accurately classify and segment a variety of different images<sup>5</sup>, including biomedical images.

Although these new technologies are being widely used with incredible results in many diverse fields, their adoption in the medical community has been slow to say the least, this has been due to many different reasons like the fact that the training data needed to provide a good accuracy model needs to come from a wide variety of patients, hundreds at least, from all around the world, from all age groups and sexes. This in it by itself is a great challenge to put together for a medical institution let alone for an individual, and even after gathering the data, a great deal of effort needs to be put into anonymizing the data. This is extremely important because by law any medical records have to be completely private and cannot be used without the expressive permission of the patient, so in order to facilitate this data many hospitals will anonymize the data so it cannot be tracked down to the patient.

The following thesis will try to provide an approach on segmenting and classifying biomedical images, specifically heart MRI images taken by a trained professional, using a series of steps, which include deep learning, to accurately determine the volume of the heart's left ventricle when it is in diastole, the largest volume of a heart cycle, and systole, the smallest volume of a heart cycle, with this measurement one can calculate the ejection fraction, often described as the most important measurement for early detection of heart disease<sup>1-4</sup>.

As stated before an accuracy high enough to be used in actual medical scenarios will be tried to be achieved. The data used for the training for the deep learning model was supplied by Kaggle, an online competition oriented platform designed to solve many of today's difficult problems.

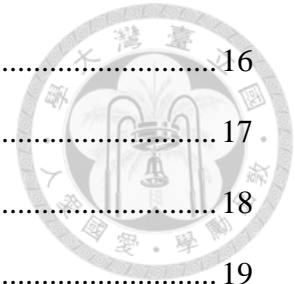
What was also tried to achieve with this research was to create a way to track foreign objects such as cancer and different other diseases, first tracking the object of interest and then using deep learning to either classify, measure or detect the objects main characteristics.



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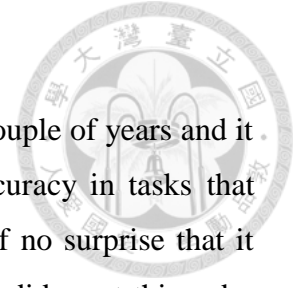
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## I. Introduction

Deep learning is a technology that has made its appearance in the last couple of years and it has taken the world by surprise, being able to achieve incredible accuracy in tasks that previously were thought to be incredibly hard<sup>5</sup>, because of this it is of no surprise that it was started to be used in the medical world, a segment that previously did most things by hand because the accuracy needed was extremely high and current computer vision techniques were simply not accurate enough, unreliable and an arduous task in developing and financing, with a final product that would take many years to make and could only be used for one task.

In the medical worlds technologies are slow to be adopted because of a series of issues that to this day have not been solved, such as the fact that the data comes from actual patients, which means that it cannot be freely distributed or utilized without the patient's consent, so it has to be anonymized to be able to be used, many times this is not even enough. Another reason is that hospitals, as many people will not realize, are businesses as well so cooperation between different medical institutions in the same country is quite difficult most of the times, let alone in between countries. This means getting a representative data set for an individual is virtually impossible, and for an institution or company it might be very expensive and complicated.

Luckily a representative data set was of heart MRI images was obtained from Kaggle which includes 1140 patients, each having a 2 chamber view, a chamber view and a series of side axis views, totaling in about 400 images per patient. This data was then used to determine the left ventricle volume in diastole and systole, the largest and smallest cycle of the heart respectfully. This volume is in term later used to calculate the ejection fraction of the heart, basically how much blood is pumped in against how much blood is pumped out in each cardiac cycle, an important measurement in early detection of heart disease.

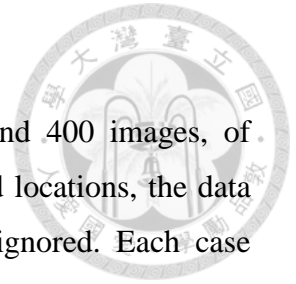
A total of 7 steps were used to calculate the final volume of the heart's left ventricle which will be described in detail in the following section but are worth mentioning here as well:

- Preprocessing
- Fourier transform approach

- Hough transform and k-means clustering
- Extraction
- Post processing
- Temporal measuring and enrichment
- Deep learning

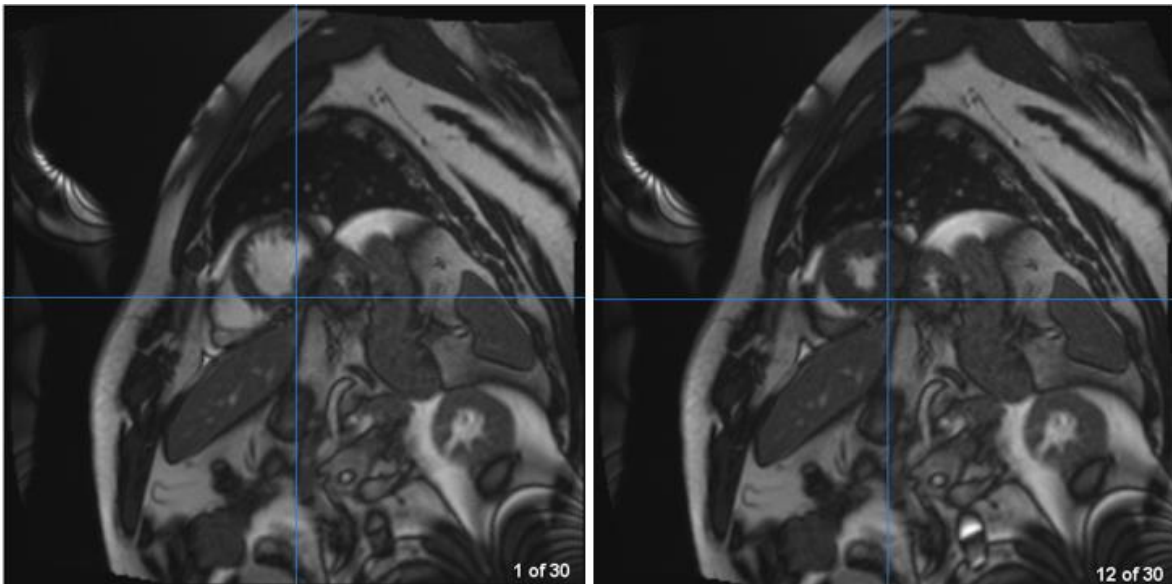


After this steps a volume is obtained with an accuracy high enough to be used in real world scenarios, hopefully this steps can also be applied to other similar medical tasks such as cancer detection and foreign object tracking.



## II. Data Set layout

The data used is divided into 1140 cases, which each include around 400 images, of anonymized heart MRI's, this data contains people of all ages, sex and locations, the data set also includes valuable header information that normally is just ignored. Each case contains a 4 chamber view, a 2 chamber view and a series of side axis slices, each containing 30 images that represent an entire heart beat cycle. This images can be said to be 4d because they represent a 3d heart over time.



**Figure 1: Diastole (Left) and Systole(Right) of the same heart**

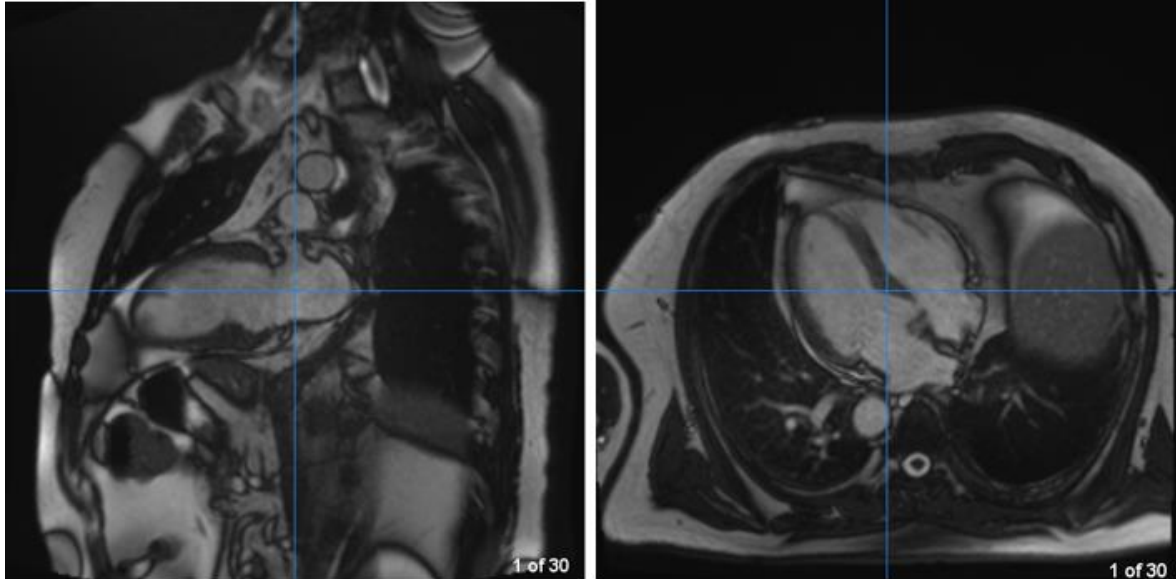
**Source: Data Science Bowl Cardiac Challenge Data**

The image above shows how the heart's left ventricle, upper left side of the blue line intersection, changes over time.



## 2.1 Heart's 2 chamber and 4 chamber views

The data set contains several other views shown bellow



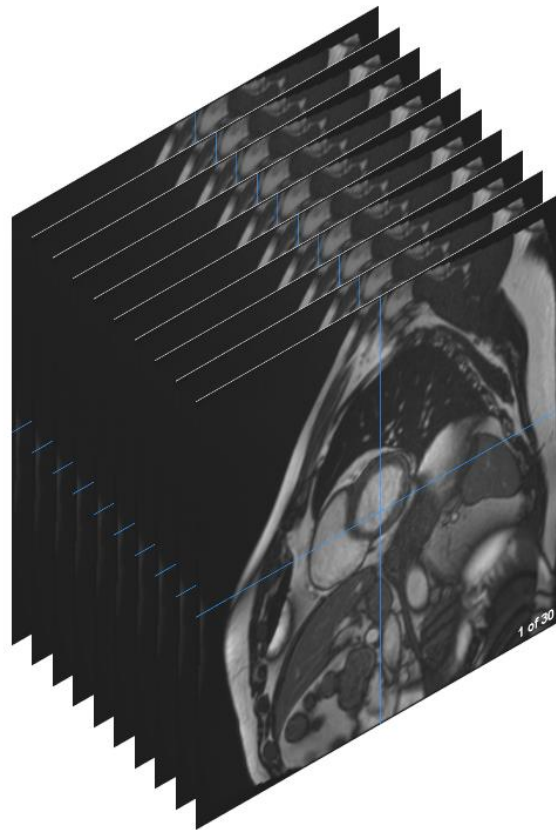
**Figure 2: 2 chamber view(Left) and 4 chamber view(Right)**

**Source: Data Science Bowl Cardiac Challenge Data**

The figure above also shows the same heart but in a different view, the 2 chamber and 4 chamber view, this images also contain a lot of useful information that can be used to calculate the volume of the left ventricle, but often they are missing or damaged, so the approach described here will not use them.

## 2.2 Heart's side axis views

This images are taken by a professional medical technician who carefully aligns the x-ray or MRI machine to take a series of “videos” at different z positions to create a quasi 3d model of a heart.



**Figure 3: Side Axis view 3d model representation**

**Source: Data Science Bowl Cardiac Challenge Data**

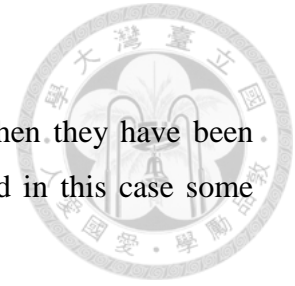
As seen above the side axis view act as a 3d model to represent a cardiac cycle, this is then repeated 30 times across a cardiac cycle to get a 4d model.

### **III. Step 1: Preprocessing**

The preprocessing stage consists in normalizing the data as much as possible.

#### **3.1 Orienting the images**

Orient images in a specific manner, this is done to make it easier for the deep learning to correctly classify the images, the images are set in a portrait mode whenever possible.

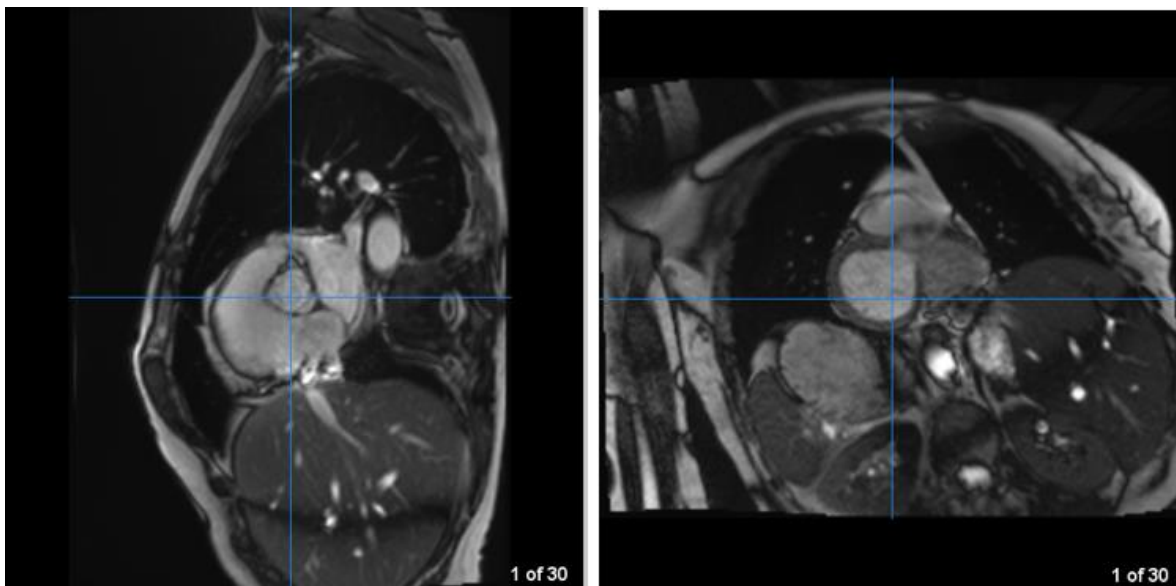


### 3.2 Separate images

Separate images where there are more than 30 slices, for example when they have been mislabeled or misplaced, sometimes there are less than 30 images and in this case some images are repeated to fill out the 30 image cardiac cycle.

### 3.3 Normalize different sized images

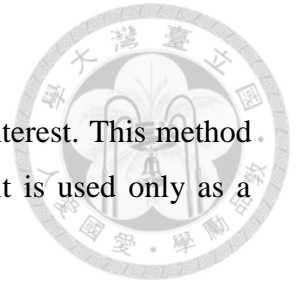
This might be the hardest part of step 1 as there is no easy way of doing this, sometimes the technician will move the MRI machine or repeat the procedure at a certain state due to an error, in this cases the images are sometimes of different size and orientation, but this can't be easily detected, a small script is executed to find sets of images in the same patient that have different sizes, this are separated into sub patients and processed independently until step 4.



**Figure 4: Variation of size and orientation in a single patient**

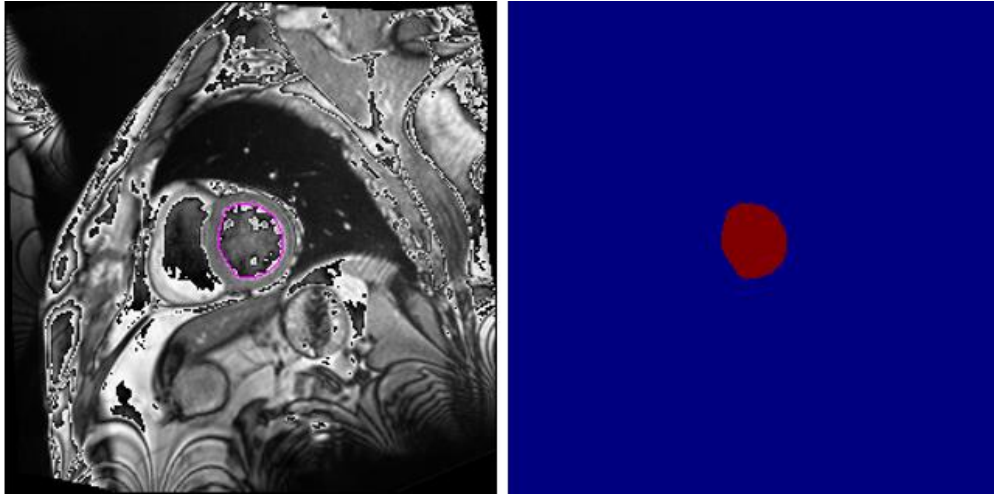
**Source: Data Science Bowl Cardiac Challenge Data**

The Images above both correspond to the same patient but it is not easy to tell how these are oriented, the header information contains position coordinates but it is not always reliable, so the left ventricle is found using the data from step 3 and orient them with that.



#### IV. Step 2: Fourier transform approach

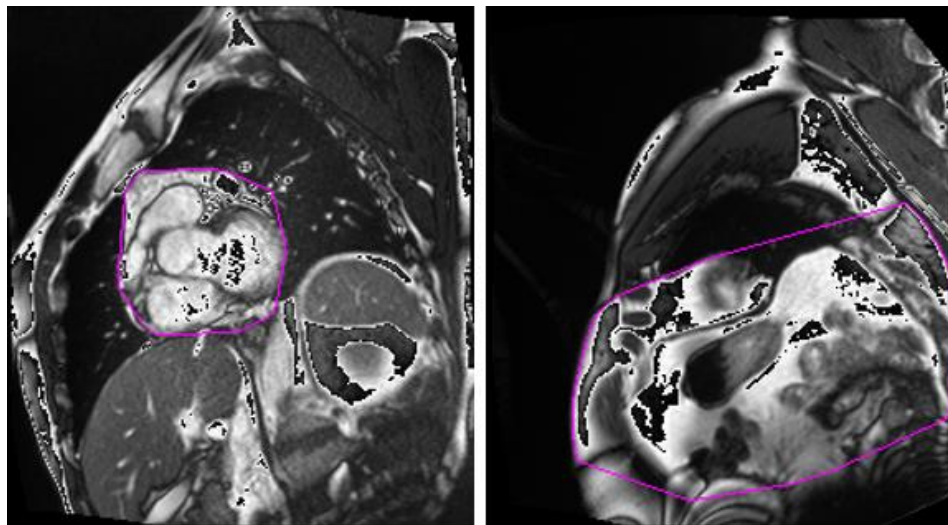
In this step a Fourier transform approach<sup>7</sup> is used to label the area of interest. This method manages to get an average result at best, but fails in so many cases it is used only as a guidance for the next steps.



**Figure 5: Correct segmentation of the area of interest using a Fourier transform approach**

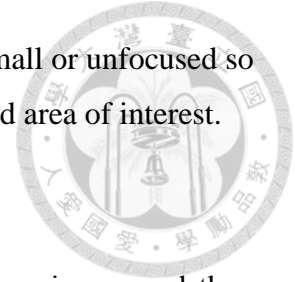
**Source: Original image from Data Science Bowl Cardiac Challenge Data**

The correct segmentation can be seen in the image above; this exemplifies a perfect segmentation.



**Figure 6: Incorrect segmentation of the area of interest using a Fourier transform approach**

**Source: Original image from Data Science Bowl Cardiac Challenge Data**



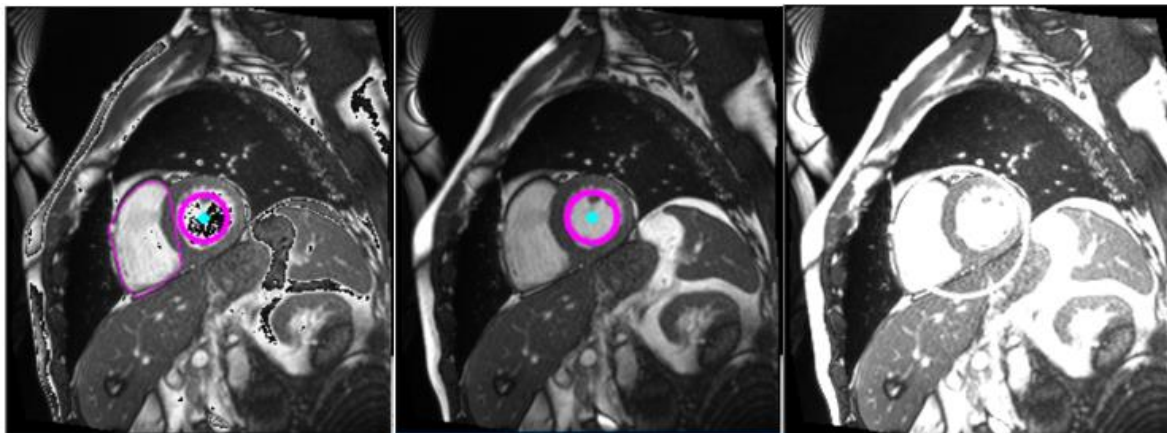
Most cases are like the shown above, the area of interest might be too small or unfocused so this method will fail to correctly segment it, resulting in an overestimated area of interest.

### V. Step 3: Hough transform and k-means clustering

In this step a Hough Transform method<sup>8</sup> was used to find “blobs” in an image and then follow it across the set to determine the center of the left ventricle, this step is repeated 3 time varying different parameters in order to find the optimal center, in this step several other minor steps are taken.

#### 5.1 Dynamic and local grayscale normalization

The images are grayscale normalized individually based on the area of interest found in step2, if the area found in step 2 is incorrect then the image is grayscale normalized using 80% of the maximum value of the image, in the second iteration this value changes to the maximum value of the center region of the image and in the third iteration it is 25% of the maximum value of the whole image, giving an underexposed, overexposed and localized views of the image.



**Figure 7: First iteration(Left), second iteration(Middle) and third iteration(Right) color normalization**

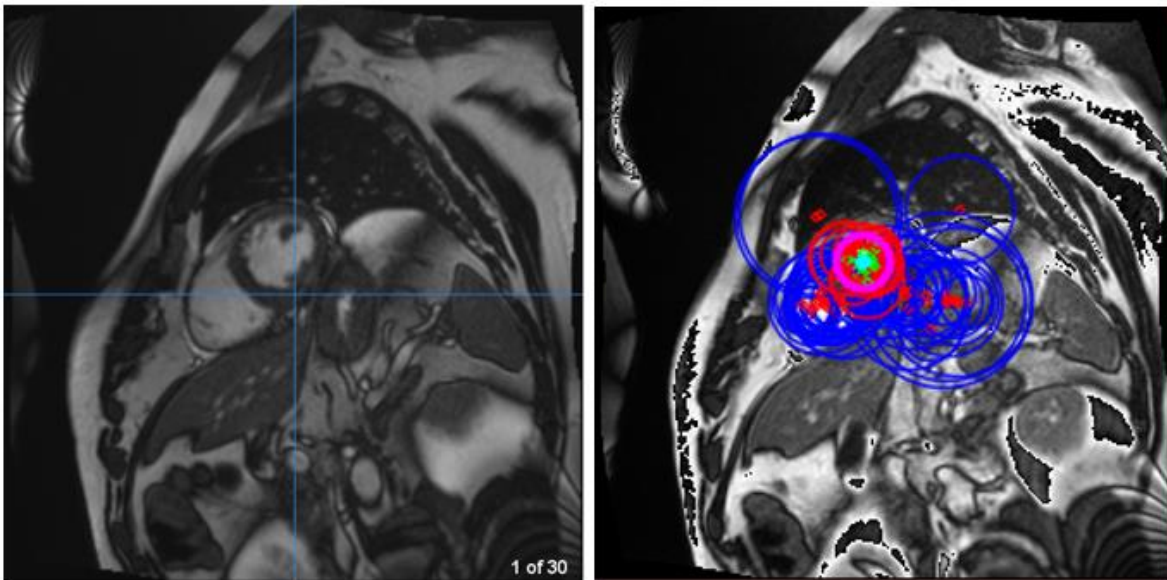
**Source: Original image from Data Science Bowl Cardiac Challenge Data**

The 3 iteration procedure will only continue if no center is found, in the above images you can see the first two iterations found a correct center, but the third found an overestimated center.



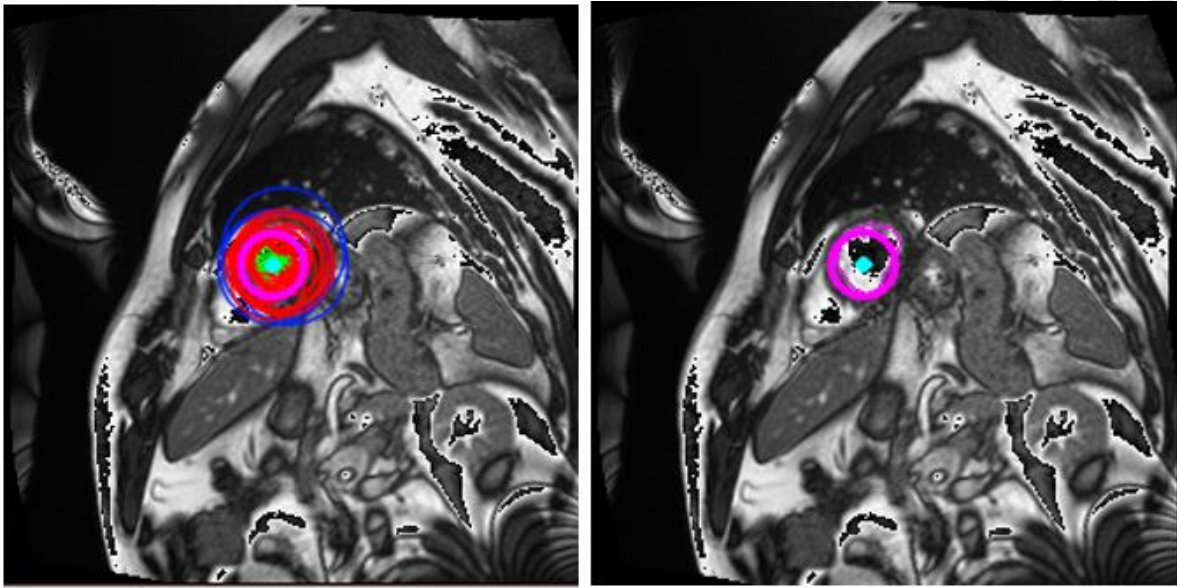
## 5.2 Blob detection

After the image has been color normalized a Hough transform<sup>8</sup> approach along with the data from step 2 is used in the first iteration to detect blobs of blood in the images, since there are 30 images per slice the detected blobs of each image are followed and reduced to only one. Many blobs will disappear or move erratically and because of this they will be removed, if by the end of the first iteration a correct blob has not been found then in the second and third iteration k-means clustering will be used to further aid the process.



**Figure 8: Original image(Left) and initial blob findings(Right)**

**Source: Original image from Data Science Bowl Cardiac Challenge Data**



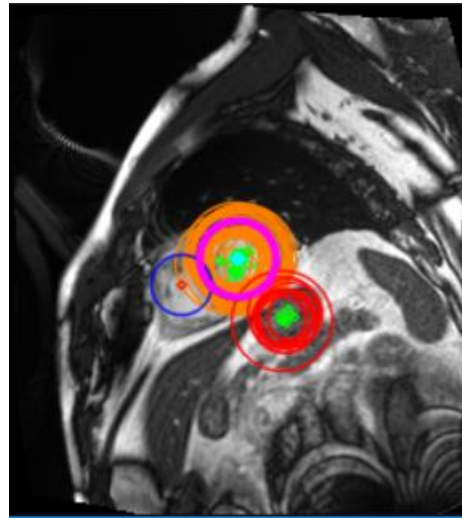
**Figure 9: Reduced blob count(Left) and final blob(Right)**

**Source: Original image from Data Science Bowl Cardiac Challenge Data**

Figure 8 shows that at the initial step many false blood pools are found, later in figure 9 this blood pools are narrowed down to the most likely candidate across the 30 images resulting in the final detected blob.

### **5.3 K-means clustering**

In case the first iteration fails to find the correct center then the second and third iteration uses K-means clustering to group the located blobs across the slices to find the most likely candidate, 3 clustering groups are used and their centers are compared against each blob to properly group them, this process is useful in about 25% of the cases because some images have more than one pool of blood that changes across time, this might be other section of the heart or body that is visible in the MRI, using K-means clustering an accurate differentiation can be found between the left ventricle and other parts of the body.



**Figure 10: K-means clustering applied to blob detection**

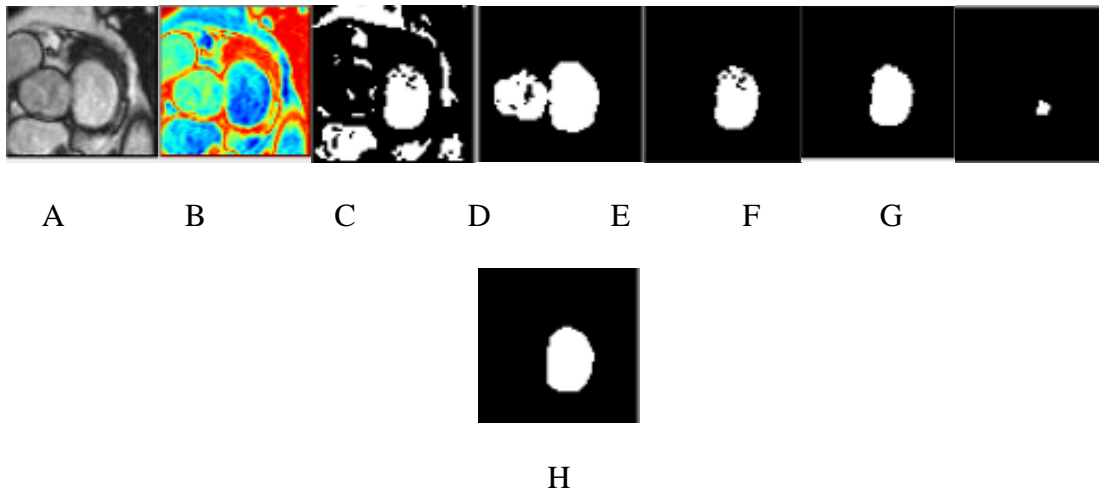
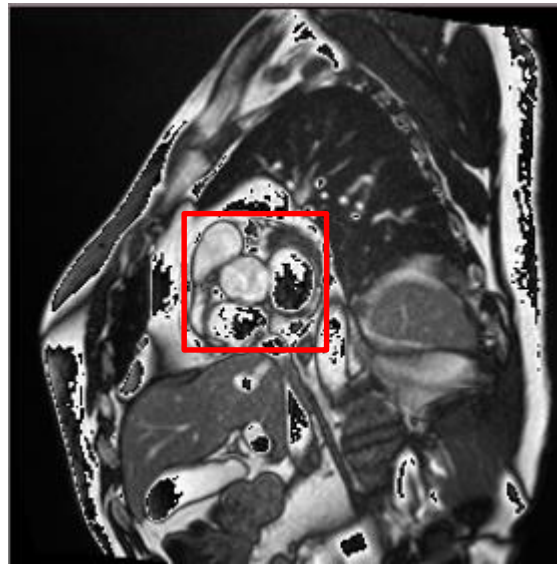
**Source: Original image from Data Science Bowl Cardiac Challenge Data**

Figure 10 demonstrates the usefulness of k-means clustering in separating blobs of blood from the left ventricle, in the end a successful detection is achieved.

#### **VI. Step 4: Extraction**

Deep learning is an incredibly useful tool that has revolutionized modern computer vision technologies but in order to take the most advantage out of it the images need to be trimmed of unnecessary information as much as possible, especially in biomedical images where this are packed full of different moving objects and body parts that are not helping in the detection of the left ventricle.

The data from step 3 is then used to determine a rough area of interest and then a double thresholding method is used, along with different computer vision techniques like dilations, erosions, closings and a lot of connected components segmentations, this allows us to extract in most cases exactly the left ventricle without the unnecessary surrounding regions.



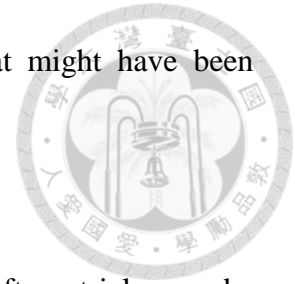
**Figure 11: Different steps in the extraction process**

**Source: Original image from Data Science Bowl Cardiac Challenge Data**

Figure 11 shows some of the complicated process to extract the left ventricle and removing unnecessary sections, the original image shows a side axis view that is really high up in the z axis, some algorithms won't count this as part of the left ventricle but it is used here to display the cleansing process of the extraction step.

Figure 11: A) shows the original image cut to 150% of the coordinates obtained in step 3. B) a mask is applied to identify the major blood pools C) and D) show both threshold applied to the image, one slightly higher than the other to preserve as much information as possible, E) is the 2 threshold images subtracted from one another, F) shows the dilated temporary

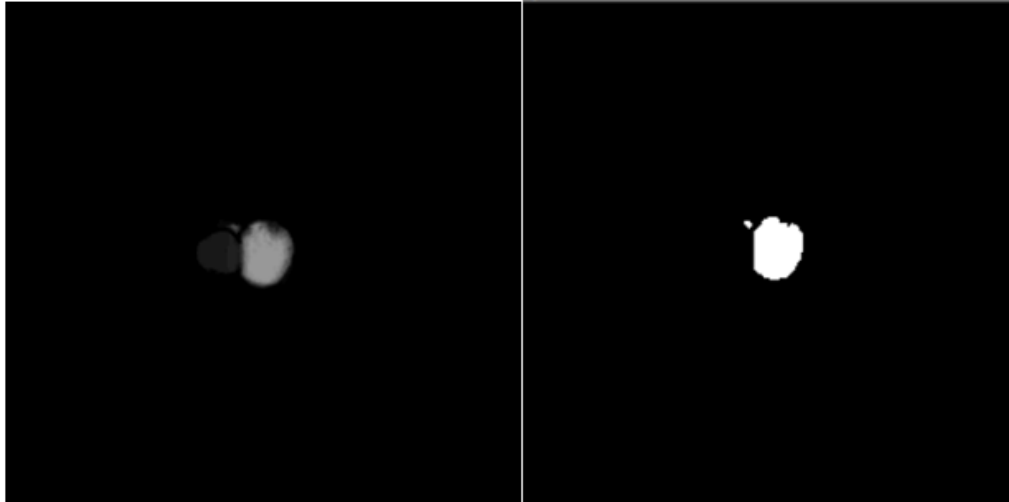
image, G) is an eroded version used to remove pools of blood that might have been mistakenly included and H) is the final extracted left ventricle area.



## VII. Step 5: Post processing

Since the images are part of a 4d model the adjacent final extracted left ventricles can be used to detect any errors the algorithm might have made, most of the time it is removing sections of unneeded information that have been grouped together with the left ventricle, sometimes the algorithm failed to correctly identify the left ventricle so the area is empty, but by comparing it with its neighboring image in the cardiac cycle, this types of errors are easily found and fixed by repeating the extraction process in that particular image using the average coordinates of the rest.

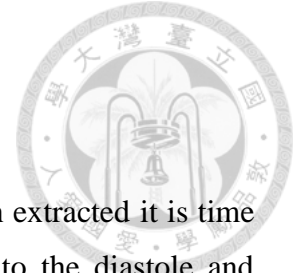
This technique can be applied to the 30 images in a cardiac cycle and to the 10 or so side axis slices.



**Figure 12: Removal of unnecessary areas in post processing**

**Source: Original image from Data Science Bowl Cardiac Challenge Data**

It can be seen in the above image that some lighter areas of the image are removed, this is done by superimposing all the 30 extracted left ventricles and determining which sections appear only in a couple of images, this can be ruled out as errors and removed.



## VIII. Step 6: Temporal measuring and enrichment

### 8.1 Determining diastole and systole images

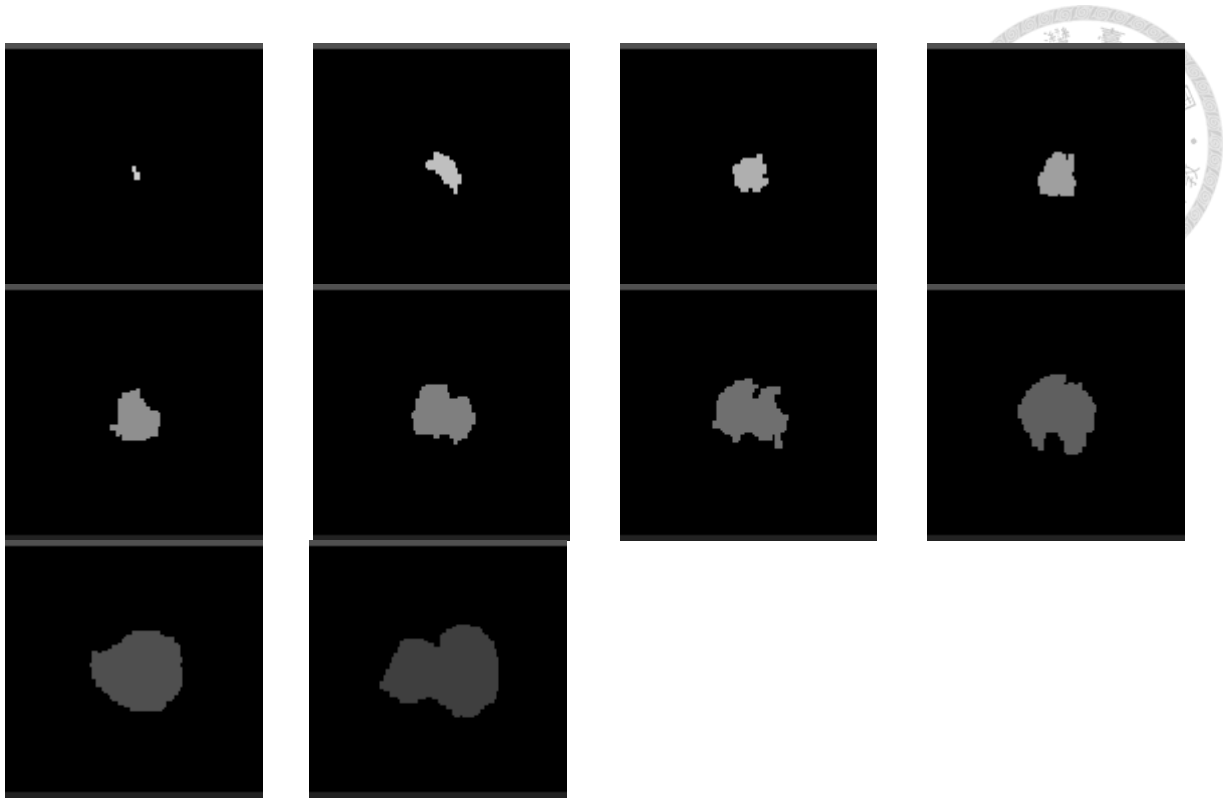
After all the images have been processed and the left ventricle has been extracted it is time to extract about 24 images out of 400, this images will correspond to the diastole and systole, about 12 images for each. One image will be extracted out of each side axis slice for diastole and systole, this is done by simply calculating the area of each image of the cardiac cycle and adding it to its counterpart in the remaining side axis views, basically grabbing two images out of the 30 of each slice of a heart.

### 8.2 Frustum calculation and enrichment

When all the areas of the left ventricle are successfully extracted a temporal volume is calculated for both the diastole and systole, a frustum-like area is calculated based on the scaled areas. The images are scaled to their real life size using the coordinate and scaling information in the headers, this information corresponds to a ratio of pixels to millimeters that the MRI machine automatically saves to each image.

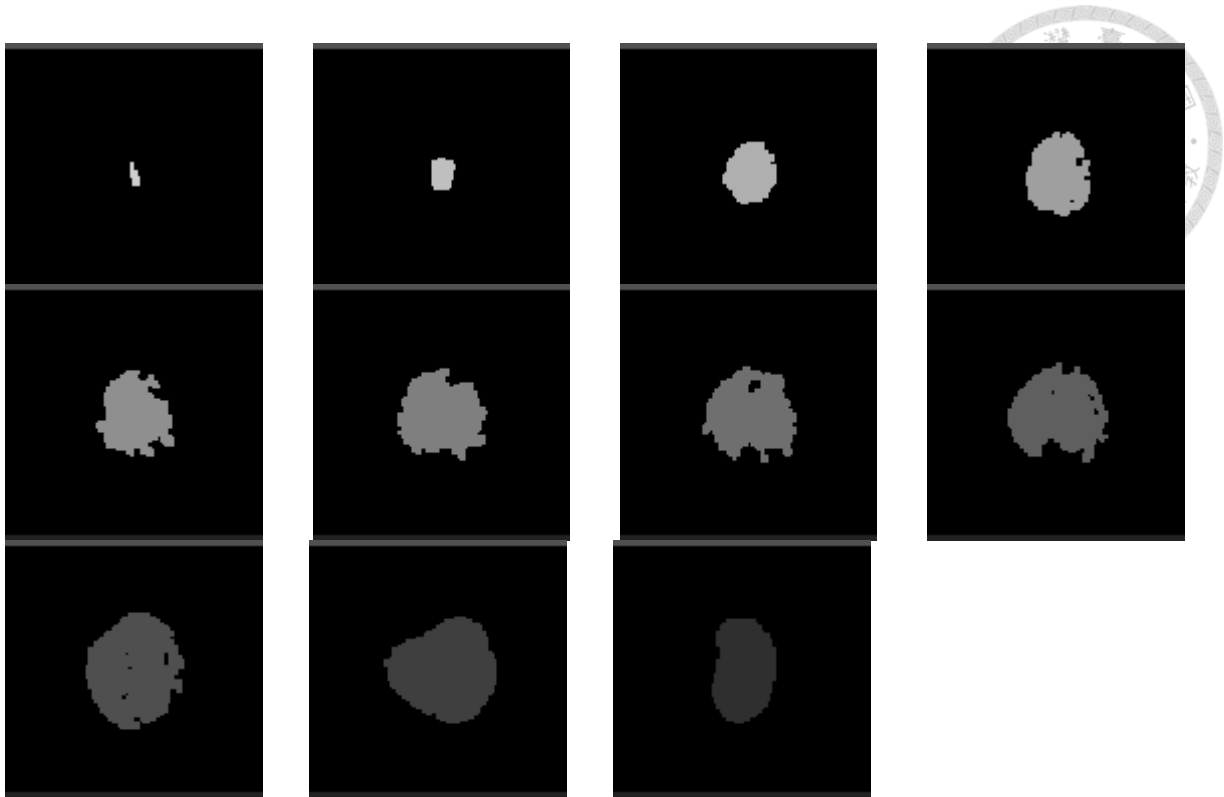
For the frustum calculation the slice thicknesses are also required, luckily this information is also available in the header and can be mapped to each slice, when this information is not available an average of 10mm is assumed.

When the frustum has been calculated it will be on average about 15ml off the correct volume for both diastole and systole, not accurate enough for real world usage, so this images are further enriched by adding new features corresponding to the age, a range from 1-100 in the image, and sex, on for male and off for female, the images are now ready for the deep learning step.



**Figure 13: Systole enriched left ventricle images**

**Source: Original image from Data Science Bowl Cardiac Challenge Data**



**Figure 14: Diastole enriched left ventricle images**

**Source: Original image from Data Science Bowl Cardiac Challenge Data**

With the extracted images successfully scaled and classified into diastole and systole, the deep learning phase can start.

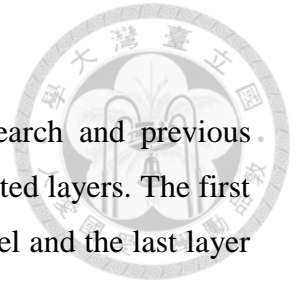
## **IX. Step 7: Deep learning**

The images are then compacted into a csv file and fed to the deep learning model.

### **9.1 Setting up the images**

In order to feed the images to the model in MXNET as memory efficient as possible they are loaded into memory and arranged into a csv file of size  $128 \times 128 \times 12 \times 1140$ ,  $128 \times 128$  being the size of the image, then 12 images for diastole and 12 images for systole and finally 1140 cases, 2 csv files are obtained from this process, which in turn are separated into testing, training and validation sets.

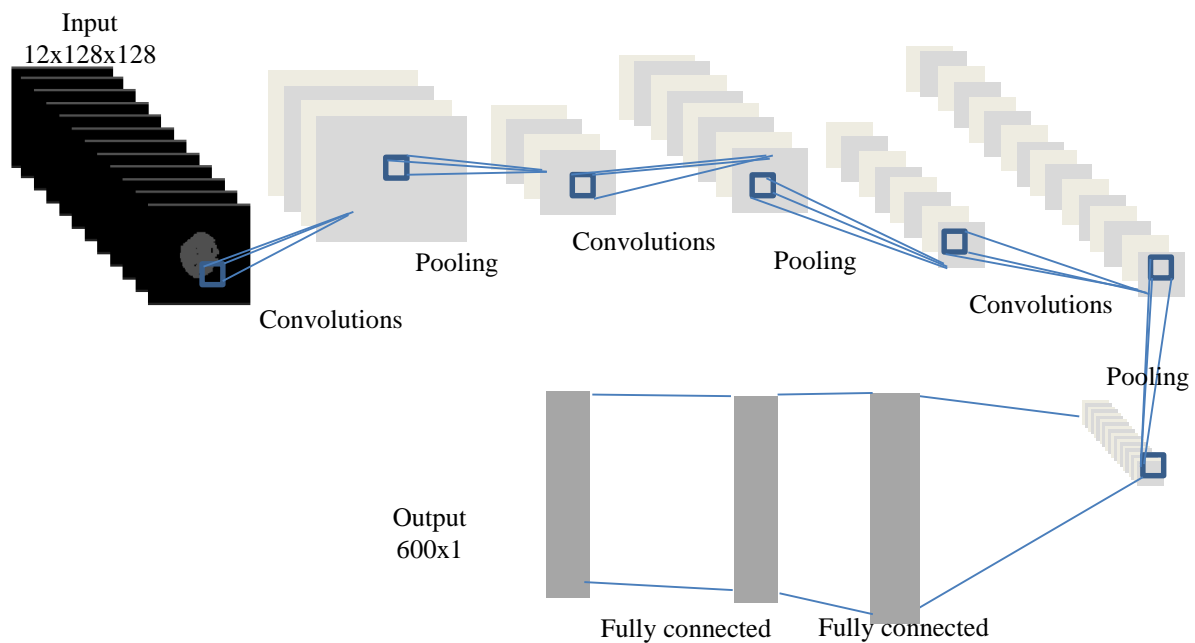




## 9.2 Model

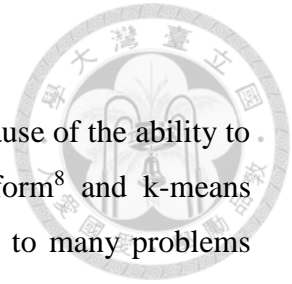
A CNN, convolutional neural network, model based on current research and previous models success<sup>11-12</sup> is used with 3 convolution layers and 2 fully connected layers. The first convolution layer using a 7x7 kernel, the second layer using a 5x5 kernel and the last layer using a 3x3 kernel. Each convolution layer also uses batch normalization, a ReLU type activation and pooling to speed up the training process.

The final 2 fully connected layers have 1024 neurons and 600 neurons respectively, since 600 is the size of the desired output, a logistic regression is applied at the end to map and clip our results to a range of 0-1 for each 600 outputs.



**Figure 15: Model visualization**

The image above gives a basic view of the model used to determine the hearts left ventricle volume in diastole and systole.

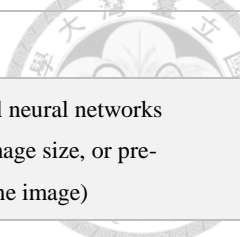


## X. Results

The approach described has several advantages over other methods because of the ability to track an object across time and depth, thanks to the Hough Transform<sup>8</sup> and k-means clustering, this combined with deep learning might provide a solution to many problems that before were solved by hand, for a simple example the left ventricle detection is done by hand by professional technicians and takes about 20 minutes per case<sup>10</sup>, this results in time consuming, expensive and most often than not inaccurate measuring, varying not so much by the time of the day at which it is measured<sup>6</sup> but by the method used<sup>13</sup>. With this new technological age medical institutions should be quick to adopt this approaches to try and solve, or at least start, problems such as early detection of cancer, foreign object tracking and many other diseases that involve human assessment of biomedical images.

The results obtained from the approach described were accurate enough to be used in real world scenarios, achieving an average error rate of about  $\pm 2$ ml and took about 19 hours from start to finish, including training, using a GTX 980 GPU. It is hard to compare it to current manual results since this vary widely depending on the method used to calculate them, but when compared to the winner of the Kaggle competition, who's average error rate was  $\pm 1$ ml but took 4 days to train, the results seem quite promising.

Manual approaches pose no comparison when put side by side with deep learning, of course medical professionals will always be needed to further interpret this results but technology should be used to aid as much as possible to get accurate and timely results.



<b>Approach</b>	<b>Time</b>	<b>Error</b>	<b>Method</b>
<b>Kaggle competition winner</b>	8 days using a GTX 970 and a GTX 980Ti card	+1ml	10 different fully convolutional neural networks (different architecture, input image size, or pre-processing transformation on the image)
<b>Approach described in this paper</b>	19 hours using a GTX 980 card	+2ml	Initial Computer vision preprocessing followed by a CNN model
<b>Same approach but without preprocessing</b>	9 hours using a GTX 980 card	+35ml	CNN model only, feeding it the original images
<b>Manual labeling</b>	20 minutes per case	15-30% (not ml)	Human segmentation followed by either an area or volume calculation method <sup>13</sup>

**Table 1: Comparison of different methods and their respective results**

The results show that CNN's are the method to go for, but as stated before a larger dataset would largely improve the results obtained, currently the dataset is relatively small which might be causing problems with overfitting with CNN models that are trained for a large amount of time.

## **XI. Future Work**

Improving the deep learning model to take advantage of enriched data by tuning the parameters is something that would increase the results by a certain amount and could even decrease the training time.

Getting a more representative set of data could further improve the model making it a more compelling alternative to manual calculation.

The Hough transform approach used still made a couple of identification errors that could be corrected to further increase the accuracy.



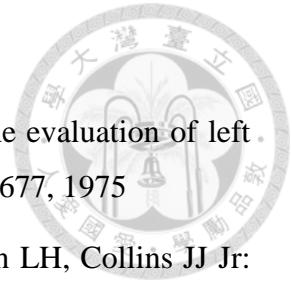
## **XII. Libraries Used**

- OpenCv for image manipulation
- SciKit-sklearn for kmeans-clustering
- Pandas data analysis
- Numpy for array manipulation
- MxNet for deep learning
- Python as the language of choice

## **XIII. Conclusion**

Heart failure, cancer, brain hemorrhage etc... are life threatening diseases that have a very small survival rate, they are responsible of killing millions of persons and doctors have the best chance at treating them when detected early, this thesis was made with that purpose in mind, giving a concrete example of the usage of deep learning in the calculation of left ventricle ejection fraction, this type of approaches can, and have been, applied in several areas, but so far the medical world has been slow to adopt them. For reasons that might not be simple to be solved, the future of biomedical image analysis lies in deep learning and CNN's, and the earlier they are embraced the more lives can be saved.

Medicine will be a field that no matter what will always involve the human factor, and technology will never be able to replace that but it will, and must, certainly seek to improve it.



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