Development of a thresholding algorithm for calcium classification at multiple CT energies

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Abstract. The objective of this study was to develop a thresholding method for calcium classification with different concentration using single-energy computed tomography. Five different concentrations of calcium chloride were filled in PMMA tubes and placed inside a water-filled PMMA phantom (diameter 10 cm). The phantom was scanned at 70, 80, 100, 120 and 140 kV using a SECT. CARE DOSE 4D was used and the slice thickness was set to 1 mm for all energies. ImageJ software inspired by the National Institute of Health (NIH) was used to measure the CT numbers for each calcium concentration from the CT images. The results were compared with a developed algorithm for verification. The percentage differences between the measured CT numbers obtained from the developed algorithm and the ImageJ show similar results. The multi-thresholding algorithm was found to be able to distinguish different concentrations of calcium chloride. However, it was unable to detect low concentrations of calcium chloride and iron (III) nitrate with CT numbers between 25 HU and 65 HU. The developed thresholding method used in this study may help to differentiate between calcium plaques and other types of plaques in blood vessels as it is proven to have a good ability to detect the high concentration of the calcium chloride. However, the algorithm needs to be improved to solve the limitations of detecting calcium chloride solution which has a similar CT number with iron (III) nitrate solution.

1. Introduction

According to the review done by George and Matthew, the ranking for atherosclerotic cardiovascular diseases in causing of death is the top which takes up about thirty percent of all deaths in the worlds [1]. There was about fifty percent of contracted acute coronary syndrome in the patients who did not show any symptoms. Thus, there is importance in identifying atherosclerosis in the early stage. Calcium is one of the compositions which appears in plaque calcification in the coronary vessels. The formation of atherosclerotic plaques and the total coronary plaque burden in coronary correlated closely with calcification (Hong, Bae, and Pilgram 2003)[2]. CT is a non-invasive method to diagnose and help in the prognosis of coronary artery calcification. The CT numbers can be varied for different types of plaques and the attenuation rate of calcium is high compared to other types of plaque. Thus, the efficacy and sensitivity for detection of calcification plaque in coronary are high [3-6]. A lot of studies were performed in order to detect the calcification and identify the composition of the plaque forming in the coronary. The Agatston score system which was introduced by Dr. Authur Agatston has collaborated in cardiac CT routine and has widely been mentioned in many studies in order to characterize the calcified
plaque. The Agatston score is a semi-automated tool; it is used to compute the calcification score in coronary arteries and will characterize the calcified tissue if the threshold value is greater than 120 HU for the images obtained at the 120 kV in single energy [7]. The Agatston score only analyses the calcification level and is unable to distinguish between the calcification plaque and iron deposit plaque as the CT number of these two types of plaque was too close.

Computed tomography was invented by Sir Godfrey Newbold Hounsfield from London in the early 1970’s [8]. The x-ray tube rotates 360 degrees along to the gantry rapidly to produce 2D images of the patients. Detectors were installed around the gantry to measure transmitted radiation, and then these readings were used to reconstruct the final images. In the 1980’s, the slip ring technology was invented. It allows the x-ray tube to continuously rotate along the gantry and the spiral scan was developed in computed tomography at that time. Slip ring technology solved the problem of acquiring a single slice of CT image with scanners in the past. Single-energy computed tomography (SECT) scanners only use a single x-ray tube to perform the scanning at a fixed tube voltage.

Elementary composition of each material was different and the attenuation coefficient of the photons was affected by this. The absorption and scatter of the photons resulted in the reducing of the intensity of the x-ray when it penetrates through a matter. When the x-ray energy increase the photoelectric effect will decrease and the compton scattering effect will increase. These will affect the attenuation coefficient of the materials. Generally, different materials will have different attenuation values or CT numbers and it is represented on grayscale [9]. Thus, when an image is acquired from conventional CT, the images will show the useful structural information of objects or materials.

Nowadays, a lot of the diagnostic processes are performed using a computer which is also known as a computer-aided diagnosis (CAD). The use of this system to analyse the image automatically has significantly improved the data handling process and reduced human errors. The diagnosis results obtained from the system are fast and reliable when collaborated with high-performance computers. There were several problems faced when performing segmentation in CT images, for example, the uniformity of the intensity, artefact and the similarity attenuation value of the soft tissue. Thus, in medical image processing, there were no common algorithms especially when applying the automatic segmentation technique to evaluate the images [10].

In many medical image processing studies, thresholding, edge detection, K-mean and others are commonly used while performing segmentation [10-13]. The thresholding technique is the fastest and easiest method compared with other methods [10, 13]. The threshold level can be determined either with the global thresholding method or local thresholding method. For global thresholding methods, the suitable threshold value will be defined according to the observer’s preferences. The threshold value can be defined using the trial and error method or through observation of the histogram modes of that particular image, to differentiate between that targeted object and the surroundings. Multiple thresholds were set for multiple window regions in the local thresholding method [13,14]. This technique is used to separate the object and divide them into different areas in the image according to the color, brightness and contrast [10]. The multi-thresholding method had been used in this study for the image processing section to distinguish the various concentrations of calcium chloride solution, iron (III) nitrate and sunflower oil.

2. Materials and Methods
A total of eight PMMA tubes were filled with the solutions in this study. All five tubes were filled up with calcium chloride anhydrous grade of analytical reagents (Grade AR) with concentration of 20.98 mg/ml, 70.89 mg/ml, 152.10 mg/ml, 204.93 mg/ml and 356.75 mg/ml, respectively. The sixth and seventh tubes were filled up with iron (III) nitrate with a concentration of 51.71 mg/ml and 96.85 mg/ml respectively. The eighth tube was filled up with sunflower oil. All tubes were held by a holder and placed in a cylindrical-shaped PMMA container. The diameter and the height of the PMMA container are 10 cm by 10 cm (Figure 1). Difference concentration of calcium chloride and iron (III) nitrate is to stimulate
the difference level of calcification in the plaque. The PMMA container was filled up with water and various materials were scanned in single energy mode in this study.

The 128-detector single-source dual-energy CT (Somatom Definition; Siemens AG, Wittelsbacherplatz Muenchen, Germany) was used in this study. This scanner is capable of producing single-energy and dual-energy images. Five different tube voltages were set (70 kV, 80 kV, 100 kV, 120 kV and 140 kV) for single-energy scanning. In this study, the current tube was automatically set using the CARE DOSE 4D. The automatic current modulation software from Siemens reduces the dose and maintains the quality of the images concurrently. The slice width was set to 1 mm for all the energy levels.

Figure 1. (A) PMMA tube placed in the holder (B) Top view of the phantom (C) Side View of the phantom after filled with water

The output DICOM images from SECT were analysed using a Java-based open source software which is ImageJ 1.5g, developed by the National Institute of Health (NIH) [15]. The area, mean (CT number) and standard deviation of the selected region of interest (ROI) of each material were then measured by ImageJ. The results were exported and saved in an Excel file.

The DICOM format CT images acquired from the scanned images were also imported into the developed system. MATLAB® software v. R2014a was used to develop the new algorithm. The algorithm of the developed system was applied to the image in order to compute the ROI to obtain the value of the area, the mean CT number and the standard deviation for that selected ROI. The location and the size of the area of the ROI placed in develop system were the same with the ROI placed in the ImageJ. The DICOM images which imported to the developed system were in pixel value. Thus, a conversion from pixel value to CT numbers was needed. Equation 1 was used to convert the pixel value of the images to CT numbers of the ROI of each material with different solution concentration.

\[ \text{CT numbers (HU)} = \text{Pix} \times \text{RescaleSlope} + \text{RescaleIntercept} \] (1)

The CT numbers (HU) obtained from the developed software using the pixel value (Pix) multiply with the RescaleSlope (Rslope) and add with the RescaleIntercept (RIntercept). The value of the Rescale slope and the Rescale Intercept could differ if the images are obtained from different systems. The value of the Rescale Slope and Rescale Intercept can be found in the metadata in the DICOM file [16]. The results converted from pixel value to CT numbers of the ROI of each material in the images were stored in an array format. The information stored in the array form will be used to compute the mean value of the CT numbers and the standard deviation value for each ROI from each material.

DICOM images were imported to the developed software where initially the dimension was in pixel-based units and not in length-based units. A conversion was required to convert the pixel-based units to length-based units. Equation 2 was applied to convert the pixel-based units’ value for the area of ROI to the length-based units which are in millimetres (mm). The size of the area of the ROI was used to make the selection at the same location and area on DICOM images in ImageJ software.

\[ \text{Area of ROI (mm}^2\text{)} = (\text{PixLength} \times \text{PS}) \times (\text{PixWidth} \times \text{PS}) \] (2)

From Equation 2, the PixLength and the PixWidth refer to the length and width of the rectangular shape, respectively. The pixel spacing (PS) refers to the vertical and the horizontal distance between two pixels which are adjacent to the unit of millimetre (mm). Basically, the distance between 2 pixels
was measured from centre to centre. The algorithm was evaluated using the same images which were analysed by ImageJ. The location and area of the ROI placed on each material in the images were same. The mean and the standard deviation was then computed and stored in an array format. The results from the ImageJ and the new system were compared and the percentage difference was calculated. The purpose of comparison between ImageJ and the developed software is to ensure the conversion value of the developed system was correct in the first place before applying these values to the segmentation section.

The segmentation process of the new algorithm is working based on a multi-thresholding technique. The minimum and maximum threshold value for each material were set based on the mean CT numbers and the standard deviations obtained from the new algorithm. This system was able to segment only one material at a time. The system will perform the segmentation process after the user inserts the value of the tube voltage and selects the type of material desired for segmentation, after the input of the DICOM image. The system converts the pixel value to a CT number for the DICOM image and compares the CT number of every pixel in the images with the threshold range predetermined in the system. The CT numbers within the range will be segmented and displayed in a binary image.

3. Results and discussion
The developed software was used to evaluate the CT numbers of the DICOM images and the results were compared with the ones acquired from the ImageJ. The comparison and verification processes were carried out to ensure that the conversion was performed correctly before proceeding to the segmentation stage. ImageJ software was chosen for the verification process. While obtaining the CT number and standard deviation with ImageJ, the ROI size and location were placed carefully in the same slice number. In this study, the ROI with an area of 0.41 cm\(^2\) was used. The average of the CT number and standard deviation were computed for every material for single energy images, for all five energy levels. The results of the CT number for each material for all energy levels acquired from the developed software and ImageJ were illustrated in figure 2.

![Figure 2](image-url)

**Figure 2.** The obtained CT number from the new algorithm compared with the CT numbers obtained from ImageJ at different energy levels in SECT.

Figure 3 illustrates the process of segmentation for the developed software. After the user imported a DICOM image into the system, the system would require the user to manually input the specific energy level (70, 80, 100, 120 and 140) for the image which was imported and the material (from 1 to 8) which the user intends to segment. Then, the system would convert the DICOM image in pixel value to CT number and compare the value of the CT number across the entire pixel in the image. If the CT number of that particular pixel falls within the ranges set, the system will label and segment it. The system will only able to segment one material at a time.
The algorithm was tested with the CT images from all five energy levels for all materials. Figure 4 shows the set of results of the segmented CT images of various concentrations of calcium chloride in various energy levels. The algorithm in the system was unable to distinguish between calcium chloride (20.98 mg/ml) and iron (III) nitrate (51.71 mg/ml) in all energy levels (figure 4(G) and 4(H)). Although these two were a different material, the CT number of these two materials at these concentrations produced a very similar CT number. Thus, the system was unable to differentiate them. In contrast, the algorithm showed a promising result to distinguish the calcium chloride solution with high concentrations for all energy levels (figure 4(A) to 4(F)). The measured CT numbers for these high concentrations can be distinguished very easily by the thresholding segmentation technique.

4. Conclusion
The results of the applied multi-thresholding technique algorithm to distinguish different types of materials with various concentrations are promising across all energy in single energy scanned. This technique might be helpful in distinguishing different types of plaques which form in blood vessels. Identifying the type of plaque is very important in clinical studies. The clinical doctor will provide a proper and better treatment plan for a patient if the system is able to identify the type of plaque.

Although there are two materials consisting of different elementary compositions, the CT number obtained will sometimes be very close or similar to each other such as it happened in this study. In low concentration of both calcium chloride (20.977 mg/ml) and iron (III) nitrate (51.706 mg/ml), their...
CT number were very similar to each other. In clinical studies, there is a limitation of differentiating the calcium deposit plaque with iron deposit plaque as the CT numbers are too close such as in this study. Therefore, other techniques would be required to collaborate with this technique in order to differentiate between the materials which consist of very close CT numbers. We can further improve the system by including the material decomposition technique into our algorithm. To perform the material decomposition technique, dual energy images would be needed as these images are able to provide extra information than single energy images. This extra information could be used to further distinguish between those materials.

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