Chapter

# Medical Image Processing and Analysis Techniques for Detecting Giant Cell Arteritis

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## Abstract

Medical image segmentation and classification algorithms are commonly used in clinical applications. Several automatic and semiautomatic segmentation methods were used for extracting veins and arteries on transverse and longitudinal medical images. Recently, the use of medical image processing and analysis tools improved giant cell arteries (GCA) detection and diagnosis using patient specific medical imaging. In this chapter, we proposed several image processing and analysis algorithms for detecting and quantifying the GCA from patient medical images. The chapter introduced the connected threshold and region growing segmentation approaches on two case studies with temporal arteritis using ultrasound (US) and magnetic resonance imaging (MRI) imaging modalities extracted from the Radiopedia Dataset. The GCA detection procedure was developed using the 3D Slicer Medical Imaging Interaction software as a fast prototyping open-source framework. GCA detection passes through two main procedures: The pre-processing phase, in which we improve and enhances the quality of an image after removing the noise, irrelevant and unwanted parts of the scanned image by the use of filtering techniques, and contrast enhancement methods; and the processing phase which includes all the steps of processing, which are used for identification, segmentation, measurement, and quantification of GCA. The semi-automatic interaction is involved in the entire segmentation process for finding the segmentation parameters. The results of the two case studies show that the proposed approach managed to detect and quantify the GCA region of interest. Hence, the proposed algorithm is efficient to perform complete, and accurate extraction of temporal arteries. The proposed semi-automatic segmentation method can be used for studies focusing on three-dimensional visualization and volumetric quantification of Giant Cell Arteritis.

**Keywords:** Giant Cell Arteritis, Enhancement, Detection and Classification, Segmentation

## 1. Introduction

Giant cell arteritis (GCA), also called temporal arteritis or cranial arteritis is a systemic inflammation of medium to large-sized vessels [1]. The cause of the disease is currently unknown; however, autoimmunity is one hypothesis [2].

GCA most commonly occurs in females (female to male ratio 2-4:1) over the age of 50 years [3]. Temporal artery involvement classically presents with sudden onset of severe headache associated with inflammatory and ischemic symptoms; [1] however, GCA may involve other large-sized arteries, namely the aorta, subclavian, iliac, ophthalmic, occipital, and vertebral arteries, which have different presentation and may be involved independently from the cranial arteries [4].

Left untreated, GCA can lead to permanent visual loss and various systemic complications; therefore, there is a need for effective diagnosis. The American College of Rheumatology proposed criteria for the diagnosis of GCA [5]. The diagnosis mainly relies on clinical presentation, inflammatory markers (typically high erythrocyte sedimentation rate (ESR)), and usually histological confirmation by temporal artery biopsy. Temporal artery biopsy has been the standard test to confirm the diagnosis of GCA, which although highly specific, is considered invasive and lacks sensitivity [2, 6, 7]. Consequently, diagnosis of GCA often relies on the combination of clinical symptoms, serum inflammatory markers, and radiological imaging.

## 2. Diagnosis of GCA by radiological imaging

The role of radiological imaging is becoming increasingly important in the diagnosis and follow-up of GCA. Generally, the different radiological imaging modalities visualize different aspects of the involved vessel wall thickening and luminal stenosis. The first line imaging modality, especially for cranial GCA is color duplex sonography (CDS) [4, 8, 9]. CDS assesses vascular wall anatomy and luminal lining and diameter. A characteristic finding of GCA on CDS is the (halo) sign, which is homogenous, hypoechogenic circumferential vessel wall thickening. Another finding is the lack of compressibility of the artery manifested by the application of transducer-imposed pressure on the temporal arteries (compression sign) [4, 8]. The (halo) sign has a sensitivity ranging from 55 to 100% and specificity of 78 to 100% in the diagnosis of temporal arteritis [8]. The wide range of sensitivity may be attributed to operator experience and arterial involvement. A systematic review published in 2016 discussed the use of the different imaging modalities in the diagnosis and follow-up of GCA [10]. The review findings suggest that CDS is an easy, cost-effective diagnostic imaging tool for the evaluation of cranial vessels, as well as the carotid, subclavian, axillary, and brachial vessels. The reliability of the unilateral halo sign is debatable; however, the presence of a bilateral (halo) sign discards the need for temporal artery biopsy. Many studies have compared ultrasound (US) imaging versus temporal artery biopsy in the evaluation of GCA [11–15]. In a prospective cohort study published in 2019, Zou *et al.* discussed the results of clinical examination following the US versus biopsy of the temporal artery biopsy directly, considering MRI as a reference diagnostic data. The study included 980 patients with a mean age of 61.12 ± 6.56 years who complained of at least one symptom consistent with GCA but have not been diagnosed or treated with glucocorticoids [11, 14]. US and MRI imaging included bilateral temporal arteries, axillary arteries, and their branches. The study concluded that the clinical examination following US detection of GCA had high accuracy and a lower risk of overdiagnosis and unnecessary glucocorticoid treatment of low to medium risk GCA [2]. Moreover, there was a higher number of false-negative diagnoses reported by temporal artery biopsy. These results are consistent with other studies like the TABUL study [1].

Other important noninvasive imaging modalities are contrast-enhanced computed tomography (CT) scan and CT angiography (CTA). Both scans visualize cranial and extracranial arteries, the aorta for example, and can visualize associated

complications [16, 17]. On CT, the diseased vessel wall appears edematous with concentric enlargement and usually shows late contrast enhancement. CTA on the other hand is better for visualization of the luminal vascular pathology. Both modalities are excellent for the diagnosis of GCA when the involvement of a large-sized vessel other than the temporal artery is suspected. However, there is a scarcity of data on the use of CT/CTA in the diagnosis of GCA. Berthod *et al.* discussed in a case–control study CT imaging of the aorta in suspected GCA, which included 174 participants (64 with GCA, 43 with polymyalgia rheumatica, and 67 controls) [18]. The study results showed that using CT in the evaluation of the aorta is diagnostic of GCA which is morphologically different that atheromatous lesions. The study set an aortic wall thickness of ≥2.2 mm as pathological and indicative of GCA.

Additionally, magnetic resonance imaging (MRI) and MR-angiography (MRA) have a prominent role in the diagnosis of GCA. The t2 weighted MRI images show a hyperintense rim at the edematous segment of the vessel wall. Moreover, t1 weighted images depict mural thickening and contrast enhancement. MRA, as CTA, better visualizes irregular luminal lining and can assess the extent of arterial wall damage and the effectiveness of treatment [8]. The use of MRI in the clinical setting is available; however, its diagnostic accuracy is still indefinite as the available literature has approached this issue differently. A systematic literature review and meta-analysis discussed the diagnostic accuracy of MRI imaging of the temporal and occipital arteries. They reviewed six studies with 509 patients that used either clinical diagnosis or temporal artery biopsy as the reference standard. They found that when the clinical diagnosis was used as the reference standard, MRI had a lower pooled sensitivity and specificity (73%, 88%) than that of the US (77% and 96%, respectively). However, when compared with temporal artery biopsy, MRI had a higher sensitivity (93% vs. 70%) and a similar specificity to sonography (81% vs. 84%). Thus, they advised that both modalities have good diagnostic accuracy of superficial temporal arteries GCA [17].

Furthermore, fluoro-D-glucose integrated with computed tomography (FDG-PET/CT) is also currently used in the diagnosis of large-sized vascular wall inflammation. This modality shows the increased uptake of glucose by the inflammatory cells lining the vessel wall [19].

The choice of image processing technique depends on the available imaging modality and the level of expertise in the clinical setting, taking on consideration the risks of radiation or contrast exposure, in contrast to the benefit of timely and accurate diagnosis of GCA versus the overdiagnosis and overtreatment of GCA based on conventional diagnostic criteria. The European League Against Rheumatism (EULAR) has issued recommendations on the use of different imaging modalities in the evaluation of large vessel vasculitis [20]. However, currently, there is no clearly defined protocol for imaging in suspected GCA; yet, there is increasing attention over the advantages and disadvantages of using each imaging modality in accordance with the clinical presentation.

## 3. GCA image processing and analysis

Recently, the use of medical image processing and analysis tools improved GCA detection and diagnosis using medical imaging. These tools provide physicians with semi-automatic detection and quantification of suspected regions of interest and enhance GCA diagnosis.

Medical imaging processing refers to the process of digital imaging by using computer software. This process includes several types of techniques and operations such as image enhancement, segmentation, registration, and visualization [21].

The rapid advancement of image processing and analysis improved the medical care process in clinical applications.

The current advances in medical imaging made in medical fields such as imaging modalities, diagnostics, and treatment applications are designed on digital imaging technology processing and analysis. Medical image processing has been recognized as a source of innovation in the advanced medical care process including medical informatics, artificial intelligence, and bioinformatics. Recently, many libraries, tools, and software products can process and manipulate images from different modalities (CT, MRI, US, PET) and are available for clinical application and research purposes [22].

Medical image segmentation and classification algorithms are commonly used in clinical applications. Several automatic and semiautomatic segmentation methods were used for extracting veins and arteries on transverse and longitudinal medical images [23]. The deformable contour model, connected threshold, fast marching method, and many other methods were used for extracting the arteries from US images. Other studies reported the application of region growing, diffusion-based filter, edge detection combined with morphology methods, and Hough transforms [12, 23, 24]. In this chapter, we proposed several image processing and analysis algorithms for detecting and quantifying the GCA from patient medical images. The chapter introduced the connected threshold segmentation approach on two case studies for temporal arteritis using US and MRI imaging modalities extracted from the Radiopedia Dataset [12].

## 4. GCA image processing and analysis software

The GCA detection procedure was developed using the 3D Slicer Medical Imaging Interaction software as a fast prototyping open-source framework [25]. The 3D slicer is a free open-source software system providing extendibility by plug-ins development that interacts with the application core. It is an open-source software platform for medical image informatics, image processing, and three-dimensional visualization. Built over two decades through support from the National Institutes of Health and a worldwide developer community, Slicer brings free, powerful cross-platform processing tools to physicians, researchers, and the general public.

The main focus of the 3D slicer is to enable the creation of highly interactive medical imaging software applications; it integrates different tools for medical imaging, computational modeling, computer graphics, deep learning, and numerical modeling for building applications with complex interaction mechanisms. It also provides a graphical user interface, multiple consistent views for the same data, 3D rendering, data retrieval, hierarchical organization for data objects, advanced visualization of multi-modal imaging, and support for 3D + t data.

3D slicer is an object-oriented cross-platform library implemented in C++ that supports Windows, Linux, and macOS. It integrates and extends widely-used open-source C++ libraries which are the Visualization Toolkit (VTK) and the Insight Toolkit (ITK), both supported by Kitware Inc. The ITK is an open-source, cross-platform library that provides an extensive suite of software algorithms for image analysis, it builds a set of fundamental algorithms especially for segmentation and registration. While the VTK supports a wide variety of visualization algorithms and advanced modeling techniques.

In addition to ITK and VTK, third-party packages can be integrated and used with MITK, such as the DICOM Toolkit (DCMTK, supported by Offis in Germany), and other commonly used C++ libraries (Boost, Qt, OpenCV among others). The

software includes numerous modules, extensions, datasets, pull requests, patches, issues report, suggestions—is made possible by users, developers, contributors, and commercial partners around the world. This development is funded by various grants and agencies [26].

## 5. Giant cell arteritis detection using medical image processing and analysis

Medical imaging is a commonly used method for detecting GCA and the diagnosis of arteries related diseases. Nowadays, medical image processing and analysis methods are used to facilitate the identification of the boundaries of internal organs from medical images and thus enhance the diagnostics of specific abnormalities. Patients with GCA may be indicated for medical imaging examination for initial diagnosing or monitoring of the disease activities.

GCA detection can be defined as the procedure in which the GCA region of interest can be detected and identified from medical images. In clinical application, the GCA diagnostic planning is defined as the process in which it is planned, using the computer system, where the GCA disease can be detected and quantified.

GCA detection passes through two main procedures: the pre-processing phase and the processing and analysis phase. The pre-processing phase improves and enhances the quality of an image after removing the noise, irrelevant and unwanted parts of the scanned image. The enhancement of image quality is obtained by the use of filtering techniques, removal of noise, and contrast enhancement methods. The processing phase includes all the steps of processing, which are used for identification, segmentation, measurement, and quantification of GCA.

GCA segmentation is composed of a series of image processing algorithms that depend on the medical image type and quality. The core image processing algorithms include:

a. The image enhancement and denoising algorithms:

   1. Gaussian Blur Module and Gaussian Blur Batch Make Module: these modules convolve the image with a Gaussian kernel wherein the Gaussian has a standard deviation specified by the user (GUI field "sigma") and the kernel width in each dimension is 6 times the standard deviation of the Gaussian.

   2. The Median Image Filter is commonly used as a robust approach for noise reduction. This filter is particularly efficient against 'salt-and-pepper' noise. In other words, it is robust to the presence of gray-level outliers. Median Image Filter computes the value of each output pixel as the statistical median of the neighborhood of values around the corresponding input pixel.

   3. Image editing tools include cropping, adding and subtracting, cutting, change the directions and orientations.

b. Image processing and analysis that includes:

   1. Threshold selection based on pixel intensity histogram analysis.

   2. Image segmentation with the selected threshold result and the use of an interactive segmentation tool that allows physicians to edit, and modify the segmented region as requested.

c. Region of interest post-processing that includes surface or volume reconstruction, measurements, deformation, and simplifications for clinical application. The measurements include the calculation of ROI area, volume, distances from organs, and other basic measurements and statistics (Mean, median, SD...etc).

The proposed method for detecting the GCA is shown in **Figure 1**. The image enhancement and the segmentation based on the threshold method are calculated from 2D MRI and US image slices. The US image shows the left temporal artery, and the MRI shows the right temporal right artery segmentation.

This approach of segmentation allows the semi-automatic detection of the outlines of the artery in the enhanced medical image. The methods of segmentation by the threshold, region growing, and interactive segmentation is commonly used in the literature. In this chapter, we tested the methods on two case studies using semi-automatic methods for detecting the GCA.

The semi-automatic segmentation is done by studying the histogram and the threshold analysis of the 2D US and MRI images. The histogram analysis is used to identify the pixel densities of all areas of interest. In this study, we assumed that there are differences calcification density distribution between the blood,

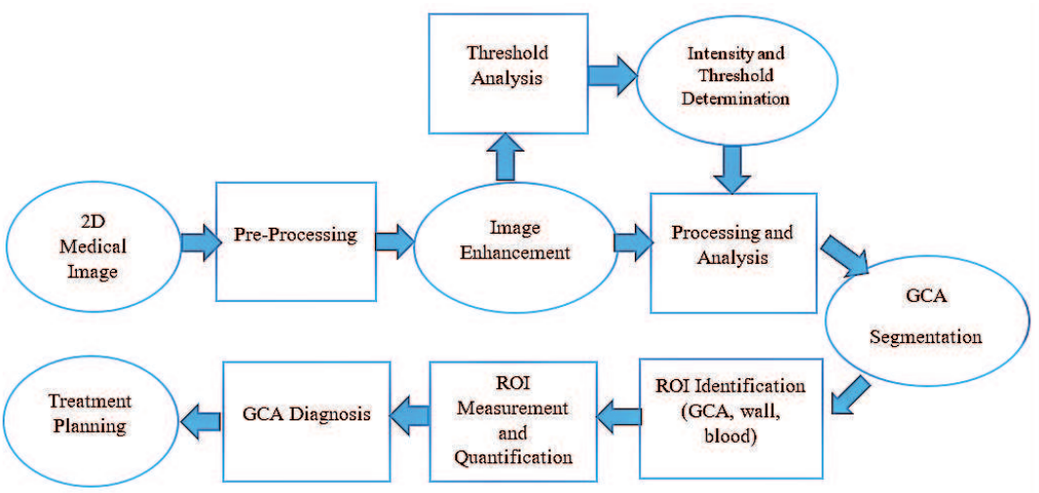


**Figure 1.**
*The flow chart GCA detection method.*

| | Volume [$cm^3$] | Threshold (Pixel Densities) | Diameter [mm] | Surface area [$mm^2$] | Roundness |
|---|---|---|---|---|---|
| **US image Case Study** | | | | | |
| Temporal Artery Wall | 3.29 | −85 – −25.3 | 181 | 8622.2 | 0.12 |
| GCA Wall Thickening | 0.73 | −87– −32.9 | 160 | 1989.5 | 0.25 |
| **MRI Image Case Study** | | | | | |
| Temporal Artery Wall | 2.31 | −376 – −127.6 | 201 | 4618.9 | 0.18 |
| GCA Wall Thickening | 0.28 | −400 – −157.4 | 88 | 594.3 | 0.35 |

**Table 1.**
*The US and MRI histogram and statistical analysis.*

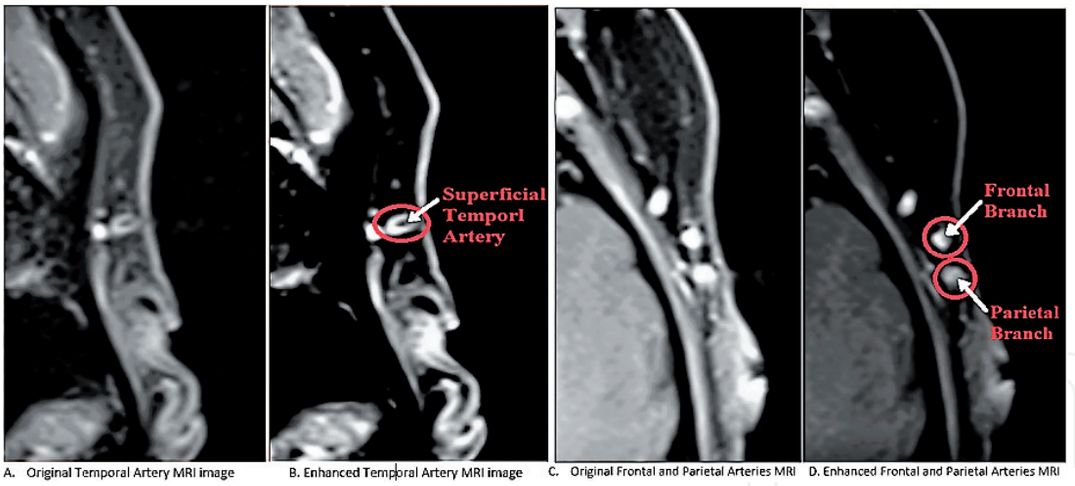


**Figure 2.**
*Pre-processing filters and algorithms for the enhancement of MRI image of a 50 years old female patient.*

artery wall, and the GCA region since the density of the GCA region is often lower than the blood and the normal wall densities. The image histogram analysis is summarized in **Table 1**. The temporal artery wall and the GCA wall thickening diameters were calculated in both images, the results in **Table 1** show an increase in the artery wall in both cases (160 mm and 88 mm). Furthermore, the GCA artery wall roundness was higher than the normal artery roundness in both cases (0.25 mm and 0.35 mm), respectively. The pixel density threshold analysis shows that there are few differences between the normal and GCA regions as indicated in **Table 1**.

In the pre-processing phase, various filtering and thresholding algorithms are applied successively to obtain the artery contour and boundary. This contour is separated and segmented into three contours (regions): the artery wall, the blood, and the abnormal region (GCA). Results in **Figure 2** show the two cases before and after image pre-processing.

The segmented regions were quantified and measured using the 3D slicer measurement and quantification tools.

## 6. Giant cell arteriti's case studies

In this chapter, two case studies were conducted to assess the connected threshold and region growing segmentation algorithms as a semi-automatic detection and quantification of temporal arteritis on US and MRA images. The histogram threshold analysis was performed to analyze and study the pixel distribution in both mages. Otsu's method was used to divide the images into two parts, namely; foreground and background regions. To segment the temporal artery, we performed the threshold segmentation algorithm on the foreground region by comparing two different statistical distributions. The semi-automatically segmented regions were compared with manually segmented regions. The segmentations were validated by experts and the different similarity metrics were used to identify the variations in segmentation.

### 6.1 US case study

In the clinical application, the temporal artery characteristics can be found and detected using US images. GCA detection compared to the normal artery is

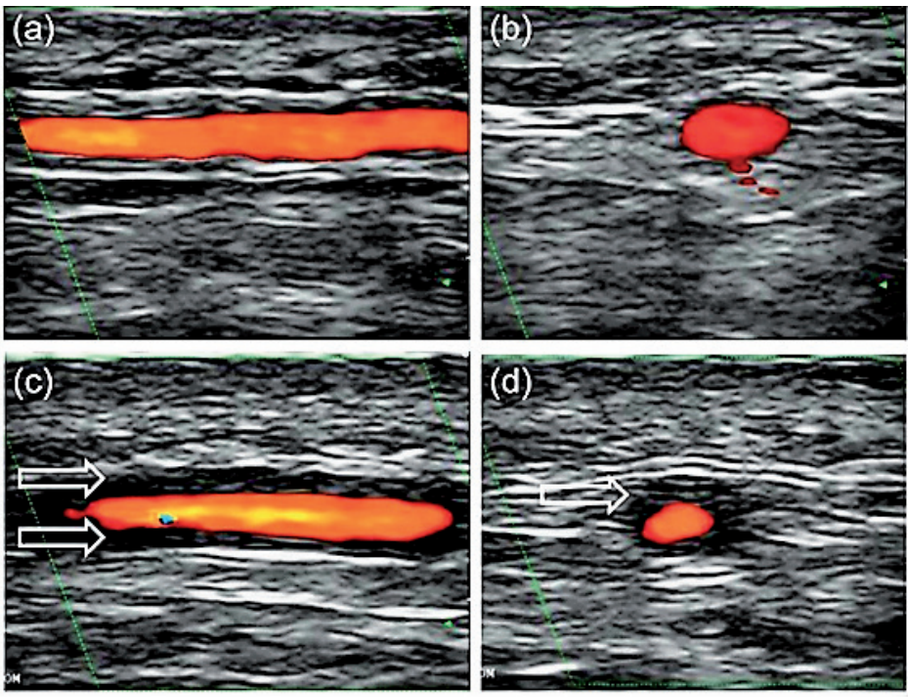


**Figure 3.**
*Color doppler ultrasound showing longitudinal (a) and transverse (b) views of normal temporal artery and acute temporal arteritis. (c, d) The arrows indicate the vasculitis wall swelling [27].*

shown in **Figure 3** [27]. The data in **Figure 3(a)** and **(b)** show the longitudinal and transverse views of normal temporal artery and acute temporal arteritis in **Figure 2(c)** and **(d)** of an adult women aged 45 years old. As seen in **Figure 2**, the arrows indicate the vasculitis wall swelling. The ultrasonography features showed a hypoechogenic halo of the temporal artery in longitudinal (left) and transverse (right) view. The data show that the normal artery diameter is 0.3-1 mm and the temporal artery diameter is 1-2 mm.

In our proposed method, the US image data of a 40 years old female patient with a visible thickening of the left temporal artery that causes a chronic left temporal headache was used to test our segmentation method. [Radiopaedia.org/GCA case studies] The data is validated by comparing the artery wall segmentation results with the manual ones from experts. The typical US image used in this chapter is shown in **Figure 4(a)** and **(b)**. **Figure 4(a)** shows a longitudinal view of GCA with wall thickness on the lower side of the temporal artery. **Figure 4(b)** shows the results of segmented regions using the threshold segmentation. The area in yellow represents the wall segment, the red indicates the blood segment while the green area represents the GCA region of interest. The temporal artery has been well-segmented and the clinical characteristics have been identified and documented. The results show the diameters of the lumen, wall, and the blood flows velocity at the region of interest along with the superficial temporal artery. The diameter of the artery wall was significantly thicker than the normal artery. The GCA region of interest diameter was 1.6 mm with an area of 19.9 $cm^2$.

### 6.2 MRI case study

The MRI case study represents a patient of a 50-year-old female with clinical suspicion of temporal arteritis, the left temporal artery and its frontal and parietal branches show significant wall thickening [12].

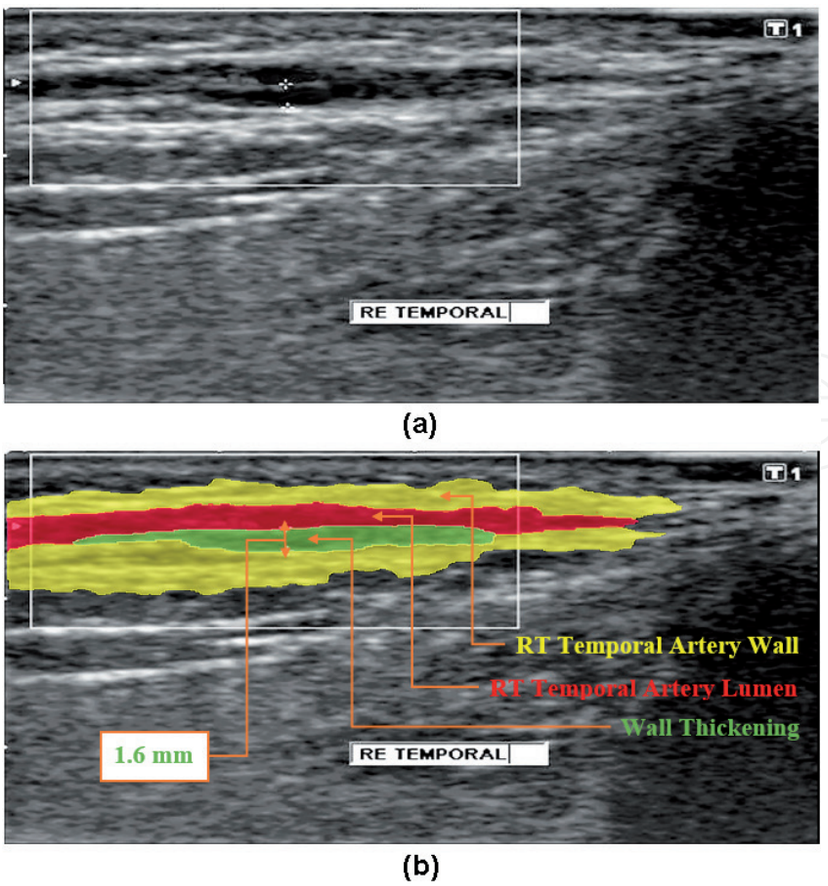


**Figure 4.**
*The left temporal artery of 40 years female patient, (a) shows the temporal artery before segmentation, (b) the threshold segmentation of GCA region of interest [12].*

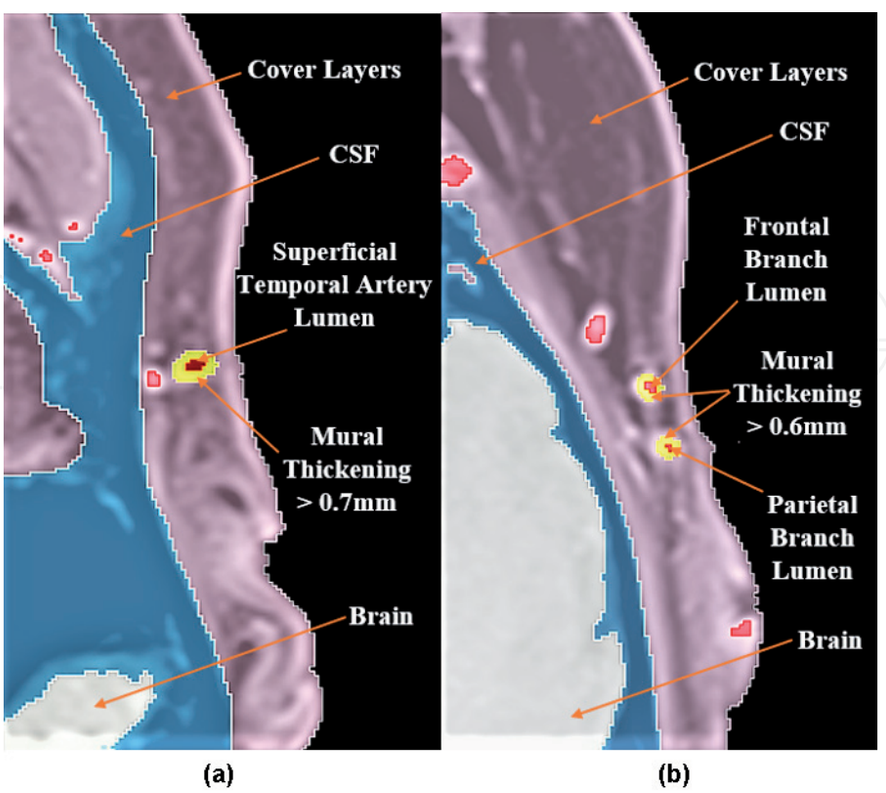


**Figure 5.**
*The left temporal artery of 50 years female patient, (a) shows the temporal artery before segmentation, (b) the threshold segmentation of GCA region of interest [12].*

Prominent mural enhancement is identified in these arteries when compared to the contralateral side. The contralateral temporal artery and its branches show a normal appearance.

The high-resolution MRI imaging of the superficial temporal artery is shown in **Figure 5(a)** and **(b)**. The arrow in **Figure 5(a)** shows the position of the abnormal temporal arteries. The images in **Figure 5(b)** show the frontal branch and the parietal branch after image pre-processing and enhancement. The region growing segmentation of the region of interest in both images shows the GCA regions. The average superficial temporal artery wall thickness was 0.71 mm. According to the literature mural thickening >0.5 mm was considered as a sign of mural inflammation [28].

## 7. Conclusion

In this chapter, we discussed the use of medical image processing and analysis in detecting and quantification of GCA. We discussed a semi-automated segmentation of temporal arteries from 2D temporal artery US and MRI images using image processing and analysis algorithms. These algorithms depend on various image processing algorithms, including image enhancement, noise reduction, pixel densities histogram analysis, and statistical analysis tools. First, the Gaussian filters and noise reduction algorithms are applied to enhance the temporal artery structures, which effectively enhances the temporal artery contrast, because the shape information of the blood flow is considered. Afterward, seed points are detected automatically through threshold pre-processing operation. Based on the set of seed points and threshold analysis, region growing is applied, which grows in the target region. Then, the temporal artery region is extracted by connected threshold and region growing approaches, which are capable of segmenting the artery due to the pixel intensity thresholds and the seed point approach. Three regions of interest were extracted, the temporal artery wall, the blood flow, and the GCA region. Then the statistical and measurement tools are used to quantify the diameters, area, and volume of the GCA regions, and to detect and identify the size and location of the GCA region. The semi-automatic interaction is involved in the entire segmentation process for finding the segmentation parameters. Hence, the proposed algorithm is efficient to perform complete, and accurate extraction of temporal arteries. The proposed semi-automatic segmentation method can be used for studies focusing on three-dimensional visualization and volumetric quantification of Giant Cell Arteritis.

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