Study on De-noising Extraction and Digitization Methods of Blood Vessel

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Dedication

To my parents; whose guidance, consistent belief and support always encouraged me when I was in a difficult time and let me enable to catch my dreams.

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Study for Ph.D is like a long long journey, which is hard and difficult. Fortunately, I was helped and accompanied by many people in this period. Therefore, I really can’t stop myself from gratefully appreciating everyone at this juncture of my life.

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My deepest appreciation goes to my loving parents, who sacrificed many things in order to provide me with the quality of life and support me to study and live in Japan as a private foreign student.

This thesis is dedicated to my parents and all my family members, especially to the memory of my grandfather who has passed away. I will never forget what you taught me: to be a good kind-hearted person in my life.

Cong Wu, D.Eng.
Study on De-noising Extraction and Digitization Methods of Blood Vessel
Thesis directed by Professor Koichi Harada.

In this thesis, we mainly focus on two research fields of blood vessels --- 1) De-noising for blood vessel images origin from Laser Speckle Contrast Analysis (LASCA); 2) Extraction and Digitization of blood vessel images applied in Traditional Chinese Medicine (TCM). Both of them have deep relation with medical image processing, which becomes a hot research topic in modern time.

Laser speckle contrast imaging (LSCI) technique is a new modality to monitoring blood flow dynamics with high spatio-temporal resolution. It records the full-field spatio-temporal characteristics of microcirculation without the need of scanning in real time. Laser speckle contrast analysis (LASCA) is a non-scanning, non-invasive technique that produces 2-D map of blood flow by analyzing speckle images captured by CCD camera. However, when LASI is applied, the details of time-varying speckle are difficult to discriminate. It needs for spatial or temporal statistics to de-noising while preserving the details. Because the time cost in spatial LASCA and the space cost in temporal LASCA are huge, it becomes an important research objective for us that use less frames of time-varying speckle to gain higher quality imaging. Our research is to develop the image quality of low frame image and make it reach the quality of high frame image by using image processing techniques.

Wiener filtering is a kind of adaptive filtering, which can effectively noise restraining and protect the edge, and is widely used in image processing. However, badly in detail discriminate, it would easily cause thin line, curve, etc lost and damaged. The nonlinear filters are proved to be effective in suppressing or eliminating fix-value impulse noise. Moreover, nonlinear filters preserve the details and edges of an image during the process of de-noising .Wavelet is an effective tool for signal restoration, which has good performance in de-noising and preserving details, but cause edge fuzzy for its soft threshold.

Therefore, we propose a novel hybrid filtering method which combines wiener filtering, order-statistic filtering and wavelet fusion, for de-noising of LASCA images.

Meanwhile, blood vessel, which is a promising biometric feature, has drawn lots of researches in Traditional Chinese Medicine (TCM). Blood vessel owns many outstanding characteristics, such as branches detection and hard to forgery. These days, the digitalization of Chinese medicine diagnoses has becoming a hot topic in TCM and computer communities with recent progress of electronic and computer technology. "Differentiation of syndromes by observing eyes" is one kind of diagnosis by observing, which observing the changing of the Sclera-conjunctiva region and the

state of its vessel. This diagnosis method collects the features of Sclera-conjunctiva (especially the vessel feature) to discriminate the diseases in the whole body. The digitalization of "Differentiation of syndromes by observing eyes" can help to build an objective and quantitative diagnostic standard for TCM.

The thesis mainly has conducted the research on the below contents:1) Based on Hybrid De-noising a research on the blood vessel LASCA imaging de-noising method; 2)Based on wavelet fusion a research on the blood vessel LASCA imaging de-noising method; 3)Research on blood vessel extraction and reproduction method of white eyeball region.

1) Based on Hybrid De-noising a research on the blood vessel LASCA images de-noising method
A de-noising approach is proposed that based on the combination of wiener filtering, nonlinear filtering and fusion of wavelet, which de-noise the LASCA (Laser Speckle Contrast Analysis) image of blood vessels in Small Animal. The approach first performs laser spectral contrast analysis on cerebral blood flow and brain blood flow in rat, get their spatial and temporal contrast images. Then, a de-noising filtering method is proposed to deal with noise in LASCA. The image restoration is achieved by applying the proposed admixture filtering， and the subjective estimation and objective estimation are given to the de-noising images.

2) Based on wavelet fusion a research on the blood vessel LASCA images de-noising method
A de-noising approach is proposed that based on the combination of wiener filtering, nonlinear filtering and wavelet fusion, which de-noise the LASCA (LAser Speckle Contrast Analysis) image of blood vessels in Small Animals. The approach first performs laser spectral contrast analysis on brain blood flow in rats, get their spatial and temporal contrast images. Then, a de-noising filtering method is proposed to deal with noise in LASCA. The image restoration is achieved by applying the proposed admixture filtering, and the subjective estimation and objective estimation are given to the de-noising images. As our experimental results shown, the proposed method provides clearer subjective sense and improved to over 25db for PSNR.

3) Research on blood vessel extraction and reproduction method of white eyeball region
Moreover, the edge feature parameters are gained, which can be used to reconstruct the blood vessels. Experimental results show that the algorithms can obtain blood vessels information fast and accurately.
This paper presents 1) algorithms for blood vessels extraction in sclera-conjunctiva images, which can be applied in syndrome differentiation by observing human eyes (named Ocular Diagnostic in Traditional Chinese Medicine); 2) digitization of extracted vessels. First, sclera-conjunctiva region is isolated by optimal threshold segmentation and mathematical operation; Scanning and edge detection methods are

used to gain the edge of the blood vessels.

Our work is to convert those sclera-conjunctive image into grayscale image and finally to binary image. After that, the digitization method will be applied to gain the parameters of attributes of blood vessels. Those result will greatly help the diagnosis of "Differentiation of syndromes by observing eyes" --- which is a traditional medicine in China.

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Chapter 1 Introduction

1.1 Blood Vessel Imaging and Segmentation

In many medical diagnoses, the analysis of blood vessel has valuable effect for researchers, especially in cardiovascular disease diagnosis. For example, the structure and orientation of blood vessels provide important information in cardiovascular disease and liver cancer diagnosis. Due to the improvement of people's living standard, cardiovascular disease has become the most major disease causes of death. It is told that 12 million people died for cardiovascular disease every year, nearly 25% of the total number of deaths in the world, which becomes the No.1 health problem for human being. Therefore, blood vessel imaging technique is very important for blood analysis and diagnosis.

Nowadays, there are two kinds of blood vessel imaging techniques: Tomography Angiography and Ultrasound. The Angiography way for example: CT radiography (Computer Tomography Angiography, CTA), MRI radiography (Magnetic Resonance Angiography, MRIA), X beam radiography (X Radiography Angiography, XRA) and so on imaging methods. The supersonic way is the supersonic imaging method (Ultrasound, US), which is excellent for non-invasively imaging and diagnosing a number of organs and conditions, without x-ray radiation. Moreover, LSCI has some applications in blood vessel imaging. It will be introduced in section 1.2.

The imaging results of (Computer Tomography Angiography, CTA), (Magnetic Resonance Angiography, MRIA) and (X Radiography Angiography, XRA) have clear effects, therefore, widely used around the world. The researchers also use those methods to perform segmentation on the images.

The supersonic imaging method (Ultrasound, US) has the characteristic of non-invasive, non-pain, the non-ionisation radiation as well as inexpensive. It also can realize the real-time imaging, which enables itself to be the important way to disease general survey and disease diagnose. But the medical supersonic imaging technique also has its imaging mechanism limitation: the picture quality is not high. Because of the non-uniformity of the imaging organ or the organizational structure, some small structures cannot be distinguished. In addition, the acoustic signal interference, which has formed the unique spot noise on the supersonic image, reduced the supersonic image quality greatly. It causes high difficulty for the blood vessel image segmentation.

In order to solve the real issue, for example the diagnosis and the matching, it still need the blood vessel segmentation based on vessel imaging picture. Such one segmentation method can not be suitable for all imaging method. The image segmentation method relies on the imaging modality and the application domain. The segmentation algorithms and techniques can be divided into six kinds based on the theory: [1]

A. Pattern Recognition Technique,

（1） Multi-criterion method

（2） Based on skeleton method

（3） Region growing method

（4） Based on crest line method

（5） Based on differential geometry method

（6） Matched filter method

（7） Mathematics morphology method

B. Based on model method,

（1）Deformation model, including parameter deformation model (i.e. active outline model) and geometry deformation model

（2）parameter model

（3）Pattern plate match model

（4）General circular cylinder method

C. Based on track method,

D. Artificial intelligence Based on artificial intelligence method,

E. Based on neural network method,

F. Complex tube structure examination method.

1.2 Blood vessel LASCA imaging technology and image processing

Laser speckle contrast imaging (LSCI) technique is a new modality to monitoring blood flow dynamics with high spatio-temporal resolution. It records the full-field spatio-temporal characteristics of microcirculation without the need of scanning in real time [2]. Laser speckle contrast analysis (LASCA) is a non-scanning, non-invasive technique that produces 2-D map of blood flow by analyzing speckle images captured by CCD camera [3]. Our research is to develop the image quality of low frame image and make it reach the quality of high frame image by using image processing techniques. Laser speckle contrast imaging applies the 1st order spatial statistics analysis, the method of spatial statistics of Time-varying Speckle was proposed by Briers in 1980s [4]. It calculates contrast value on the local image (sub-image or statistics window), and convert into pseudo color image [5]. In fact, it can be considered as the 1st order spatial statistics analysis on speckle image, and the temporal statistics analysis is first proposed in 1976 by Ohtsubo and Asakura [6]. Serov applied this method in Laser doppler perfusion imaging and use CMOS fast imager, the sampling rate can be 9000 pps [7]. Cheng applied this in LSTAC (Laser Speckle Temporal Contrast Analysis) to gain the two dimension imaging of blood vessel distribution, which performs temporal statistics on each point around m frames images [8].

However, when LSCI is applied, the details of time-varying speckle are difficult to discriminate. It needs for spatial or temporal statistics to de-noising while preserving the details. Because the time cost in spatial LASCA and the space cost in temporal LASCA are huge, it becomes an important research objective for us that use less frames of time-varying speckle to gain higher quality imaging.

Wiener filtering is a kind of adaptive filtering, which can effectively noise restraining and protect the edge, and is widely used in image processing. However, badly in detail discriminate, it would easily cause thin line, curve, etc lost and damaged [9].The nonlinear filters are proved to be effective in suppressing or eliminating fix-value impulse noise [10]. Moreover, nonlinear filters preserve the details and edges of an image during the process of de-noising [11].Wavelet is an effective tool for signal restoration, which has good performance in de-noising and preserving details, but cause edge fuzzy for its soft threshold [12].

Therefore, we propose a novel hybrid filtering method which combines wiener filtering, order-statistic filtering and wavelet fusion, for de-noising of LASCA images. This approach first performs wiener filtering, add nonlinear filtering with the result, change the luminance; Meanwhile, makes wavelet transform on the noisy image, and via inverse wavelet transform. Finally, the result is the fusion of wavelet and those two. The experimental results show that the hybrid filtering has better performance than each single filtering, which de-noising while preserve the edge and other details of images.

1.3 Characteristic extraction method to the winds the arteries image from white eyeball region

In China and also other countries in the world, there are still many people benefit by Traditional Chinese Medicine (TCM) for the early diagnosis. No need much diagnosis equipment, TCM diagnosis can provide cheaper and quicker diagnosis process to the patients than western ways [13]. Traditional Chinese Medicine has been the cornerstone of oriental traditional medicine, which comprise of other variants of Hindu, Arab, Korea and Japan. One of the most unique features among oriental traditional medicine is Non-intrusive Diagnosis and Treatment, and it is best exemplified by Chinese traditional medicine's famous Four Methods: Looking, Palpating, Asking and Listening/Smelling, with which a doctor diagnose the patients thoroughly, analyze, and follow up measures. This methodology has been working very well for the past 2000 years, and made a significant contribution on human health. However, it's not without drawback on the other hand. Comparing to its strong competitors—Western Orthodox Medicine, TCM has came up short of diagnosis precision and, in particular, is lack of concrete basis on which to make a sound judgment, which in turn makes it difficult for inexperienced doctor to diagnose [14].

The digitization of TCM diagnosis can develop its correctness which is usually doubted by the public. Blood vessels as a promising biometric feature have drawn lots of researches in Traditional Chinese Medicine (TCM). Blood vessel owns many outstanding characteristics, such as branches detection and hard to forgery .

Therefore, for the above reasons, these days, the digitalization of Chinese medicine diagnoses has becoming a hot topic in TCM and computer communities with recent progress of electronic and computer technology [15]. “Differentiation of syndromes by observing eyes” is one kind of diagnosis by looking into eyes, which searching the changing of the Sclera-conjunctiva region and the state of its vessel. This diagnosis method collects the features of Sclera-conjunctiva (especially the vessel feature) to discriminate the diseases in the whole body. Fig 1.1 shows the patient’s eye diagnosed by “Differentiation of syndromes by observing eyes” Method in TCM.

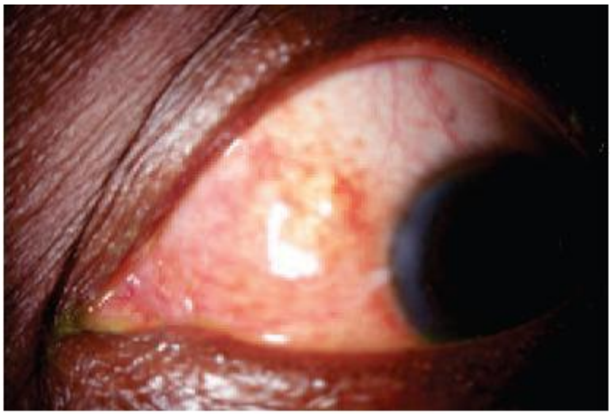

Fig 1.1 The patient's eye diagnosed by "Differentiation of syndromes by observing eyes" Method in TCM

The digitalization of "Differentiation of syndromes by observing eyes" can help to build an objective and quantitative diagnostic standard for TCM [15].

In recent researches, there are a lot of methods applied in medical image processing, such as edge detection, region growing, mathematical analyze, snakes, level-sets and so on. Particularly, in blood vessel extraction, ZHU Guidong et al. proposed an automatic vessel extraction for Sclera-conjunctiva images based on exploratory tracking [16], which successfully isolate the Sclera-conjunctiva region and extract the blood vessels in it. However, it is lack of supporting the reconstruction of information of blood vessels.

Vessel segmentation is very important in an automatic processing system for Sclera-conjunctiva images. Incomplete vessel removal usually causes a false positive in detection. Paripurana et al. proposed a segmentation method based on fractal dimension in spatial-frequency domain [17].

T. Pappas and J. Lim [18] proposed a window based method, which involves looking at a small region of the image and extracting possible blood vessel pixels based on local image characteristics. It was done in the mapping of arteries in angiograms. A model was created for blood vessel densitometry and matched to regions of angiograms to determine blood vessel location as well as diameter and cross-sectional area.

S. Chaudhuri et al [19] attemptted to match the gray-scale intensities of regions of a retinal image to a Gaussian profile and thereby locate the blood vessels.

A. Pinz et al [20] proposed edge detection method, in which parallel edges were connected and identified as blood vessels.

Pattern recognition is utilized to eliminate spurious blood vessels [21].

However, while success has been achieved on normal retinal images, on abnormal or diseased images - for which accuracy is more crucial than ever - the algorithms frequently fail. For instance, popular convolution approaches suffer from variable retinal background and low contrast between vessels and surrounding pixels. Tracking algorithms fail in special cases on abnormal images; they are often sidetracked by light objects and sometimes experience difficulty locating starting points. Current levels of success are still frequently inadequate for wide scale implementation [22].

Also, there is not so much researches focus on establishing digital vessel model applied on TCM diagnosis. Like ZHU’s research, he proposed an automatic vessel extraction, however, lack of enough support for digitization of the extracted vessel data [16].

In this paper, we propose a scanning method for extracting the blood vessels successfully, and give an original solution for pseudo vessel removal in order to decrease the false positive in detection. We also propose a digital vessel model by using several setting feature parameters for reconstructing the blood vessel, which can be used in further medical researches.

1.4 Main research content of the thesis

The LASCA imaging can provide the high spatial and temporal resolution to the living specimen biology micro-cycle blood stream system for the real-time entire audience imaging. Because it has the merits of non-contact, non-wound and fast imaging processing, the LASCA imaging technology is suitable extremely for the blood micro-cycle survey, survey of the blood vessel calibration, the blood vessel density and any other micro-cycle parameters such as speed of blood flow and blood stream irrigation [23]. When the LASCA imaging technology is used, because the detail information of initial image is not easy to distinguish, we have to use the time-variable speckle imaging based on the space statistical method or the space statistical analysis to maintain the image during eliminating spot noise from the detail information. Because the time cost of spatial statistical method is large, and the spatial cost in time statistical method also takes in a big way, therefore, how to use the few frame number of the initial image to obtain a clearer real imaging picture becomes an important research topic in medical image domain. The thesis proposes the LASCA imaging method, and also proposes an original de-noising method correspondingly based on combining several filters and wavelet fusion method in order to represent a complete blood vessel imaging and processing method.

In blood vessel image characteristic extraction aspect, in view of the fact that at present on eye blood vessel extraction, some researchers has already proposed method based on the tracking, and gave good solution of white eyeball region extraction and blood vessel extraction in white ball region. However, as the valuable diagnosis essential method of “Differentiation of syndromes by observing eyes” in the Chinese medicine, it is still lacked of the dialogue eyeball area blood vessel image complete parameterization and the numerical description. Our thesis proposes the blood vessel extraction and the reconstruction method in order to do some contribution on this field.

The thesis mainly has conducted the research on the below contents: Based on Hybrid De-noising a research on the blood vessel LASCA imaging de-noising method; Based on wavelet fusion a research on the blood vessel LASCA imaging de-noising method; Research on blood vessel extraction and reproduction method of white eyeball region.

1. Based on Hybrid De-noising a research on the blood vessel LASCA images de-noising method

A de-noising approach is proposed that based on the combination of wiener filtering, nonlinear filtering and fusion of wavelet, which de-noise the LASCA (Laser Speckle Contrast Analysis) image of blood vessels in Small Animal. The approach first performs laser spectral contrast analysis on cerebral blood flow and brain blood flow in rats, and gets their spatial and temporal contrast images. Then, a de-noising filtering method is proposed to deal with noise in LASCA. The image restoration is achieved by applying the proposed admixture filtering, and the subjective estimation and objective estimation are given to the de-noising images.

2. Based on wavelet fusion a research on the blood vessel LASCA images de-noising method

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3. Research on blood vessel extraction and reproduction method of white eyeball region

Moreover, the edge feature parameters are gained, which can be used to reconstruct the blood vessels. Experimental results show that the algorithms can obtain blood vessels information fast and accurately.

Our research presents 1) algorithms for blood vessels extraction in sclera-conjunctiva images, which can be applied in syndrome differentiation by observing human eyes (named Ocular Diagnostic in Traditional Chinese Medicine); 2) digitization of extracted vessels. First, sclera-conjunctiva region is isolated by optimal threshold segmentation and mathematical operation; Scanning and edge detection methods are used to gain the edge of the blood vessels.

Our work is to convert those sclera-conjunctive image into greyscale image and finally to binary image. After that, the digitization method will be applied to gain the parameters of attributes of blood vessels. Those result will greatly help the diagnosis of "Differentiation of syndromes by observing eyes" --- which is a traditional medicine in China.

Chapter 2 Laser speckle contrast imaging

2.1 The Principle of Laser Speckle Contrast Imaging (LSCI)

The use of Laser speckle contrast imaging technique for monitoring blood stream's variation is actually through the establishment of mathematical model, to obtain the related statistics relation between blood stream speed and the laser speckle image. When laser light illuminates a diffuse surface, the high coherence of the light produces a random interference effect known as laser speckle. The properties of laser speckle can only be described statistically. When an object moves, the speckle pattern it produces changes. This phenomenon has come to be known as "time-varying speckle"[24].

The main scatterer in blood vessel is the red blood cells with diameter from 5 mm to 8 mm [25]. The flowing of red blood cells has reflected the change of blood stream, therefore, the undulation of speckle intensity can reflect the variation of blood stream speed. It is considered that speckle contrast is related with blood stream speed. Speckle contrast is defined as the ratio of standard deviation of speckle luminous intensity to average intensity (as Formula 2.1 shown), which is a physical quantity to describe the relative undulation of speckle luminous intensity.

The movement of scatterer causes the variation of speckle pattern. This kind of variation of the speckle pattern is a stochastic process of ergodicity. The temporal statistical property of intensity change in any point of space is consistent with the spatial statistical property of intensity change of neighbourhood of the point in a certain time.

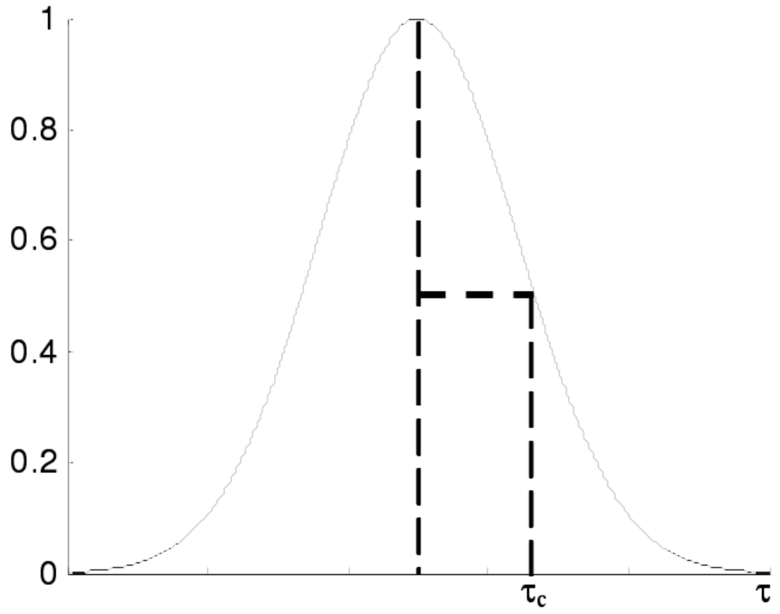


Fig 2.1 Self-correlation function of the time-varying signal

The luminous intensity measured by the detector is the integral of luminous intensity in the detector exposure time. The movement of scatterer will cause the speckle pattern fuzzy. The bigger the movement speed, the bigger the fuzzy degree. When the movement speed tends to infinite, the intensity of each point will tend to be consistent.

A parameter C --- speckle contrast from spatial statistics field is used to describe the fuzzy degree. Speckle contrast C is defined as the ratio of standard variance σ to the mean value I of intensity:

$$C = \frac{\sigma}{\langle I \rangle} \qquad (2.1)$$

Supposes luminous intensity causes by the scattered along with the time variation undulation is I(t), then its self-correlation function G (τ) may be indicated by the equation below:

$$G(\tau) = \int I(t) I(t+\tau) dt \qquad (2.2)$$

The related time c_τ defines as time independent variable τ for the speckle luminous intensity normalization correlation coefficient falls to 0.5, as shown in Figure 2.1. Thus, the macroscopic movement of scatterer can be expressed by the size of self-correlation time c_τ.

If the average speed of movement is quick, the curves in Fig 2.1 drop quickly, the corresponding related time is smaller. Otherwise, the related time is bigger. Therefore, the related time c_τ has an inverse relation with average speed of scatterer movement u, which can be defined as:

$$u = k / \tau_c \qquad (2.3)$$

Factor k is decided by different speed distributed model. Based on Goodman et al. in early work of speckle statistics [20], the spatial variation of time-varying speckle intensity σ s can be inferred, as well as self-correlation function of light intensity fluctuation:

$$\sigma_s^2(T) = \frac{1}{T} \int_0^T C_t(\tau) d\tau \qquad (2.4)$$

T is the CCD exposure time, $C_t(\tau)$ represents the single speckle luminous intensity in the time self-correlation function.

Here, self-correlation function defines as $C_t(\tau) = \left\langle \left(I(t) - \langle I \rangle_t\right)\left(I(t+\tau) - \langle I \rangle_t\right) \right\rangle_t$, $<>_t$ which expresses the speckle luminous intensity in the time average, and suppose it obeys Lorentz distribution along with the time variation distribution [26], then between the self-covariance function and the correlation time the following negative exponent relations can be established [27]:

$$C_t(\tau) = \langle I \rangle_t^2 \exp(-2\tau / \tau_c) \qquad (2.5)$$

τ_c is defined as:

$$\tau_c = \frac{1}{ak_0 v} \qquad (2.6)$$

v is the average speed, k0 is the laser wave number, a is one factor relies on the Lorentz width and the organization scattering parameter[28].

Formula (2.4) establishes the relation between the laser Doppler speed measuring technique and the laser speckle speed measuring technique [29]. Substitutes (2.5) in (2.4), we can obtain

$$\sigma_s^2(T) = \left(\langle I \rangle_t^2 / T\right) \int_0^T \exp(-2\tau / \tau_c)\, d\tau \qquad (2.7)$$

Removes the sign of integration:

$$\sigma_s^2(T) = \left(\langle I \rangle_t^2 \tau_c / 2T\right)\left[1 - \exp(-2T / \tau_c)\right] \qquad (2.8)$$

From the definition of speckle contrast (ratio of correlation time to integration time), we can obtain

$$K = \frac{\sigma_s}{\langle I \rangle} = \left[\frac{\tau_c}{2T}\left\{1 - \exp\left(\frac{-2T}{\tau_c}\right)\right\}\right]^{\frac{1}{2}} \qquad (2.9)$$

Therefore, the above equation represents the relation between spatial contrast and correlation time [28]. Using the above equation, we can draw a relational curve of the spatial contrast value and T/τ_c, as shown in Fig 2.2.

Because T/τ_c is related with the speed of scatterer movement, therefore, this figure is also representing the relation between the spatial contrast value and the scatterer speed.

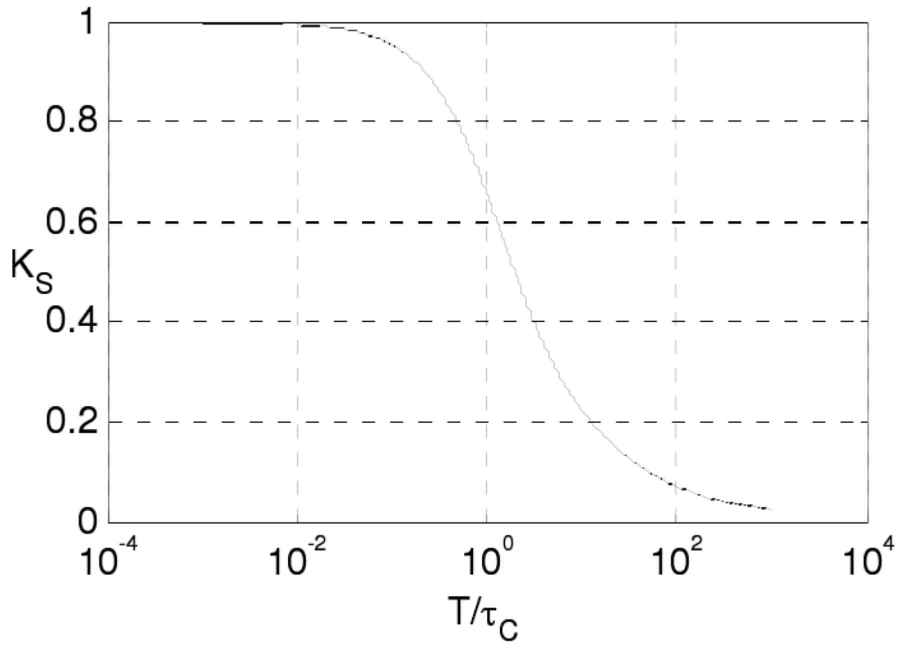


Fig 2.2 Plot of spatial contrast and T/τ_c

Using CCD to gather the laser speckle images, and carries on 1st order spatial statistics to the speckle images (i.e. spatial contrast statistics), can gain speckle contrast value of each pixel by using formula (2.1). Then carry on the Newton iterative computation to (2.9) to compute related time τ_c, and substitutes to formula (2.6), finally can gain the average speed distribution. Therefore, take the correlation time τ_c as the bridge, relation between the laser speckle contrast and the speed can be established.

Although the above formulas theoretically can calculate the absolute value of average speed u, factor k in the formula (2.3) relies on the different speed distributed model. The following factors are needed to consider in order to establish different speed distribution model: the blood vessel caliber sizes, the blood vessel type, the speed of flow distribution model, multiple scattering of the coherent light, influence of the static organization diffused light, the organization optics parameter influence, the size and shape influence of the scattering (blood corpuscle), the non-Newtonian flow phantom, the non-Gaussian statistics of small number of scatterers, scatterer revolving and so on. So many influence factors cause it difficult to establish accurate speed distribution model, therefore, the absolute value of speed is also difficult to be determined [30]. However, in most clinical practices, the relative variation quantity is more important, such as the research on response of blood stream circulation for exterior stimulation. Especially, the relative variation quantity can reduce the noise and other element of certain influence.

2.2 Spatial LASCA (Spatial LAser Speckle Contrast Analysis)

The LSCI uses 1st order spatial statistical analysis, the following will introduce the spatial statistical analysis algorithm first. Through the LASCA image, the key of computing speed distribution is 1st order spatial statistics of speckle image. The time-varying speckle image spatial statistical method was proposed in the beginning of 1980s by Briers [27][31][32]. The 1st order spatial statistics of laser speckle contrast performs on the partial image (sub-graph, or statistical window), and transforms into the pseudo color image [33][34][35]. Suppose there is an $M \times N$ pixel image, in the image the grey level of the random point (x, y) is I (x, y). The grayscale level is decided by the CCD camera. In this paper it is 12 bits, then $I(x, y) \in [0\sim4095]$, the speckle image may be represented as

$$F = I(x, y) \qquad x = 1,2,...,M; \quad y = 1,2,...,N$$

Performing 1st order statistics processing to the speckle image to obtain the speckle contrast ratio function directly

$$C(x', y') = L(I(x, y)) \quad x' \leqslant M; \quad y' \leqslant N$$

x ', y ' are the different value according to the statistical method, L is the partial image element speckle contrast computation function, which is defined as the computation on the neighbourhood of (x, y). The neighbourhood is defined as a sub image whose central point is (x,y) and the size is the $O \times P$. Usually, choose a $O = P$

=m square as neighbourhood, the size of sub image as m2 pixel. A laser speckle 1st order spatial statistical method calculates the sub image contrast value. The average value and the standard variance of sub image are separately defined as

$$\bar{I}(x',y') = \frac{\sum_{a=-m/2}^{m/2}\sum_{b=-m/2}^{m/2} I(x+a,y+b)}{m^2} \tag{2.10}$$

$$\sigma(x',y') = \sqrt{\frac{\sum_{a=-m/2}^{m/2}\sum_{b=-m/2}^{m/2}\left(I(x+a,y+b)-\bar{I}\right)^2}{m^2}} \tag{2.11}$$

Then the contrast value

$$C(x',y') = \frac{\sigma(x',y')}{\bar{I}(x',y')} \tag{2.12}$$

To calculate C(x',y'), the mask (sub-image) moves from left-top of the image. For each step, compute the contrast value in the central point of sub-image.

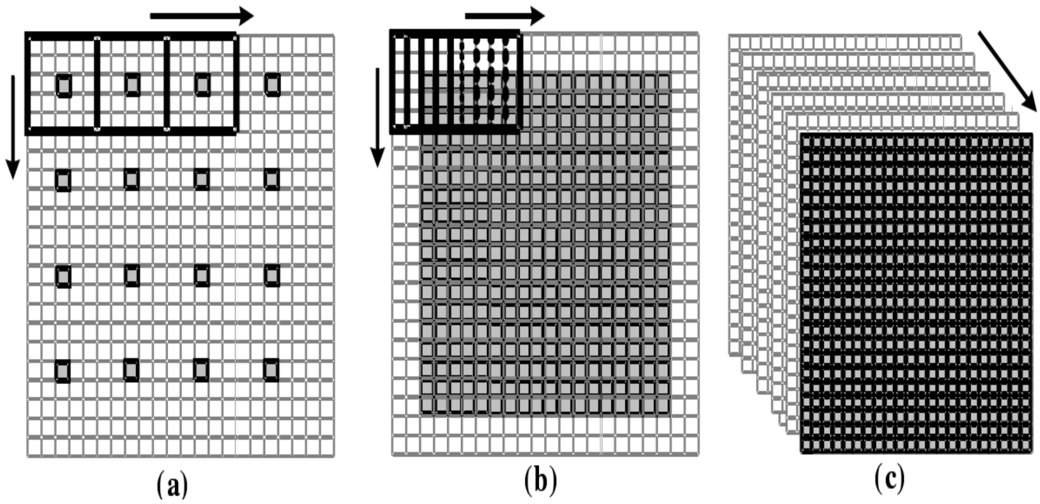


Fig 2.3 Spatial and temporal statistical processing of speckle image. Each minimal block in the images represents one pixel. Bold-type large block consists several pixels is sub-image. For example, one sub-image consists of 5×5 pixels. The minimal block filled by gray located in the center of sub-image represents the post-processing pixel (contrast in spatial statistical processing).Arrows indicate the statistical processing directions.(a)is spatial statistical processing method;(b)is modified spatial statistical processing method and(c)is temporal statistical processing method

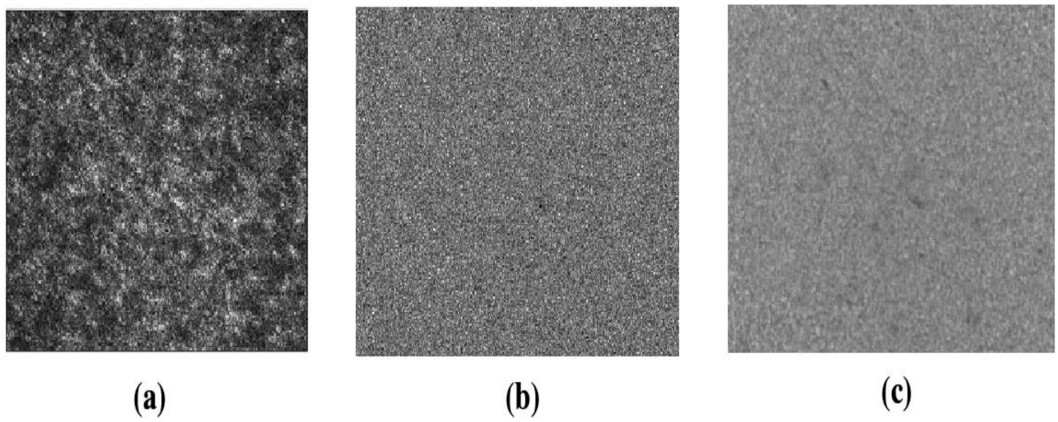


Fig 2.4 Speckle images of static rough surface of white paper.(a)origin speckle image (b) speckle contrast image after spatial statistical processing by 3×3 sub-image;(c)speckle contrast image after spatial statistical processing by 11×11 sub-image

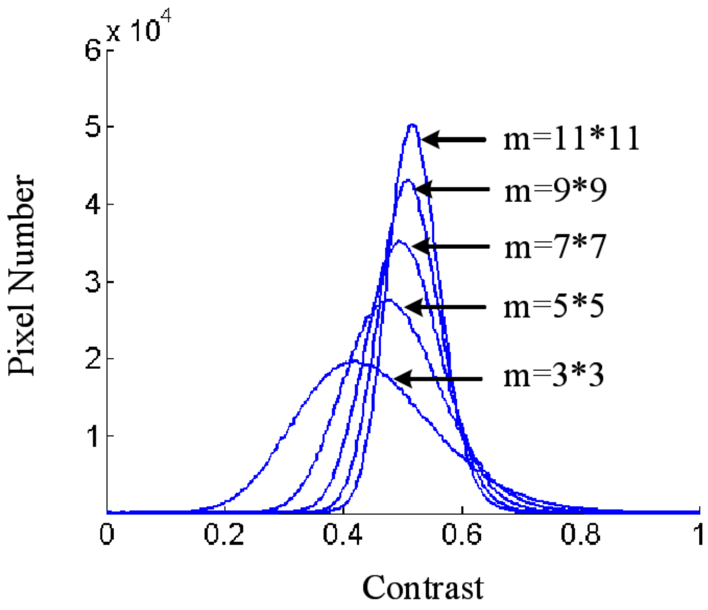


Fig 2.5 Speckle contrast variation during the different pixels size sub-images processing. m is pixel number of sub-image. Each curve represents contrast histograms.

In practical application, it is found that the size choice affects the result of speckle contrast very much. Fig 2.4 shows speckle images of static rough surface of white paper. Using different size of masks and some results are shown as Fig 2.4(b) and (c). Fig 2.5 shows speckle contrast variation during the different pixels size sub-images processing (3×3,5×5,7×7,9×9 and 11×11).

The choice of the number of pixels over which to compute the speckle contrast is important: too few pixels and the statistics will be compromised, too many and spatial resolution is sacrificed. In practice, it is found that a square of 7×7 or 5×5 pixels is usually a satisfactory compromise. (A square with sides of an odd number of pixels was chosen so that the computed contrast could be assigned to the central pixel.)

2.3 Temporal LASCA (Temporal LAser Speckle Contrast Analysis)

Temporal LASCA was firstly proposed by Ohtsubo and Asakura in 1976[36]. At that time only using the following formula to calculate the speed of a single point:

$$N_t = \frac{<I^2> - <I>^2}{<I>^2} \qquad (2.13)$$

$<I>$ and $<I^2>$ are time average and time mean square value of the time-varying speckle intensity in time t. Then Nt is inverse ratio with the scatterer speed. Serov applied this method on the laser Doppler's irrigation image formation, and used the CMOS for fast imaging, and achieved 9000 pps[37]; Cheng applied this method on the laser speckle imaging for temporal statistics processing to obtain the two-dimensional imaging of the blood stream distribution, using the following formula to calculate each point on m frames image [38]

$$V_{i,j} = \frac{<I_{i,j,t}>_t^2}{<I_{i,j,t}^2> - <I_{i,j,t}>_t^2} \qquad (2.14)$$

Ii,j,t is intensity value of the t-th frame on the i-th and the j-th point. Calculate their time average and the time mean square value separately. Temporal statistics schematic is shown in Fig 2.3(c). As same as spatial LASCA, the speed of flow model is very complicate, it is also unable to give the precise speed of flow model at present, therefore, V i, j is only the relatively average velocity.

2.4 Laser speckle contrast imaging system and experimental results

2.4.1 LSCI system

The schematic setup for the experiment is shown in Fig 2.6. A rat was anesthetized and fixed in a stereotaxic instrument. An approximately 5.0 ×5.0-mm cranial window with intact dura was formed by removing the skull overlying one side of the parietal cortex with a high speed dental drill (Fine Science Tools, USA) under constant saline cooling. A beam of He-Ne laser (Melles Griot,America; 632.8 nm and 15 mW) was expanded and collimated to illuminate the cranial window at about 30-deg incidence. 30 frames of statistically independent laser speckle images were acquired by a 12-bit charge-coupled device (CCD) camera (PixelFly QE, PCO Computer, Germany; pixel size =6.45×6.45 μm) attached to a microscope (Z16 APO,Leica, Germany; working distance 97 mm)for data processing.The CCD exposure duration was 20 ms and the frame interval time is approximately 87 ms. The system magnification is adjusted to 3.15×, and the aperture diaphragm is well controlled to ensure the average speckle size of the images to be approximately two pixels. A variable attenuator was used in the light path to ensure the light intensity within the dynamic range of the CCD camera. The whole setup was placed on a vibration-isolator table (VH3036W, Newport)

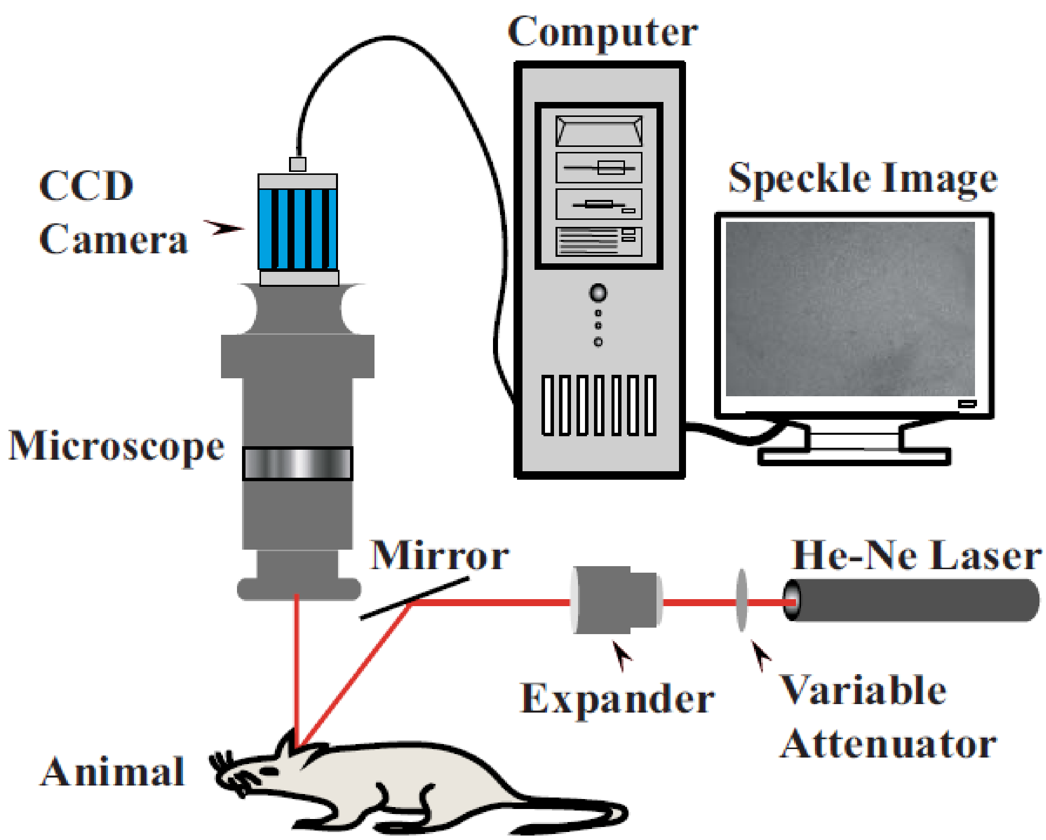


Fig 2.6　Scheme of laser speckle contrast imaging system.

System constituted by laser light source, microscope, CCD camera and computer.

The experimental setup for laser speckle contrast imaging is very simple. Diverging laser light illuminates the object under investigation, which is imaged by a CCD camera (or equivalent). The image is captured by a frame grabber (or equivalent) and the data passed to a personal computer for processing by custom software.

2.4.2 Spatial LASCA and Temporal LASCA

As illustrated in Fig. 2.7, the laser speckle contrast analysis can be performed based on spatial statistics and temporal statistics. The spatial LASCA performs speckle contrast calculation in the spatial domain using a spatial window. It achieves high temporal resolution with the loss of spatial resolution, impeding its application on monitoring blood flow changes in small vessels. The temporal LASCA method, which is based on temporal statistics, computes speckle contrast images using a sequence of speckle images acquired along a few time points instead of using a spatial window. It preserves the original spatial resolution by sacrificing the temporal resolution, making it inappropriate in applications where video frame rate visualization of blood flow is required.

2.4.3 Application of LASCA on blood vessel images of small animal

From Fig 2.8 to Fig 2.10, it shows the spatial, temporal (10 Frames) and temporal (100 Frames) LASCA images, respectively. TABLE 2.1 shows objective estimation between spatial and temporal LASCA with Base Image.

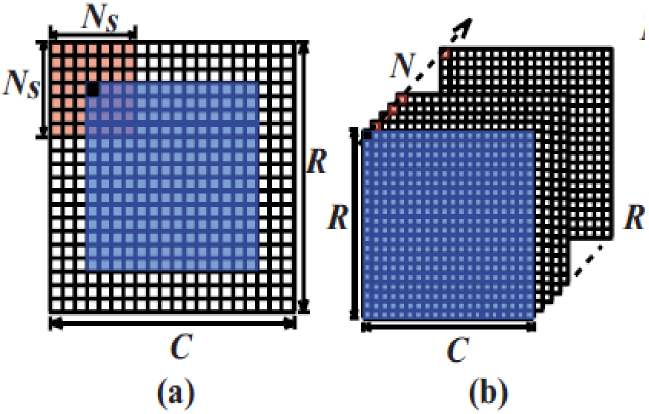


Fig 2.7 (a) Spatial LASCA and (b) Temporal LASCA

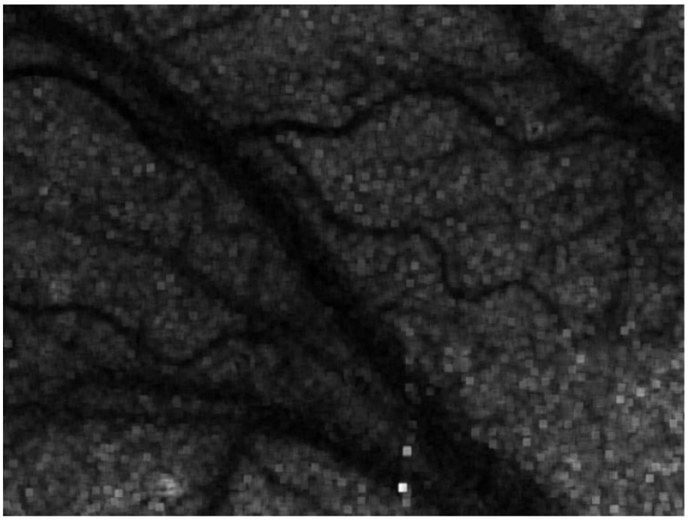


Fig 2.8 spatial LASCA

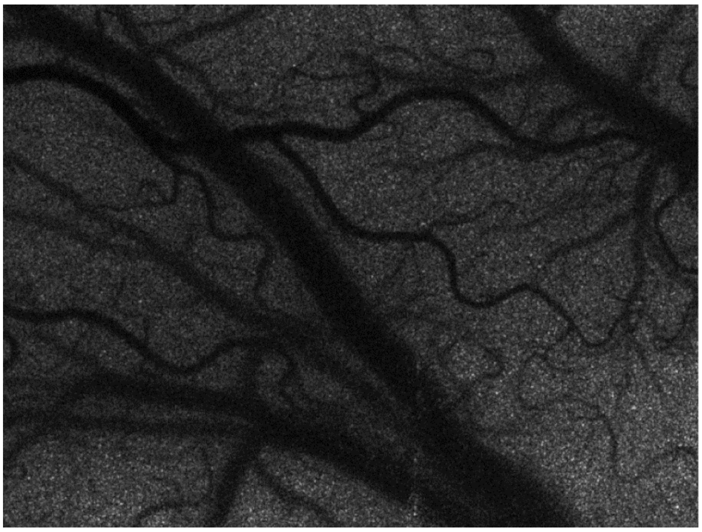


Fig 2.9 temporal LASCA 10 Frames

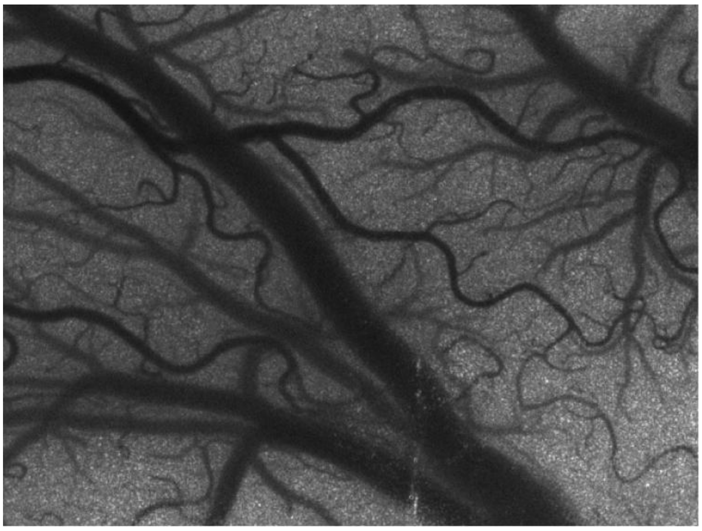


Fig 2. 2 temporal LASCA 100Frames (Base Image)

TABLE 2.1 Objective Estimation between spatial and temporal LASCA with Base Image

	Spatial LASCA	Temporal LASCA (10Frames)
MSE	0.14349	0.12686
SNR	1.5838	1.4046
PSNR	15.964	16.304

2.5 Conclusions

This chapter discussed the principle and the method of the laser speckle contrast imaging, introduced laser speckle contrast imaging system using in this thesis's research. Using this laser speckle contrast imaging system, we proposed a LASCA experiment on the big mouse model based on the spatial statistical method and the temporal statistical method. The result indicated that,

1. States two kinds of LASCA methods used in this chapter to be possible to obtain the spatial LASCA image and temporal LASCA image. Those two kinds of image contrast principles are proved to be correct and feasible.

2. The objective evaluation of spatial LASCA and temporal LASCA explained that, surpasses certain frame, the latter processing effect surpasses the former.

3. Using two kinds of LASCA methods, the obtained images both include the noise signal. The de-noising processing is needed.

Chapter 3 Proposed De-noising Methods on LASCA Images of Blood Vessels

3.1 Wiener, Nonlinear (Order-Statistic) and Wavelet Filtering

The inverse filtering is a restoration technique for de-convolution, i.e., when the image is blurred by a known low-pass filter, it is possible to recover the image by inverse filtering or generalized inverse filtering. However, inverse filtering is very sensitive to additive noise. The approach of reducing one degradation at a time allows us to develop a restoration algorithm for each type of degradation and simply combine them. The Wiener filtering executes an optimal tradeoff between inverse filtering and noise smoothing. It removes the additive noise and inverts the blurring simultaneously. The Wiener filtering is optimal in terms of the mean square error. In other words, it minimizes the overall mean square error in the process of inverse filtering and noise smoothing. The Wiener filtering is a linear estimation of the original image. The approach is based on a stochastic framework.

The wiener filter performs lowpass-filter on a greyscale image that has been degraded by constant power additive noise. It uses a pixelwise adaptive wiener method based on statistics estimated from a local neighbourhood of each pixel.

The detail is shown as below:

It estimates the local mean and variance around each pixel.

$$\mu = \frac{1}{NM} \sum_{n_1, n_2 \in \eta} a(n_1, n_2)$$

and

$$\sigma^2 = \frac{1}{NM} \sum_{n_1, n_2 \in \eta} a^2(n_1, n_2) - \mu^2 ,$$

where η is the N-by-M local neighbourhood of each pixel in the image.

The method applies to an image adaptively, tailoring itself to the local image variance. Where the variance is large, wiener filter performs little smoothing. Where the variance is small, wiener filter performs more smoothing.

The merit and limitation of Wiener filter is that [39]:

This approach often produces better results than linear filtering. It is more selective than a comparable linear filter, preserving edges and other high-frequency parts of an image. Wiener filter, however, does require more computation time than linear filtering. Wiener filter works best when the noise is constant-power ("white") additive noise, such as Gaussian noise.

A nonlinear filter is a signal-processing device whose output is not a linear function of its input. Terminology concerning the filtering problem may refer to the time domain (state space) showing of the signal or to the frequency domain representation of the signal. When referring to filters with adjectives such as "band-pass, high-pass, and low-pass" one has in mind the frequency domain. When resorting to terms like "additive noise", one has in mind the time domain, since the noise that is to be added to the signal is added in the state space representation of the signal. The state space representation is more general and is used for the advanced formulation of the filtering problem as a mathematical problem in probability and statistics of stochastic processes.

Order-statistic filter as a famous and frequently used nonlinear filter, was firstly introduced by Bovik et al. [40]. In his work, the signal is assumed to be a constant and the noise statistics are known. Thus a set of optimal coefficients of the order-statistic filter can be derived in terms of the correlation matrix of the noise. However, the limitation is that the methodrequires at least one clean reference image, otherwise the results have been shown to be even worse than a straightforward median or Gaussian filter [41].

The wavelet filter is good at removing Gaussian-type noise, while it can leave some kind of photon noise (very hot pixels for example). Thus an option is provided in the form of an optional adaptive median filter. This filter will detect pixels that differ from their context by more than a given multiple of the neighbourhood's standard deviation. If marked as outlying, the pixel value is replaced by the median value of the neighbourhood. A suggested default value is 1.6 * sd. The idea behind this filter is that if an adequate sampling was chosen upon acquisition, no such outlying (extreme value) pixels should be found.

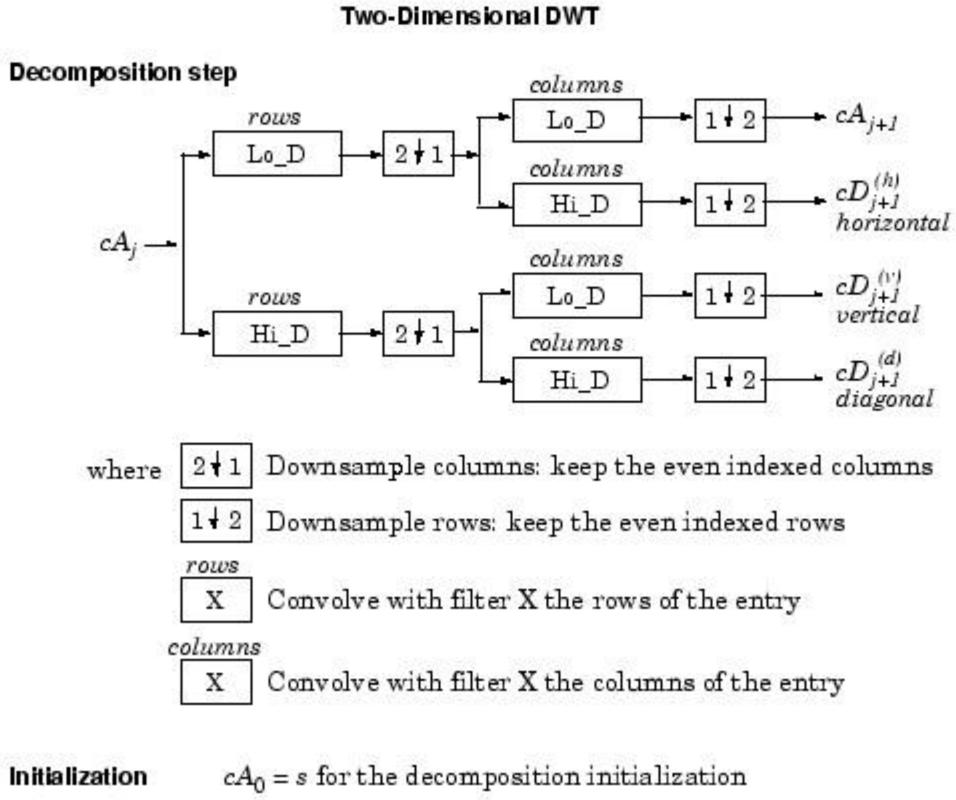
The general wavelet de-nosing filter procedure is as follows:

(1)Apply wavelet transform to the noisy signal to produce the noisy wavelet coefficients to the level which we can properly distinguish the PD occurrence.

(2)Select appropriate threshold limit at each level and threshold method (hard or soft thresholding) to best remove the noises.

(3)Inverse wavelet transforms of the thresholded wavelet coefficients to obtain a de-noised signal.

The following chart describes the basic decomposition step for images:



3.2 Proposed De-noising Method

3.2.1 De-noising Method using Hybrid filtering

Wiener filtering is a kind of adaptive filtering, which can effectively noise restraining and protect the edge, and is widely used in image processing. However, badly in detail discriminate, it would easily cause thin line, curve, etc lost and damaged.

The order statistics filters are designed to suppress noise of different nature, they can remove impulsive noise and guarantee detail preservation [42]. On the other hand, the filters based in the wavelet domain provide a better performance in terms of noise suppression in comparison with different space domain filters [43].

Our proposed method considers the two weak-points of wiener and order-statistic filter, cascade the two filters in proposed order to protect edge information and preserve the detail also. Moreover, we add wavelet filter for the better performance in noise suppression. The experimental results will show the reliability of our proposed method.

Based on the comparison of several filtering methods discussed above, considering their advantages, we put forward a hybrid de-noising method oriented for LASCA images, which combined with wiener, nonlinear and wavelet filtering.

The process is shown below:

(1) Apply spatial statistic analysis or temporal statistic analysis on LASI (time-varying speckle) images, to gain f01(i,j) from spatial LASCA and f02(i,j) from temporal LASCA for small number of frames (no larger than 10 frames). They are all noisy images.

(2) Perform wiener filtering on f01(i,j) (or f02(i,j)) to gain processing image fw(i,j).

(3) Perform order-statistic filtering and grayscale processing on fw(i,j) to gain fNL(i,j).

(4) Divide fNL(I,j) into 2 layers and perform wavelet transform to gain WTf1(i,j) and WTf2(i,j), then inverse transform for each. Finally, reconstruct wavelet de-nosing image ff(i,j) from those two.

(5) The result of admixture filtering is the de-noising image we gain.

The framework is shown as below.

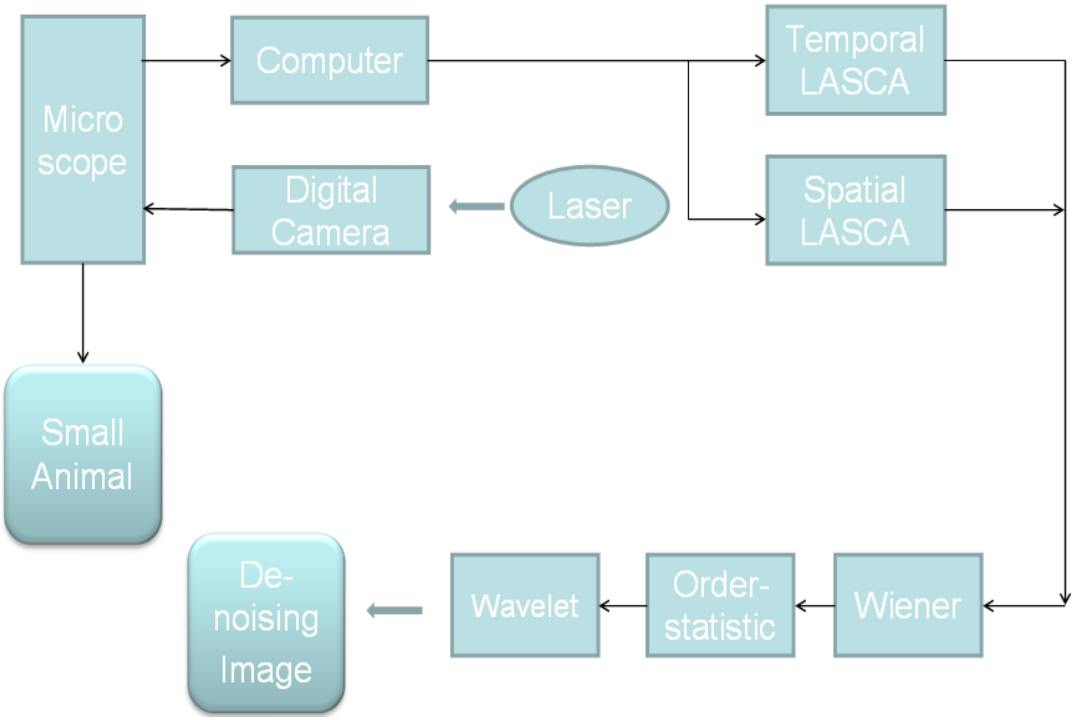


Fig 3. 1 Framework of Blood Vessel Imaging and De-noising

3.2.2 De-noising Method using wavelet Fusion

The principle of image fusion using wavelets is to merge the wavelet decompositions of the two original images using fusion methods applied to approximations coefficients and details coefficients [44].

The general method for image fusion using the wavelet decomposition is as follows [45]:

1. The wavelet decomposition of the source images is performed, having chosen the wavelet basis and the depth or level of decomposition.

2. The best trees for the images are found on the basis of some entropy-based criterion and the tree which has the greatest number of leaf nodes is chosen as the composite tree structure to be populated.

3. The wavelet coefficients are then selected from the source images according to a fusion rule to populate the tree.

4. The wavelet reconstruction of this synthetic or composite tree gives the required fused image.

Based on the comparison of several filtering methods discussed above, considering their advantages, we put forward a hybrid de-noising method oriented for LASCA images, which combined with wiener, nonlinear, wavelet filtering and image fusion.

The process is shown below:

（1）Apply spatial statistical analysis or temporal statistical analysis on LSCI (time-varying speckle) images, to gain spatial LASCA and temporal LASCA for small number of frames. They are all noising images.

（2）Perform wiener filtering, nonlinear filtering (order-statistic filtering) and luminance adjust on the noisy image.

（3）Meanwhile, perform wavelet de-noising on the same image.

（4）Fusion those two midterm results, in order to get the final de-noising image.

The framework is shown as below.

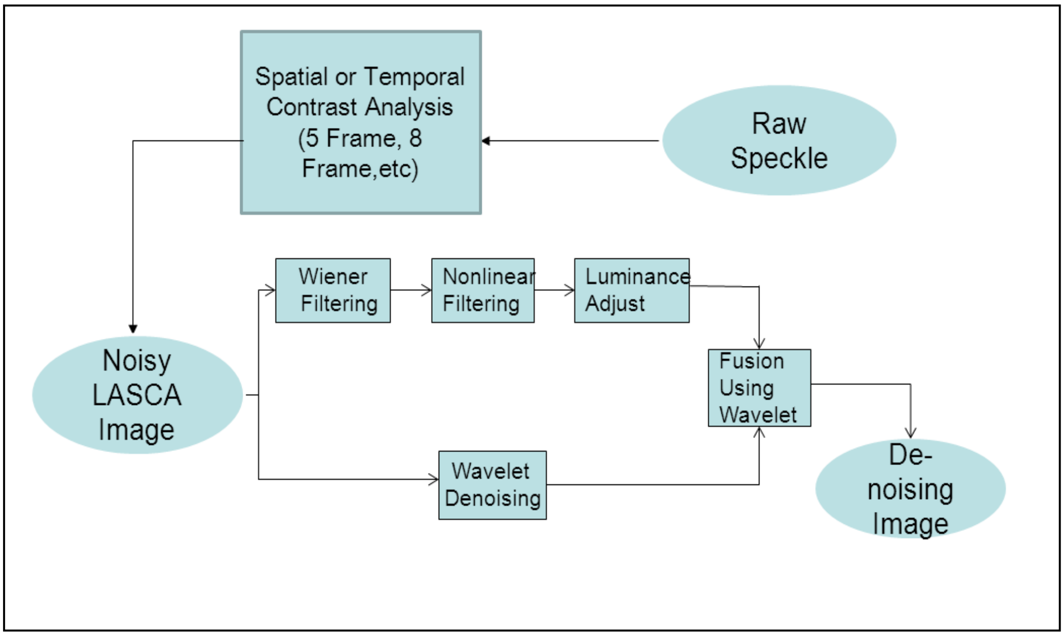


Fig 3. 2 Framework of Proposed Hybrid De-noising Method

Compared with our former method, we add image fusion using wavelet. This addition will smooth the image although increase the consuming time of process.

3.3 Evaluate Criterion

Because the Temporal Contrast Analysis (100Frames) has a fine performance, in our research, it is considered as the base image, which is used in objective estimations --- MSE, SNR and PSNR. The objective quality measurements are save time more than subjective quality measurement [46] [47]. In fact, MSE and PSNR are the most common measures of image quality in image processing [48].

The above three objective measurements are selected and used for our research study. Definition: x(m,n) denotes the base image, x^(m,n) denotes the de-noising image. M and N are number of pixels in row and column directions, respectively.

(1)Mean Square Error (MSE)

The simplest of image quality measurement is Mean Square Error (MSE). In statistics, the MSE of an estimator is one of many ways to quantify the difference between values implied by an estimator and the true values of the quantity being estimated. MSE is a risk function, corresponding to the expected value of the squared error loss or quadratic loss. MSE measures the average of the squares of the "errors." The error is the amount by which the value implied by the estimator differs from the quantity to be estimated. The large value of MSE means that image is poor quality. MSE is defined as follow:

$$MSE = \frac{1}{MN}\sum_{m=1}^{M}\sum_{n=1}^{N}\left(x(m,n)-\hat{x}(m,n)\right)^2$$

MSE represents the mean square difference between the original image and the processed image. The less the MSE value, the more approximated the processed image is with the original one. An MSE of zero, meaning that the target image is the ideal, but is practically never possible. Therefore, the MSE is usually used in image restoration. In our case, the smaller the MSE value, the de-noising performance is better.

MSE is the most basic evaluate criterion in image processing filed, although it has its weak point that it asks for the original image for comparing. In some practical cases, the original can not easily be extracted.

(2)Signal to Noise Ratio (SNR)

Signal-to-noise ratio (often abbreviated SNR or S/N) is a measure used in science and engineering to quantify how much a signal has been corrupted by noise. It is defined as the ratio of signal power to the noise power corrupting the signal. A ratio higher than 1:1 indicates more signal than noise.

SNR is defined as follow:

$$SNR = \frac{P_{signal}}{P_{noise}} ,$$

Where P is average power.

(3)Peak Signal to Noise Ratio (PSNR)

The phrase peak signal-to-noise ratio, often abbreviated PSNR, is an engineering term for the ratio between the maximum possible power of a signal and the power of corrupting noise that affects the fidelity of its representation.

The small value of Peak to Noise Ratio (PSNR) means that image is poor quality. PSNR is defined as follow:

$$PSNR = 10 \log \frac{255^2}{MSE}$$

The PSNR is most commonly used as a measure of quality of reconstruction of lossy compression codecs (e.g., for image compression). The signal in this case is the original data, and the noise is the error introduced by compression. When comparing compression codecs it is used as an approximation to human perception of reconstruction quality, therefore in some cases one reconstruction may appear to be closer to the original than another, even though it has a lower PSNR (a higher PSNR would normally indicate that the reconstruction is of higher quality).

As a part of estimation, we do in this way: mainly compare the subjective performance between the base image and our hybrid de-noising image. Also, we provide the performance of 3 single de-noising methods we apply, in order to ensure the effectiveness of our hybrid method. Three former researchers' works (Med, TV and Linear Filters) are added in our comparison at last.

Total variation de-noising (TV de-noising), also known as total variation regularization is a process, most often used in digital image processing that has applications in noise removal. It is based on the principle that signals with excessive and possibly spurious detail have high total variation, that is, the integral of the absolute gradient of the signal is high. According to this principle, reducing the total variation of the signal subject to it being a close match to the original signal, removes unwanted detail whilst preserving important details such as edges [49].

This noise removal technique has advantages over simple techniques such as linear smoothing or median filtering which reduce noise but at the same time smooth away edges to a greater or lesser degree. By contrast, total variation de-noising is remarkably effective at simultaneously preserving edges whilst smoothing away noise in flat regions, even at low signal-to-noise ratios [50].

3.4 Experimental results for Hybrid Filtering method on blood vessel

3.4.1 Experimental results for Hybrid filtering method on rat's cerebral blood vessel

From Fig 3.3 to 3.8, it shows de-noising results applied on Fig 2.8 and Fig 2.9 by using single filters --- Wiener, nonlinear and wavelet. From Fig 3.9 to 3.10, it shows the results by using our proposed filter.

For objective estimations, we choose MSE, SNR and PSNR to be criterions. In computing, the base image (temporal LASCA 100 Frames) is used to be compared with TABLE 3.1 and 3.2 show the specific data of those three.

（1） Results of Single Filtering

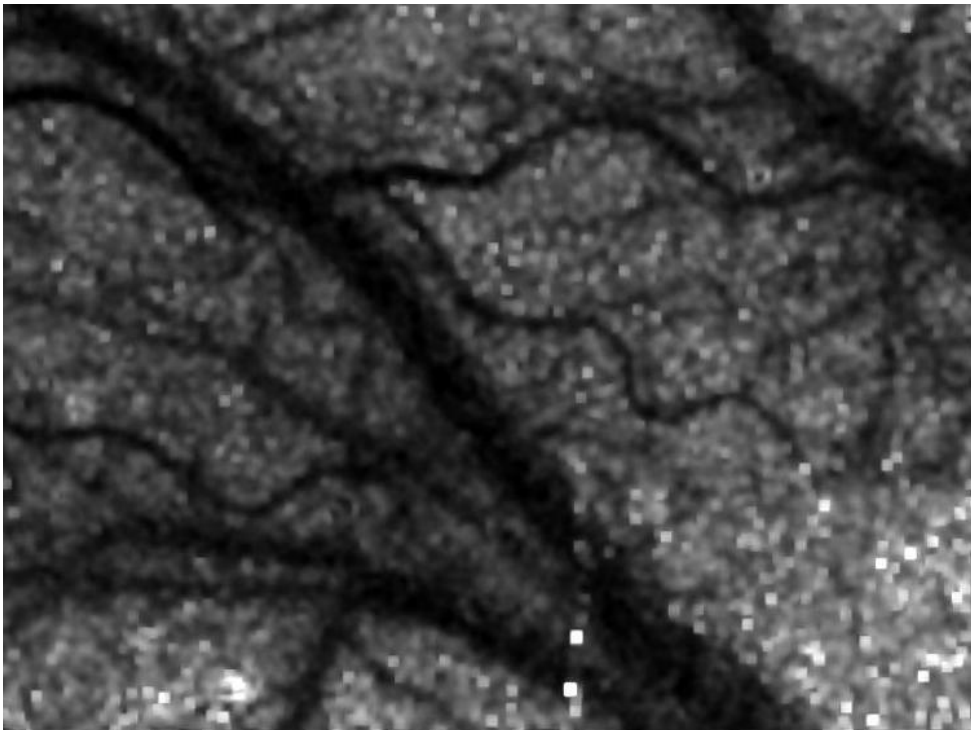


Fig 3. 3 Result for Fig 2.8(Wiener)

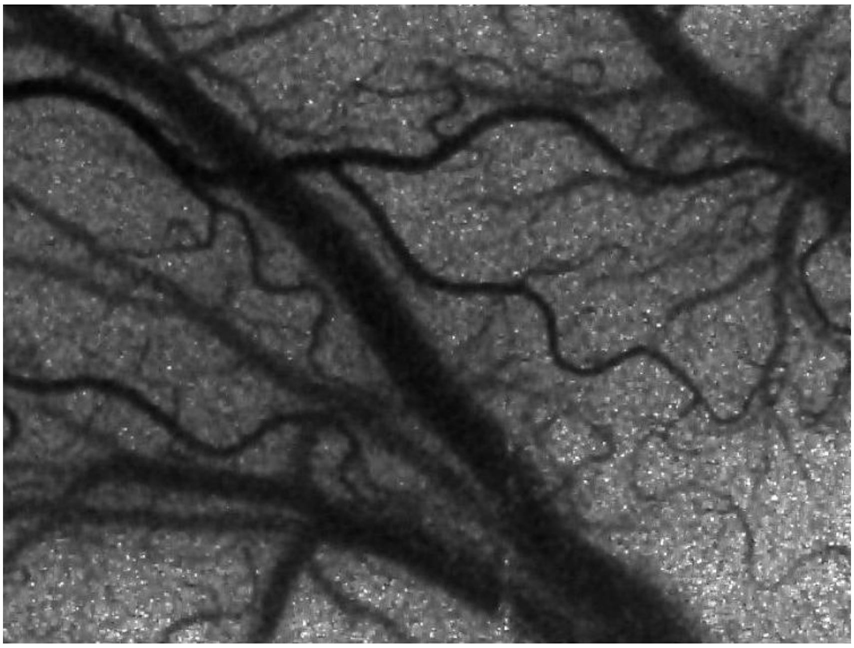


Fig 3. 4 Result for Fig 2.9(Wiener)

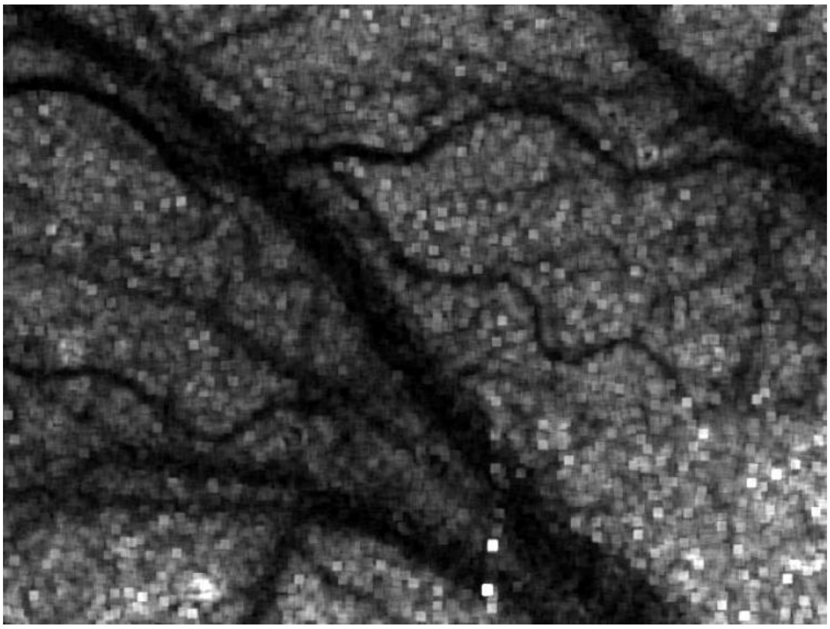


Fig 3. 5 Result for Fig 2.8(Nonlinear)

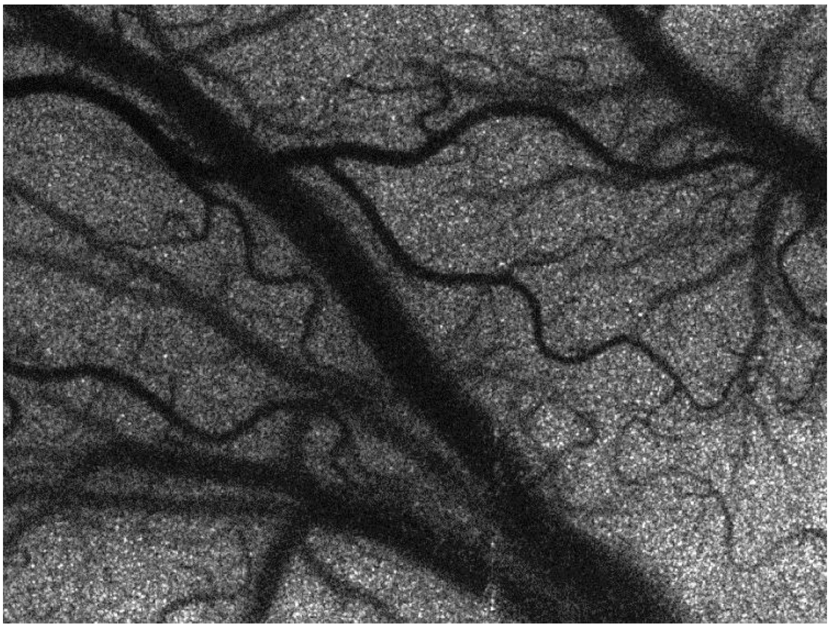


Fig 3. 6 Result for Fig 2.9(Nonlinear)

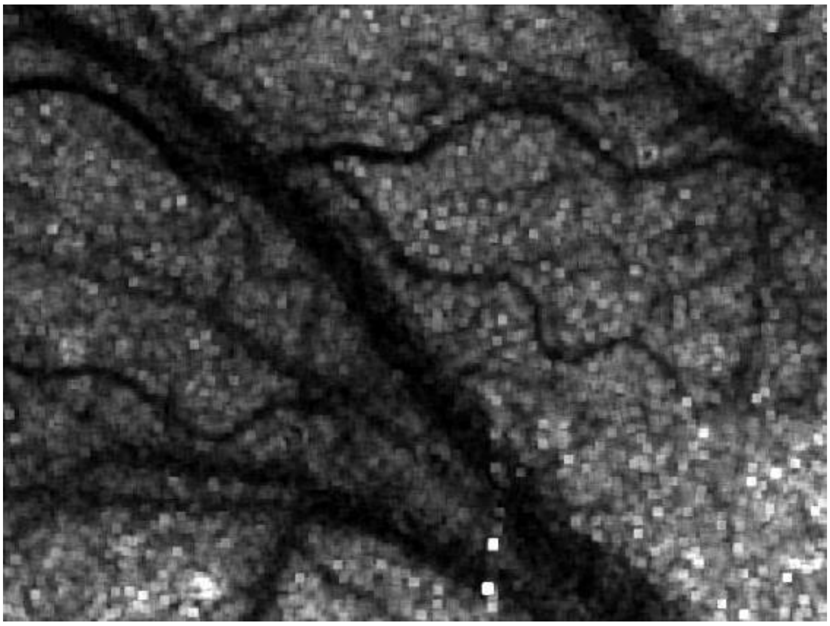


Fig 3. 7 Result for Fig 2.8(Wavelet)

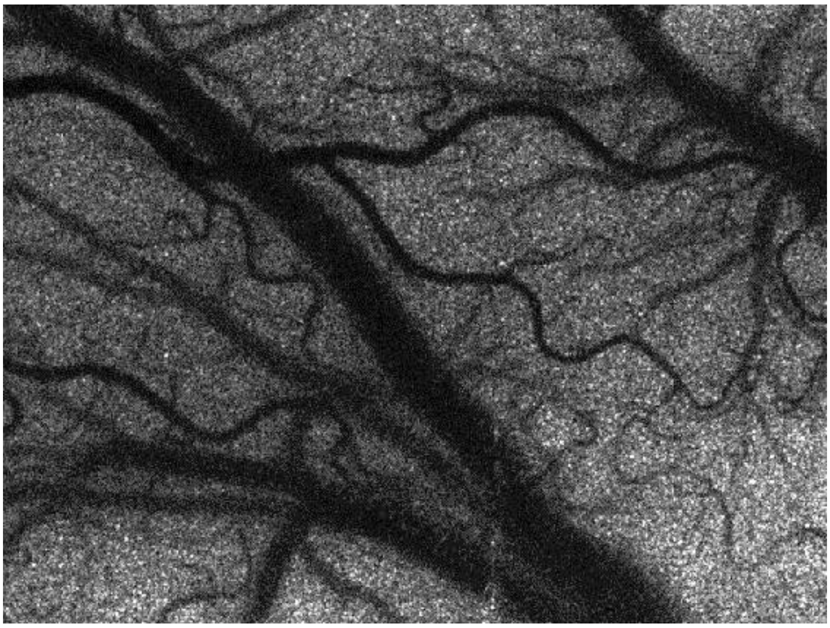


Fig 3. 8 Result for Fig 2.9(Wavelet)

（2）Result of Hybrid Filtering

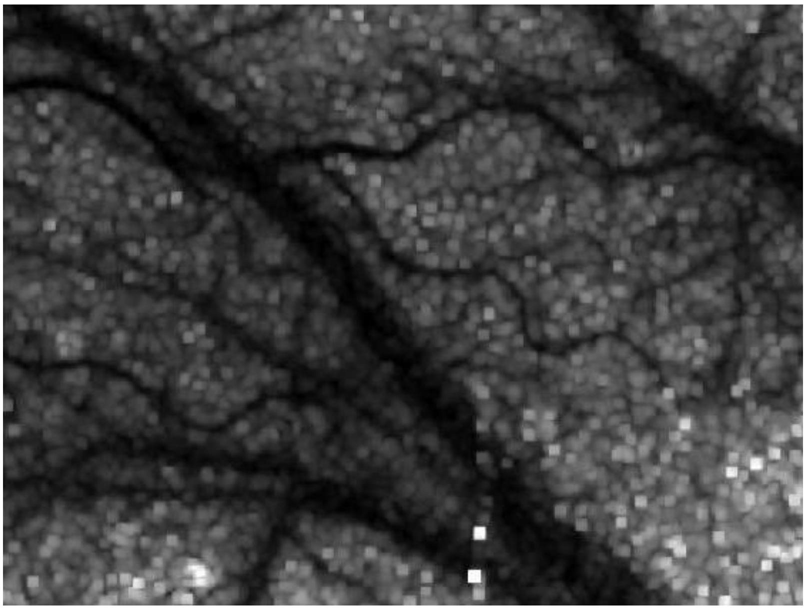


Fig 3. 9　　Result for Fig 2.8

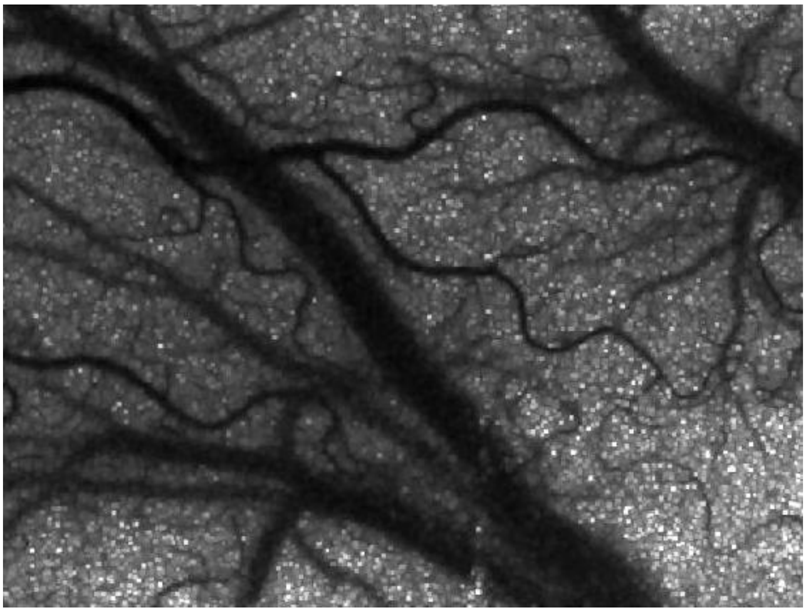


Fig 3. 10　　Result for Fig 2.9

（3）Objective Estimation for each filtering method

TABLE 3. 1 Objective estimation of Fig 2.8

	Original	Hybrid	Single		
			Wiener	Nonlinear	Wavelet
MSE	0.14349	0.016318	0.032712	0.03317	0.033109
SNR	1.5838	8.1698	9.4593	6.4932	6.5077
PSNR	15.964	20.243	18.822	20.024	20.029

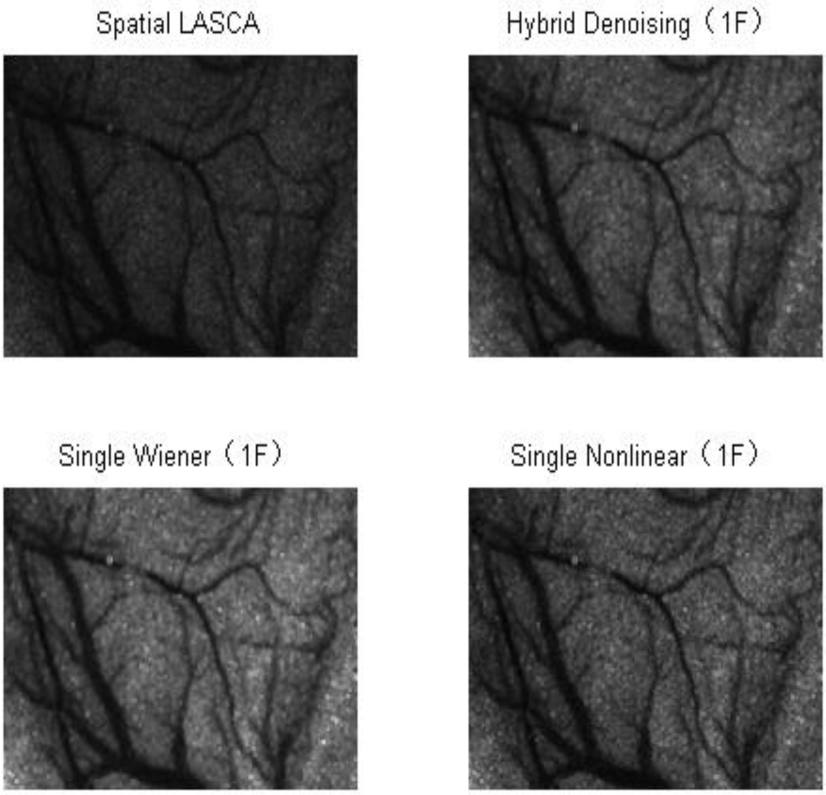
TABLE 3. 2 Objective estimation of Fig 2.9

	Original	Hybrid	Single		
			Wiener	Nonlinear	Wavelet
MSE	0.12686	0.001201	0.059582	0.0031516	0.002892
SNR	1.4046	13.3	12.655	9.0205	9.0134
PSNR	16.304	22.538	20.125	19.925	19.918

3.4.2 Experimental results for hybrid filtering method on rat's brain blood vessel

3.4.2.1Experimental results and analysis of Spatial LASCA image de-noising

We show the results of each de-noising filter in Fig 3.11--- from original (noisy LASCA image), our proposed filter to each single filter, also, we add other researcher's methods such as Linear de-noising and so on. From the widely compare, it is firmly shown that, our hybrid de-noising have the best objective performance. Moreover, TABLE 3.3 shows the specific data of objective estimations.



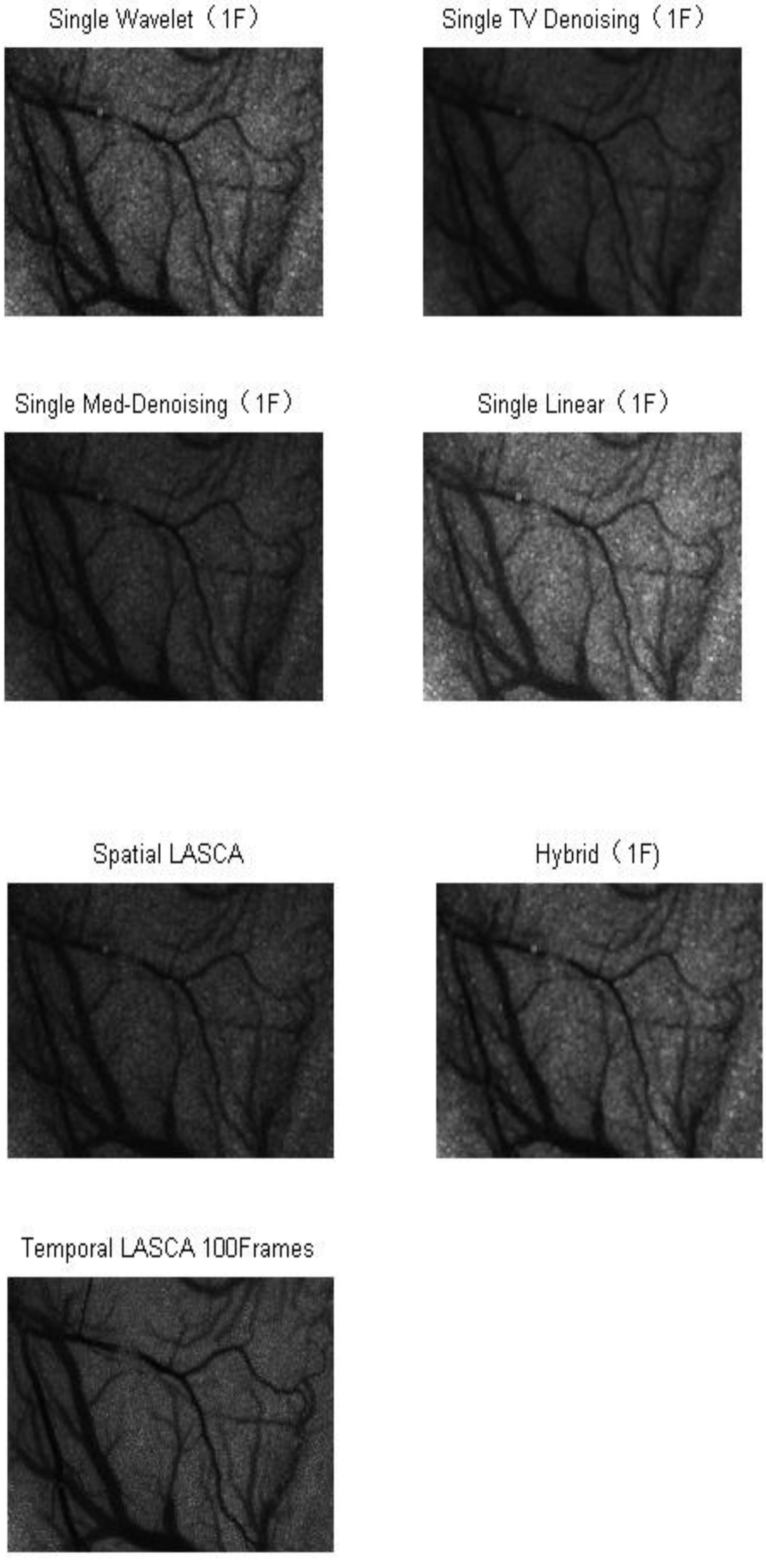


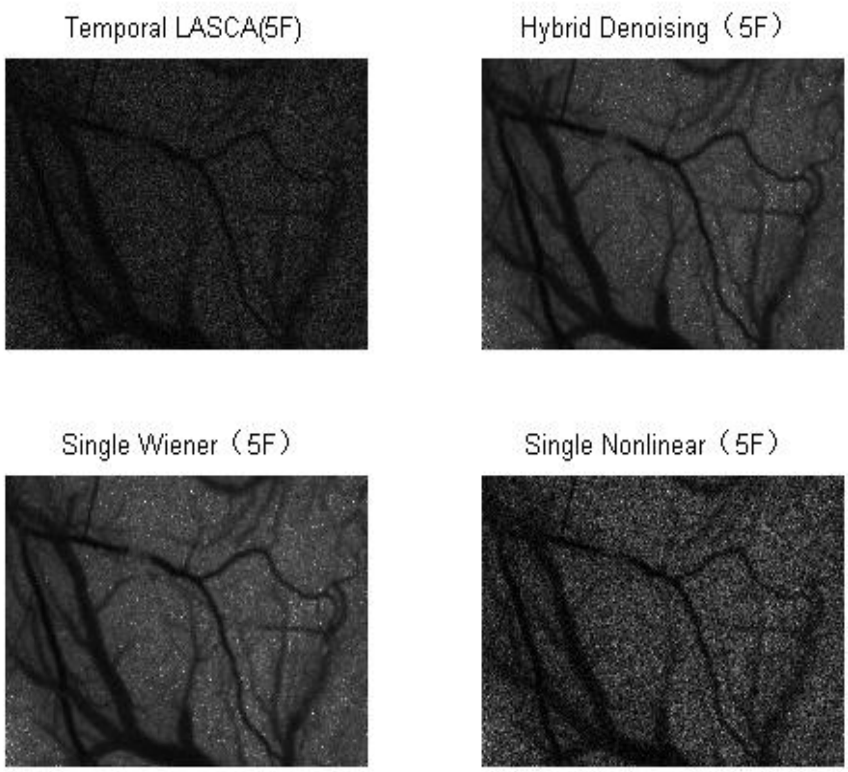
Fig 3. 11 Results of Spatial LASCA image de-noising

TABLE 3. 3 Estimation of de-noising (Spatial)

	Original	Hybrid	Single			Others		
			Wiener	Nonlinear	Wavelet	TV	Med	Linear
MSE	0.0477	0.0383	0.1138	0.0525	0.0525	0.0485	0.0479	0.1487
SNR	8.3454	11.9030	7.7906	10.3830	10.3926	4.3915	8.3791	5.7848
PSNR	15.0007	20.1797	16.3509	19.3908	19.4030	6.8904	14.5771	14.9426

3.4.2.2 Experimental results and analysis of temporal LASCA

（1）Experimental results and analysis of Temporal LASCA (5F) image de-noising



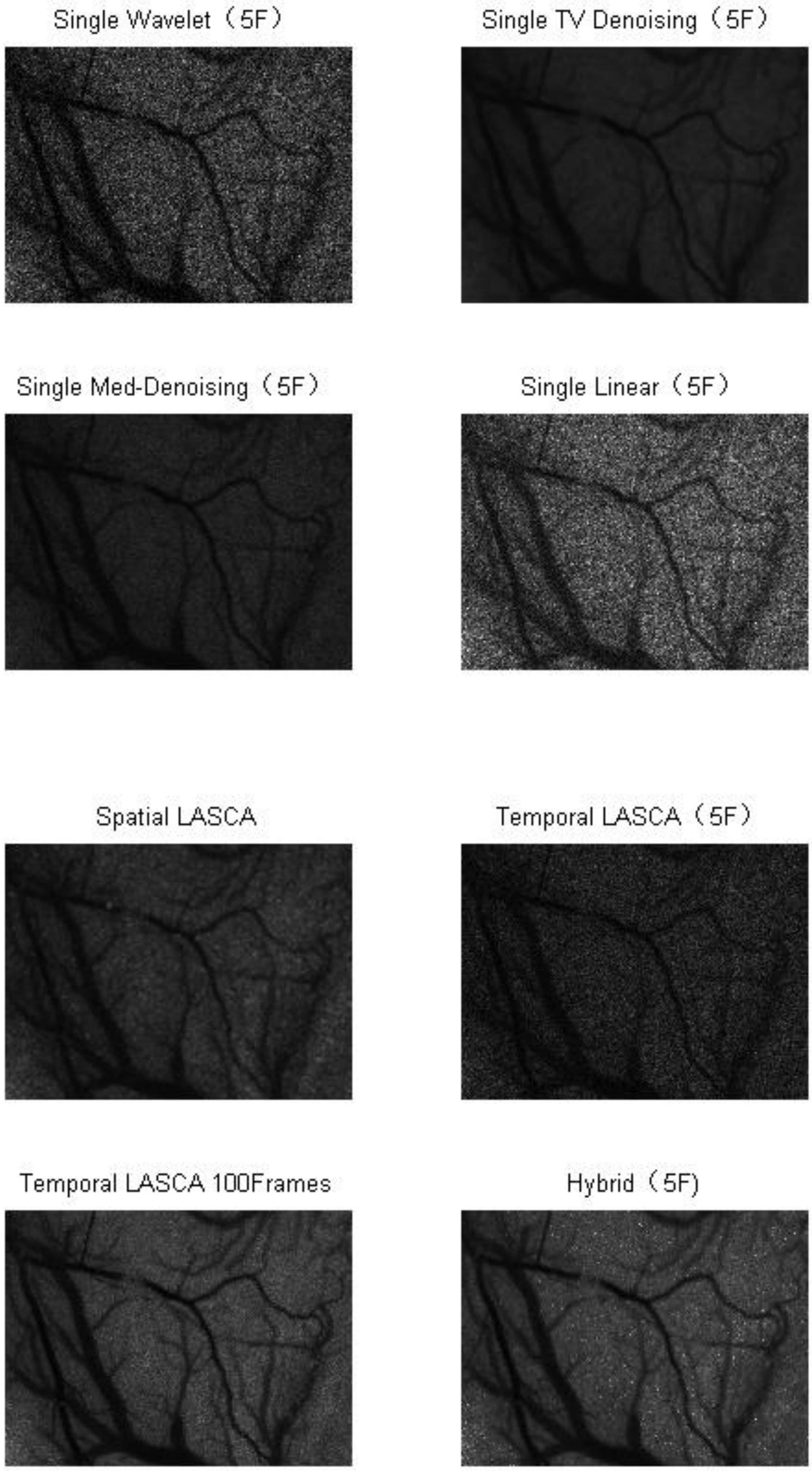


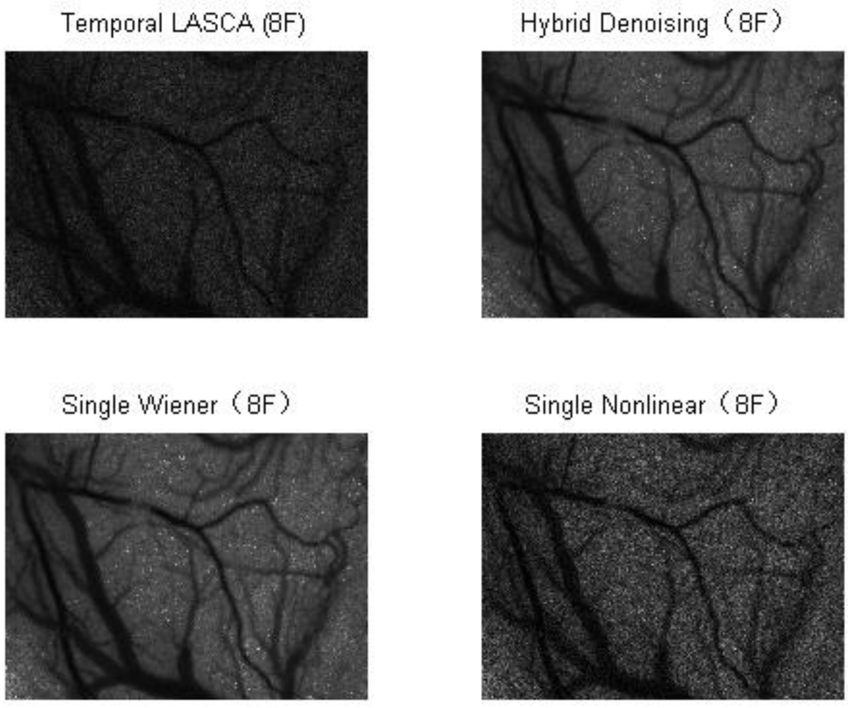
Fig 3. 12　Results of Temporal LASCA (5F) image de-noising

TABLE 3. 4 Estimation of de-noising (5 Frames)

	Original	Hybrid	Single			Others		
			Wiener	Nonlinear	Wavelet	TV	Med	Linear
MSE	0.0766	0.0119	0.0373	0.0077	0.0076	0.0802	0.0806	0.0765
SNR	3.9292	14.0343	11.9009	6.8384	6.8502	4.2700	3.4655	5.9091
PSNR	14.0777	26.6278	24.2052	21.0845	21.0770	5.6558	7.9792	17.8743

The subjective estimation results are shown in Fig 3.12, the objective estimation results are shown in TABLE 3.4.

（2）Experimental results and analysis of Temporal LASCA (8F) image de-noising



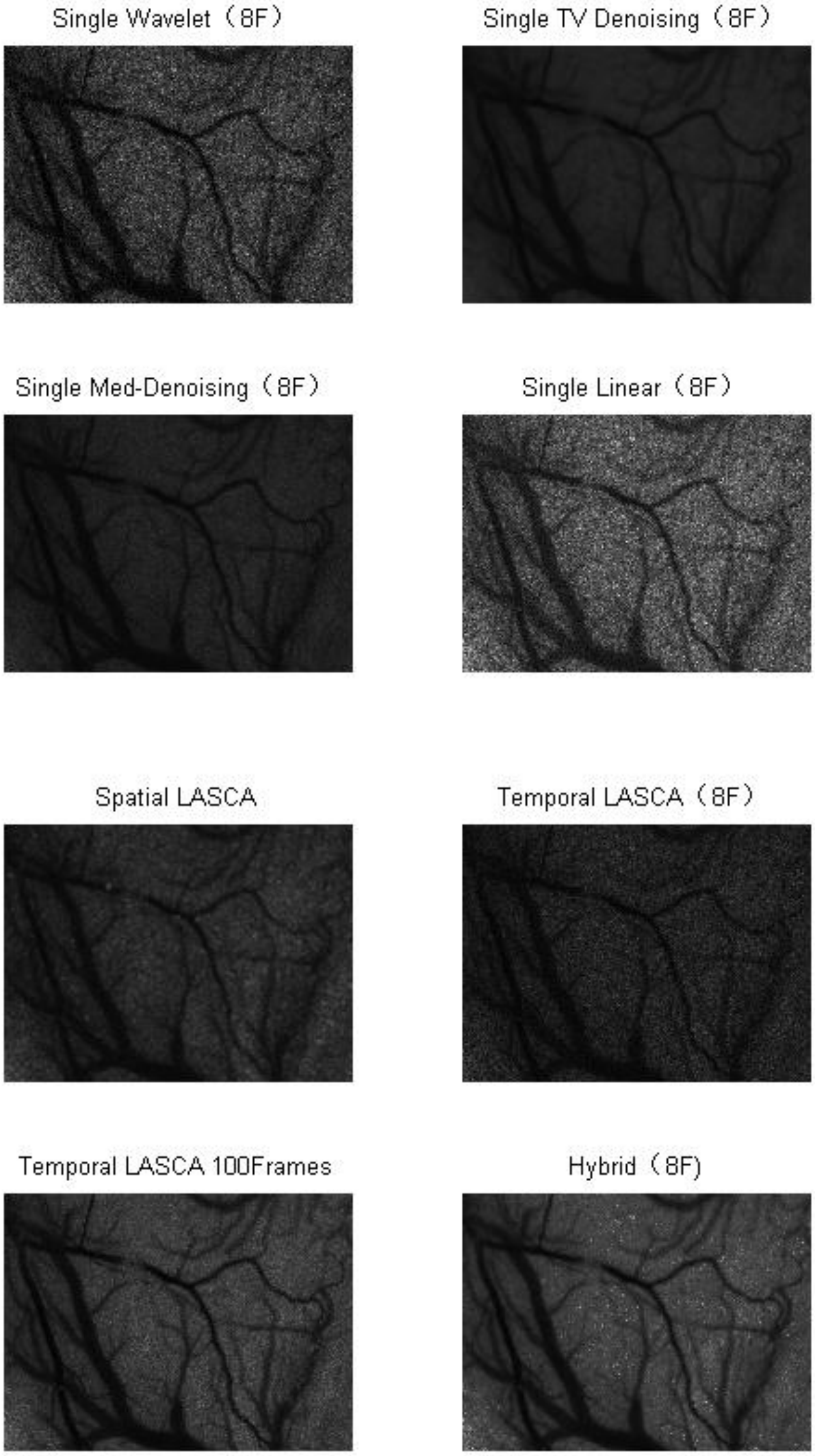


Fig 3. 13 Results of Temporal LASCA (8F) image de-noising

TABLE 3. 5 Estimation of de-noising (8 Frames)

	Original	Hybrid	Single			Others		
			Wiener	Nonlinear	Wavelet	TV	Med	Linear
MSE	0.0719	0.0230	0.0500	0.0022	0.0022	0.0747	0.0750	0.0884
SNR	4.9965	13.9797	11.3387	8.9911	9.0024	6.8801	4.5431	6.4365
PSNR	13.7477	25.9501	23.5541	21.8760	21.8966	8.2378	9.5101	18.3410

The subjective estimation results are shown in Fig 3.13, the objective estimation results are shown in TABLE 3.5.

3.5 Experimental results for Wavelet Fusion method on blood vessel

3.5.1 Experimental results and analysis of Spatial LASCA image de-noising

We show the results of each de-noising filter in Fig 3.14--- from original (noisy LASCA image), our proposed filter to each single filter, also, we add other researcher's methods such as Linear de-noising and so on. From the widely compare, it is firmly shown that, our hybrid de-noising have the best objective performance. Moreover, TABLE 3.6 shows the specific data of objective estimations.

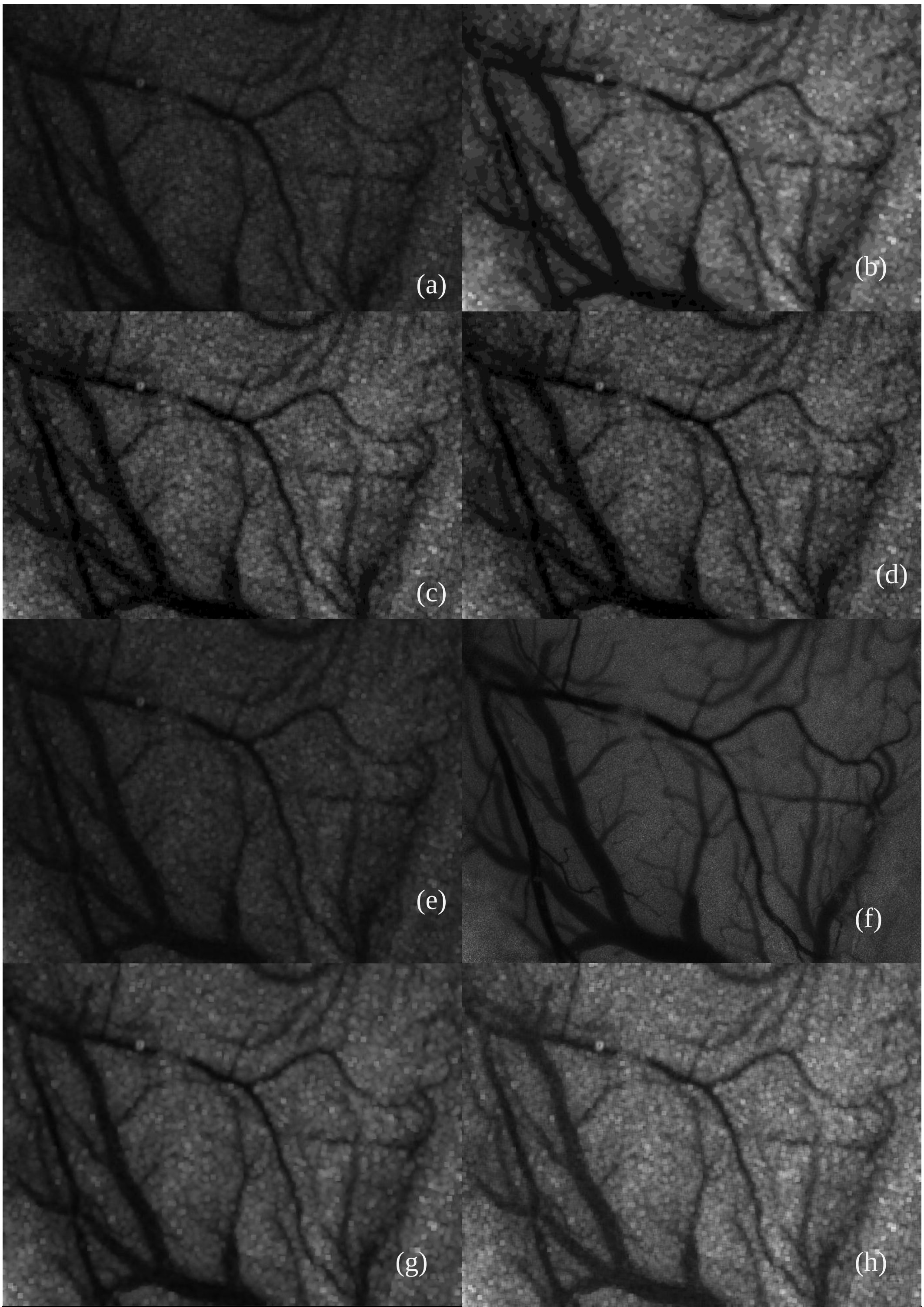


Fig 3. 14 Spatial LASCA De-noising (a) noisy LASCA image (Spatial) (b) wiener de-noising (c)order-statistic de-noising (d)wavelet de-noising (e)Med de-noising (f) Linear de-noising (g)base image (h) Proposed hybrid de-noising and wavelet fusion method

TABLE 3. 6 Estimation of de-noising (For Spatial LASCA)

	Original	Fusion	Single			Others	
			Wiener	order-statistic	Wavelet	Med	Linear
MSE	0.0477	0.0052	0.1138	0.0525	0.0525	0.0479	0.1487
SNR	8.3454	11.7621	7.7906	10.3830	10.3926	8.3791	5.7848
PSNR	15.0007	20.0085	16.3509	19.3908	19.4030	14.5771	14.9426

3.5.2 Experimental results and analysis of Temporal LASCA image de-noising

We choose sampling frame parameter as 8 frames in temporal LASCA. Similarly with Spatial LASCA, in Temporal experiment, the same comparison has been down. The subjective estimation results are shown in Fig 3.15, the objective estimation results are shown in TABLE 3.7.

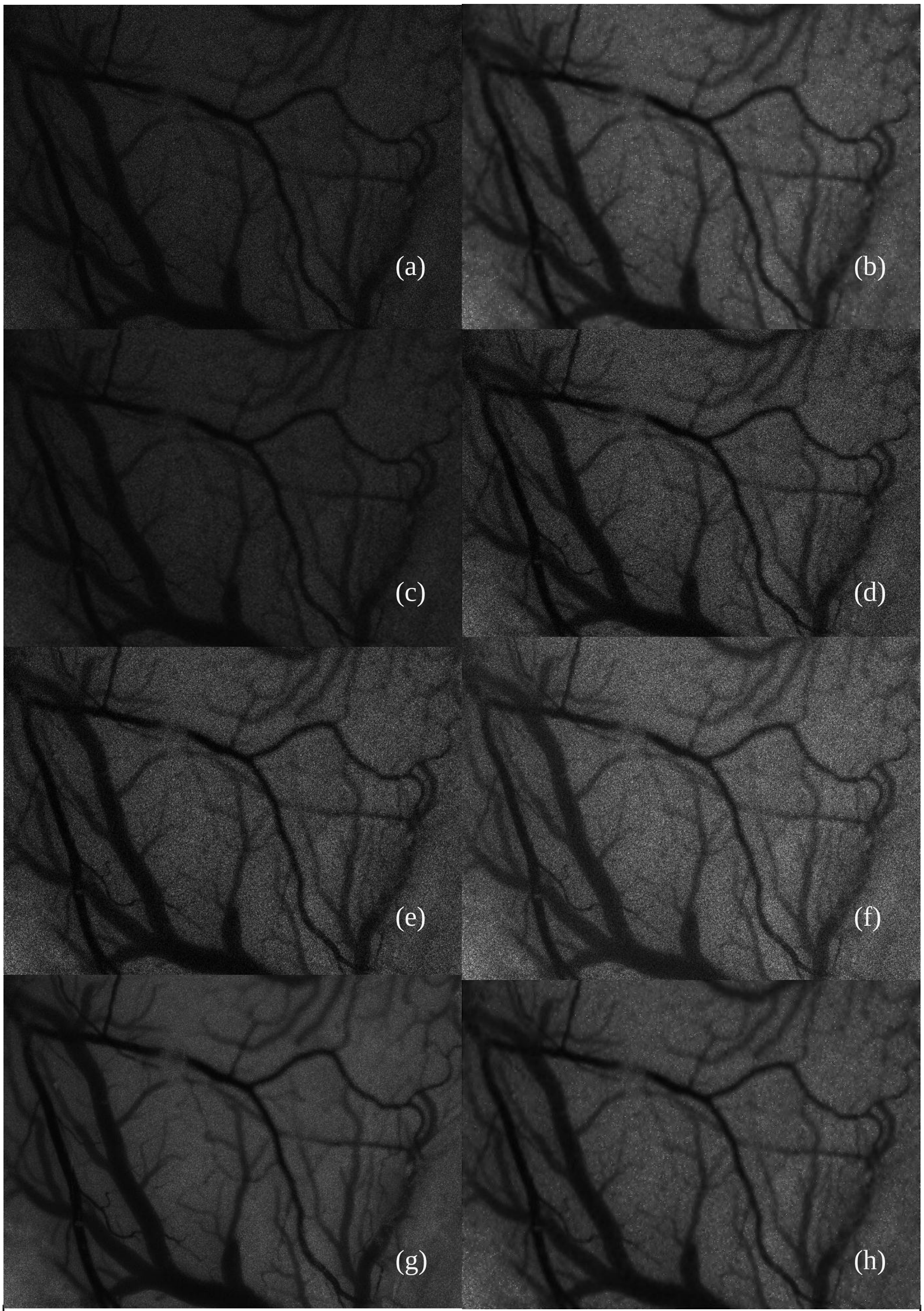


Fig 3. 15 Temporal LASCA De-noising (a) noisy LASCA (Temporal 8 Frames) (b) wiener de-noising (c)order-statistic de-noising (d)wavelet de-noising (e)Med de-noising (f) Linear de-noising (g)base image (h) Proposed hybrid de-noising and wavelet fusion method

TABLE 3. 7 ESTIMATION OF DE-NOISING (FOR TEMPORAL LASCA)

	Original	Fusion	Single			Others	
			Wiener	order-statistic	Wavelet	Med	Linear
MSE	0.0719	0.0056	0.0500	0.0022	0.0022	0.0750	0.0884
SNR	4.9965	13.9630	11.3387	8.9911	9.0024	4.5431	6.4365
PSNR	13.7477	24.6753	23.5541	21.8760	21.8966	9.5101	18.3410

3.5.3 Experimental results and analysis of Proposed Method under different frame parameters

In this section, the performance of our proposed de-noising method under different contrast frame parameters is provided and discussed.

For 6 groups of noisy Temporal LASCA images (contrast parameter varies from 5 frames to 40 frames), our de-noising method is proposed, the experimental results are shown in Fig 3.16, the objective estimation results are shown in TABLE 3.8.

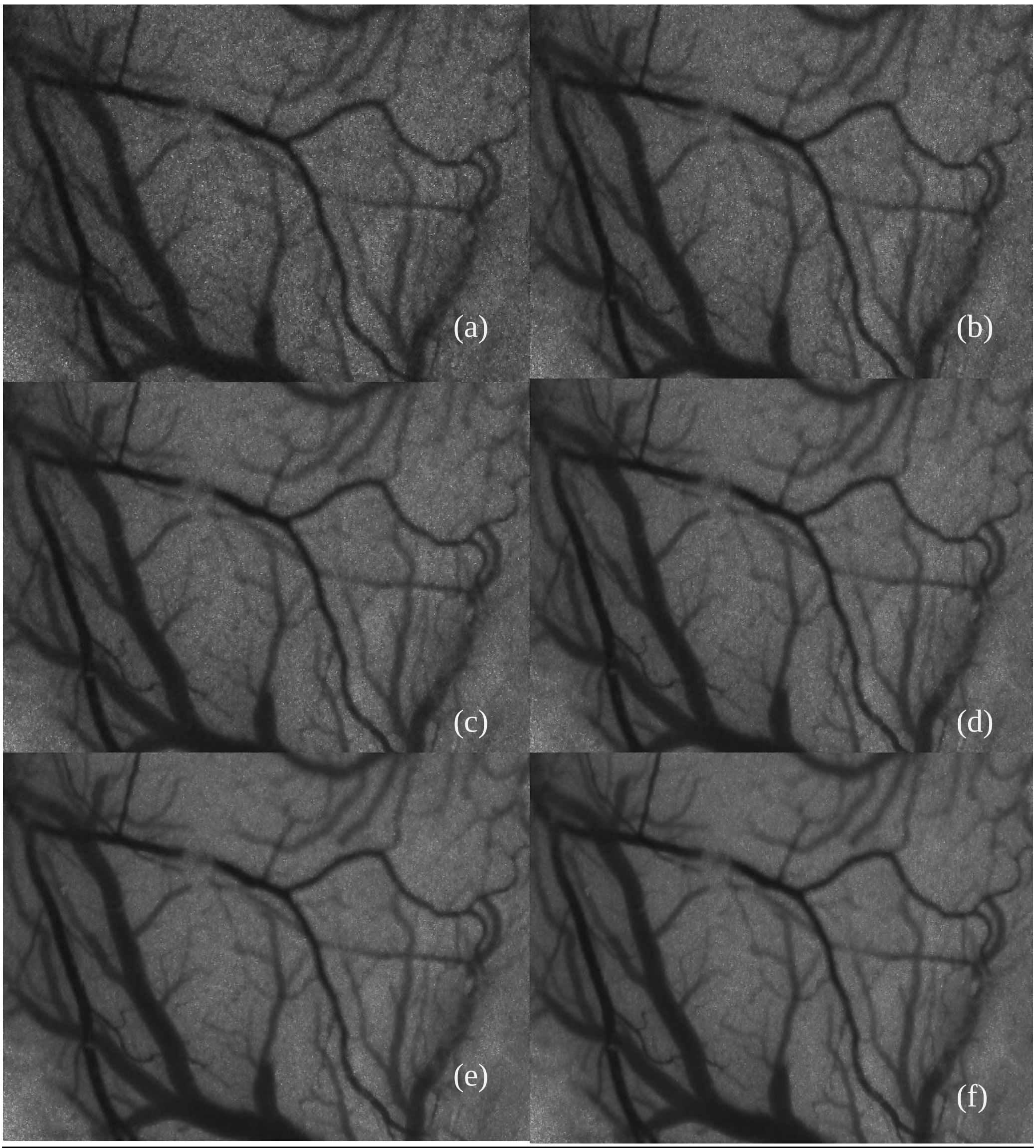


Fig 3. 16 De-noising Results of Proposed Method under (a) 5 Frames (b)8 Frames (c) 12 Frames (d)18 Frames (e)27 Frames (f) 40 Frames Temporal LASCA

TABLE 3. 8 De-noising Results of Proposed Method under different frames

	5F	8F	12F	18F	27F	40F
MSE	0.0080	0.0056	0.0110	0.0156	0.0184	0.0193
SNR	13.9222	13.9630	13.9494	13.8020	13.7424	13.7872
PSNR	23.5268	24.6753	25.2742	25.4974	25.5786	26.0673

From the table above, the graphical result can be generated as Fig 3.17 shown. The horizontal vector shows the value of frame while the vertical vector shows the dB value of each objective estimation factor.

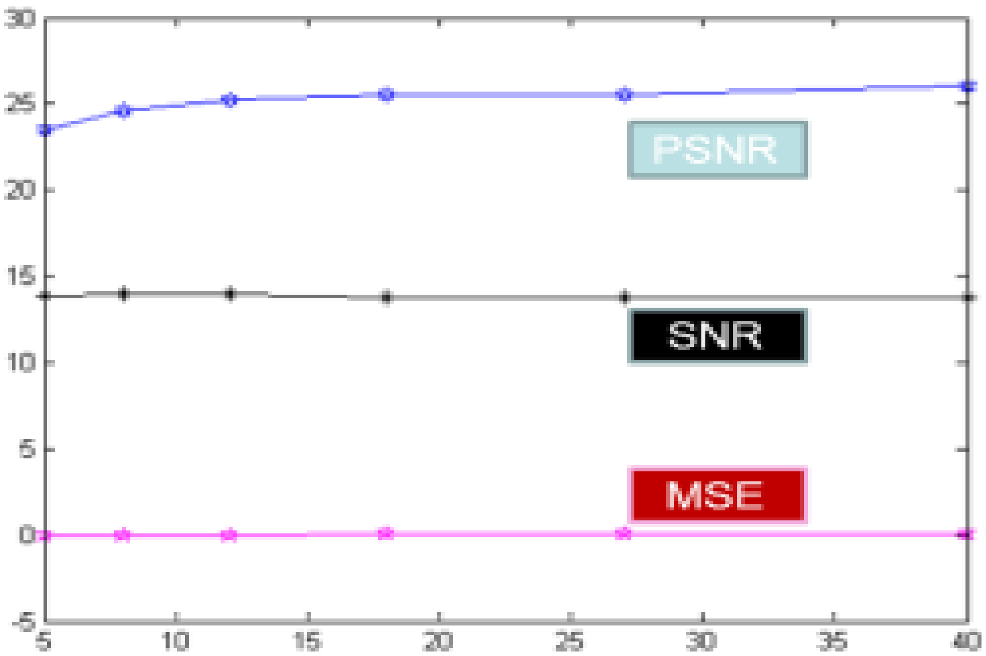


Fig 3. 17 Plot Result

From Fig 3.17 and TABLE 3.8, it is clear shown that, while the contrast parameter increases, the corresponding MSE value changes from 0.0056 to 0.02, and has not obvious variation. The SNR value changes from 13.7 to 13.96, also not much variation. The PSNR value increases from the range of 5 to 10 frame, however, when bigger than 10 frame, the changing becomes tiny.

TABLE 3. 9 CONSUMING TIME FOR DIFFERENT METHOD

Applied Method	**Consuming Time (s)**
Spatial LASCA	4.2695
Temporal LASCA (100F)	5.6777
Temporal LASCA (10F)	0.3226
Temporal LASCA (8F)	0.1769
Proposed De-noising	1.0286

TABLE 3.9 shows the time cost for different cases. Temporal LASCA (100F) can provide the highest quality of image around all the methods referred. However it costs much longer time compare with the others.

3.6 Discussion

Consider the results of Spatial and Temporal LASCA images de-noising, our proposed method has good subjective performance around all methods we provide (shown in Fig 3.3 to Fig 3.16). Meanwhile, our method performs the best in MSE, SNR and PSNR estimation, shown in TABLE 3.1 to TABLE 3.8 (That means MSE has the least value and SNR/PSNR have the largest value).

From the performance under different contrast parameter, we can claim that the number of frames does NOT affect our method's performance much. The de-noising under small number of contrast can be close to the large number of contrast image (such as 100 Frames in our research). The effectiveness of our method is proved.

From TABLE 3.9 we can conclude that using the consuming time of applying LASCA (8F) and our de-noising method is even smaller than just applying LASCA (100F). Also, the experimental results have shown that they have similar performance.

Therefore, we can state that our research have its significance that decrease the consuming time while preserve the performance in order to realize the real time LASCA processing.

3.7 Conclusion

This chapter proposes a novel hybrid filtering for LASCA in de-noising of medical images. Regrouping Wiener filtering, order-statistic filtering, Wavelet de-noising and fusion technology, the laser speckle imaging based on spatial contrast or temporal contrast has been down, and the de-noising is performed. From the experiment, we can conclude that

1. The proposed hybrid filtering for spatial and less frame contrast image (5F, 8F, etc) has high value of PSNR and good subjective performance.

2． The hybrid filtering absorbs all the benefits of each filtering.

3． From the results, both subjective and objective performance, the hybrid filtering is the best or one of the best. Therefore, it is considered that it has better performance than other single filtering.

One of our research motivations is that doctors find it delay when they using Temporal LASCA to do real time diagnosis. The high quality LASCA result (such as 100F) would costs more time, while the low quality (such as Spatial or 5F) can not provide good image. Our attempt by using de-noising method in image processing filed can improve the image quality in less time than performing high frames LASCA. Our hybrid de-noising method absorbs the benefits of single de-noising method while the time consumption doesn't change a lot.

Chapter 4 Extraction and Digitization Method of Blood Vessel in Sclera-conjunctiva Image

4.1 Transformation from true-color image to binary image in Sclera-conjunctiva region

In the research of medical image processing, usually we will do some pre-processing on the target image before formal process, in order to short cut the processing time, improve the performance and so on. For these reasons, there is no exception in our case. In this section, the following processes are introduced: greyscale processing, automatic threshold choosing, binary processing, noise removal.

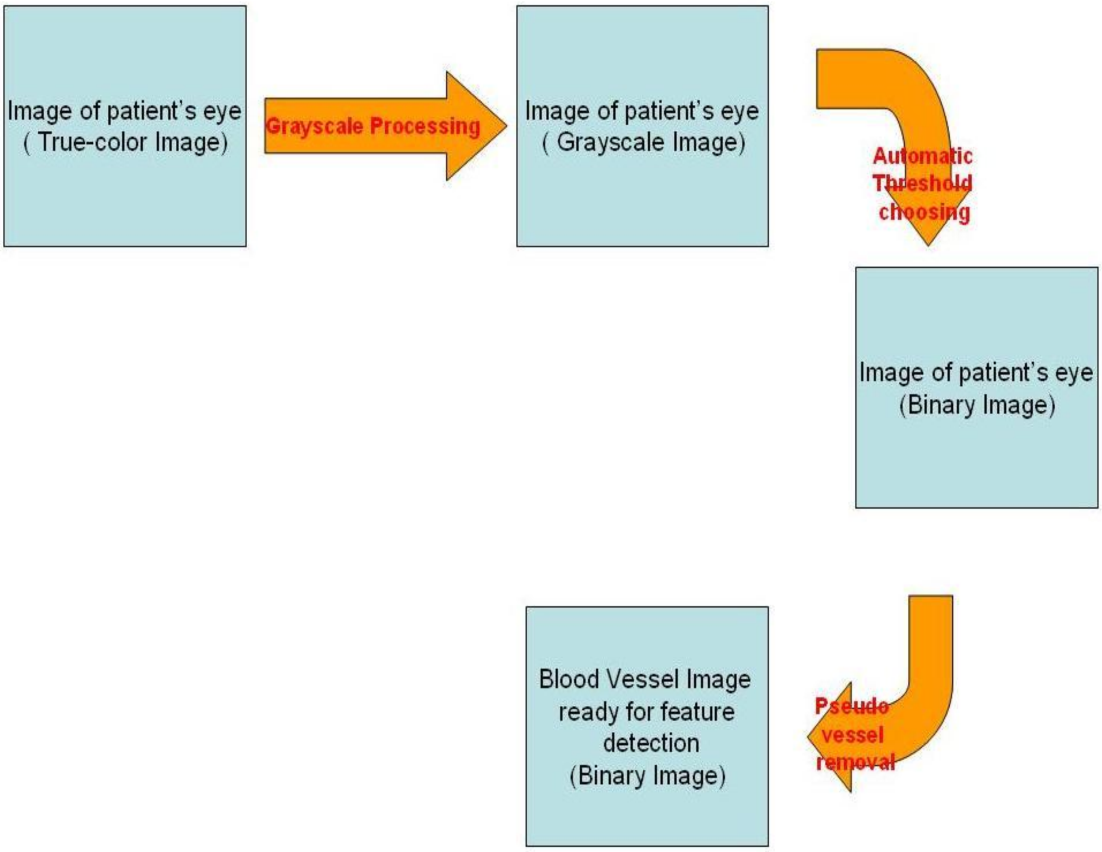


Fig 4. 1 Framework for Preprocessing

4.1.1 The grayscale processing

A greyscale image (also called gray-scale, gray scale, or gray-level) is a data matrix whose values represent intensities within some range. MATLAB stores a greyscale image as an individual matrix, with each element of the matrix corresponding to one image pixel. By convention, the variable name I is referred to greyscale images.

In order to decrease the processing time, we convert the true-color image of the blood vessel into greyscale, then binary analysis. Conversion of a color image to greyscale is not unique; different weighting of the color channels effectively represents the effect of shooting black-and-white film with different-colored photographic filters on the cameras. Our strategy is to match the luminance of the greyscale image to the luminance of the color image. To convert any color to a greyscale representation of its luminance, first one must obtain the values of its red, green, and blue (RGB) primaries in linear intensity encoding, by gamma expansion. Then, add together 30% of the red value, 59% of the green value, and 11% of the blue value (these weights depend on the exact choice of the RGB primaries, but are typical). Regardless of the scale employed (0.0 to 1.0, 0 to 255, 0% to 100%, etc.), the resultant number is the desired linear luminance value; it typically needs to be gamma compressed to get back to a conventional greyscale representation [51].

In our experimental environment---MATLAB, the true-color image RGB is converted to the greyscale intensity image I by using I = rgb2gray(RGB). rgb2gray converts RGB images to greyscale by eliminating the hue and saturation information while retaining the luminance.

4.1.2 The binary processing

An image may consist of a single object or several separated objects of relatively high intensity, viewed against a background of relatively low intensity. This allows figure/ground separation by thresholding. In order to create the two-valued binary image a simple threshold may be applied so that all the pixels in the image plane are classified into object and background pixels. A binary image function can then be constructed such that pixels above the threshold are foreground ("1") and below the threshold are background ("0").

In our experimental environment---MATLAB, when processing the greyscale image in Sclera-conjunctiva region , it is transformed into a binary image by using g=im2bw(f,T),which is a logical array.

4.1.3 Automatic threshold choosing

From section 4.1.2 we know that the threshold to separate the foreground and background in greyscale image is very important for transform it into binary image.

Thresholding is an important form of image segmentation and is a first step in the processing of images for many applications. Therefore, the objective and automatic threshold choosing method is introduced. The selection of suitable thresholds is ideally an automatic process, requiring the use of some criterion on which to base the selection. One such criterion is the maximization of the information theoretic entropy of the resulting background and object probability distributions. [52]

To set a global threshold or to adapt a local threshold to an area, we usually look at the histogram to see if we can find two or more distinct modes—one for the foreground and one for the background.

The introduced Otsu's algorithm assumes that the image to be threshold contains two classes of pixels (e.g. foreground and background) then calculates the optimum threshold separating those two classes so that their combined spread (intra-class variance) is minimal.

Otsu's threshold method involves iterating through all the possible threshold values and calculating a measure of spread for the pixel levels each side of the threshold, i.e. the pixel that either falls in foreground or background. The aim is to find the threshold value where the sum of foreground and background spreads is at its minimum [53].

From our experiment result ---shown in Section 4.3, it is clear that the binary image would be much better by applying Otsu's method, however, the "isolated island" noise remains.

Therefore, in next section, an original noise removal method is proposed.

4.1.4 The pseudo vessel removal

Because of the quality of the picture influenced easily by the natural texture of the eyeball surface, the changing of illumination state and any other vestiges, the pseudo targets unavoidably exist. To reduce the wrong judging in the result, it is necessary to do the pseudo vessel removal.

Usually, the vessel branches have the features as follows:

The single branch has curve feature and connectivity. It is distributed as tree or net shape. However, the pseudo blood vessel is represented as discrete block or point.

Based on these features of attribute we concluded, only the branch which have certain length and laid on certain orientation can be considered as real vessels. Otherwise, it is pseudo target and should be eliminated.

The algorithm is as follows:

1) Take the point in the binary image whose value is 0 to be the possible target;

2) For each searched point, do the "isolated island "judging: If there is a isolated block, in which all points are value=0(or 1) and the points around it are value=1 (or 0), then it is considered as "isolated island", and should be eliminated;

3) Continue to search the next "isolated island ", if not, then remain it.

```
for i=2:row
    for j=2:col
        if(I2(i,j)==0)&&(I2(i-1,j-1)==1)&&(I2(i,j-1)==1)&&(I2(i+1,j-1)==1) %Isolated island judging
            I2(i,j)=1;
        end
    end
end
```

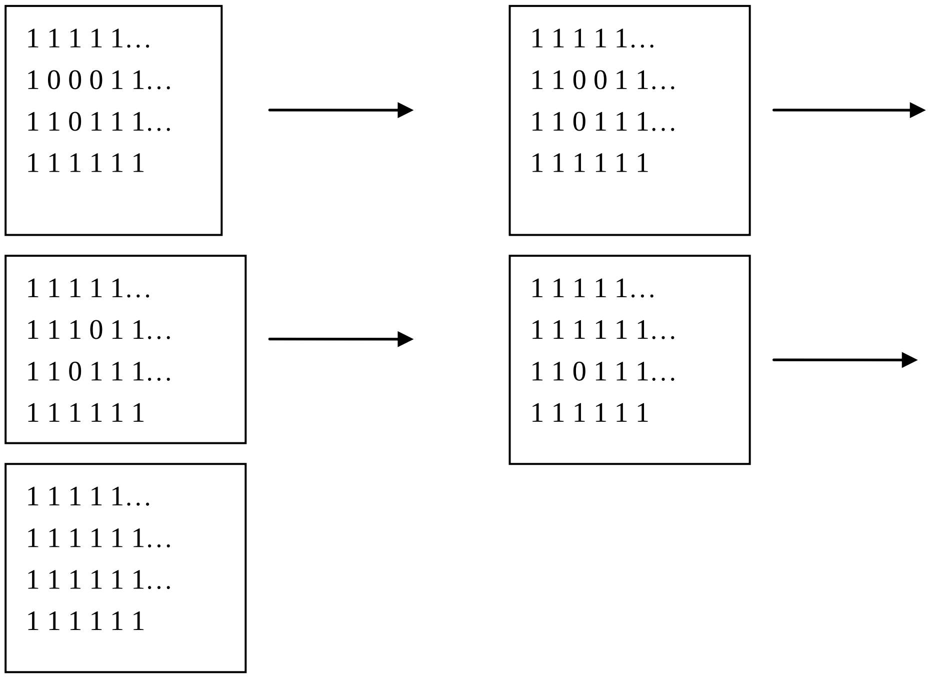


Fig 4. 2　Example of pseudo vessel removal

The simple example is shown in Fig. 4.2. We also add key part of codes above.

4.2 The digitization of blood vessels in Sclera-conjunctiva region

4.2.1 Gather the edge information from the blood vessel images

After the binary processing and the elimination of the pseudo target, the next work is the confirm of edge of blood vessels.

In the existing method, when the value of a point is 0 and the eight neighbor point is 1, then it is considered as inner point and be eliminated. After looping this process, we can gain the boundary of the blood vessel.

However, in order to additional processing of boundary, the formal method is not applied in our proposed method algorithm, instead, a new method is proposed by searching and reserve the boundary point in the designated array:

Take the 0 value point in binary image as the possible boundary point.

(1) Make the edge judging on the searched possible point , that means when scanning, if the point value has been changed compared with its neighbours, then it is considered as boundary point, and put it into boundary point array orderly;

(2) Continue to search the boundary point, otherwise eliminate it.

```
for i=1:row % Searching the leftside of blood vessel
    for j=2:col
        if I1(i,j)>I1(i,j-1)
           x(i,j)=0;
        end
    end
    for j=1:(col-1) % Searching the rightside of blood vessel
        if I1(i,j)>I1(i,j+1)
             x(i,j)=0;
        end
    end
end
```

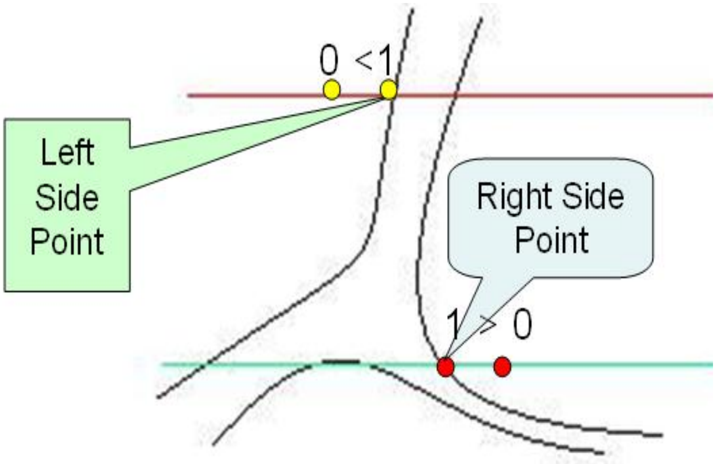


Fig 4. 3 Search the boundary point

4.2.2 Feature Parameters of edge of blood vessel

The edge of blood vessel is the main feature, which is important for medical research on TCM, and of great moment for "Differentiation of syndromes by observing eyes". Thus, the establishment of the feature parameters is necessary work in the whole research.

The feature matrix R is considered as

$R = R(\lambda_1, \lambda_2, \lambda_3)$

λ_1 is the extending feature, λ_2 is the branching feature, λ_3 is the two-sides feature. The creation methods of each parameter are shown as below.

4.2.2.1 Parameter of Extending Attribute λ_1

In order to express the extending attribute, we choose the sequence number in vertical axis to be the extending features.

The algorithm is as follows:

In the x-y plain of blood vessel picture (binary image), we set the y coordinate of the boundary point orderly as the extending feature value.

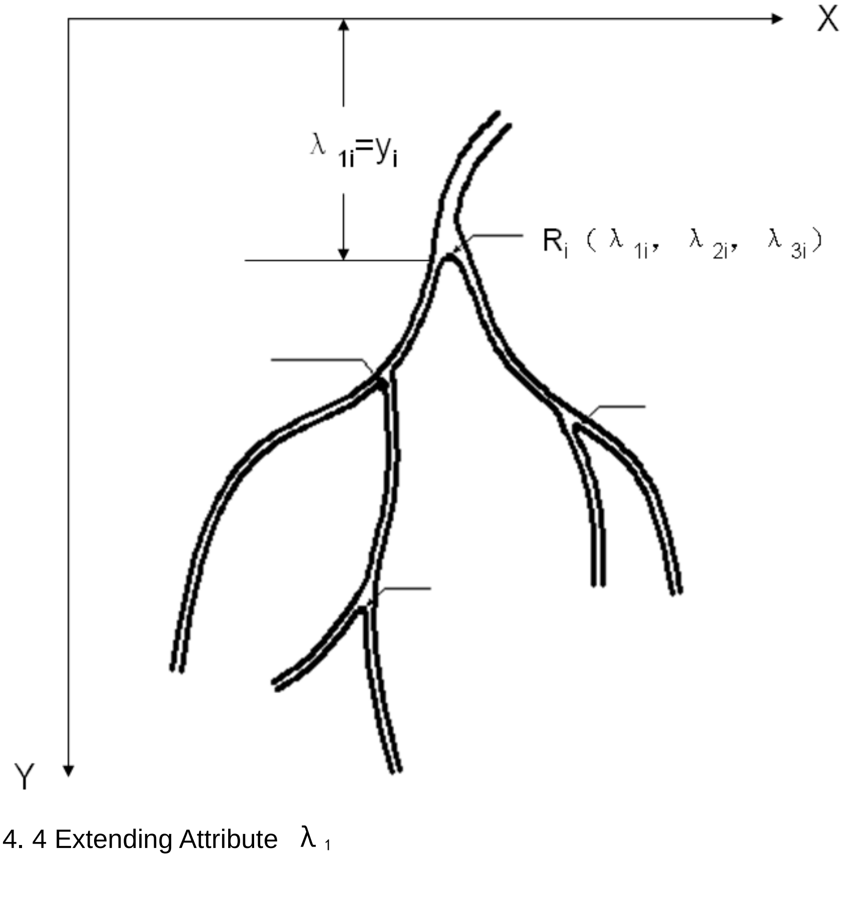


Fig 4. 4 Extending Attribute λ_1

4.2.2.2 Parameter of Branching Attribute λ_2

The branch is one of the most important factor of vessel image. In order to express the branching information accurately, we describe the vessel the as follows:

The curve of branch is separated into sub-curves, such as main branch ， 1st-level branch， 2nd-level branch and so on.

We choose the vertical parameter y in the branch point to be the branching attribute

We define "00" as the main vessel without branch, and "01" as the first level branch in the left, "02" as the first level branch in the right, and also, “011”,”012”,”013”,…;”021”,”022”,”023”,…;as the second level branch and so on.

```
%ascertain T2
        if (KK(i)<2)&&(i>KK1(1))&&(x(i,j)==0) % main vessel
            t2(i,j)=T20;
        end
        if (KK(i)<2)&&(i>=KK1(2))&&(x(i,j)==0)&&(jj<3)&&(jj>0)
            t2(i,j)=T21; % 1st branch on the left
        end
         if (KK(i)<2)&&(i>=KK1(2))&&(x(i,j)==0)&&(jj>2)
            t2(i,j)=T22; % 1st branch on the right
         end
          if (KK(i)>1)&&(i>KK2(1))&&(x(i,j)==0)
            t2(i,j)=T22;
          end
        if (KK(i)<2)&&(i>=KK1(3))&&(x(i,j)==0)&&(jj<3)&&(jj>0)
            t2(i,j)=T221; % 2nd branch on the left
        end
        if (KK(i)<2)&&(i>=KK1(3))&&(x(i,j)==0)&&(jj>2)
            t2(i,j)=T222; %2nd branch on the right
        end
         if (KK(i)>1)&&(i>KK2(2))&&(x(i,j)==0)
            t2(i,j)=T222; %
         end
```

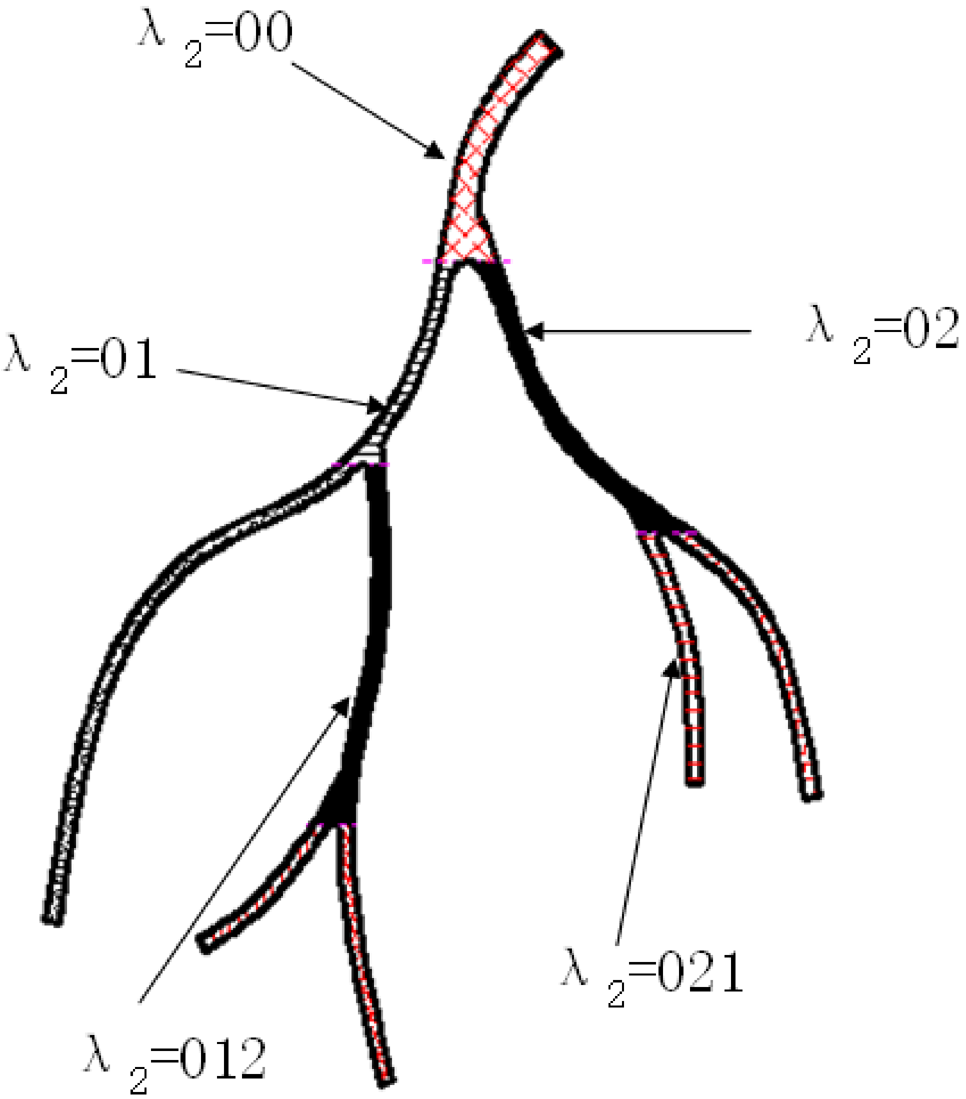


Fig 4. 5 Branch Attribute λ_2

4.2.2.3 Parameter of Two-sides Attribute λ_3

After fixing on the branching feature, the two-sides feature thus can be ensured.

The whole vessel region is separated into a certain numbers of sub-curves. Each sub-curve is enclosed by two-sides boundaries. For each one, it should be discriminate both two sides. Here, Two-sides Attribute λ_3 is used to represent the one side of the boundary (include main vessel and each sub-vessel).

The left side is defined as 0 and right side as 1.

```
%ascertain T3
          if (x(i,j)==0)&&(jj==1)    % 1st edge point of column i
             t3(i,j)=T31;
          end
          if (x(i,j)==0)&&(jj==2)    % 2nd edge point of column i
             t3(i,j)=T32;
         end
         if (x(i,j)==0)&&(jj==3)    % 3rd edge point of column i
             t3(i,j)=T31;
         end
         if (x(i,j)==0)&&(jj==4)    % 4th edge point of column i
             t3(i,j)=T32;
         end
   end
```

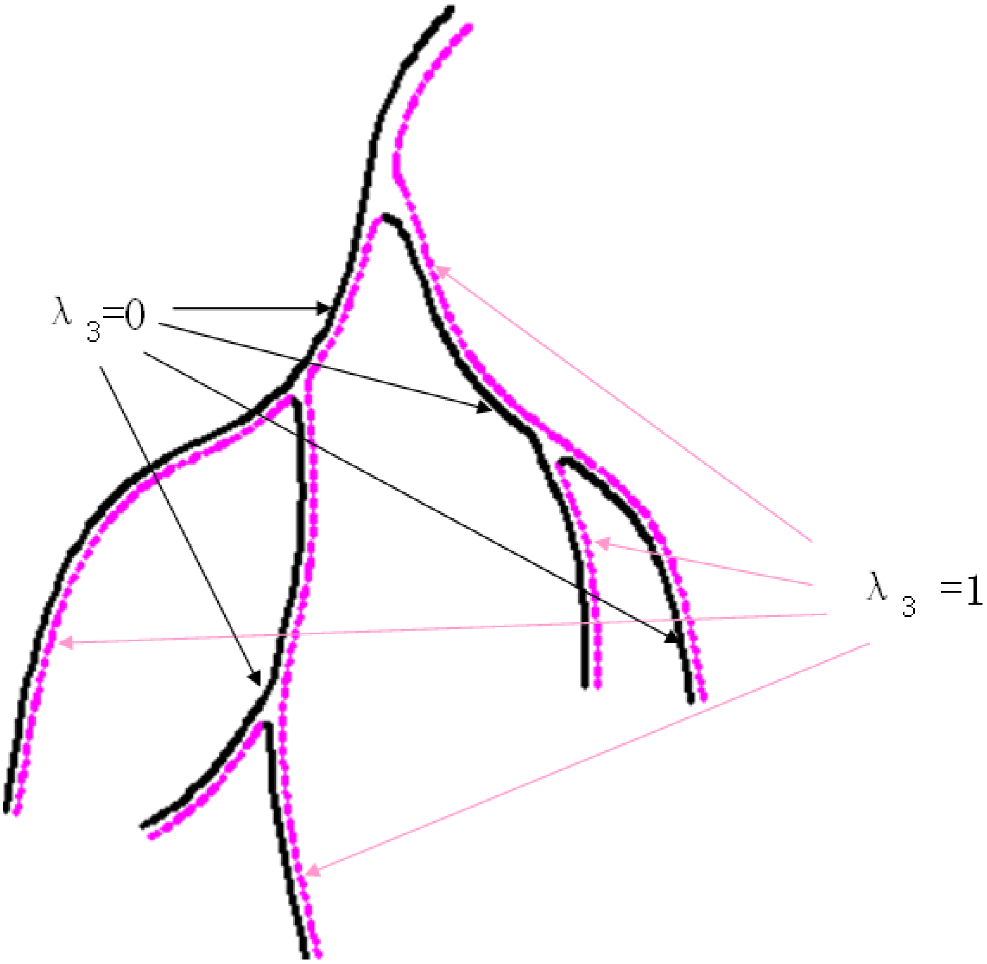


Fig 4. 6 Two-sides Attribute λ_3

4.2.2.4 The Width Attribute b

The value of R can be expressed as the value of x coordinate of boundary point along x coordinate orientation. The width of the vessel along the changing boundary, is approximately as the difference of the two sides of the boundary.

Therefore, the width parameter can be given from this formula as follows:

$$b(\lambda_1, \lambda_2) = R(\lambda_1, \lambda_2, \lambda_{3A}) - R(\lambda_1, \lambda_2, \lambda_{3B})$$

R is the x-coordinate of boundary point value. λ_{3A} λ_{3B} represents the right and left boundary respectively. The difference of two boundary points is the width of the blood vessel.

```
b12(i)=y(i,2)-y(i,1);
b34(i)=y(i,4)-y(i,3);
```

4.3 Experiments And Results

The experiments are based on 50 eye images from different volunteers in Hiroshima University. These images are captured by CCD as 4 orientations (Up, Down, Left, Right) to gain the whole region of Sclera-conjunctiva.

The method for transformation from true-color image to binary image in Sclera-conjunctiva region has been given in Section 4.1, here, the results are shown as follows.

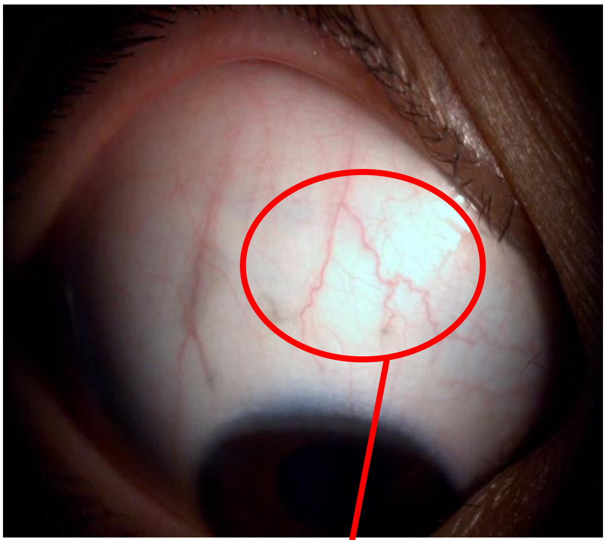


Fig 4. 7 The Original Image

Fig 4. 8 The Sclera-conjunctiva Image

Fig 4.7 and Fig 4.8 show the original image of blood vessel in Sclera-conjunctiva.

Fig 4. 9　SCI in Grayscale

Fig 4. 10　SCI in Binary

Fig 4.9 shows the result of grayscale transformation. Fig 4.10 shows the result of binary transformation.

Fig 4. 11 SCI in Binary (Otsu)

Fig 4. 12 SCI in Binary (After Pseudo Vessel Removal)

Fig 4.11 shows the result by applying Otsu's method, and Fig 4.12 shows the result after "isolated island" removal.

The method of edge detection has been given in Section 4.2. The results of the parameters of edge of blood vessel have been shown as follows.

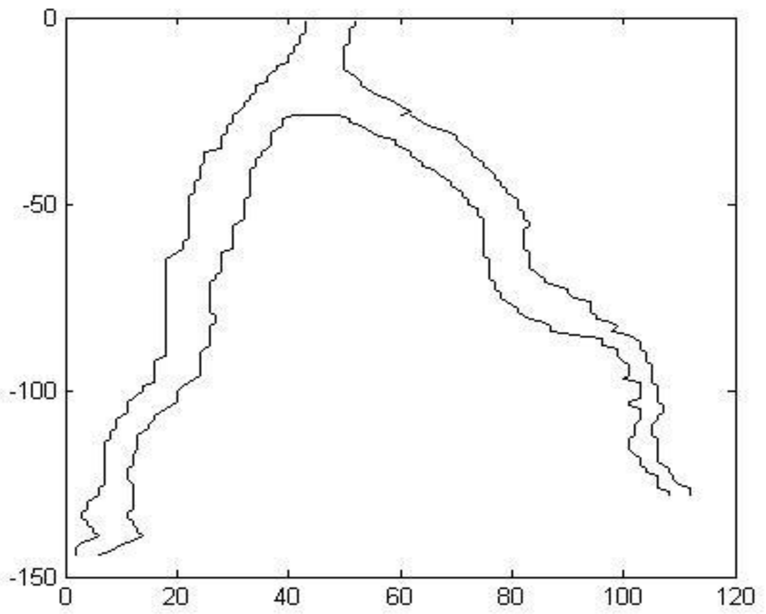


Fig 4. 13 Boundary

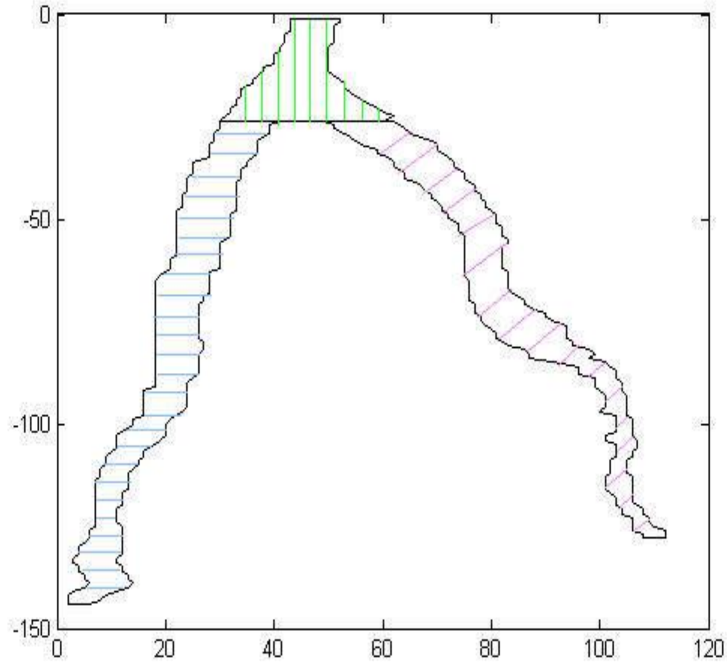


Fig 4. 14 Branching Attribute λ_2

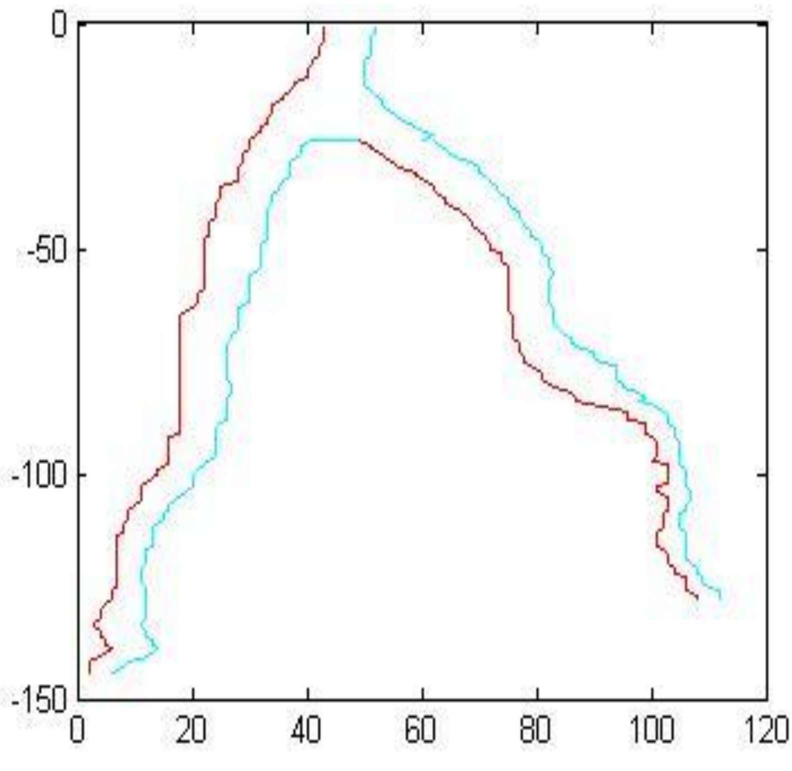


Fig 4. 15 Two-sides Attribute λ_3

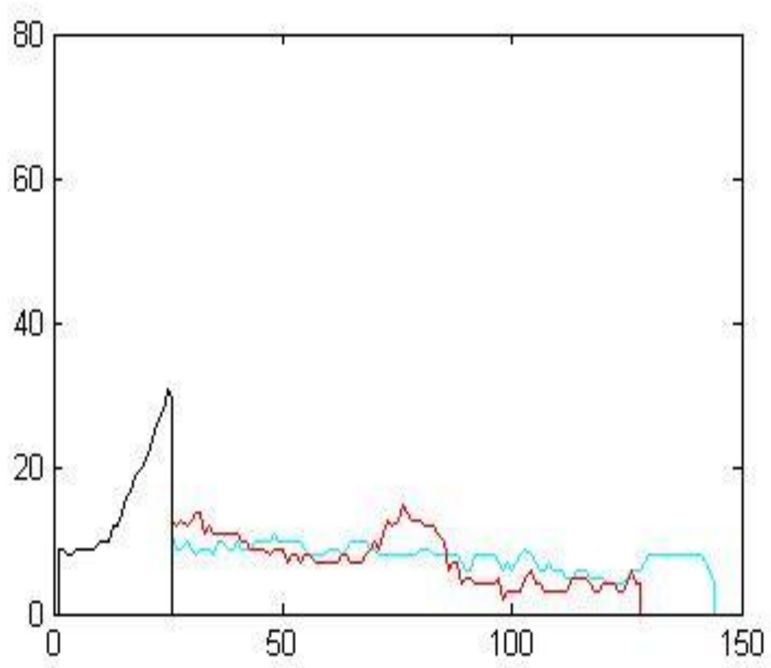


Fig 4. 16 The width Attribute b

Fig 4.13 shows boundary, Fig 4.14 shows the Parameter of Branching Attribute λ_2 .Fig 4.15 shows Parameter of Two-sides Attribute λ_3 and Fig 4.16 shows the width attribute b.

4.4 Conclusion

In this paper, scanning and edge detection methods are used to gain the edge of the blood vessels. We apply Otsu's method to gain the thresh value automatically in the pre-processing, which is proved to improve the performance of detection. Also, we propose an original pseudo vessel removal method to remove the noise. Meanwhile, the edge feature parameters are gained, which can be used to reconstruct the blood vessels. We propose a scanning method for extracting the blood vessels and setting feature parameters for reconstructing the blood vessel, which can be used in further medical researches.

Another contribution is we establish an original digital vessel model by using the attribute parameters we proposed, which can represent the vessel features directly.

In light of the experimental results of this work, the following conclusions can be drawn.

1. When comparing the results provided in Figure 4.11 with Figure 4.12, it can be found that the method to remove the pseudo vessel is effective.

2. Digitization method of blood vessel in sclera-conjunctiva image is presented in the paper; from sclera-conjunctiva original image to profile parameters obtained, is achieved successfully.

With these result, we are able to not only get an unprecedented high quality image of blood vessel of patient, but also better explain to the patients of their symptoms, store and transfer all pertaining information readily.

As our future work, we will completely study on the relationship between the parameters by our extraction and the diagnostic from human beings. The objective and quantitative result is expected to given for the further objective --- computer-aided diagnosis in TCM.

Chapter 5 Conclusion

The thesis has mainly carried on the following research works: hybrid de-noising method on LASCA images of blood vessels; wavelet fusion de-noising method on LASCA images of blood vessels; white eyeball blood vessel extraction and reconstruction method research.

5.1 Main research results of the thesis

The thesis has obtained the following main research results:

1. The proposed hybrid filtering for spatial and less frame contrast image (5F 8F) has low value of MSE, high value of SNR PSNR and good subjective performance.

The hybrid filtering absorbs all the benefits of each filtering.

From the results, both subjective and objective performance, the hybrid filtering is the best or one of the best. Therefore, it is considered that it has better performance than other single filtering.

2. The proposed hybrid de-noising combining wavelet fusion for spatial and less frame contrast image (5F, 8F, etc) has low value of MSE, high value of SNR PSNR and good subjective performance.

The hybrid filtering absorbs all the benefits of each filtering. Also, the wavelet fusion can increase the performance in same cases.

From the results, both subjective and objective performance, the hybrid de-noising and wavelet fusion method is the best or one of the best. Therefore, it is considered that it has better performance than other single filtering.

By comparing de-noising results under different frames, using our method in 8Frame can gain good enough performance and provide low processing time.

3. In the thesis, scanning and edge detection methods are used to gain the edge of the blood vessels. Meanwhile, the edge feature parameters are gained, which can be used to reconstruct the blood vessels. We propose a scanning method for extracting the blood vessels and setting feature parameters for reconstructing the blood vessel, which can be used in further medical researches.

5.2 Main innovations of the thesis

Summarizes the above research content and the conclusion, main innovation of the thesis displays in following several aspects:

1. Using Hybrid De-noising and the wavelet fusion technology, to perform filter processing based on the Spatial LASCA as well as the few frame number base in the Temporal LASCA, is a new method for following processing of LASCA. Using this method can obtain the good de-noising subjective and objective performance. The existed high frame temporal LASCA is not suitable for the need of real time diagnosis for live animal blood vessel. Our proposed de-noising method based on low frame temporal LASCA provides a solution for this filed.

2. Proposing and establishing a new method for the white eyeball blood vessel image automatic numerical reconstruction. The method has realized the blood vessel image outline extraction, and made the characteristic analysis to the blood vessel boundary. The experimental results show the exact data has been achieved by our

digitization method, which provide a solution for increasing the reliability of TCM diagnosis.

5.3 Research forecast

Based on achievement foundation of the thesis, we may consider continue to following several aspects to launch the research:

1. As an important step for online LASCA succeeding processing, use Hybrid De-noising or the wavelet fusion technology, a prompt filter processing method to LASCA is need to be researched.

2. Research on each kind of complex shape (for example lattice, complex dendritic structure) of the blood vessel image for the outline extraction methods, then makes the characteristic analysis to the blood vessel boundary. Explore the general method of automatic numerical reconstruction.

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Referred International Journal Publications

1) Cong Wu and Koichi Harada, "Extraction and Digitization Method of Blood Vessel in Sclera-conjunctiva Image", International Journal of Computer Science and Network Security, Vol.11 No.7, p113-118, July 2011
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1) Cong Wu and Koichi Harada, "Research on Extraction and Digitization Method of Blood Vessels for TCM diagnosis", 2011 Workshop on Digital Media and Digital Content Management, Hangzhou, China, p223-228,May 2011