

Nailfold Capillaryscopy Techniques –A Review

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Abstract: In this paper we have conducted a review of the techniques which lead to the evaluation of the nailfold capillaryscopy techniques to the present level. This paper also discusses main diseases which can be diagnosed with the help of NFC (Nail fold Capillaryscopy). We have worked on identifying issues related to the implementation of the nailfold capillaryscopy for diagnoses as well as the basic steps for doing nailfold capillaryscopic techniques.

Keywords: blood cells; nailfold capillaryscopy; velocity measurements.

I. INTRODUCTION

Whenever we try to capture the nail fold capillary video for in *Vivo* microscopic studies for diagnosis of pulmonary hyper-tension, sclerosis etc. the electron microscope typically captures video which may be blurred and the moving entities like Red Blood Cells, White Blood Cells, Plasma and other fluid particles need extra attention for their movement calibrations. Also, since the nail fold vessels are not rigid in shape, the method for blood cell tracking becomes a challenge and the cluttering due to overlapping of the objects that appear and disappear instantaneously creates a problem.

Therefore it is a challenging job to segment particular cells and track its moment in terms of its speed with respect to time in particular direction. The video recording of blood capillary flows allows identifying the co-relations of the parameters associated with diseases like Hyper-tension, fibrosis, arthritis, sclerosis etc which is otherwise a difficult task. Therefore its accurate measurement to correctly diagnose is paramount and is excellent non invasive diagnosis investigation technique.

The review paper is organized as Section I includes Introduction, section II includes Literature Review and Section III includes Conclusion and Future scope.

II. LITERATURE REVIEW

Nailfold capillaryscopy (NFC) is a technique which uses a lens for the analysis of the capillary morphology and microcirculation of nailfold. It is a non invasive, simple, repeatable, highly sensitive, inexpensive and direct method for evaluating micro vascular abnormalities [1].

Before, 1663 when Johan Christophorus Kolhaus used a primitive microscope for observing small vessels surrounding the nails, several other methods such as viewing through magnifying glass, ophthalmoscopy, dermatoscopy and wide-field capillary microscopy were employed for studying the micro vasculature.

Giovanni Rasori (1766-1873) was the first to conduct morphological study of micro circulation using magnifying glass. He was able to establish a relationship between conjunctival inflammation and the presence an “inextricable knot of capillary loops”. Subsequently researchers started using optical magnifying systems to study capillaries at different body sites like conjunctiva, lips, malleoli, nailfolds and fingertips [2,3]. Ever since, from the early 20th century investigators have started using NFC for studying several diseases [4,5].

In these investigations microscopes with 100 - 300X magnification power were used, which could provide details of the a few capillary loops in a limited microscopic field. In 1911, it was Lombard who observed that putting a drop of immersion oil on the periungal skin capillaries made observation of capillaries easier [6]. Weiss [7] on the basis of these findings standardized capillaryscopic techniques and using a primordial camera produced first images of the capillaries.

Numerous capillaryscopic studies were carried out during this period; in fact in 1939 Müller [8] a large volume of color capillaryscopic atlas was published. However, because of high morphological variability of individual capillary loops and absence

of proper controls in most of these studies, the narrow field (because only a limited area could be investigated under a microscope or a magnifying glass) approach became extensively subjective and the results were not reproducible. As such, NFC became less popular and was ignored for a very long time.

It was only in the mid of 20th century when Maricq [9] directed attention towards capillary landscape, recognized and established the benefits of utilizing panoramic capillaroscopy for the diagnosing of connective tissue diseases that investigators envisaged some interest in NFC.

Bollinger in 1979 [10] described a new technique of video microscopy based on Fluorescent tracers. This technique involves administering a bolus injection of 20% solution of Sodium fluoresces in into the antecubital vein that enables the dye to reach the capillaries. This technique enables the visualization of trans capillary and interstitial diffusion of the dye. Cutolo (2000) [11] introduced a further refinement of the findings of Maricq.

A simple history of nailfold capillaroscope is depicted in Table I.

TABLE I. A SIMPLE HISTORY OF NAILFOLD CAPILLAROSCOPE FOR DIAGNOSING RHEUMATIC DISEASES

Name Of Author	Year	Technique Used
Johan Christophorous Kolhaus	1663	Used primitive microscope firstly.
Giovanni Rasori	1766-1837	First noted the relationship and capillary abnormality
Brown and O'Leary	1925	Abnormal vasculature of scleroderma
Müller	1977	Large capillaroscopic arteries
Hildegard Maricq	1977	Recognition of micro vascular landscape
Alfred Bollinger	1979	Pioneer of fluorescence video microscopy
Maurizio Cutolo	2000	Capillaroscopic training course

Reference – Chen *et al* (2009)

Recently there has been a shift towards computer based nailfold video capillaroscopy system, which can record images, enhance image quality and show real time blood flow and velocity.

Anderson *et al* (2005) [12] developed a computer based nailfold video capillaroscopy system. Using frame registration software, digitized video images from the microscope were combined to form a panoramic mosaic of the nailfold. They reported that newly developed system improves reproducibility of nailfold capillary measurements by allowing measurements of the same capillaries by different

observers. The new system by allowing access to previous measurements may improves reliabilities in longitudinal studies and as such has the potential of being a valuable outcome measure of micro vessel disease. A multicentre study on the reliability of qualitative and quantitative nailfold video capillaroscopy was conducted by Hofstee *et al* (2011)[13].

The studies found that inter and intra observer reliability of quantitative parameters showed substantial to almost perfect agreement. Qualitative parameters showed moderate to substantial intra observer reliability and substantial intra observer reliability. This study reinforced earlier findings which cite inherent difficulties in tracking of circulating cells and micro particles and retrieval of their behavior characteristics. The task of automated blood cell tracking is particularly challenging because of the blood cell's non rigid shapes, the instability inherent in videos, the abundance of moving objects and their super imposition [14].

Vennemann, P., Lindken, R., Westerweel, J.,(2007) [15] in their study discussed *in vivo* whole-field blood velocity measurement techniques. According to them there are three principles of full field velocity which are suitable for monitoring capillary flow namely laser Doppler velocimetry (including time-varying speckle), laser speckle contrast imaging and particle image velocimetry (including particle tracking).

Table II gives a brief overview of the reviewed methods in terms of spatial and temporal resolution.

TABLE II. SPATIAL AND TEMPORAL RESOLUTION IN VIVO FULL FIELD BLOOD VELOCITY MEASUREMENT TECHNIQUES

Method	Velocity Component	Spatial Resolution (μm)	Measurement Duration (S)	Remarks
Scanning laser Doppler	1	10^1	10^0	Standard diagnostic tool
Multi-probe laser Doppler	1	10^2	10^2	Under development
Profile laser Doppler	Standard 1 upto 3	10^{-1}	10^{-3}	Under development
Laser speckle contrast imaging	1	10^2	10^{-3}	Standard research tool for animal model
Particle image velocimetry	Standard 2 up to 3	10^1	10^{-3}	Used in animal research

Ultrasound particle image velocimetry	2	10^2	10^{-2}	Used in animal research
Nuclear Magnetic Resonance imaging	Standard 1 up to 3	10^2	10^{-2}	Used in animal research

Reference-Vennemann *et al* (2007)

Based on the review of literature Eden *et al* (2005) [14], Acton, S.T., Wethmar, K., Ley, K., (2001) [16] and Allen *et al* (British Machine Vision Conference) [17] computer based system for the analysis of nailfold capillary pattern is built up through a series of steps which can broadly be arranged in the following sequence:

- Reading the video frame by frame.
- Segmenting the vessels from each frame
- Denoising, deblurring the video.
- Analysis and tracking of Red Blood Cells and White Blood Cells in the vessels.
- Measuring features in terms of their count, their size, velocity and relative positions.

A. Instrument Used In Doing Nail Fold Capillaryscopy

The major instrument that is used are Electron Microscopes, these are scientific instruments that use a beam of highly energetic electrons to examine objects on a very fine scale.

Electron Microscopes (EMs) functions exactly as their optical counterparts except that they use a focused beam of electrons instead of light to "image" the specimen and gain information as to its structure and composition.

The basic steps involved in all Electron Microscopes for observations include is to get the focus onto the sample using magnetic lens, this is done by a stream of electrons (formed by the Electron Source) and accelerated toward the specimen using a positive electrical potential. The interaction of the beam with the sample is then observed for the potential findings, it may also require confirmation of the focused stream using apertures.

B. Video Microscopy

The use of a high-quality video camera or other fast camera (such as a charge-coupled device) attached to a research-quality light microscope for the purpose of real-time or high-speed imaging of samples on a microscope stage. These images are

recorded at regular intervals (often at "video rate" of 30 images per second), and the time-lapse sequence can be played back in the form of a movie. The term "video microscopy" originally referred to microscope imaging using true video (30 frames per second) but now generally refers to rapid time-lapse imaging techniques. Video microscopy is used frequently to image small structures that move rapidly within cells as well as movement of whole cells. This motion can be quantitated, and in the case of fluorescence microscopy, changes in fluorescent intensity (reflecting the local chemical environment of the fluorescent molecule or the number of fluorescent molecules) can be quantities as well.

C. Factors Affecting The Accuracy Of Measurements In Image Processing Technique

- Quality of video microscopy.
- Process of image/video registration and normalization of foreground and background of each frame of video.
- Type of edge detection operator.
- Vessel segmentation which is always preferred that segmentation occurs when maximum information is available which is typically possible in frequency domain.
- Computational time and complexity should be minimum.
- Consideration of temporal features like mean, median, variance etc. and color feature.
- Frame by frame analysis of the blood flow and cell path within the vessel.

D. Use Of Nailfold Capillaroscopy

The maximum usage of nailfold capillaroscopy technique is in diagnosis of diseases related to skin tissues e.g. Systemic sclerosis [1], it is a clinically heterogeneous, systemic disorder which affects the connective tissue of the skin, internal organs and the walls of blood vessels leading to tension and hardness of the skin. It is characterized by alterations of the microvasculature, disturbances of the immune system and by massive deposition of collagen and other matrix substances in the connective tissue.

Typically, the major criteria in identifying this disease is skin tightness, skin thickening as well as presence of abnormal nailfold capillaries. There further class of sclerosis which might occur, and the classification criteria is based on the incidence of sclerosis on particular part of body or simply to what extent it is limited or spread on hands, faces, feet, forearms, presence of or absence of anticentromere antibodies and presence of pulmonary tension. The

most important of these criteria are the calibrations related to blood flow movements .In general this disease affects the connective tissue, predominantly of the skin and vessel wall and, to a lesser extent, of the gastrointestinal tract, heart, lungs and kidneys.



Figure 1. Patient Infected From Nailfold Disease



Figure2. Patient Infecting From Nailfold Disease

This condition may lead to future complications related to disease which based on condition of bone and muscles also, typical there is weakness in muscles and we might need to correlate the finding of nailfold capillarscopy test to arthritis.



Figure3. Irregular nail fold capillaries as shown by capillaroscopy

Prominent finding of nailfold capillaroscopy are normally related to vascular abnormalities which can be noted in capillaries and small blood vessels. Affected capillaries are characterized by distorted and irregular loops. The changes include reduced numbers of capillaries and the presence of a vascular areas as shown by nail fold capillaroscopy, even in the preclinical stages a show above, On the ultra structural level the earliest changes consist of large gaps between endothelial cells, vacuolization of endothelial cytoplasm, an increase in the number of basal lamina-like layers, and disruption of endothelial cell cytoplasm membranes.

Since, early diagnosis and sound prognosis of various chronic diseases like sclerosis, arthritis, auto immune diseases etc. require reliable information pertaining to blood flow in the micro vessels, it is therefore of paramount importance to have a technique which is simple, repeatable, highly sensitive and inexpensive method of evaluating micro vascular abnormalities.

III. CONCLUSION AND FUTURE SCOPE

Since, early diagnosis and sound prognosis of various chronic diseases like sclerosis, arthritis, auto immune diseases etc. require reliable information pertaining to blood flow in the micro vessels, it is therefore of paramount importance to have a technique which is simple, repeatable, highly sensitive and inexpensive method of evaluating micro vascular abnormalities, so that issues related to the accuracy of the measurement are achieved to highest level, this can be attained by including better segmentation techniques and bringing each frame of Nail fold video into frequency domain and the doing the calculations of the flow that includes velocity measurements.

All the future methods must yield average values well within the experimental error limits of the techniques. The speed of moving particles in the capillaries of the human nailfold must be evaluated non-invasively more so that the patients do not undergo hardship of invasive methods.

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