An Analysis of Nailfold Capillaroscopy Imaging as A Diagnostic tool for Various Microvascular Disorders

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Abstract— **Nailfold Capillaroscopy (NFC) is a non-invasive, portable device used to acquire the image of capillaries at the nailfold region. The capillaries which play a vital role in microcirculation helps to diagnose various microvascular disorders such as systemic sclerosis, myositis, rheumatoid arthritis, diabetes, glaucoma, systemic erythematosus etc., as the physiology of internal organs is highly correlated with these microcirculation. The changes in microcirculation can also influence the cardiovascular and renal functions, which may lead to pulmonary pathologies, cardiac dysfunction and renal abnormalities. The qualitative parameter such as capillary morphology (tortuous capillaries, giant capillaries, ramified capillaries, bushy capillaries etc.) and quantitative parameter such as capillary height, capillary diameter, arterial and venous limb diameter, intercapillary distance etc. are measured to analyze the capillaries for diagnosing various diseases. The Study of capillary pattern can aid in diagnosis as well as treatment of various vascular abnormalities. This survey discusses the method to acquire the NFC images, studies involved in analyzing the morphology of capillaries and their pattern in various vascular disorders from NFC images.**

Keywords— ***Nailfold Capillaroscopy, Microcirculation, Capillary Morphology, Autoimmune conditions, Connective tissue diseases, vascular disorders.***

I. INTRODUCTION

The blood vessel which helps to deliver nutrients to and remove waste products from the blood and the surrounding tissues in human body is capillaries; hence it is important for vascular function .The nailfold is among the most accessible region to analyze abnormal changes in capillaries in various vascular disorders. The microcirculation in the dermis includes superficial and deep horizontally oriented plexuses. As seen in figure 1, the superficial plexus consist of 1-3 capillary loops per dermal papilla, which due to 90-degree positioning with surface of skin appear as visible dots & commas and it is positioned 1-2 mm underneath the surface of the skin [1]. Characterizing alterations in the microvasculature can offer helpful hints for determining a disease's diagnosis and prognosis. In the last few decades, the nailfold capillarascopy has been improved for diagnostic purposes. Along with connective tissue diseases, its possible role in other systemic and dermatological conditions is currently under investigation. Even though capillaries are tiny, any abnormalities in their functioning might create noticeable symptoms or even significant clinical disorders. As it provides essential information about the health of an individual, it has a major part in medical diagnostics. The capillaries of the nailfold are normally long, straight and thin, but they can vary in length, thickness, and tortuosity occasionally. Vascular abnormalities such as aneurysms, saccular dilatations, Raynaud's disease, scleroderma, acrocyanosis, polycythemia, hypertension and autoimmune conditions such as arthritis, myositis is highly associated with irregular arrangement of capillary loops. The interrelationship between blood flow resistance and the blood pressure level in the human skin capillaries attracts rheumatology researchers to study microcirculation and its associated abnormalities. Mapping of RBC velocity with morphological changes in the capillaries can aid detection and treatment of microvascular conditions. The increase in capillary count and larger blood vessels is a key way that cancer may promote its own growth. Age-related macular degeneration is influenced by abnormalities of the retinal capillaries. People with cardiovascular risk factors and coronary heart disease have decreased capillary density. The vascular bed is inaccessible for research on human capillary function. On the other hand, the capillaroscopy technique makes it simple to study skin capillaries and allows the researcher to evaluate blood flow velocity and density. Proximal nailfold (PNF) capillaries can be examined using a reliable, noninvasive, painless, and reasonably priced technique called nailfold capillaroscopy (NFC) [2]. It's used to investigate diseases that affect the microvasculature, such as connective tissue disorders. Magnifying lens was used in the earlier period of time to obtain capillaries image from NFC and later wide-field and ophthalmoscopes were employed. The most recent dermatoscopes and videocapillaroscopy devices include high magnification (~200×), polarization, and advanced software that make studying capillary morphology easier. These more recent systems also have real-time control over the acquisition, storing and processing of images, together with integrated software for millimeter (mm) measurement [3–4]. Factors such as age of the subjects, presence of pigmentation in the skin, ethnicity, and formation of edema and inter observer variance highly influence the results obtained with NFC. [5–11]. This review will outline the methods utilized to conduct these assessments as well as some potential shifts between normal and abnormal conditions.

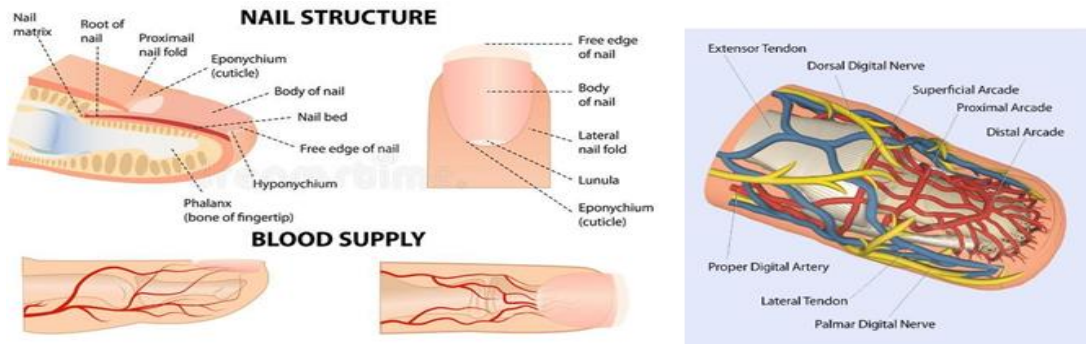


Fig. 1.Visibility of Microvasculature in the nail [1]

A. Capillaroscopic Microvascular morphology

The capillary morphology to be examined during NFC examination includes tortuosity, capillary loop diameter and density of capillaries, avascular areas, angiogenesis and visibility of subpapillary venous plexus, microhemorrhage and architectural structure.

(a) Capillary Dimensions

When examining capillary anomalies, factors such as capillary thickness (capillary width), capillary height (capillary length), size of venous and arterial limb, exterior and internal diameters, and apex thickness are taken into account. The measurement of capillary height has a crucial role in differentiating various abnormal capillaries but due to the changes in transparency of the skin it is difficult to accurately measure the length. The mentioned capillary dimensions can be measured by using various image processing techniques. A schematic diagram representing the important capillary dimension is shown in figure 2. The height of capillaries in fourth and fifth finger is usually longer when compared with other fingers. Normal capillaries will have an average height of 475µm and an elongated capillaries will have a height greater than 700µm [13]. An increased capillary size i.e. greater than 20µm is an indicator of excessively big capillary loop.

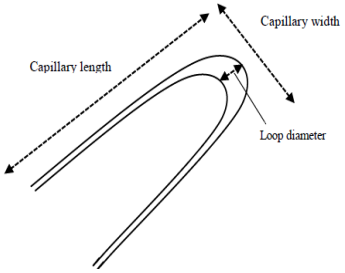


Fig.2. Schematic diagram representing a capillary dimension

Giant capillaries or mega capillaries are capillaries whose diameter is larger than normal capillaries i.e. more than 50µm. The development of homogeneously and irregularly expanded capillary loops indicates the abnormality or the progression of the disease. The capillary thickness parameter has been given several values in the literature. The widest point of the capillaries is referred as capillary thickness otherwise termed as "loop thickness", "maximum loop thickness", "total thickness" , "total caliber of the loop", "capillary loop amplitude", "totals capillary thickness" and "external diameter" [17] and they can be measured either automatically or manually.

(b) Tortuosity

The capillaries beneath the nailfold region generally look like "hairpin or reverse U-shaped in healthy subjects. An uneven or undulating appearance with one or more crossovers that resemble "treble clef" loops, "antler" loops, "trefoil" loops, or "glomerule" loops is known as tortuosity. Although tortuosity has little diagnostic significance, in some conditions it may be an indication of angiogenesis. [12].

(c) Density

Capillary density is the count of capillaries within the given area of skin. There are one to three capillaries at the nailfold of each dermal papilla. Ten to thirty capillaries per square millimeter, or nine to thirteen capillaries per millimeter, are present. Measurements of capillary density can be used to determine the total density of vessels or the functional density of capillaries in a particular situation [13].

(d) Angiogenesis

Capillary neoformation can have a range of traits. Capillary loop clusters that resemble trees and extremely twisted are a sign of angiogenesis. These clusters are often encompassed by a dropout of regular capillary loops. Angiogenesis is indicated by extremely elongated loops, extremely tortuous, coiled, branching, bushy capillaries and thin interconnected capillaries.

(e) Avascular area

This condition denotes a reduction in the number of capillaries or their loss within a 500µm field. Additionally, it has been linked to illnesses that proceed more quickly; therefore it also has prognostic importance.

II. METHODS

The equipment used to examine capillaries is ophthalmoscopes, dermatoscope, videocapillarascope and wide field microscope. It is easier to conduct a clinical

examination if the microscope can be moved over the skin region of interest rather than the patient. To do this, the optics can be mounted on a normal mounting block and then attached to a focusing block, which is then connected to an arm that allows movement top and bottom, left to right, and tilting in two planes. Hence digital videocapillaroscopy, an instrument that uses a digital video camera embedded in a microscope is used to measure and evaluate capillaroscopy characteristics. The scientific camera, illuminator, objective lens, processor and the software tool as in figure 3 are the essential components in videocapillarascope. Since, its magnification is very high, it can differentiate distinct

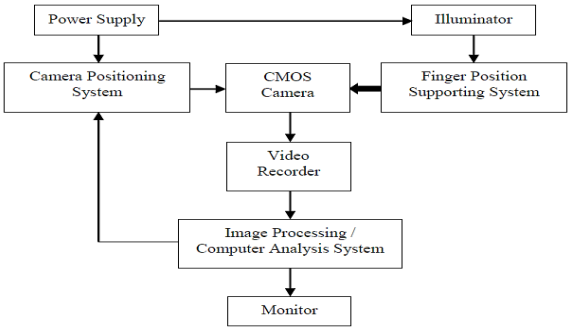


Fig. 3. Block diagram for nailfold capillaroscopy.

capillaries based on visible details, even though the magnification capability is low. Direct contact with a nailfold and evaluation of patients with severe finger flexion contractures are also made possible by it. A videocapillaroscopy makes direct contact with the nailfold of a patient. Reflections arise in videocapillarascopy can be reduced by adjusting its contact angle and orientation. A clear picture of the capillary branches can be produced by utilizing the camera head and manually adjusting the focusing mechanism. Optical probes have magnification levels ranging from 100x to 1000x; in clinical practice, a 200x magnification is commonly used. Although capillaries are more visible at this level of magnification, each capillaroscopic image acquired in this way can only cover 25% of the nailfold's surface area [14-16]. Before examination, the patients will be advised to thoroughly cleanse their hands with antimicrobial soap & water and then pat them dry with sterile gauze. Prior to the test, patients have to sit at room temperature of 20–25°C for 15–20 minutes in order to help them relax. The examination process also needs to be described to them. In order to have a good resolution, vegetable oil is applied to the finger nail which is to be examined. The fourth and fifth fingers of both hands are typically considered for in-depth morphological studies of the capillaries. Presence of nail paint, physical injuries in the nail region should be excluded from examinations and it has to be ensured that participants should abstain from smoking or consuming caffeine 4-6 hours prior to examination. There is usually little to no capillary flow when the patient feels uneasy or the examination room is cool. Once the gadget is focused, a ten- to twenty-second video clip and one static image are captured near the middle of a nailfold. The accurate region for acquiring the image is the distal layer of the capillaries present underneath the papilla. The finger nailfold is used to capture a video sequence of blood flow in the capillaries at a 200x magnification. Figure 4 describes the procedures to extract the nail bed's microvasculature. These procedures involve extracting frames for various parameter analysis. The frame from the video that was captured from the nailbed utilizing capillaroscopy is shown in Figure 4. It is simple to observe the capillaries in Figure 5, from which various capillary parameters such as density, loop height, avascular zone can be analyzed.

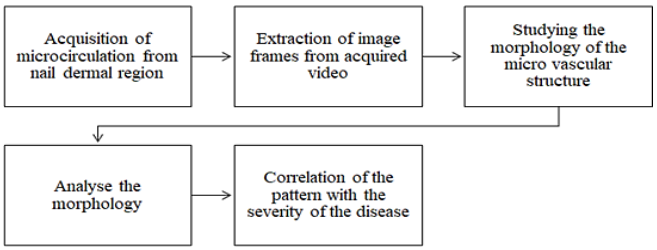


Fig. 4. Flowchart to study the microvascular morphology.

Fig. 5. Capillary image acquired from NFC

III. ANALYSIS OF MICROVASCULAR PATTERN USING NFC

A. NFC in Rheumatic Diseases

NFC is a useful device for examining microvascular abnormalities in rheumatic conditions, especially in systemic rheumatic conditions like raynaud's phenomenon and scleroderma [54]. It also be utilized to differentiate stages of disease, particularly in dermatomyositis and to identify primary and secondary raynaud's phenomenon [55]. Specifically, video NFC makes capillary data measurement and storage more precise and helps in detecting systemic sclerosis at its early stage. In pediatric rheumatology, the evaluation of morphological irregularities of the microcirculation, NFC has proven to be beneficial, especially in the cases of juvenile systemic sclerosis, raynaud's phenomenon juvenile dermatomyositis and idiopathic arthritis [56]. The capillary parameters that are considered to analyze them are given in table I. The conventional method to evaluate capillary density was direct observation method in which direct observation of capillary loops and marking of distal loops are done. In 90^{o} method, the capillary loop is classified as distal loop if the angle formed between capillary tip and the tip of its two adjacent capillaries is larger than 90^{o} [57]. The height and thickness of capillaries can be evaluated both automatically and manually. In automated measurement, principle component analysis was used to assess the thickness and height of the capillaries. [27]. The normal capillaries are

differentiated from abnormal conditions based on it enlargement as in figure 6. The largest distance between two neighboring capillaries, or the intercapillary distance, can be measured manually or semi-automatically.

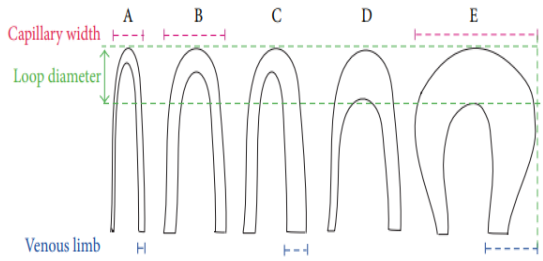


Fig. 6. (A)Capillary loop of normal group; (B) Afferent capillary loop in dilated condition; (C) Efferent capillary loop in dilated condition; (D) Dilated apical capillary loop and (E) Mega capillary loop with horseshoe shaped.[27]

TABLE I. SIGNIFICANT CAPILLARY PARAMETERS AND THEIR NORMAL RANGE

Capillary Parameter	Normal Range
Capillary Density	6–7.3 capillaries per mm(Children) 7.3–10.3 capillaries per mm (Adults)
Capillary thickness	27– 59.5 μm (upper limit)
capillary height	92 - 295 μm (upper limit)
Arterial limb size	7 to 17 μm
Venous limb size	11 to 20.6 μm
Loop size	8 - 21 μm
Internal diameter	18 to 21 μm.
Apex thickness	26 to 39 μm
Intercapillary distance	96 to 166 μm

In semi-automated measurement image processing algorithms was applied to preprocess the image and the distance was calculated by marking the intersection line of the capillary apices manually [60]. The subpapillary plexus is the term used to describe the vascular network into which capillaries drain near the base of a finger nailfold. These will gradually disappear in adults but if the person is diagnosed with any microvascular abnormalities, the sub papillary plexus will be visible. The abnormal findings of capillaries are given in table II.

B. NFC in Raynaud's Phenomenon

A disorder with reduced microcirculation due to persistant contraction of blood vessels in that region is called raynaud's phenomenon. Primary RP (PRP) and Secondary RP (SRP) are the two primary types of RP. PRP is a benign condition, While SRP is often considered as a sign for Systemic Sclerosis (SSc), myositis, rheumatoid arthritis etc. NFC is useful for differentiating these PRP and SRP. A machine learning approach can be employed to classify raynaud's phenomenon and SSc. The mean intercapillary distance measured in arbitrary units was 18.1 (9.0) and the mean capillary thickness was observed to be 16.9 (4.6) [84]. Random forest and Regression approach been followed for the classification of blood vessels (Supervised learning) and orientation & thickness of capillaries respectively [61]. Patient with systemic sclerosis and Primary Raynaud Phenomenon were classified by measuring statistical differences among them. Structural measurements (capillary density, mean and maximum thickness, disorganization of capillaries, shape score, mean flow velocity) and Capillary flow in the capillaries have been taken as important parameter for statistical analysis [62]. Though raynaud's phenomenon is a connective tissue disease, it is also considered as one of the major symptoms in other conditions which include arthritis, myositis, systemic sclerosis and systemic lupus erythomatosus etc. Multiclass logistic regression and support vector machine algorithms were implemented to classify RP from SSc [84].

TABLE II. ABNORMAL FINDINGS OF CAPILLARIES

Abnormal parameters	Findings
Enlarged Capillaries	>4 times the normal diameter
Elongated capillaries	Capillary loop longer than 300 um
Giant capillaries	Arterial or venous limb size > 50 μm
Dilated capillaries	• The diameter of Arterial limb > 15 μm • Venous limb has its diameter wider than 20 μm
Avascular areas	• 2 or more capillaries missing • Inter capillary distance > 500 μm

C. NFC in Systemic sclerosis

Systemic sclerosis (SSc), one of the connective tissue diseases with a sign of autoimmunity, fibrosis of external and internal organs and Raynaud's phenomenon. The arrangement of nailfold capillaries observed in SSc is referred as 'Scleroderma pattern' which has avascular areas, giant capillaries, ramified capillary loops and haemorrhages. 82-95% of people affected with SSc shows the sign of scleroderma pattern and also associated with raynaud's phenomenon [63]. This scleroderma pattern is categorized into early, active and late stage as given in table III based on which the severity of the disease can be examined. At the nailfold, capillary abnormalities were observed in almost 90% of SSc patients.

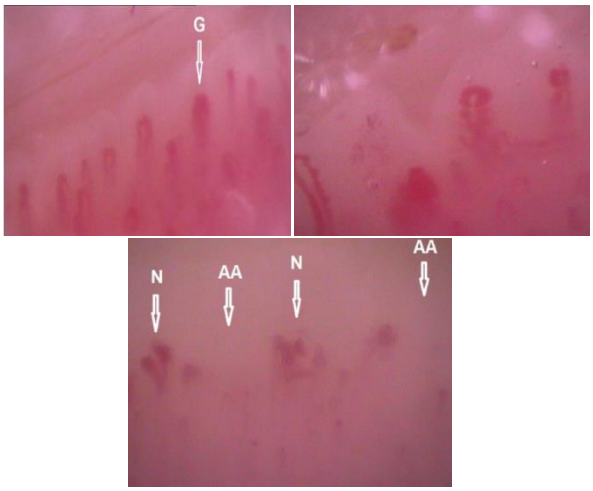


Fig. 7. Scleroderma pattern in SSc ((a) Early, (b) Active, (c) Late). G - Giant capillary; N - Neoangiogenesis; AA - Avascular Areas) [40]

TABLE III STAGES OF SCLERODERMA PATTERN

Early	Active	Late
Few giant capillaries	Frequent giant capillaries	Few or absence of giant capillaries
Few capillary haemorrhage	Frequent capillary haemorrhage	Absence of haemorrhage
No significant loss of capillaries	Moderate loss of capillaries	severe loss of capillaries
Well preserved capillaries distribution	Mild disorganization	Severe disorganization
No ramified capillaries	Some ramified capillaries	Frequent ramified capillaries

The primary problems found in SSc patients are deorganization of nailfold microvascular network, larger loops, capillary neoformation and avascular regions. [81]. Increased capillary thickness, disorganization in the overall direction of the capillaries, lack of straight edges, increased intercapillary distance with avascular areas were reported in SSc conditions [84]. The capillaroscopic findings obtained using NFC from SSc provides significant diagnostic information from which the capillary structure and its parameter can be determined as given in table IV [32]. On a quantitative basis, capillary diameter [32] and capillary density [40] is used as significant parameters to diagnose and differentiate SSc from other connective tissue disorders. The correlation between systemic sclerosis and the scleroderma pattern is also noted in cases of pulmonary arterial hypertension. Avascular regions identified in systemic sclerosis indicate the occurrence of digital ulcers. In a research involving 36 systemic sclerosis patients, digital ulcers were found in 36% of the participants. [32]. Chi square test and multinominal logistic regression was applied to differentiate stage of scleroderma pattern in SSc patients [62]. NFC images provides a significant outcome for SSc patients to study the disease activity after treatment [82]. Figure 7 shows the abnormal conditions observed in systemic sclerosis.

D. NFC in Glaucoma

Glaucoma is a condition which causes damage to optic nerve due to increased intraocular pressure as a result of insufficient blood supply. Primary Open Angle Glaucoma (POAG) which is a class of glaucoma which occur due to absence of retinal ganglion cells. It shows dysfunction in haemo-dynamic activities in ocular and systemic circulation when compared with normal group [62 -64]. Laser Doppler flowmetery and Color Doppler Imaging were used to analyze the blood flow at the retinal region in POAG Patients. But the flow of blood cannot be analyzed in pericapillary region of POAG with these techniques [65 – 69]. The density of capillaries and capillary blood flow in these patients were found to be reduced when compared with normal groups [41]. Multiple Linear Regression analyses was applied to differentiate nailfold capillaries of POAG from normal group [41]. Normal Tension Glaucoma (NTG) is a kind of glaucomatous condition with intraocular pressure in the normal range. In this type, Capillary density is found to be decreased when compared with normal group. Disc haemorrhage (11% - 42%), microbleedings and enlargement of capillaries is more frequently observed in NTG as in figure 8. Capillary blood flow velocity is considered as a dynamic parameter for analysing microcirculation in NTG patients, which is significantly reduced as compared with health individuals [47]. Table V shows the abnormal capillary parameters observed in glaucoma conditions.

Fig. 8. NFC image of a patient with NTG [47]

D. NFC in Diabetes mellitus

Type 1 and type 2 Diabetes mellitus affects macro and micro vasculature due to the change in capillary blood flow and blood flow velocity and these effect on vasculature leads to the destruction of capillaries. Diagnosis of vascular damage with capillaroscopy can be an effective method in treating diabetic patients. People who have the history of vascular disorder, clinical cardiovascular and microvascular disease, collagen vascular disease, hypertension, skin allergies, hepatopathy, smoking, infection, vascular effective drug use should be excluded from diagnosis [28]. Ectasia and

giant capillaries, arborified capillaries, branched, avascular areas, tortuous, haemorrhages, cuticulitis, presence of the subpapillary venous plexus (SPVP) and Scleroderma pattern are the parameters considered for analyzing the micro-architecture of capillaries in people with diabetes mellitus.

TABLE IV CAPILLAROSCOPY FINDINGS IN SSC PATIENTS

Abnormal findings	Observations
Shape of the capillaries [32]	• Giant capillaries • Avascular areas • Neoangiogenesis • Dearrangement of capillaries • Elongated capillarie
Haemorrhage [62]	Present
Capillary size [32]	45 µm
Arterial or venous limb size [40]	>50 µm
Intercapillary distance [84]	35.7 (23.4) [mean (Standard deviation)]
Capillary thickness [84]	20.0 (5.7) [mean (Standard deviation)]

About 63% of diabetic patients under study have shown the presence of tortuous capillaries, 59% has cross linked capillaries, 48% have avascular areas in the capillaries and 31% have ectasias. Giant and ramified capillaries are seen in very few subjects. Among the diabetic group, each individual has atleast 2 capillarascopic alterations [29].Tortuous capillaries were highly seen in diabetic group in contrast to healthy group. [29, 30]. The Abnormal capillarscopic findings given in figure 11 were observed in Diabetes Mellitus conditions. Microvascular involvement in both the cases was dominant and these could be precisely detected with Nailfold videocapillarascopy [30, 31]. When comparing type 1 DM patients to healthy people, it is observed that they have more dilated and tortuous capillaries as well as a higher capillary density. [47].

E. NFC in Arthritis

Arthritis is condition which is caused due to swelling and tenderness of one or more joints. The vascular system's conditions are crucial for the onset or advancement of disease disorders. Therefore, NFC can be used to analyze and study the microvascular pattern in patient diagnosed with arthritis conditions. Figure 9 shows the capillary pattern in arthritis conditions. Capillary density which is one of the significant parameter to study the disease condition is found to be reduced in Psoriatic Arthritis (PsA) when compared with normal group [46].

In PsA conditions, a reduction in the diameter of both the venous and arterial branch in capillary loop has been reported. [70]. Around 30.6% of individuals living with Rheumatoid Arthritis (RA) have been related to Raynaud's phenomenon. [46].The mean capillary height is observed to be larger in RA conditions. [46, 49] while it was found to be reduced in PsA [46]. The abnormal capillarascopic pattern observed in RA and PsA is given in table VI. NFC can be used to analyze the capillary pattern with both quantitative and qualitative measurement in RA arthritis patients [49]. About 99.5% and 74.7% of patients with RA conditions have been observed with tortousity & angiogenesis respectively, also increased efferent / afferent limb ratio is observed in RA conditions [49].

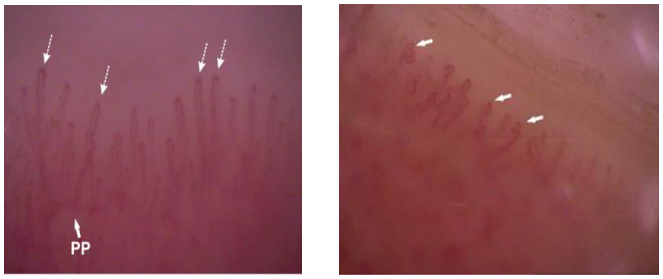


Fig. 9. (a) Capillary pattern in RA (b) Capillary pattern in PsA

(PP - visibility of subpapillary plexus)

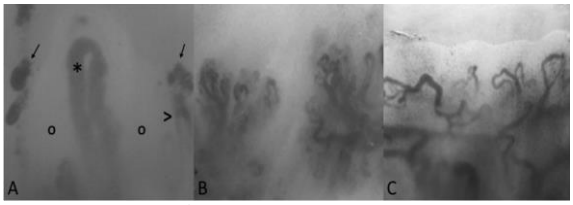


Fig. 10. NFC images of DM (A) Giant capillaries (marked with asterisk), (B) Bushy Capillaries (C) Loss of capillaries [34].

TABLE V. CAPILLAROSCOPY FINDINGS IN GLAUCOMA

Abnormal findings	Observations
Capillary density in POAG[41]	8.8 ± 1.0 (Mean ± Standard Deviation)
Capillary blood flow (pL/s) [41]	19.9 ± 9.4 (Mean ± Standard Deviation)
Shape of capillaries in NTG [43]	• Tortuous capillaries • Branched capillaries • Dilated capillaries • Meandering capillaries • Avascular areas
Haemmorhage [41, 43]	Present (in both POAG & NTG)
Capillary diameter in NTG Diameter of megacapillaries (NTG)	>20µm >50 µm

F. NFC in Myositis

Myositis is an autoimmune condition caused due to prolonged weakness and muscle fatigue. NFC is used as a tool for diagnosing few types of Myositis because of their active involvement in vascular endothelium leading

to microangiopathy [71 -73]. Scleroderma pattern is highly observed in patients diagnosed with dermatomyositis (DM) [74]. About 74% of patients diagnosed with Juvenile dermatomyositis (JDM), a type of DM associated with rash and muscle weakness has been observed with the sign of scleroderma pattern [75 – 76]. In JDM, reduced capillary density and increased capillary area as compared with normal group was reported [74].The most frequent early alteration seen in JDM was the morphological appearance of microthrombosis and microhemorrhages, capillary regeneration [36]. Reduced RBC velocity is observed in DM [76]. As compared with DM, PM does not show much significant changes in the capillaries. In a few cases of PM, scleroderma pattern was observed and in few it was absent but at the same time microhemorrhages, decreased capillary density, and capillary enlargement were seen in PM but very little in DM. [34].Since, NFC provides significant information on vascular pattern in myositis condition, it act as a biomarker that can be used to analyze the advancement of the disease in the skin and muscles. [37]. The abnormal capillary parameters observed in myositis conditions are given in table VII.

G. NFC in Systemic Lupus Erythematosus

Systemic Lupus Erythematosus (SLE) an autoimmune condition, where immune cells attack the tissue and internal organs leading to inflammation and damage in the affected regions. NFC is a useful tool in assessing microvascular involvement and disease activity in SLE. Studies show that patient diagnosed with SLE is associated with raynaud's phenomenon. 15.3% of this condition report scleroderma pattern [78]. The density of capillaries is found to be reduced in SLE. Microhaemorrhages were more common in patients with active SLE condition. [79]. About 9% of SLE has found to have an alteration in their blood flow [80]. The existence of extended capillaries was seen in 43% (13/30) of the cases, high tortuosity in 70% (21/30) of the cases, and a large subpapillary plexus in 60% (18/30) of the cases were the most common capillaroscopic abnormalities in SLE conditions. Eighty percent (24/31) of the patients had dilated capillaries. One important analysis for determining the capillary abnormalities in SLE patients is the existence of the scleroderma pattern. [83]. Figure 12 and table VIII shows the abnormal findings observed in SLE patients.

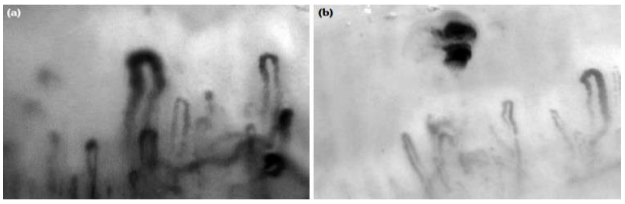


Fig . 12. (a) Systemic lupus erythematosus NFC image with Enlarged capillaries (20-50 μm), megacapillaries (>50 μm) and disruption of RBC. (b) Bleeding and absence of capillaries seen in NFC image of systemic lupus erythematosus condition [51]

TABLE VI. CAPILLAROSCOPY FINDINGS IN ARTHRITIS CONDITION

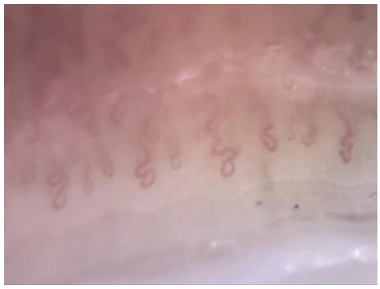
Abnormal findings	Observations
Shape of capillaries (in RA & PsA)	• Giant capillaries • Avascular areas • Bushy capillaries • Ramified capillaries • Elongated capillaries
Subpapillary Plexus in RA [46, 49]	Visible
Mean Capillary height in RA [70]	0.265± 0.086 mm
Arterial limb diameter in RA [46]	0.018± 0.005 mm
Mean Capillary height in PsA [46]	0.166± 0.09 mm
Mean capillary density in PsA [46]	8± 1 capillaries/mm

TABLE VII. CAPILLAROSCOPY FINDINGS IN MYOSITIS CONDITION

Abnormal findings	Observations
Shape of capillaries [33]	• Widened capillaries • Massive busy capillaries • Giant Capillaries • Elongated capillaries • Enlarged Capillaries • Avascular area
Mean Capillary Density in JDM [77]	4.5 capillary/mm
Capillary height [33]	>300um
Intercapillary distance [33]	>500 um
Haemorhage [77]	Present

TABLE VIII. CAPILLAROSCOPY FINDINGS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Abnormal findings	Observations
Shape of capillaries [53]	• Tortuous capillaries • Ramified Capillaries • Corkscrew capillaries
Capillary Diameter [52]	• Dilated (20 - 50μm) • Giant capillaries (>50 μm)
Capillary height [52]	>300um
Intercapillary distance [52]	>600 um
Haemorhage [52, 53]	Present

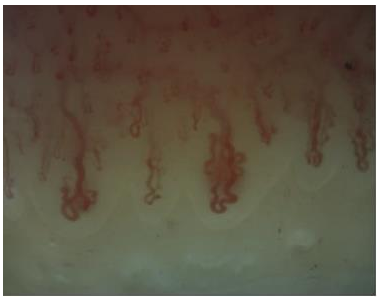


a.Tortuosity
(crossed capillaries with 1 mm in length)

b. Neoformation
(Twisting, bushy capillaries exhibiting significant variation in size)

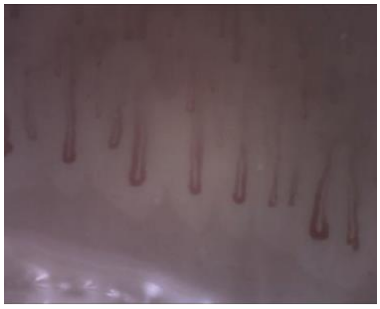
c. **Microhemorrhage**
(2 or more punctate bleeds around a single capillary)

d. Extravasation
(Bleeding in capillaries)

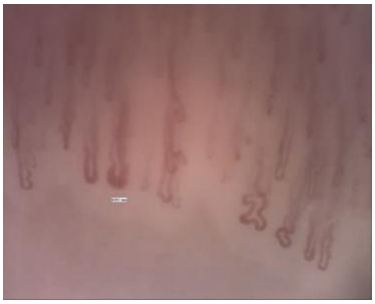


e. Avascular area and Neoformation
(Absence of capillaries or ≤6 capillaries over each 1 mm length)

f. Bizaree Capillary
(No definite shape and structure of capillaries)



g. Capillary Ectasia
(The size of capillary wall range from 0.02 to 0.05 micrometers)



h. Megacapillary
(capillary wall size >0.05 micrometers)

Fig.11.(a-h) Abnormal Findings Of Naifold Capillaries In Diabetic conditions [31]

H. NFC in secondary connective tissue diseases

In the above conditions, NFC is used as a diagnostic tool in analyzing the capillary pattern to diagnose and also to study the progression of diseases. Those vascular abnormalities at their active stage, affects other internal organ (skin, heart, lung) function leading to secondary connective tissue diseases. Digital ulcers, a type of skin disease are reported in systemic sclerosis. SSc Patients having sign of avascular areas are highly associated with digital ulcers. Decreased capillary density was found to observe in digital ulcers. Greater intercapillary distance was reported in patients with active ulcers [log (intercapillary distance), P = 0.03] [44]. In case of Ssc, advanced capillary loss is highly correlated with digital ulcers [45]. In leprosy patients abnormal capillary findings such as micro-haemorrhages, dilated, bushy and corkscrew capillaries was observed [47]. In case of psoriasis, the mean capillary density was <9 capillaries/mm, mean arterial limb diameter was 11.37 ± 2.434μ mean venous limb diameter was found to be 15.89 ± 3.131μ and length of the loop was 152.51 ± 57.21μ. Tortuous capillaries, ramified capillaries, avascular areas and haemorrhage were observed in patients diagnosed with psoriasis [48]. Autoantibodies and circulating immune complexes can cause vascular inflammation and damage to endothelial cell damage causing multiple organ dysfunctions. NFC is used to monitor any damage in the organ during the development of SSc, e.g., to predict the risk of hypertension in pulmonary region after the diagnosis of SSc. The clinical signs of SLE include cardiac involvement, neurological involvement, vasculitis, hematologic involvement, periungual vasculitis, and renal involvement. [78]. Most of the patients diagnosed with connective tissue diseases reported to have hypertension and cardiac insufficiency, those patient's capillaries are observed to be elongated longer than 300 μm in case of hypertension and it is appear to be

shorter in individuals with cardiac abnormalities [58].Pulmonary hypertension are also observed in systemic sclerosis at late stage [47]. Thus, NFC has a significant role in diagnosis and analysis of microcirculation in these secondary diseases.

IV. CONCLUSION

NFC is invaluable in diagnosing connective tissue diseases and also their influence on other internal organs by analyzing the microcirculation. The qualitative and quantitative parameters of capillaries that include shape, structure, density, length, thickness, capillary diameter, intercapillary distance are the factors considered for differentiating microvascular disorders. These factors are also helps in identifying the stages of disease thereby its progression can be studied. Hence, NFC is a highly specific and sensitive diagnostic tool for detecting various microvascular abnormalities. This paper provides a survey on the importance of NFC, methodology implemented to acquire the nailfold capillary images and the protocol to be followed during acquisition. The pattern of capillaries present in SSc, glaucoma, diabetes mellitus, arthritis and SLE has also been reviewed. The impact of connective tissue on internal organs and their capillary pattern reported in various literatures was studied in this paper. Thus, this paper provides an insight on NFC as a valuable tool and its application on various microvascular disorders along with their qualitative and quantitative parameters. With this, one can differentiate various vascular patterns and also able to use various image processing and machine learning algorithms on the capillary images for classification and for predicting the disease progression.

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