Nailfold capillaroscopy (NC) is the in vivo microscopic examination of the capillaries found in the skin just proximal to the nail. The capillaries in this area run parallel to the surface of the skin, and can be easily visualized with appropriate lighting and magnification. Using only a magnifying glass, the 19th century Italian physician Giovanni Rasori was able to describe abnormal capillaroscopic findings and related them to conjunctival inflammation. In the twentieth century, the practice of NC was refined and now it is used most prominently to detect markers of rheumatological disease, such as systemic sclerosis. However, there are indications that NC may also be helpful in the diagnosis and prognosis of various hereditary conditions that involve the microvasculature. In this article, we hope to illustrate a general approach to NC as a tool in assessing rheumatological pathologies as well as its potential utility in the context of genetic disease.

Procedure

Traditionally, NC has been performed with a light microscope. The patient is seated and acclimatized to the ambient temperature of the examining room. Immersion oil or clear gel is applied to the nailfold area to enhance transparency of the skin and make the capillaries more visible, and the light source is positioned at a 45 degree angle to the nailfold. A green LED or green-filtered light is often used to further enhance visibility, as light in the blue-green part of the spectrum is preferentially absorbed by hemoglobin. A wide view of the terminal capillaries can be obtained with a 10x-60x magnification.
magnification, and more detailed views can easily be achieved with higher magnification (250x-1000x). Photomicrographs can be taken at the time of examination for further study or archival purposes.

The capillaries can also be examined with hand-held instruments, such as an ophthalmoscope or a dermatoscope, although these often make it more difficult to spot areas of diminished vascularity. More recently, specialized videocapillaroscopic systems have been developed to facilitate the analysis of capillary abnormalities, although the expense of these systems may be prohibitive for some clinicians.

The more common findings in patients with microvascular abnormalities include the presence of large or giant capillaries, disorganization of the vascular array, tortuous vessels, microhemorrhage, loss of capillaries, and ramified, or “bushy,” capillaries.

**Rheumatological Findings**

Classically, nailfold capillaroscopy has been utilized to differentiate patients presenting with isolated Raynaud’s phenomenon (RP) from those who may have underlying connective tissue disorders causing secondary RP. The nailfold capillaries of healthy patients and isolated RP patients appear as parallel hairpin loops with visible afferent, transitional and efferent portions (Figure 1). In contrast, secondary RP patients may possess deviatory capillary patterns directing the clinician to investigate for certain connective tissue or autoimmune rheumatic diseases.

The scleroderma pattern has been extensively characterized and represents a multitude of nailfold capillary changes seen in patients with systemic scleroderma. Three variations of the scleroderma pattern have led to the categorization into early, active and late phases (Figure 2). Specific findings that have been described include giant capillaries proposed to be a result of an autoregulatory response to tissue hypoxia, capillary microhemorrhages due to early vascular damage, avascular fields due to increasing hypoxia and architectural disruption of capillaries.

Similar to systemic sclerosis, variations of the scleroderma pattern are also seen in patients with other connective tissue diseases such as dermatomyositis, systemic lupus erythramatosus, antiphospholipid syndrome, Sjogren’s syndrome and occasionally rheumatoid arthritis.

![Figure 1. Normal nailfold capillaries. (Courtesy of Dr. Joerg Piper)](image)

**Nailfold Capillaroscopy in Hereditary Hemorrhagic Telangiectasia**

An autosomal dominant disorder characterized by easily bleeding telangiectases on the skin and mucosal surfaces, hereditary hemorrhagic telangiectasia (HHT; OMIM 187300) can lead to arteriovenous malformations in many organs and paradoxical septic emboli. Therefore, early diagnosis is important for better prognosis. Currently, three typical telangiectases are required to make the diagnosis of HHT, with genetic testing only positive for a small subset of families. If not diagnosed, arteriovenous malformations and septic emboli may be missed. One study demonstrated that over 80 percent of patients with HHT show enlarged afferent portions of the capillary loop, a finding that was not evident in matched patients without HHT. More importantly, five of nine patients without visible macroscopic cutaneous telangiectases but having a clinical diagnosis of HHT showed enlarged afferent capillary loops. Although further studies are needed to validate this, nailfold capillaroscopy appears promising as a diagnostic aid when a definitive diagnosis of HHT can’t be
made based on clinical information alone (for example, if it is suspected but not yet proven).

**Capillary Blood Flow Measurements and Glaucoma**

As one of the leading causes of blindness in the world, glaucoma represents a significant threat to ocular health and day-to-day function. One of the most common subtypes, primary open-angle glaucoma (POAG; OMIM 137760), is known to have a significant genetic component, as the prevalence of POAG among those with a positive family history is 5- to 20-fold greater than the normal population. The progression of POAG is often insidious, and it is estimated that more than half of those with the disease remain unaware of their condition until their vision begins to deteriorate. Thus, screening measures for those who have a family history of POAG and others at increased risk have an important role in preventing the progression of glaucoma to visual damage and blindness. Unfortunately, the classic sign of developing glaucoma, a high intra-ocular pressure, is only detectable in about half of those with the disease.

Although the precise pathophysiology of POAG is complex and still not completely understood, it has been noted that aberrations in systemic blood flow are often correlated with the incidence of glaucoma. One such abnormality is the degree of peripheral capillary vasospasticity after a period of cooling. Using capillaroscopy, it is possible to measure blood flow in the nailfold vessels and estimate the extent to which flow...
stops in response to cold. Patients with POAG often show an exaggerated vasospastic response relative to normal controls, which may indicate a systemic abnormality of blood flow regulation. Thus, capillaroscopic examination in patients with risk factors for POAG may be useful in research and eventually in screening for this disease, especially when an elevated intra-ocular pressure is not detectable.

**Capillary Abnormalities and Psychiatry**

One of the more intriguing domains of medicine that can be examined with capillaroscopy relates to hereditary mental illness, namely schizophrenia. As early as 1939, researchers discovered that a disproportionate number of patients with schizophrenia exhibited abnormalities of the nailfold capillaries and increased visibility of the nailfold plexus, the dense subcutaneous network of capillaries found proximally adjacent to the fingernail, which is generally not visible past puberty. Typical findings upon examination of the nailfold include a highly visible capillary plexus (Figure 3), and oddly-patterned individual capillaries with numerous horizontal anastamoses.

Subsequent studies in the 1960’s and onwards aimed to establish an objective scale for measuring visibility of the plexus and concurrently found evidence that the endophenotype of high plexus visibility was positively correlated with familial, rather than sporadic, schizophrenia, as well as more severe and more negative symptoms. Conversely, it is estimated that 70% of patients with familiar schizophrenia have an elevated plexus visibility. This demonstrates that schizophrenia is a more complex disease, with abnormalities that extend beyond the brain in many patients.

Taken together, these data suggest that an elevated plexus visibility has the potential to be a suitable non-invasive biomarker for those at risk of developing hereditary schizophrenia or schizotypic personality features. Given the young age at which many patients with schizophrenia begin to show symptoms, the ability to screen for nailfold abnormalities could possibly enable families with a history of schizophrenia to be mindful of early manifestations of mental illness and seek appropriate treatment. Active research in this area is underway, and it is hoped that being able to identify a distinct subclass of people with schizophrenia may assist in future genetic studies aimed at discovering the underlying etiology for a truly debilitating disease.

**Figure 3. Nailfold venous plexus images with associated Maricq plexus visibility scores (0 = no visible plexus, 4 = highly visible plexus). (A) Normal, 0/4 on Maricq scale. (B) Abnormal, 4/4 on Maricq scale. (Courtesy of Dr. John Vuketich)**

**Conclusion**

Nailfold capillaroscopy is a tried and true clinical method that has applications to many disparate pathologies. While the usual investigations that comprise genetic workups cannot be replaced by a simple observation of nailfold capillaries, a thorough examination of the microvasculature can often yield clues that aid in
diagnosis and prognosis, with a minimum of expense and invasiveness. It is important to be aware that capillary abnormalities and other vascular signs can be missed if not sought and that magnification of the nailbeds in patients with many diseases can be a useful and relatively easy skill to acquire.

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References