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## Nailfold capillaroscopy



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## A B S T R A C T

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Raynaud's phenomenon

Scleroderma pattern

Systemic sclerosis

Connective tissue diseases

EULAR study group on microcirculation in rheumatic diseases

Nailfold capillaroscopy is a safe and well-established method for the assessment of structural alterations of the microcirculation. It is a crucial tool in the investigation and monitoring of patients presenting with Raynaud's phenomenon. Detection of the characteristic "scleroderma pattern" on capillaroscopy may indicate an underlying rheumatic disease, particularly systemic sclerosis (SSc). Herein, we highlight the practical aspects of videocapillaroscopy, including image acquisition and analysis, with mention of dermoscopy. Special emphasis is placed on standardized use of terminology to describe capillary characteristics. Systematic evaluation of images in discerning the normal from the abnormal using the validated European Alliance of Associations for Rheumatology (EULAR) Study Group consensus reporting framework is paramount. In addition to the relevance of capillaroscopy in the (very) early diagnosis of SSc, its emerging predictive value (especially capillary loss) for new organ involvement and disease

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progression is underscored. We further provide capillaroscopic findings in selected other rheumatic diseases.

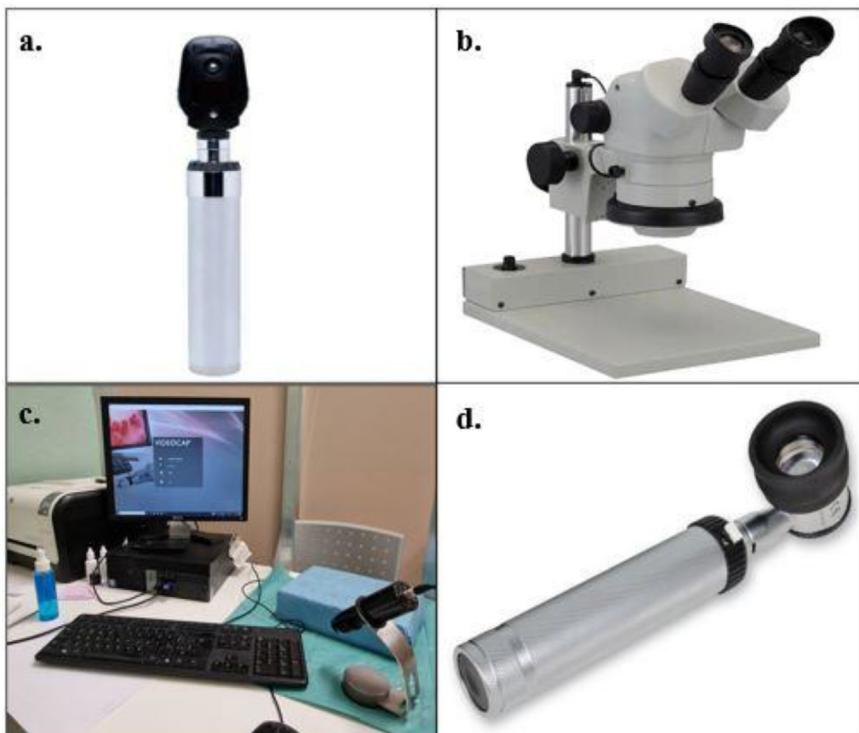
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## How to use nailfold videocapillaroscopy in daily practice

Capillaroscopy is a non-invasive imaging technique that is used for the *in vivo* assessment of the microcirculation. Its principal role is its use in the differential diagnosis of Raynaud's phenomenon (RP). It may also be used in "other" conditions [1].

Capillary microscopy can be performed with various optical instruments such as an ophthalmoscope, a dermatoscope, a photomacrogaphy system, a stereomicroscope, a conventional optical microscope, and a videocapillaroscope (Fig. 1) [2]. Only the dermatoscope and videocapillaroscope have demonstrated good validity and inter- and intra-observer reliability [3]. At present, the commercially available software for image analysis is restricted to videocapillaroscopes, allowing a standardized approach to analyzing individual capillaroscopic characteristics and use in a research setting [4,5].

The videocapillaroscope with handheld device is a technique to perform capillaroscopy that has several advantages: the technique itself can be learnt fast, even by novices; it has a handheld device (probe), which allows capillaroscopy to be performed in all circumstances, including in situations in which the use of the traditional microscope may be less convenient (such as in patients with flexion contractures) [6].



**Fig. 1.** Different imaging techniques for assessing microvascular morphology. **a.** The ophthalmoscope **b.** A stereomicroscope that has been adapted for nailfold capillaroscopy **c.** The nailfold videocapillaroscopy (NVC) device **d.** The dermatoscope.

### The videocapillaroscopy equipment

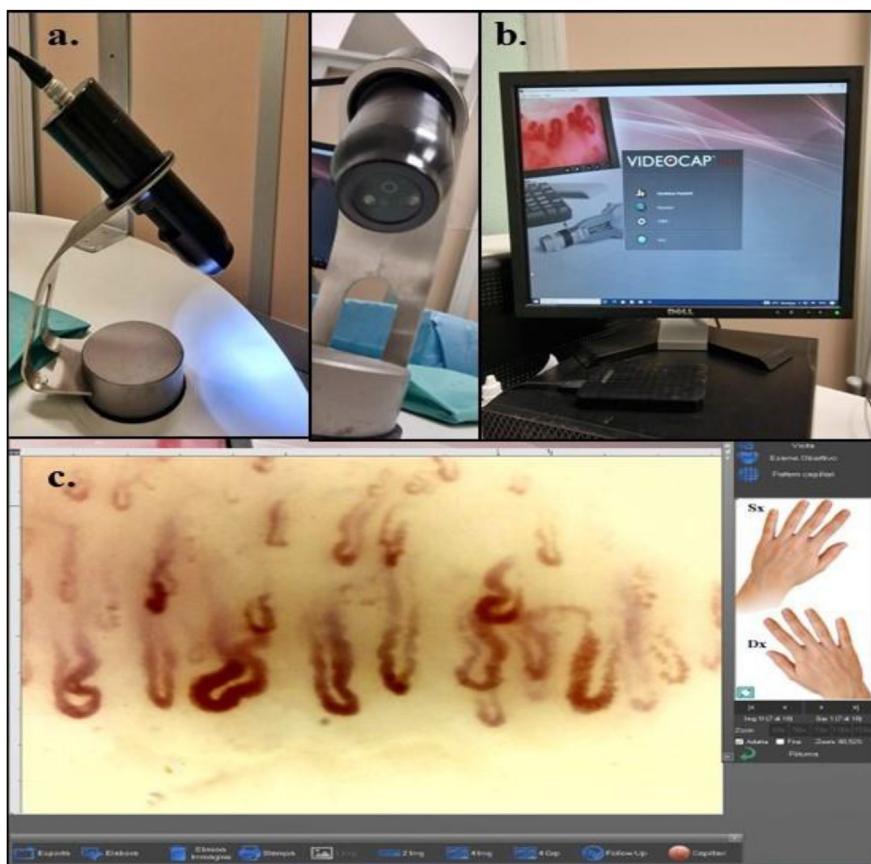
The nailfold videocapillaroscope consists of the following parts (Fig. 2).

- Digital video microscope with ultra-bright long-life white LEDs with  $\times 200$  high-resolution objective lenses, as per consensus of the European Alliance of Associations for Rheumatology (EULAR) Study Group on Microcirculation in Rheumatic Diseases and Scleroderma Clinical Trials Consortium (SCTC) Group on Capillaroscopy [7], with unpolarized light, integrated in the handheld device (probe).
- A high-resolution color monitor (e.g. 24 inch) on which images can be observed (pixel dimensions, e.g. 1920 horizontal X 1080 vertical).
- Digital image analysis software (Videocap, DS Medica, Milan, Italy).

### How to use the videocapillaroscope

#### Acclimatization of patients

Before starting the videocapillaroscopy, the patient is acclimatized in a room with constant temperature 20–22 °C for at least 15 min. In this way, undue vasoconstriction of capillaries, which can induce false positivity for avascular zones, can be avoided.



**Fig. 2.** The videocapillaroscopy equipment. **a.** The lens **b.** The high-resolution color monitor **c.** The digital image analysis software (see also below).

### *Area that is being examined*

In RP, morphologic evaluation of skin capillaries is generally performed at the nailfold ([Fig. 3](#)) because of several reasons.

- a) The fingers are an easy part of the body to perform videocapillaroscopy.
- b) The fingers are involved in the pathological process of some autoimmune disorders that give rise to a secondary RP.
- c) The observation site can be defined accurately.

*Transparency of epidermis.* As the epidermis is normally transparent, deposition of oil (e.g. cedar oil) will create a smooth surface that makes the visualization of superficial structures of the skin possible ([Fig. 4](#)).

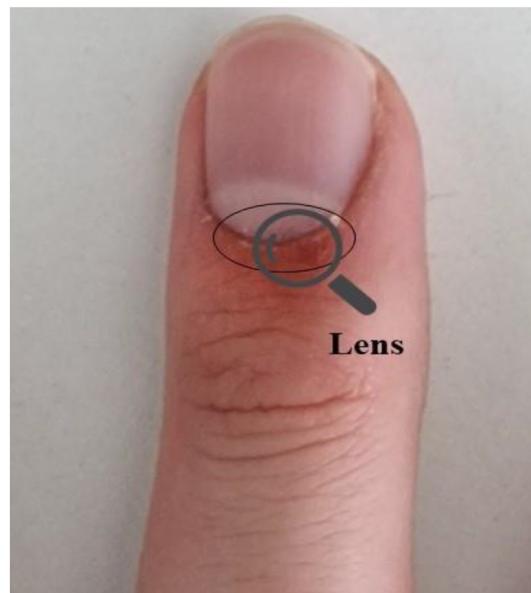
Nail polish and dirt should be removed from all nailfolds of the fingers, as they hamper the visibility. Fingers with localized trauma should not be examined, as wounds may give a false positive interpretation for hemorrhages and/or abnormal shapes (neoangiogenesis).

### *How to make the capillaroscopic image*

#### *Position of the probe*

The probe is placed on the nailfold at an angle of 90–45° ([Fig. 5](#)). The probe “rests” on the nailfold, and no pressure is exerted on the nailfold. In this way, one avoids the capillaries from being “pressed” away. Undue pressure would give false positive images of avascularity.

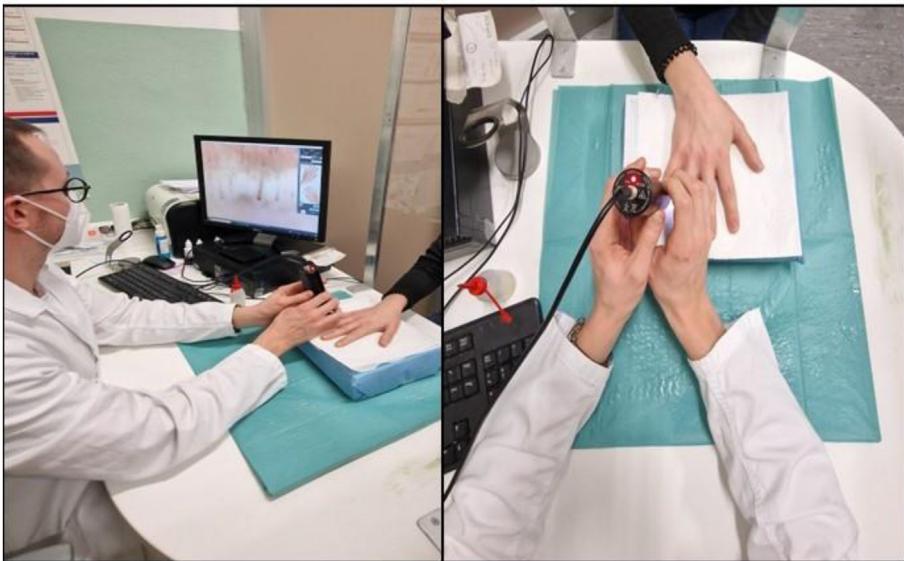
The contact probe makes it easy to explore the whole nailbed in all circumstances, including in situations in which the use of the traditional microscope may be less convenient (e.g. flexion contractures).



**Fig. 3.** Nailfold of a patient with a scleroderma-spectrum disease. Note the periungual erythema that can be seen with the naked eye.



**Fig. 4.** A drop of oil is being placed.



**Fig. 5.** Operator in front of the patient (left panel). Probe is placed on the nailfold at an angle of 90–45° (right panel).

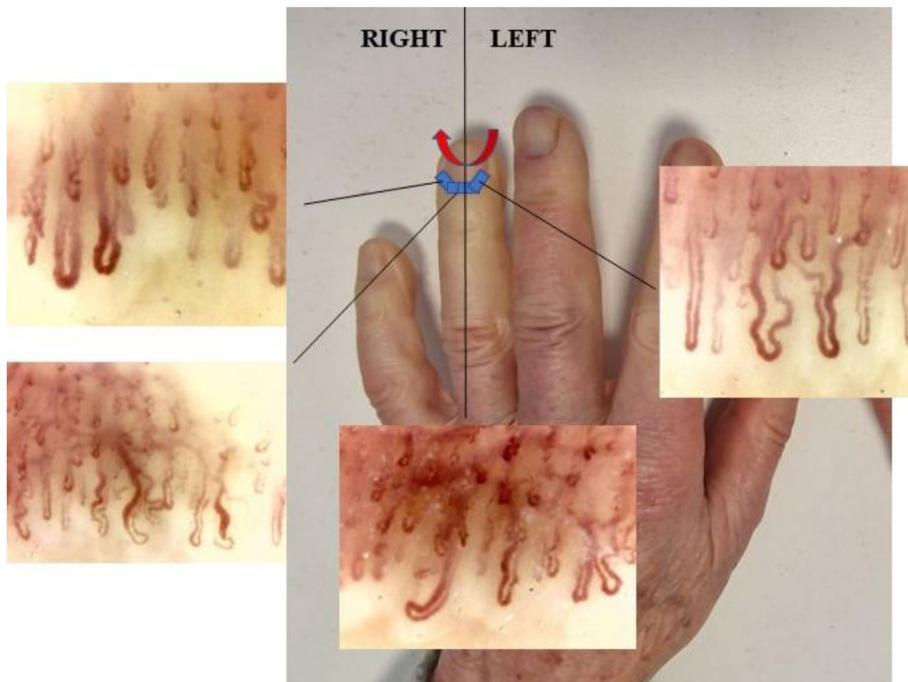
#### *Quality of the images*

Quality of the image can be obtained by, on the one hand, adapting the focus on the probe manually while looking at the high-resolution color monitor. Adaptations can be directly followed on the screen.

On the other hand, the light intensity can be adjusted by turning on the light intensity knob. Most authors agree that capillaries are best seen at the 4th finger.

#### *Capture of the capillaroscopic image*

When the quality of the image is as desired, the footswitch can be pressed and an image will be captured and stored. In this way, four images (one lateral field, two medial, and one lateral) or two images (two medial fields) per finger are taken ([Fig. 6](#)).



**Fig. 6.** From left to right, four pictures per finger are taken.

#### *Sequence of images*

The probe is used to examine the finger in the following manner: from left to right, from the operator's point of view (Fig. 6).

All fingers may be evaluated. Some schools do not evaluate the thumbs because capillaries are less well visualized there. Mostly, the 2nd, 3rd, 4th, and 5th fingers are examined ensuing in 32/16 images that are stored.

#### *Preparation and interpretation of images*

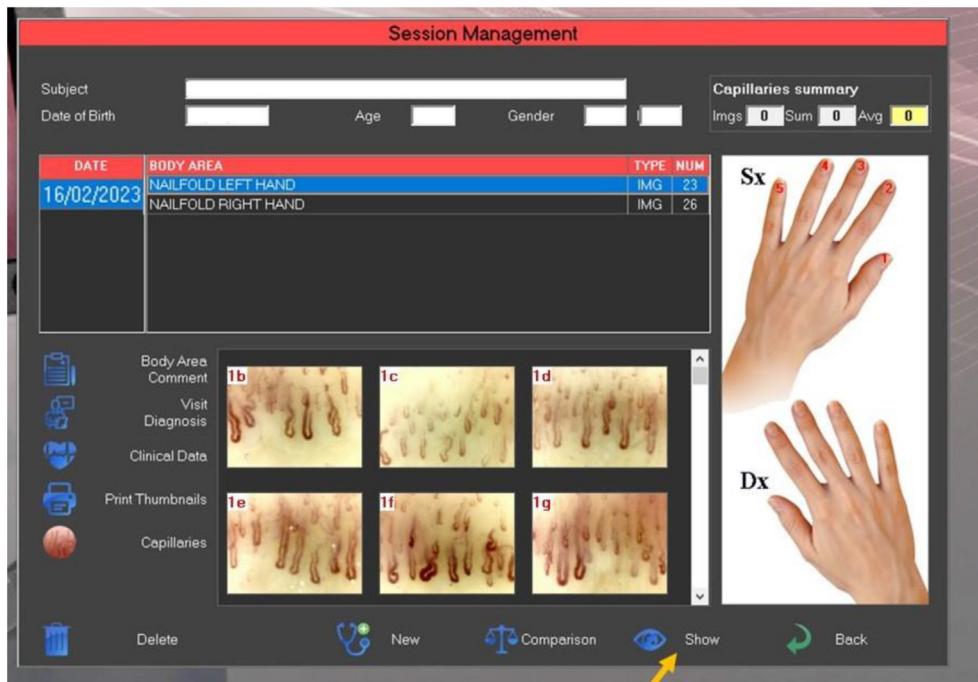
After the images are captured, the images can be assessed qualitatively and (semi-)quantitatively by reverting to the stored images. By pressing the "show" button, all images from the left and right hand are displayed consecutively (Fig. 7).

#### *Qualitative assessment of images*

The rater makes an interpretation of the images after going through the 32 (or 16) stored images and gives an "overall" evaluation or "qualitative" assessment. Based on qualitative assessment, images can readily be classified as revealing a scleroderma or non-scleroderma pattern (see below).

#### *(Semi-) quantitative assessment in the scleroderma-spectrum (SDS) diseases*

Cutolo et al. proposed in 2000 a semi-quantitative assessment of the hallmark parameters of the "scleroderma pattern": the following hallmark parameters are counted over 32 fields (four fields of 1 mm per finger, finger 2–5 of each hand, eight fingers): total amount of capillaries (normal defined as: 9/mm), giant capillaries (homogeneously enlarged loops with a diameter >50 µm), microhemorrhages (dark mass due to hemosiderin deposit), and abnormal shapes for example "ramifications" (branching, bushy or coiled capillaries, often originating from a single normal sized capillary) [8]. The semi-quantitative rating scale (0 = no changes, 1 = less than 33% of capillary alterations/reduction, 2 = 33–66% of capillary alterations/reduction, 3 = more than 66% of capillary alterations/reduction) is



**Fig. 7.** The show button is pressed to display each image sequentially.

adopted for each of the hallmark parameters. Nowadays, the quantitative assessment is frequently used. In the quantitative assessment, capillaroscopic characteristics are counted per millimeter and a mean is described per characteristic over 32 fields or over 16 fields (if two images per finger have been taken).

#### *Preparation of the images for (semi-)quantitative scoring (see supplementary file 1)*

##### *Preparation of 1-mm field: placing of grids*

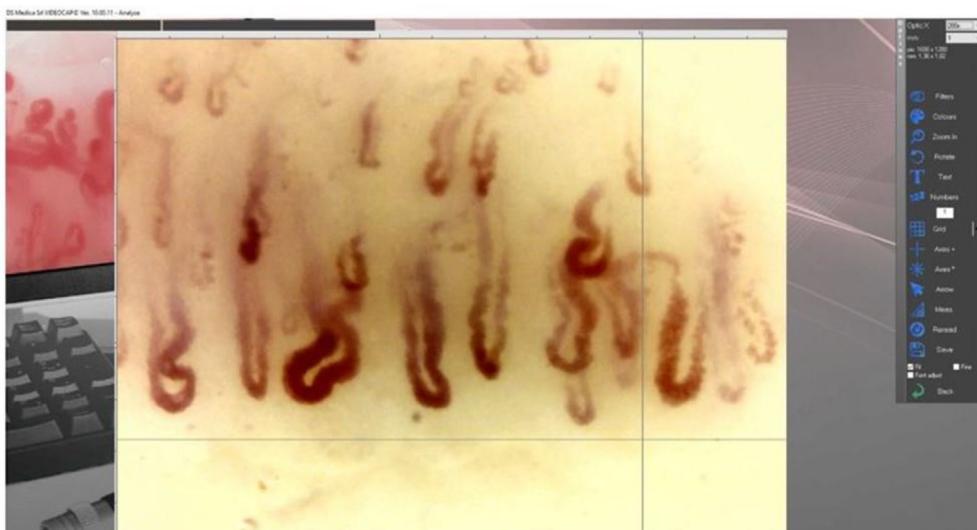
With the digital image analysis software (Videocap, DS Medica, Milan, Italy), the rater can put grids of 1 linear mm each on each image (Fig. 8). The image with grid will be saved additionally after the already four existing images that were taken during the examination of each respective finger (Supplementary Figs. 1A–1C).

##### *Preparation of counting of giants: measurement of diameter of capillaries*

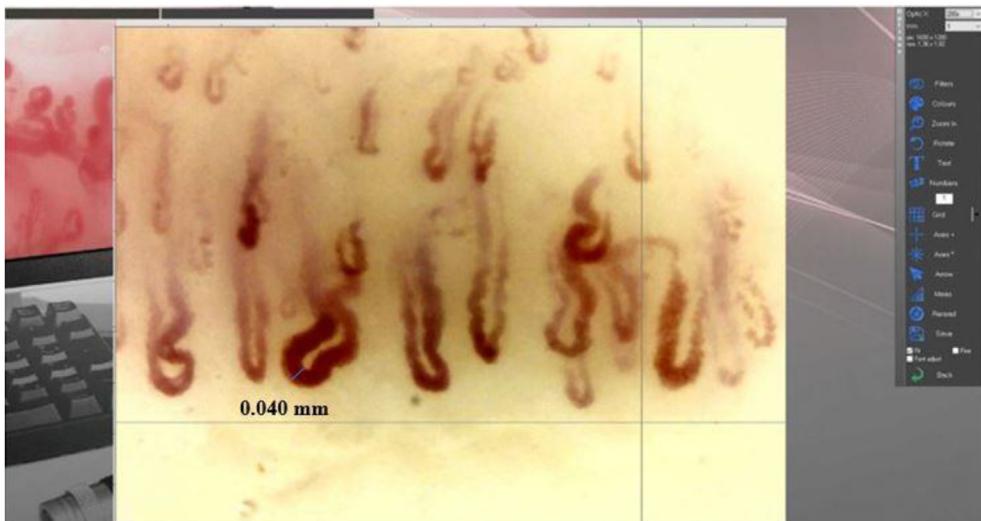
A giant is defined as: "a homogeneously enlarged loop with an apical lined diameter  $\geq 50 \mu\text{m}$ " After placing a grid, the measurement of capillary diameter can be obtained by pressing the buttons: "analyze," "measure," and "line" (Supplementary Figs. 1D–1G). The part that needs to be measured can be marked this way. The software will automatically calculate the diameter and give the option to store the image with the diameter of the marked part displayed on the capillaroscopic image (Fig. 9).

#### **EULAR and SCTC consensus-based description and the interpretation of capillaroscopy**

With the increasing use of nailfold capillaroscopy worldwide, it is of fundamental importance to have consensus concerning standard reporting of the capillaroscopic characteristics. Recent efforts between the SCTC and the EULAR Study Group on Microcirculation in Rheumatic Diseases resulted in a



**Fig. 8.** A 1-mm grid is placed on the image.



**Fig. 9.** The magnitude of the measured line is automatically displayed on the monitor (in this case 40  $\mu\text{m}$ ).

consensus framework to standardly report capillaroscopic characteristics when using a nailfold videocapillaroscope with a 200 $\times$  magnification [7].

The following capillary characteristics are evaluated when assessing an image (Table 1) while using the standard 200 $\times$  magnification: capillary density (number of capillaries per linear mm), capillary dimension (caliber of the apical limb of the capillary [see below]), capillary morphology (shape of individual capillaries), and the presence or absence of microhemorrhages. Table 1 describes the stereotypic normality, the non-specific abnormalities, which can occur in 34% of healthy subjects (non-scleroderma patterns) and the SSc-specific abnormalities (scleroderma patterns) for each of these capillaroscopic characteristics according to international consensus [7,9].

**Table 1**

EULAR Study Group on Microcirculation in Rheumatic Diseases standardized capillaroscopy evaluation chart. Adapted from Smith V et al. [7].

Capillaroscopic characteristics	CATEGORY 1					CATEGORY 2		
	Non-scleroderma pattern					Scleroderma Pattern		
	Normal	Non-Specific Abnormalities				Early	Active	Late
		If any of the capillaroscopic characteristics are abnormal (alone or in any combination) as highlighted in grey						
Density (/mm)	≥ 7	↓				≥ 7	Lowered density (4-6)	Further lowered density (≤3)
Dimension (μm)	Normal		20-50			> 50 (giant)	> 50 (giant)	-
Abnormal morphology	-			+		-	+	++
Haemorrhages	-				+	+/-	+/-	-

### Capillary density

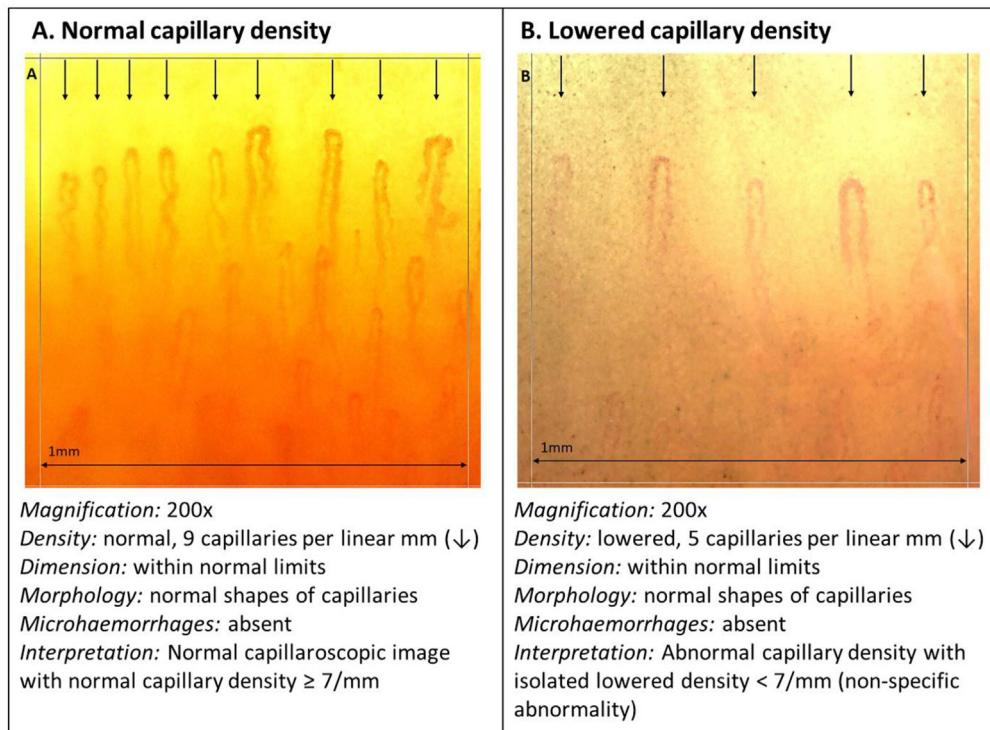
A normal capillary density in adults ranges between 7 and 12 with a mean of seven capillaries per linear millimeter, counted in the distal row of the nailfold [7,10]. A density lower than the normal indicates a loss of capillaries. “Avascular areas” is another term used to describe capillary density, which more specifically refers to the absence of adjacent capillaries. Fig. 10 depicts videocapillaroscopic images of a normal and an isolated lowered capillary density. Both these images are classified as revealing “non-scleroderma patterns” according to consensus definitions by the EULAR Study Group on Microcirculation in Rheumatic Diseases (Table 1).

### Capillary dimension

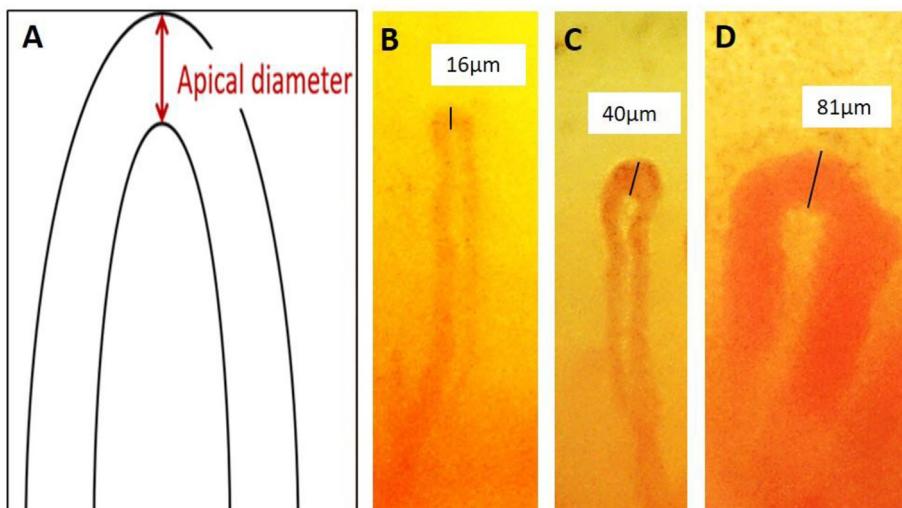
Capillary dimension is measured at the apex of the capillary loop (Fig. 11A schematic diagram). An apical diameter of  $\pm 20 \mu\text{m}$  is considered normal (Fig. 11B). Dilated capillaries are represented by a caliber of  $> 20 \mu\text{m}$  and  $< 50 \mu\text{m}$  (Fig. 11C) and are considered “non-specific abnormalities of dimension” [7,10]. Giant capillaries are described as normal shaped capillaries, homogeneously enlarged with an apical diameter of  $\geq 50 \mu\text{m}$  (Fig. 11D) [8].

### Capillary morphology

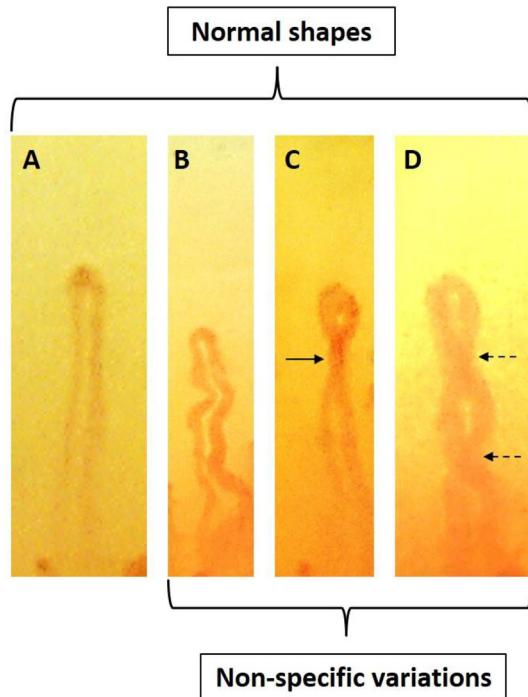
Concerning capillary morphology, literature had been disseminated with different definitions to describe the capillaroscopic characteristic capillary morphology (i.e. “ramifications” [bushy capillaries where a single normal sized capillary branches into multiple buds], “neo-angiogenesis” [clustering of twisted and bushy capillaries with marked shape and size heterogeneity surrounded by loss of normal capillary loops] or “meandering” [limbs are crossed upon themselves or with another several times], see below) with low reliability [9,11,12]. To avoid the use of confusing terminology, the EULAR Study Group on Microcirculation in Rheumatic Diseases has published by agreement a simple definition to evaluate a single capillary as “normal” or “abnormal,” adoptable to all rheumatic diseases and capillaroscopic evaluations for a standardized interpretation, which has also been incorporated in the



**Fig. 10.** Videocapillaroscopic images demonstrating capillary density. **A.** Normal capillary density (density  $\geq 7/\text{mm}$ ) **B.** Isolated lowered number of capillaries (density  $< 7/\text{mm}$ ) representing a “non-specific abnormality” **A, B.** “Non-scleroderma patterns.”



**Fig. 11.** Evaluation of capillary dimension. **A.** Schematic diagram depicting the measurement of the apical diameter of a capillary loop **B.** Normal capillary dimension, apical diameter  $\leq 20 \mu\text{m}$  **C.** Dilated capillary (apical diameter  $> 20 \mu\text{m}$ ,  $< 50 \mu\text{m}$ ) **D.** Giant capillary (homogeneous enlargement of all three limbs, normal shape, and apical diameter  $\geq 50 \mu\text{m}$ ) **B-D.** Technique: Nailfold videocapillaroscopy, 200 $\times$  magnification.



**Fig. 12. A-D.** Examples of normal capillary morphology. **A.** Stereotype “hairpin” shaped capillary **B.** Tortuous shape (afferent and efferent limbs bend but do not cross) **C.** Once crossing shape (→) **D.** Twice crossing shape (←). Note A convex capillary tip is required to define a normal shape **B-D.** Denoted as “non-specific variations of morphology” [7,13]. Technique: Nailfold videocapillaroscopy, 200× magnification.

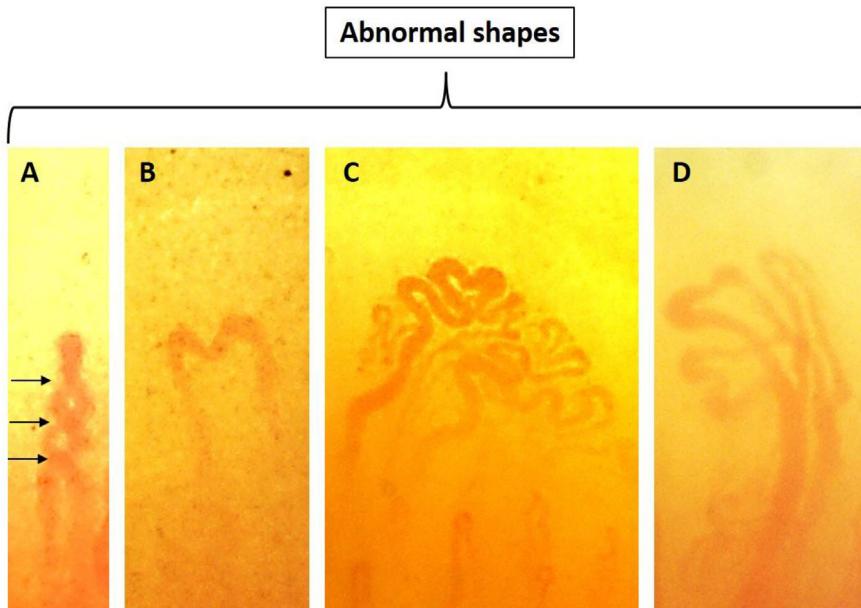
consensus framework [7]. In short, capillaries with a stereotype “hairpin” shape, a (once or twice) crossing shape, or a tortuous shape (the afferent and efferent limbs bend [undulate] but do not cross) are defined as being “normal,” with the provision that the tip of the capillary is convex (Fig. 12A–D). All other shapes are defined as being “abnormal” (Fig. 13A–D). This simple evaluation of single shapes of capillaries as “normal” or “abnormal” has attested excellent reliability when applied by novices as well as by independent expert raters in a multicenter international study [13,14].

#### Microhemorrhages

Microhemorrhages appear as red or brown hemosiderin deposits and represent extravasation of the red blood cells from a disrupted capillary wall (Fig. 14 A, B). These may occur in healthy subjects as well as in any connective tissue diseases (CTDs) and are always categorized as “non-specific abnormalities” [7]. Focal microhemorrhages may occur due to trauma in healthy subjects [9]. Algorithms that can rapidly, simply, and reliably categorize an image as a (non-)scleroderma pattern have been published after in- and external validation (see below: “the Fast Track algorithm”) [15].

#### “Non-scleroderma pattern”

A “non-scleroderma pattern” represented by several non-specific abnormalities (i.e. capillary density, capillary dimension, capillary morphology, and microhemorrhages) is shown in Fig. 15. It should be recognized that other than the stereotypical “normal” capillary pattern, isolated non-specific



**Fig. 13. A-D.** Examples of abnormal capillary shapes (morphology). **A.** Three times crossing capillary **B.** Non-convex capillary tip **C.** Capillary "ramifications" **D.** "Meandering" capillaries. **A-D** denoted as "abnormal" capillary morphology according to the EULAR Study Group consensus framework [7]. Technique: Nailfold videocapillaroscopy, 200 $\times$  magnification.

anomalies may occur in healthy individuals [9]. Underlying pathology, such as a CTD, should be suspected if several capillary non-specific abnormalities occur in the same individual.

#### "Scleroderma pattern"

The key capillaroscopic abnormalities characterizing the "scleroderma pattern" include giant capillaries, microhemorrhages, loss of capillaries, and abnormal shapes (Fig. 16) [7,16,17]. In specific, the presence of giant capillaries or the combination of an extremely lowered density of capillaries with abnormal shapes is a distinctive feature of a "scleroderma pattern" [8,15]. These morphological markers reflect the microvascular damage and are present in the nailfolds of the majority of patients with clinically evident SSc [18]. However, the "scleroderma pattern" can also be observed in other SDS disorders [19,20].

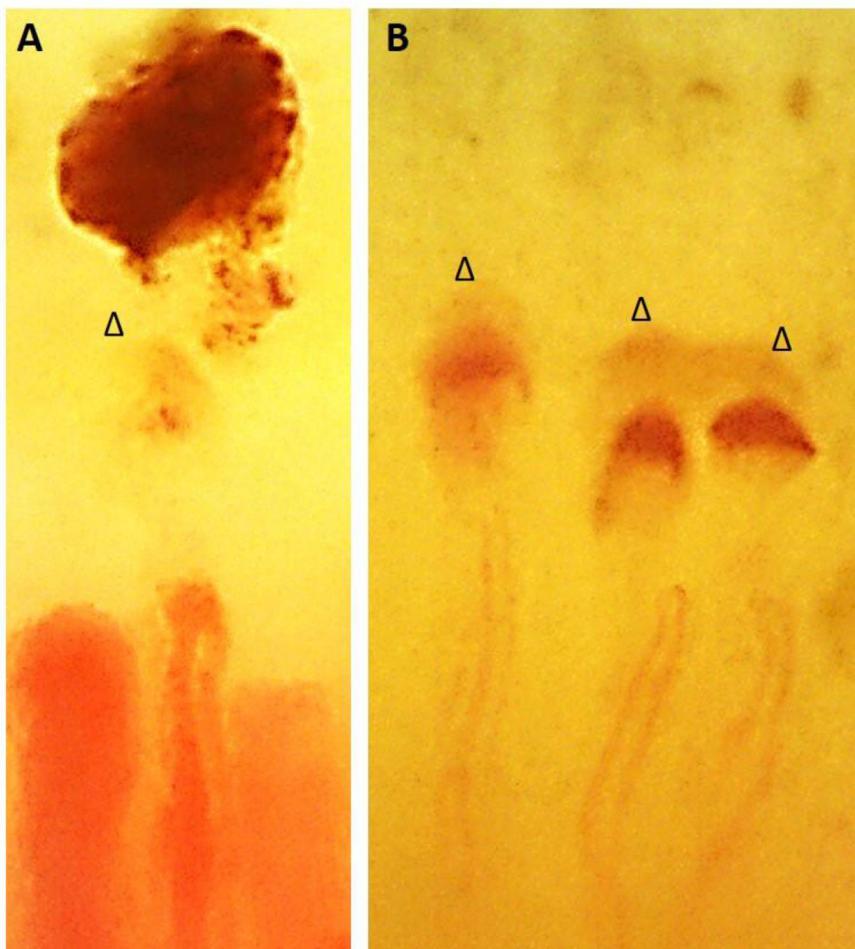
### Main role of capillaroscopy: investigation of the RP: identification of "early" SSc

#### *Investigation of patients with RP*

Microvascular abnormalities represent a key event in the pathophysiology of SSc [21]. NVC is a safe and fast diagnostic tool to detect structural alterations of the microcirculation [22]. Its use is mandatory in a patient presenting with RP, a pivotal clinical manifestation of microangiopathy, in that capillaroscopy may detect even minimal changes of the microvessel structure.

#### *Primary versus secondary RP*

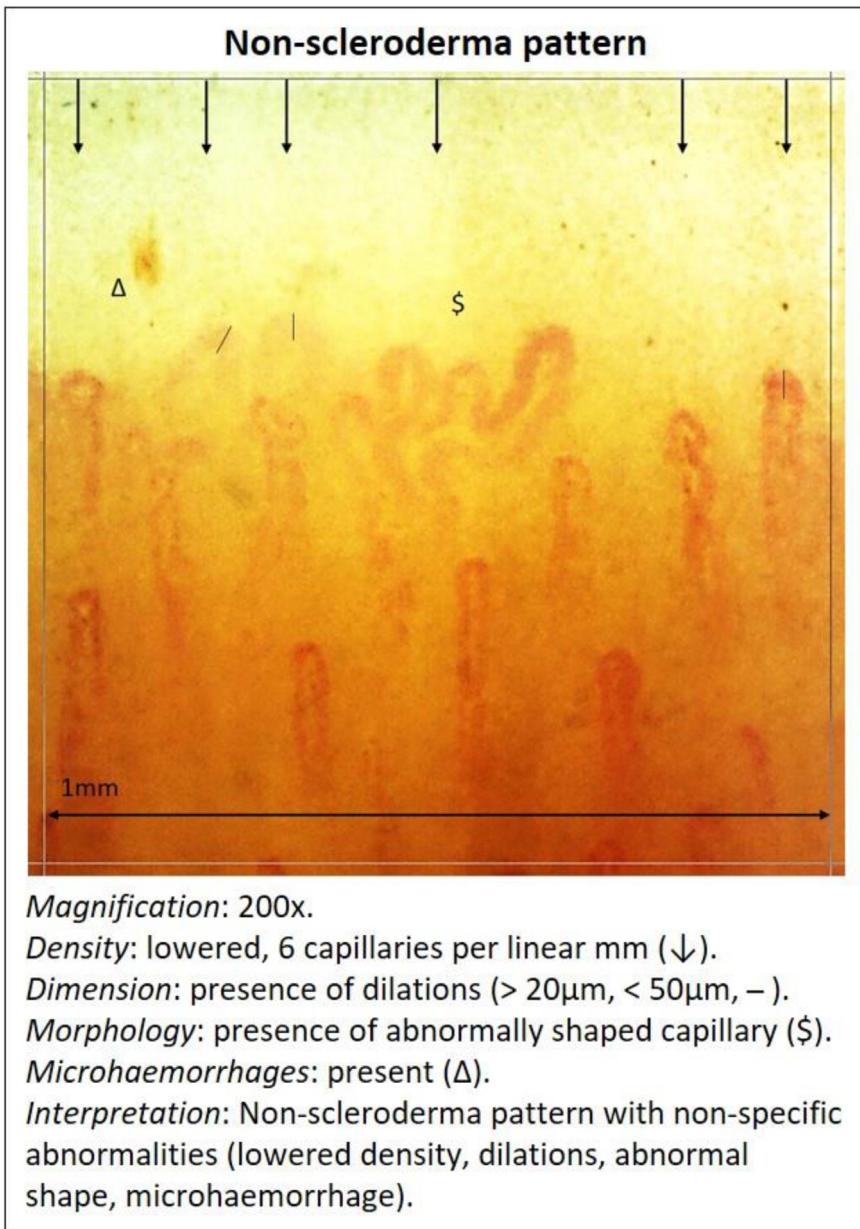
RP is characterized by episodic blanching and cyanosis of the fingers and toes after exposure to cold. Vasospasm of the digital arteries occurs in the ischemic phase (pallor-white) with subsequent dilation



**Fig. 14.** Microhemorrhages. Presence of a single (A) and multiple (B) pericapillary microhemorrhages ( $\Delta$ ). Technique: Nailfold videocapillaroscopy, 200 $\times$  magnification.

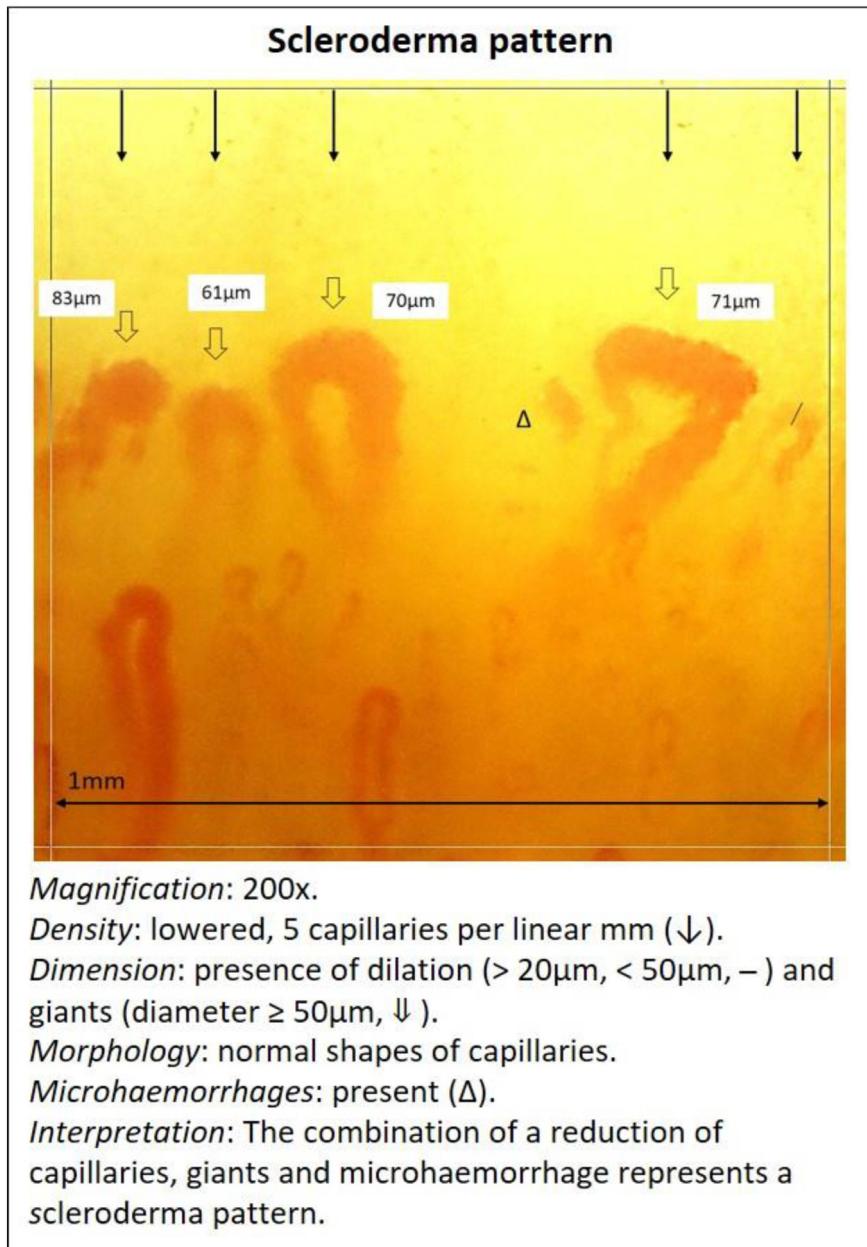
of capillaries and venules and filling of deoxygenated blood (cyanosis-blue). There may be reactive hyperemia caused by an increased blood flow into the now dilated arterioles and capillaries upon rewarming, resulting in a phase of redness of digits. Primary RP (not related to any other disease) is most often a benign functional condition and affects approximately 5% of the general population [23]. In contrast, RP may also be related to a variety of conditions/diseases (secondary RP) such as occlusive arterial or neurological disorders of the upper extremities; exposure to injurious occupational factors/chemicals (vibration tools and vinyl chloride); medication side effects (beta blockers); several oncological and hematological conditions (e.g. paraproteinemia, myeloproliferative disorders, paraneoplastic syndromes); and hypothyroidism, among others [24]. Importantly, secondary RP may also be a manifestation of an underlying CTD. For example, RP manifests in >95% of patients with SSc and 75% of patients with mixed CTD (MCTD) [25].

In 1992, LeRoy and Medsger proposed diagnostic criteria for primary RP that included, among others, the presence of normal nailfold capillaries and a negative antinuclear antibody (ANA) test (titer <1/100, all fluorescence patterns) [26]. Indeed, in a retrospective test of their proposal criteria to differentiate between primary and secondary RP at initial evaluation in a large patient database, the



**Fig. 15.** Videocapillaroscopic image of a “non-scleroderma” pattern with “non-specific abnormalities”

authors showed correct classification in 89% of 240 patients [26]. In 2014, complimentary criteria for primary RP were proposed by international expert consensus through a process of Delphi exercise that included the presence of a clinical diagnosis of biphasic RP; normal capillaroscopy; no findings of a secondary cause of RP on physical examination (such as ulceration, necrosis or gangrene, sclerodactyly, skin thickening or calcinosis); no history of CTD and a negative or low titer (1:40) of ANAs [27].



**Fig. 16.** Videocapillaroscopic image of a "scleroderma pattern"

*In primary RP: a normal capillaroscopic pattern*

A normal capillary pattern is characterized by a normal capillary density and homogeneously sized open hairpin shapes that are regularly arranged in a parallel distribution (Fig. 10A) [7,10]. Although the morphological pattern of the nailfold capillaries is fairly constant in healthy individuals, a wide range of morphological variation exists across the population. In the largest study of 800 healthy persons, using

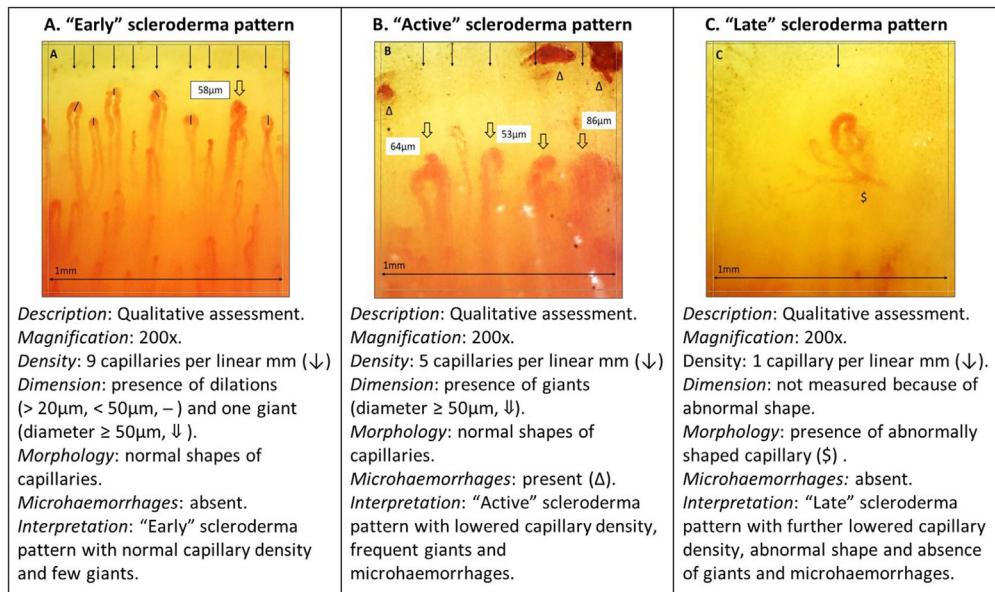
10x–16 $\times$  magnification widefield technique, Andrade et al. reported non-specific anomalies (described in the aforementioned sections) to occur in 34% of healthy individuals [9]. Importantly, one type of capillary abnormality may occur frequently in a healthy population, whereas several anomalies together rarely feature in a healthy population.

#### *In secondary RP due to systemic sclerosis: a scleroderma pattern*

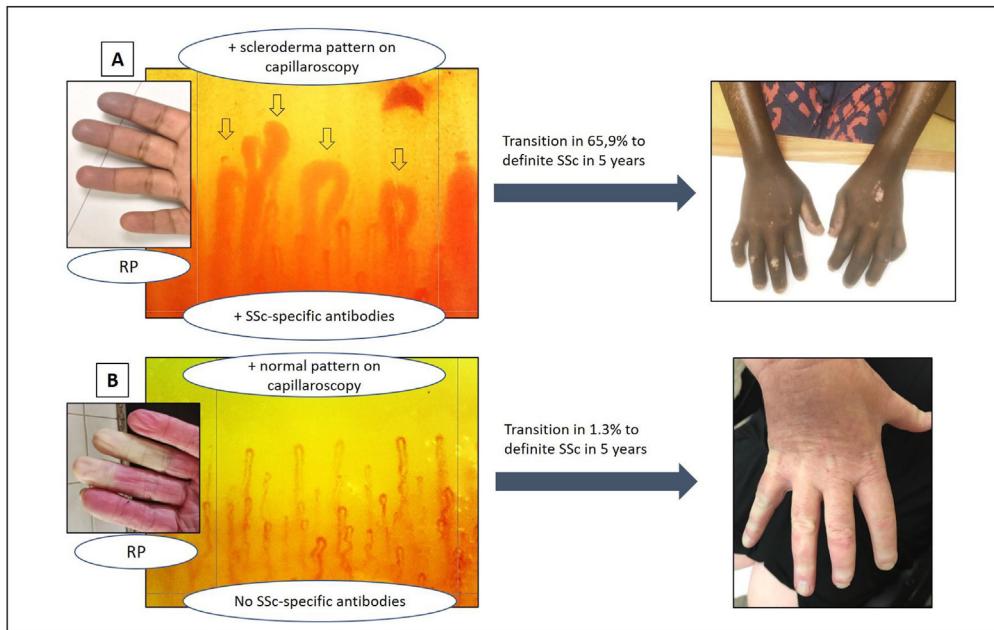
The early detection of SSc is of key importance, as it allows for vigilant monitoring of early organ involvement and timely therapeutic intervention. RP is one of the earliest clinical warning signs that may signal the development of an underlying CTD, in particular SSc [23]. In this context, capillaroscopy is a cornerstone investigation to discern a “scleroderma pattern” from a “non-scleroderma pattern” as a means to distinguish primary RP from secondary RP due to SSc [8,15]. Furthermore, RP may precede the emergence of other organ features in SSc by many years, underscoring the importance of capillaroscopy as an early diagnostic tool.

Three scleroderma patterns exist, more specifically the “early,” “active,” and “late” scleroderma patterns according to Cutolo et al., which reflect the progressive obliterative character of SSc (Fig. 17) [8]. The “early” pattern is characterized by the presence of giants (homogeneously enlarged capillaries with a normal morphology and a limb diameter of 50  $\mu\text{m}$  or more) and never presents with lowered density (cut-off  $\geq$  seven capillaries/mm) (Fig. 17A). The “active” and “late” patterns always present with lowered density (< seven capillaries/mm); however, these cut-offs are not fixed. In the “active” pattern, the loss of capillaries is combined with giant capillaries (Fig. 17B); In the “late” pattern, the loss of capillaries is combined with abnormal shapes (representing neoangiogenesis), and giant capillaries are never found (Fig. 17C) [7,8]. The three defined patterns are generally sequential and dynamic as the disease progresses and can easily be recognized by qualitative assessment (pattern recognition) of the capillaroscopic image [7,15,28].

To detect the early stage of SSc, two validated sets of criteria exist to identify that patients with RP who are at a higher risk for developing SSc. The LeRoy and Medsger criteria (proposed in 2001) for the “early” diagnosis of SSc included RP, SSc-specific antibodies, and “scleroderma-type” changes on nailfold capillaroscopy [29]. In 2008, these criteria were validated in a large 20-year prospective study



**Fig. 17.** Videocapillaroscopic images of the three “scleroderma patterns” as defined by Cutolo M et al. [8]. A. “Early” B. “Active” C. “Late”



**Fig. 18.** Criteria for “early” diagnosis of systemic sclerosis and their validation. After LeRoy EC et al. [29]; Koenig M et al. [30]. In patients presenting with RP, the probability of transitioning to definite SSc is high (65.9% in 5 years) in the presence of both SSc-specific antibodies and a “scleroderma pattern” on capillaroscopy [note Panel A: presence of lowered number of capillaries, giants (↓) and microhemorrhages]. In contrast, patients with a normal pattern on capillaroscopy (Panel B) and no SSc-specific antibodies rarely transition to definite SSc (1.3% in 5 years) [29,30]. Abbreviations: RP, Raynaud’s phenomenon; SSc, systemic sclerosis.

on patients presenting with isolated RP. The authors demonstrated that of those patients with both SSc-specific antibodies and “scleroderma-type” capillaroscopy changes present at baseline, a definite diagnosis of SSc occurred in 65.9% of patients at 5 years and almost 80% of patients at 20 years (Fig. 18A). In contrast, only 1.3% of patients with RP and “non-scleroderma” patterns and no SSc-specific antibodies developed SSc at the 5-year follow-up (Fig. 18B) [30].

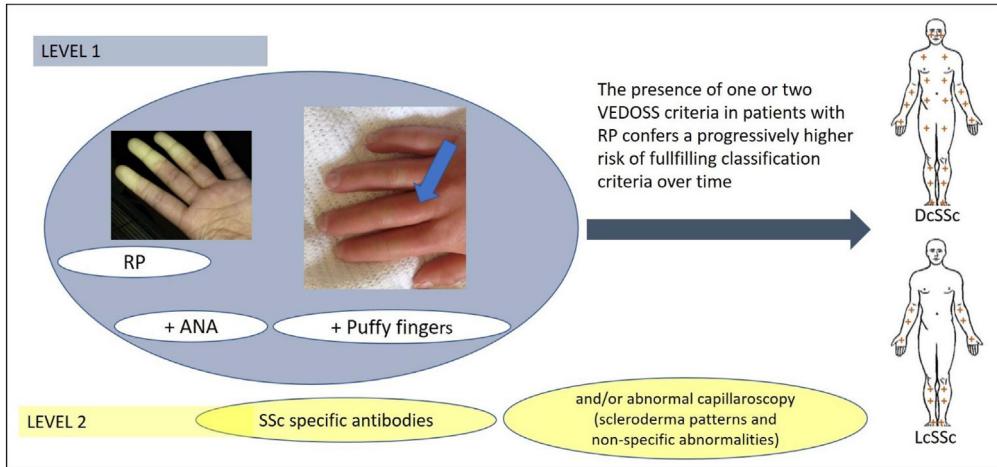
In 2011, criteria for the “very early” diagnosis of SSc (VEDOSS) were put forward and consisted of similar criteria proposed by LeRoy and Medsger [29], with the inclusion of puffy fingers (Fig. 19) [31].

Notably, the 2013 ACR/EULAR classification criteria (using a weighted score) subsequently included the LeRoy and Medsger items for “early” SSc and the VEDOSS criteria, among others features (Table 2) [33].

This was a significant step toward identifying patients with early disease. The VEDOSS criteria were prospectively validated in 2021 and the authors showed that a large proportion of patients with RP meeting the VEDOSS criteria transitioned to fulfill the 2013 ACR/EULAR criteria for SSc over 5 years (Fig. 19) [32]. In this way 94% of patients presenting with puffy fingers and SSc-specific antibodies will meet the 2013 ACR/EULAR criteria over time.

#### *The Fast Track algorithm: a fast simple and reliable algorithm to discern a “scleroderma pattern” from a “non-scleroderma pattern”*

The vast majority of “non-specific abnormalities” that may be present in a healthy population may render it difficult for the non-experienced capillaroscopist to classify an image as a “scleroderma pattern” or a “non-scleroderma pattern.” To address this, the EULAR Study Group has produced a Fast Track algorithm (Fig. 20) that has attested through internal and external validation to have a high



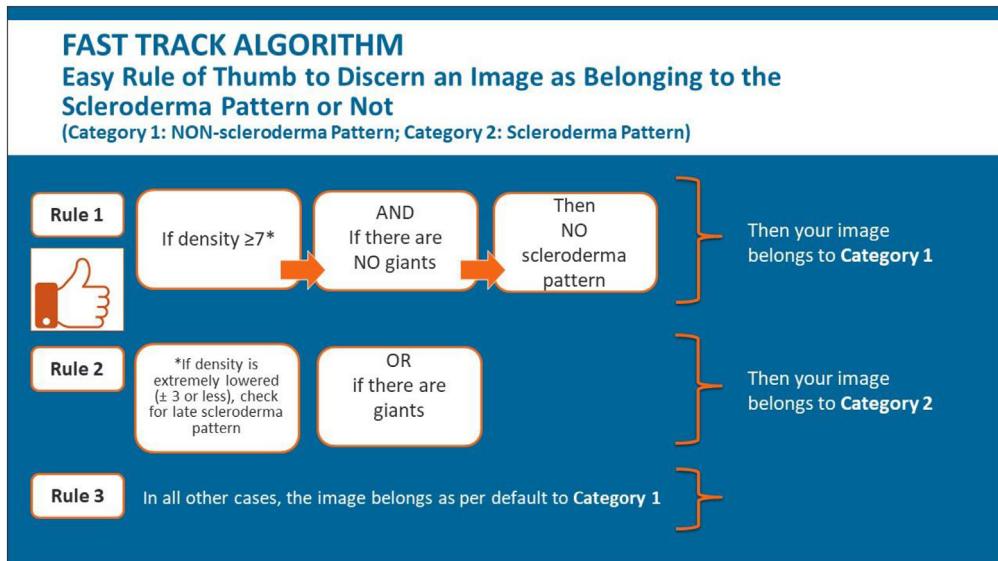
**Fig. 19.** Criteria for the "very early" diagnosis of systemic sclerosis (VEDOSS) criteria [31,32]. VEDOSS criteria: **level 1:** antinuclear antibodies (ANA) positivity and puffy fingers and **level 2:** the positivity of SSc (systemic sclerosis)-specific antibodies and/or the detection of "abnormal" (both SSc-specific as well as non-specific abnormalities) nailfold capillaroscopy [31]. After a 5-year follow-up, the proportion of patients fulfilling the 2013 American College of Rheumatology (ACR)/EULAR classification criteria [33] is as follows for the following pairs of criteria: ANA + puffy fingers: 79%; SSc-specific antibodies + puffy fingers: 94.1%; capillaroscopic abnormalities (both SSc-specific as well as non-specific abnormalities) + puffy fingers: 69.2%; capillaroscopic abnormalities (both SSc-specific as well as non-specific abnormalities) + SSc-specific antibodies: 82.2% [32]. Abbreviations: ANA, antinuclear antibodies; DcSSc, diffuse cutaneous systemic sclerosis; LcSSc: limited cutaneous systemic sclerosis; RP, Raynaud's phenomenon; VEDOSS, very early diagnosis of systemic sclerosis.

**Table 2**

Clinical features of the (very) early systemic sclerosis in the 2013 ACR/EULAR classification criteria.

ACR/EULAR 2013 Classification Criteria for Systemic Sclerosis			LeRoy & Medsger "Early" SSc	VEDOSS Criteria "Very early" SSc
Items	Sub-items	Score		
Skin thickening of fingers of both hands extending proximal to MCP joints (sufficient criterion)		9		
Skin thickening of the fingers (only count highest score)	Puffy fingers	2		✓
	Sclerodactyly	4		
Fingertip lesions (only count highest score)	Digital tip ulcers	2		
	Fingertip pitting scars	3		
Telangiectasia	-	2		
Abnormal nailfold capillaries	-	2	✓	✓
PAH and/or ILD (maximum score is 2)	PAH	2		
	ILD			
Raynaud's phenomenon		3	✓	✓
SSc-related antibodies (maximum score is 3)	Anti-centromere Anti-topoisomerase 1 Anti-RNA polymerase 3	3	✓	✓

**Legend.** The 2013 ACR/EULAR criteria: A total score of  $\geq 9$  is sufficient to classify patients with definite SSc. Abbreviations: ACR/EULAR, American College of Rheumatology and European Alliance of Associations for Rheumatology; ILD, interstitial lung disease; MCP, metacarpophalangeal joints; PAH, pulmonary arterial hypertension; SSc, systemic sclerosis; VEDOSS, very early diagnosis of SSc. After Avouac J et al. [31]; LeRoy EC et al. [29]; van den Hoogen F et al. [33].



**Fig. 20.** The Fast Track algorithm based on landmark literature for reliable capillaroscopic characteristics [15]. The Fast Track algorithm comprises three easy rules: 1) **Rule 1:** a normal capillary density ( $\geq$  seven capillaries) AND the absence of giant capillaries permits the rater to classify the capillaroscopic image as a “non-scleroderma pattern” (category 1); 2) **Rule 2:** an extremely lowered capillary density ( $\leq$  three capillaries) together with abnormal shapes (i.e. “late scleroderma pattern”) OR the presence of giant capillaries permits the rater to grade the capillaroscopic image as a “scleroderma pattern” (category 2); 3) **Rule 3:** if the image findings do not comply with rule 1 or rule 2, then the image is automatically graded as a “non-scleroderma pattern” (category 1) [15].

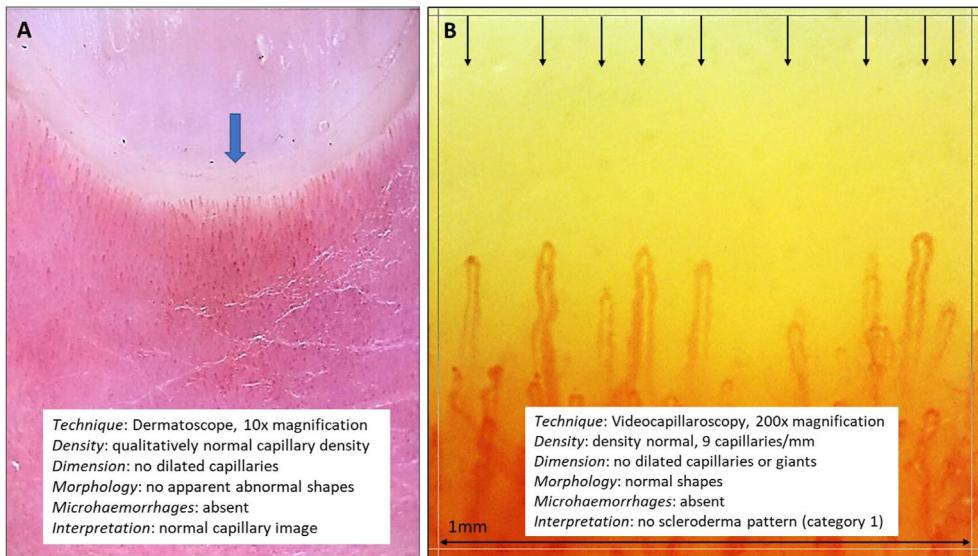
reliability to classify in a fast and simple way an image as a “scleroderma pattern” or a “non-scleroderma pattern,” even by novices in the field of capillaroscopy [15].

The present review focuses mainly on the application of NVC, the gold standard in assessing and quantifying capillary abnormalities in RP and SDS disorders. However, the dermatoscope is a more inexpensive and lower magnification instrument that is more frequently used in the United States and the United Kingdom [2,34]. Its reliability has been affirmed to be comparable to that of video-capillaroscopy in the differentiation of primary and secondary RP [35,36]. Moreover, international experts in capillaroscopy (belonging to EULAR Study Group) have recently developed a preliminary consensus algorithm to evaluate nailfold capillaries via dermoscopy [2]. Here the characteristics assessed are similar to the EULAR Study Group standardized capillaroscopy evaluation (Table 1) [7], yet less precise owing to the lower magnification of dermoscopy devices. Nonetheless, the basic principle of distinguishing normal from abnormal applies as in the Fast Track algorithm [15]. The evaluation of nailfold capillary images using a dermatoscope and videocapillaroscopy demonstrating a “normal capillary pattern” [category 1; “non-scleroderma pattern”] and a “scleroderma pattern” [category 2] is shown in Figs. 21 and 22, respectively. The gradeability for dermoscopy is lower than that for video-capillaroscopy [2,3,36]. However, it is a useful alternative for initial rapid screening in a patient with RP. Images that are not classifiable or those graded as having non-specific findings should preferably be re-evaluated using a videocapillaroscope.

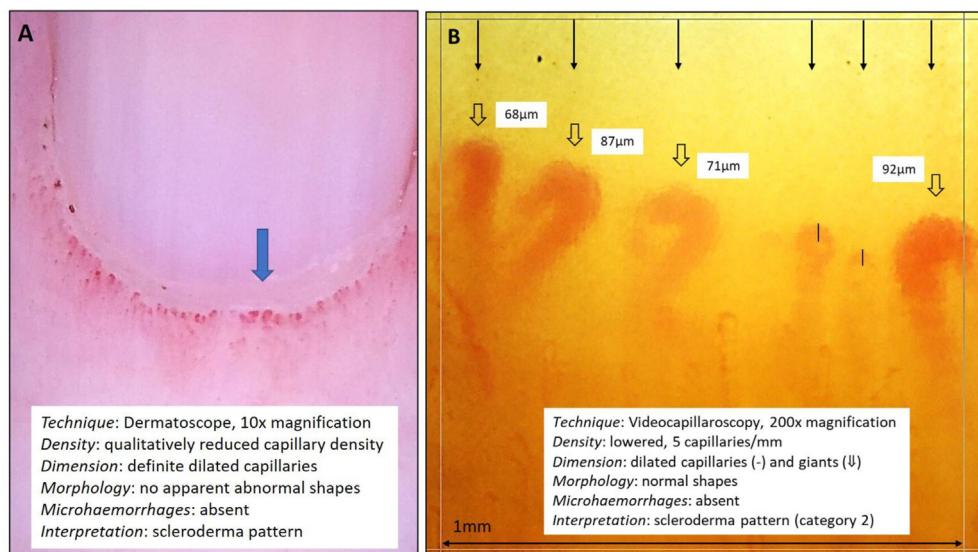
### Role of capillaroscopy in SSc: association and prediction

#### Capillaroscopy and predictive indices in SSc

The progressive vasculopathy accounts for several clinical manifestations and serious organ complications in SSc [37,38]. The microvascular damage, reflected by capillary structural alterations,



**Fig. 21.** Examples of nailfold capillary images using a dermatoscope and videocapillaroscopy showing a "normal pattern". **A.** "Normal pattern" in the area of focus (blue arrow) graded as per consensus evaluation for dermoscopy [2]. Technique: Dermlite DL3 Dermatoscope (10 $\times$  magnification) connected to the iPad for improved quality. **B.** "Normal pattern" (category 1) by nailfold videocapillaroscopy graded as per EULAR Study Group [7,15]. Technique: videocapillaroscopy, 200 $\times$  magnification



**Fig. 22.** Examples of nailfold capillary images using a dermatoscope and videocapillaroscopy showing a "scleroderma pattern". **A.** "Scleroderma pattern" in the area of focus (blue arrow) graded as per consensus evaluation for dermoscopy [2]. Technique: Dermlite DL3 Dermatoscope (10 $\times$  magnification) connected to the iPad for improved quality. **B.** "Scleroderma pattern" (category 2) by nailfold videocapillaroscopy graded as per the EULAR Study Group [7,15]. Technique: videocapillaroscopy, 200 $\times$  magnification.

parallels skin and internal organ involvement rendering nailfold capillaroscopy an attractive candidate for study in the follow-up of patients. There is growing literature to support the use of NVC as predictor of outcomes (new or worsening organ/system involvement and overall disease progression). We will mainly highlight conclusions drawn from multicenter and prospective studies (data on cross-sectional studies are not within the scope of this review but will be succinctly referred to below).

Capillary density (i.e. capillary loss), the parameter that has attested the highest interrater reliability in literature [11] has been found to be the most consistent predictor of clinical complications in SSc across studies, in particular digital ulcers (DUs), pulmonary arterial hypertension (SSc-PAH), SSc-associated interstitial lung disease (SSc-ILD), progression of skin fibrosis, and worsening of disease severity [28,39–44]. Moreover, severe scleroderma capillary patterns (i.e. “active” or “late”) associate with organ complications and progression [39,41,43–46].

Of note, loss of capillaries can be defined quantitatively (a lowered number of capillaries) or qualitatively by pattern severity (“active” and “late” scleroderma pattern). Other NVC parameters such as capillary diameter and capillary morphology have a less well-defined predictive value than that of capillary loss [44]. In addition, no reliability studies exist attesting high interrater reliability of evaluating the number of microhemorrhages.

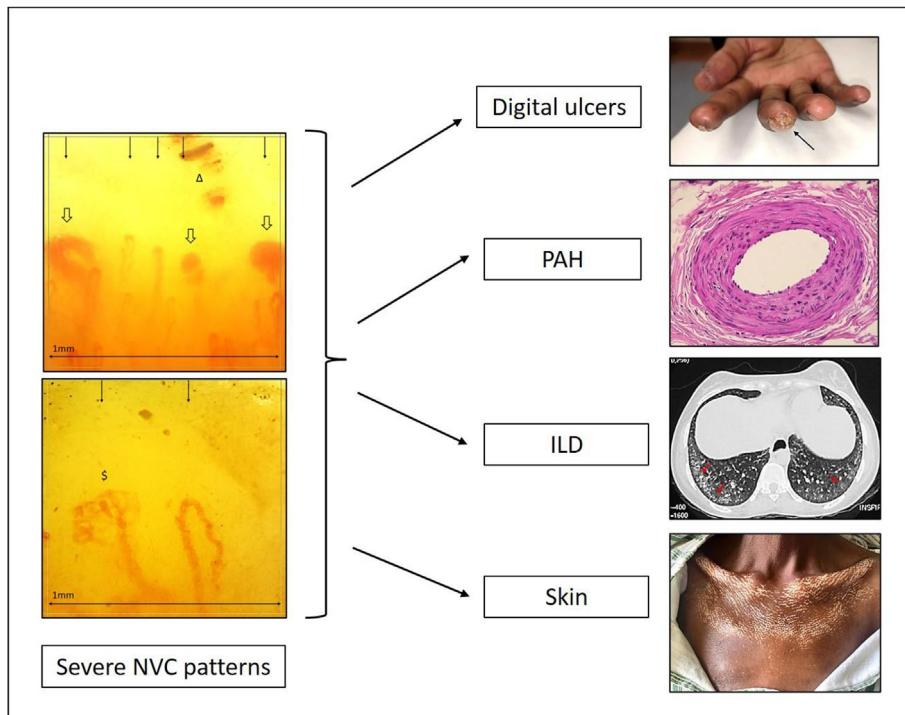
Capillary density has been associated with vascular complications (such as DUs and SSc-PAH) and SSc-ILD in a number of cross-sectional studies [47–49].

Baseline capillary density has been associated with future organ involvement and progression in SSc. In the CAP (videoCAPillaroscopy) study, a large multicenter prospective study, the mean number of capillaries per millimeter in the middle finger of the dominant hand (at study enrollment) was one of the three predictors of new DU occurrence over a 6-month period [39]. In line with this, more recently, a multicenter, multinational EULAR Study Group on microcirculation/European Scleroderma Trials and Research Group (EUSTAR) prospective study demonstrated that a normal capillary density was unequivocally associated with less new DUs and less novel overall severe organ involvement/progression (at 12 or 24 months) [41].

A change in capillary density over time has been associated with new organ involvement and disease progression. Concerning lung involvement in SSc, strong evidence has been put forward by the authors of two longitudinal studies showing that progressive capillary loss over time was associated with incident SSc-PAH (diagnosed by right heart catheterization [RHC]) [28,43]. These findings have been supported by a systematic literature review [50]. Furthermore, in one of these studies, progressive capillary loss associated with incident SSc-ILD after a 7-year follow-up [28]. Progressive capillary loss (assessed quantitatively over 3 years) has also been associated with incident DUs, progression of skin fibrosis, and overall disease progression [43].

A lower baseline capillary density, as reflected by the “active” and/or “late” scleroderma patterns, predicts organ complications/progression in SSc (Fig. 23). In the CAP study, a more severe “late” scleroderma pattern on NVC at baseline showed an increased risk of DUs at the 6-month follow-up [39], which had previously already been attested in several smaller studies [46,51]. In the latter studies, the follow-up ranged from 18 months to 3 years. More recently, evidence from a large multicenter prospective EULAR Study Group on Microcirculation in Rheumatic Diseases/EUSTAR study has shown that severe NVC patterns (“active” and “late”) at baseline significantly associated with a higher incidence of novel skin progression and novel overall organ involvement/progression at the 12- or 24-month follow-up [41]. In this study, novel organ involvement included, among others, DUs and lung involvement (SSc-ILD and PAH [by RHC], and pulmonary hypertension [by echocardiography]).

Finally, a change of scleroderma patterns over time to “active” or “late” has been shown to predict novel organ involvement in two longitudinal studies [28,43]. In a well-designed prospective study involving sequential NVC assessments of 140 patients over 3 years, progression to a “late” scleroderma pattern on NVC was associated with new DUs, incident SSc-PAH, progression of skin fibrosis, and worsening of overall disease activity [43].



**Fig. 23.** Predictive associations between severe scleroderma patterns and future organ involvement/progression. Baseline severe scleroderma patterns on NVC ("active" pattern as in left upper panel and/or "late" as in left lower panel) are associated with the development of future new organ involvement/progression in SSc (digital ulcers), PAH, ILD, and skin [39,41,46,51]. Abbreviations: ILD, interstitial lung disease; NVC, nailfold videocapillaroscopy; PAH, pulmonary arterial hypertension.

### Capillaroscopy in other rheumatic disorders

In CTDs other than SSc, capillaroscopic images may present normal capillaroscopic findings, non-specific abnormalities, or in certain CTDs (MCTD, idiopathic inflammatory myopathies [IIMs]), the scleroderma pattern.

#### *Idiopathic inflammatory myopathies*

NVC has shown to be a valuable tool for assessing microvascular abnormalities in IIMs, especially in those disease subtypes where vascular injury plays an important role in disease pathophysiology, particularly dermatomyositis (DM) and antisynthetase syndrome (ASS) [52] (Fig. 24).

A recent systematic literature review provided an interesting outline of the available NVC studies in IIMs that used image acquisition and report with a uniform standardized interpretation according to the EULAR Study Group on Microcirculation in Rheumatic Diseases and SCTC Group on Capillaroscopy [52].

The manuscript highlighted that NVC characteristics differ on group level between different types of IIMs and healthy controls (HCs), as well as between the different subsets of IIMs. From the analysis of two comparative studies with SSc, patients with DM seem to show less capillary loss than patients with SSc show (the latter show a typical progression of the microangiopathy from "early" to "late" stages over time) [53,54]. When specifically comparing patients with DM with patients with SSc with "early," "active," or "late" disease, patients with DM generally show less capillary loss than that shown by



**Fig. 24.** The left hand of a patient with dermatomyositis showing Gottron's papules and active Raynaud's phenomenon in the third and fourth digits.

patients with SSc, even though they still exhibit more capillary loss than that exhibited by patients with SSc with an “early” scleroderma pattern [54].

Interestingly, the presence of the “scleroderma-like” pattern, defined as a capillary pattern showing mixed microvascular markers of the scleroderma patterns, but not proportionally fitting the definition for the single “early,” “active,” or “late” pattern, was also found to be discriminatory between patients with IIMs and patients with SSc (Fig. 25) [55].

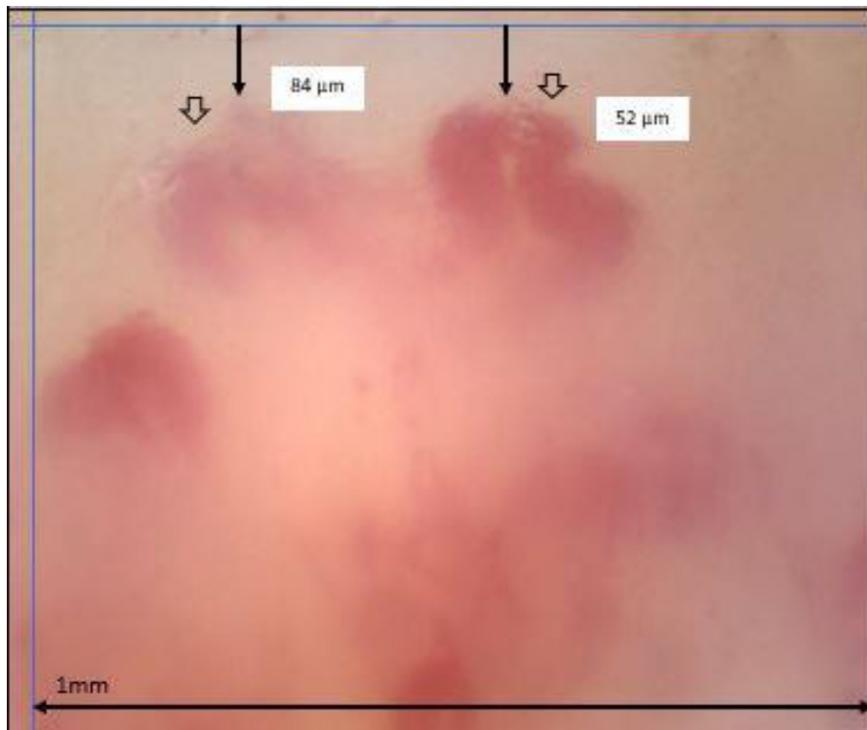
A phenotypical heterogeneity of microvascular damage among IIMs derives also from the different NVCs detectable among patients with DM, HCs, and polymyositis (PM) [56]. Indeed, in patients with DM and juvenile DM, a lower capillary density and a higher prevalence of dilations, giants, and rates of the “scleroderma pattern” have been observed than those observed in both patients with PM and HCs (detected in 69% of DM and in none of HCs and PM). Likewise, patients with ASS show more NVC alterations than patients with PM exhibit, as confirmed by recent studies showing a high prevalence of “scleroderma-like” patterns in patients with ASS [57,58].

The studies reporting correlations between NVC findings and disease activity in IIMs are scarce and conflicting ([Supplementary Table 1](#)).

Further investigation is needed to evaluate the potential use of NVC as an imaging biomarker integrated with specific antibodies and organ involvement to stratify patients with IIMs in the diagnosis and treatment response. The application of internationally consented standardized definitions in capillaroscopy is warranted to conduct homogenous larger prospective studies evaluating the associations between NVC parameters and clinical data.

#### Mixed connective tissue disease

RP is a common symptom observed in patients with MCTD being an item in many classification criteria of the disease [59]. Capillaroscopic images in MCTD may vary from “non-scleroderma” patterns, (normal images to non-specific abnormalities), as well as scleroderma patterns “early,” “active,” “late,” or “scleroderma-like.” In a classic comparative study of NVC findings between patients with MCTD vs SSc and systemic lupus erythematosus (SLE), a “scleroderma-like” pattern was detected in 64% of patients with MCTD and the authors suggested that this pattern may help differentiate MCTD from other autoimmune rheumatic diseases [60].



**Fig. 25.** Videocapillaroscopic picture of a patient with dermatomyositis naïve to glucocorticoid and immunosuppressive treatment. *Magnification:* 200×. *Density:* extremely lowered, two capillaries per linear mm (↓). *Dimension:* presence of giant capillaries (diameter  $\geq 50 \mu\text{m}$ , ↓). *Morphology:* within normal limits. *Microhemorrhages:* absent. *Interpretation:* the presence of giant capillaries combined with a reduced capillary count may prompt the reader to categorize this picture as an “active” scleroderma pattern. However, as per the EULAR/SCTC consented standardized definitions in NVC [7], the extent of capillary density reduction is generally between 4 and 6 capillaries per linear mm in the “active” pattern. This mean capillary count reduces further (< four capillaries per linear mm) in the “late” pattern, but in this pattern, giants are never found. Therefore, the combination of an extremely reduced capillary density (< four capillaries per linear mm) and giant capillaries are indicative of a “scleroderma-like” pattern. Abbreviations: EULAR, european alliance of associations for rheumatology; SCTC, scleroderma clinical trials consortium.

Interestingly, a significant association was observed between the presence of a “scleroderma-like” pattern and the development of MCTD in a cohort of 3029 patients with RP, followed up for an average of 4.8 years in a large prospective study [20].

Additionally, some reports indicate associations with disease activity because giant capillaries have been associated with the development of interstitial lung disease in patients with MCTD, especially among those with a short disease duration [61] (Figs. 26 and 27). Nevertheless, the data inherent to NVC parameters and disease activity are scarce and derive from low-sample sized studies (Supplementary Table 1).

The results of cross-sectional studies suggest that MCTD may have a different underlying microvascular pathophysiology with less avascular areas (lowered density) or capillary loss compared with those observed in patients with SSc [62]. This concept has also found basis in a follow-up study of patients with MCTD showing no progression of nailfold microvascular damage during 3 years of follow-up, displaying, at the initial assessment, a lower number of dilated or giant capillaries and a higher mean capillary density than those observed in age- and disease-matched patients with SSc [63].

A comparative study assessing NVC findings between patients with MCTD vs individuals with undifferentiated connective tissue disease showed a significantly higher frequency of “scleroderma-



**Fig. 26.** Videocapillaroscopic image of a patient with mixed connective tissue disease. *Magnification: 200×. Density:* lowered, four capillaries per linear mm (↓). *Dimension:* presence of dilation ( $>20 \mu\text{m}$ ,  $<50 \mu\text{m}$ ), and giants (diameter  $\geq 50 \mu\text{m}$ , ↓). *Morphology:* normal shapes of capillaries. *Microhemorrhages:* absent. *Interpretation:* A combination of reduced capillary density and giants is indicative of an “active” scleroderma pattern.

“like” pattern, indicating that this finding may be a potential imaging biomarker of a more aggressive disease [64].

Despite the presence of extensive microvascular changes in MCTD, the identification of a validated or specific NVC pattern is not yet possible due to the potential existence of these alterations in other SDS disorders such as IIMs [1]. A diagnostic and prognostic value may still be relevant when other clinical and serological aspects of the disease are considered [65].

#### Antiphospholipid syndrome (APS)

No specific capillaroscopic patterns are related to the APS, still microvascular abnormalities are frequently observed on NVC images [66]. APS-related pathology is attributed to the presence of pathogenic antiphospholipid autoantibodies (aPL) mediating the occlusion of small blood vessels resulting in either thrombotic events or negative placental/obstetric outcomes [67].

Non-specific capillary abnormalities such as dilations or abnormal shapes have been reported in classic observational studies suggesting the presence of microvascular damage in patients with APS [68].

A distinct NVC pattern sometimes observed in patients with APS is the “comb-like” pattern characterized by parallel hemorrhages beneath the nailfold capillaries mimicking the appearance of a comb (Fig. 28).

Two recent observational studies suggested that the “comb-like” pattern may serve as a potential capillaroscopic biomarker in patients with APS because it is more frequently observed in these patients than its occurrence in HCs and aPL carriers (reported prevalence of, respectively, 50% vs 16% vs 20%) [69].



**Fig. 27.** High resolution computerized tomography of the chest of a patient with MCTD showing severe fibrotic parenchymal changes in both lungs.



**Fig. 28.** On the left, the videocapillaroscopic picture of a patient with antiphospholipid syndrome. On the right, the same patient showing livedo reticularis in the lower legs on the physical examination. *Magnification: 200×. Density: lowered, five capillaries per liner mm (↓). Dimension: within normal ranges ( $\leq 20 \mu\text{m}$ ) Morphology: presence of one abnormal shape (\$). Microhemorrhages: present abundantly in a comb-like appearance ( $\Delta$ ). Interpretation: a combination of reduced capillary density, abnormal shapes, and abundant microhemorrhages indicative of a "non-specific" capillary pattern with comb-like microhemorrhages.*

However, larger studies are needed to determine the utility of capillaroscopy for the diagnosis and monitoring of APS, as well as its potential associations with specific aPL subtypes.

### SLE

A recent systematic review, conducted by authors of the EULAR Study Group on Microcirculation in Rheumatic Diseases summarized the results of 40 studies on NVC in patients with SLE.

The most consistent findings were a higher frequency of dilations, abnormal capillary morphologies, and microhemorrhages detected in patients with SLE than those observed in HCs [70]. Additionally, “non-specific” patterns and “scleroderma-like” patterns were more frequently observed in patients with SLE than they were in HCs (Fig. 29) [70].

Correlations between capillaroscopic changes and clinical and laboratory parameters have been described: overall disease activity (measured with heterogeneous indexes) has shown a direct association with the NVC score, in particular with the rates of abnormally shaped capillaries and microhemorrhages [71]. For other specific clinical and laboratory markers, the data are not fully conclusive (Supplementary Table 1).

Currently, the knowledge gaps in NVC features in SLE derive from the small sample sizes of the published studies and the usage of different methodologies, which pose a challenge in reaching definitive conclusions. Additionally, conflicting results have been reported regarding the density and dimensions of nailfold capillaries in patients with SLE. The absence of a consistent “SLE-specific” pattern in NVC could be due to the heterogeneity of phenotypes among patients with SLE patients and the different pathobiology of microvasculopathy in SLE compared to those of other CTDs.

An international multicenter study applying the EULAR Study Group consented standardized definitions in capillaroscopy is ongoing to clarify the relationship between NVC parameters and clinical/serological characteristics of patients with SLE.

### Sjögren's syndrome

The available evidence on NVC findings in Sjögren's syndrome (SjS) is limited, with only a few studies investigating the differences between microvascular findings in patients with SjS vs HCs [72].



**Fig. 29.** On the left panel of the image, the hands of a patient with systemic lupus erythematosus with active cutaneous and renal disease with positive anti-RNP autoantibodies. On the right, the NVC image of the same patient performed the same day: *Magnification:* 200×. *Density:* lowered, five capillaries per linear mm (↓). *Dimension:* presence of dilation (>20 µm, <50 µm.). *Morphology:* normal. *Microhemorrhages:* present. *Interpretation:* a combination of reduced capillary density, dilations, and microhemorrhages indicative of a “non-specific” capillary pattern (non-specific abnormalities). Abbreviations. RNP, ribonucleoproteins.



**Fig. 30.** The left panel shows the videocapillaroscopic picture of a patient with Sjögren's syndrome. The patient displayed, as extra-glandular manifestations, leukocytoclastic cutaneous vasculitis in the lower legs, subsequently confirmed via biopsy (right panel). *Magnification:* 200×. *Density:* lowered, five capillaries per linear mm (↓). *Dimension:* presence of dilation (>20 µm, <50 µm). *Morphology:* within normal limits. *Microhemorrhages:* absent. *Interpretation:* a combination of reduced capillary density and dilations is indicative of a "non-specific" capillary pattern.

A systematic review of seven observational studies on NVC in SjS revealed that there is limited evidence on the differences between NVC in SjS and in HCs [72].

A single article has detected a lower capillary density in patients with SjS vs HCs [73], whereas another observed a higher frequency of capillaroscopic abnormalities in patients with SjS with RP compared with patients without RP [74]. Most of the NVC abnormalities in the first group of patients were "non-specific" capillary abnormalities (Fig. 30).

"Scleroderma (-like)" patterns were also observed in a subgroup of patients with SjS with RP, potentially indicating the presence of overlap syndromes with SSc or MCTD [75].

The qualitative synthesis related to the association between serological features of patients with SjS and NVC characteristics provided conflicting results (Supplementary Table 1).

The limitations in interpreting studies on NVC in SjS are related to the lack of standardized application of NVC, the different study designs, and the inclusion of patients with different classification criteria.

The current evidence from NVC studies indicates that paying attention to early overlapping features, such as RP, ANA positivity, the presence of atypical antibodies, or puffy fingers, may be suggested for the diagnostic and therapeutic approach of patients with SjS [72]. In this respect, NVC may serve as a biomarker in SjS to identify patients with overlap features and their possible risk of evolving into another CTD. Larger studies using a standardized approach in NVC may confirm this hypothesis in the future.

## Conclusions

Given the importance of nailfold capillaroscopy in the investigation of RP, early diagnosis of SSc, and follow-up of patients with established disease, its use is crucial for rheumatologists and physicians. Standardized use of terminology and reporting on capillaroscopic findings in all CTDs is pivotal in daily practice and across research studies. Advances in automated counting systems, further research into its application for monitoring therapeutic effects (alone or in combination with other imaging techniques/laboratory investigations) is an exciting prospect for the optimal care of patients with rheumatic diseases.

### Practice points

- The gold standard to execute capillaroscopy is a nailfold videocapillaroscope with 200× magnification of the lens.
- The EULAR Study Group on Microcirculation in Rheumatic Diseases and Scleroderma Clinical Trials Consortium (SCTC) Group on Capillaroscopy has published a consented framework on standardized description and interpretation of capillaroscopy.
- Non-specific abnormalities may occur in 34% of healthy subjects and in connective tissue diseases.
- Scleroderma patterns are specific for scleroderma-spectrum diseases (systemic sclerosis, inflammatory myopathy, and mixed connective tissue diseases).
- Capillaroscopy should be used primarily in a patient presenting with the Raynaud's phenomenon.
- The Fast Track algorithm allows for simple, reliable, and fast distinction for whether there is a scleroderma pattern or not.
- A dermatoscope may also be valuable to detect a definite scleroderma pattern.
- In systemic sclerosis, a lower density at baseline and progressive loss of capillaries over time (6 months–3 years) is associated with future development of digital ulcers, pulmonary arterial hypertension, interstitial lung disease, skin progression, and overall severe organ involvement/progression.
- In systemic sclerosis, severe baseline scleroderma patterns (active and late) are associated with future severe organ involvement (digital ulcers, skin fibrosis, and overall organ involvement) at 6 months-3 years.
- Connective tissue diseases other than systemic sclerosis do not have specific patterns and associations with clinical complications and still have to be evaluated in large prospective trials.
- For the interpretability of reports of capillaroscopy as well as of studies, it is paramount to use the EULAR consented standardized description of capillaroscopic characteristics.

### Research agenda

- Prospective studies in all connective tissue diseases besides systemic sclerosis with the use of standardized terminology are highly needed to explore the role of capillaroscopy in those diseases.
- Automated fully reliable, inexpensive, fast systems generating accurate reports are needed to execute randomized clinical trials (with a view to evaluate a putative role of capillaroscopy in therapy monitoring).

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### Declaration of competing interests

The authors declare no conflicts of interest related to this manuscript.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.berh.2023.101849>.

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