

Consensus-based evaluation of dermatoscopy *versus* nailfold videocapillaroscopy in Raynaud's phenomenon linking USA and Europe: a European League against Rheumatism study group on microcirculation in rheumatic diseases project

M. Radić¹, M.H. Snow², T.M. Frech³, L.A. Saketkoo⁴, M. Cutolo⁵, V. Smith⁶

¹Division of Rheumatology and Clinical Immunology, Centre of Excellence for Systemic Sclerosis in Croatia, University Hospital Split; University of Split School of Medicine, Croatia; ²Division of Rheumatology, Dept. of Internal Medicine, University of Nebraska Medical Centre, Omaha, NE, USA; ³Division of Rheumatology, Dept. of Internal Medicine, University of Utah and Salt Lake Veterans Affairs Medical Centre, City, UT, USA; ⁴Tulane University School of Medicine, New Orleans Scleroderma & Sarcoidosis Patient Care & Research Centre, UMC Comprehensive Pulmonary Hypertension Centre, New Orleans, LA, USA; ⁵Research Laboratory and Academic Division of Clinical Rheumatology, Postgraduate School of Rheumatology, Dept. of Internal Medicine, University of Genova, IRCCS Polyclinic Hospital San Martino, Genova, Italy; ⁶Dept. of Rheumatology, Ghent University Hospital, and Dept. of Internal Medicine, Ghent University, Belgium.

Mislav Radić, MD, PhD*
Marcus H. Snow, MD*
Tracy M. Frech, MD, MS*
Lesley A. Saketkoo, MD
Maurizio Cutolo, MD
Vanessa Smith, MD, PhD

*These authors share first name authorship.

Please address correspondence to:

Mislav Radić,
Šižgoričeva 20/II,
21000 Split, Croatia.
E-mail: mislavradic@gmail.com

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ABSTRACT

Objective. Nailfold videocapillaroscopy (NVC) is the current gold standard for detection and quantification of capillary abnormalities in Raynaud's phenomenon (RP). The objective of this study is to evaluate the role of dermatoscopy as a further screening tool in RP.

Methods. Nailfold capillaries of RP patients were examined by a hand-held non-contact polarised dermatoscope connected to the digital camera (D1) and connected to an iPad (D2). Both dermatoscopic images were marked with an arrowhead. NVC examination was evaluated at the arrowhead. Single blinded reader performed all examinations. NVC was graded as per standard of European League against Rheumatism (EULAR) study group on microcirculation in rheumatic diseases. Consensus evaluation of dermatoscopy characteristics/grade was determined and each dermatoscopic image was given a final impression of 'normal', 'non-specific' or 'scleroderma' pattern. The final interpretation by both techniques was compared after completion of the blinded reading.

Results. Classification of 100 consecutive dermatoscopic images resulted in 37 (wide view) 'non-interpretable', 2 'normal', 48 'non-specific' and 13 'scleroderma' pattern with D1; 23 'non-interpretable', 4 'normal', 52 'non-specific' and 21 'scleroderma' pattern by the experts with D2; 0 non-interpretable, 4 normal, 13 non-specific and 83 'scleroderma' pattern with NVC.

Conclusion. Overall, 50% of dermatoscopic images were classified as non-specific and 30% were classified as non-interpretable in RP patients. However, all images classified by dermatoscopy as "normal" or as overt "scleroderma" pattern were confirmed by concomitant NVC analysis. These find-

ings demonstrate tenuous promise for dermatoscopy as a tool for the initial screening of nailfold capillaries in RP. Further regular work up with NVC is needed to further clarify non-interpretable and non-specific findings possibly related to non-scleroderma patterns.

Introduction

Raynaud's phenomenon (RP) is a very common clinical sign that can be seen across several medical specialties (a prevalence of 5-10% has been reported in the general population) (1). Patients are currently classified into two groups: those with primary RP, a benign form occurring alone without concomitant diseases with a favourable prognosis and those with secondary RP, which occurs in a variety of connective tissue diseases (CTDs) with variable progression and prognosis (2). Patients who initially present as RP with no signs of other CTDs but later progress to a secondary RP generally have a concomitant CTD, commonly systemic sclerosis (SSc) (3, 4). Recent studies have shown that RP may predate systemic illness up to two decades, therefore regular follow-up of patients with RP is of utmost importance (5, 6). Nailfold videocapillaroscopy (NVC) is current gold standard for detection and quantification of capillary status in RP (7). NVC is able to distinguish secondary RP from both, primary RP and healthy subjects, through determining a scleroderma pattern from a non-scleroderma pattern (8, 9). However, most rheumatologists and other health care providers that assess RP in United States do not have access to this method on a regular basis and therefore, hand-held dermatoscopy is used as a lower-cost alternative to NVC. Dermatoscopy has been shown, on the condition that images are interpretable, to be a reliable technique in the evalua-

tion of morphological nailfold changes, permitting the differentiation of primary and secondary RP (3, 9-11).

Given the important role of NVC in discerning a primary from a secondary RP and given the daily practice of United States clinicians to use the dermatoscope we wanted to evaluate the role of dermatoscopy in evaluating patients presenting the RP.

Against this background, the European League against Rheumatism (EULAR) Study Group on Microcirculation in Rheumatic Diseases (SG MC/RD) developed a project (International Comparative Image Banking for Nailfold Capillary Education in Systemic Sclerosis and Other Rheumatic Diseases) bringing together representatives from United States and Europe with an interest in both dermatoscopy and NVC which in a first step addresses this question.

Methods

An international task force (TF, MS, MR, LS, MC, VS), consisting of investigators with clinical and research experience in microcirculation in rheumatic diseases was brought together and formed a preliminary consensus (Fig. 1) based on landmark literature and in line with published consensus based NVC standard terminology (9, 12-16). Preliminary recommendation was provided as follows: 'non-interpretable' images and 'non-specific' patterns need further evaluation (ideally NVC but if it is not available then repeat dermatoscopy) and 'normal' images and 'scleroderma pattern' require that no further evaluation is needed for capillaroscopic diagnosis.

Consecutive patients from selected outpatient clinics of Utah Hospitals and Clinics underwent nailfold capillaroscopy with three different devices: dermatoscopy using two different devices and NVC with one device. All dermatoscopy and NVC examinations were performed by a single reader (MR) blinded for clinical parameters and patient status. Hand-held dermatoscopy was performed with two techniques: "D1" with non-contact polarised dermatoscope (HEINE Delta 20 T Dermatoscope, HEINE Optotechnik GmbH

1. Clarity of image ("are capillaries able to be seen in the area of focus?")

IF YES à Next step

IF NO à Step 4
2. Findings (yes/no):

Part 1- "Area of focus" (i.e. in the arrowhead)

 - a. Qualitatively reduced ("does the area of focus appear to have decreased capillary density")
 - b. Enlarged ("do any of the capillaries in the area of focus appear dilated")
 - c. Haemorrhages ("are there any hemorrhages in the area of focus")
 - d. Abnormal Shapes ("do any capillaries in the area of focus appear abnormal based on definitions for NVC")

Part 2- "Widefield view"

(same questions but the examiner is able to look at the whole image of the nailfold)
3. Interpretation (for each part):

- 'Normal' (0/4 of the above)
 - 'Non-specific' (any abnormality)
 - 'Scleroderma' (definitely dilated capillaries and decreased density)
4. Recommendation:

- 'Normal' à **no further evaluation**
 - If 'Scleroderma' pattern (meaning we have no doubt) à **no further evaluation**
 - If 'Non-specific' à **further evaluation (ideally NVC, but if it is not available then repeat dermatoscopy)**
 - If 'Non-interpretable' à **further evaluation (ideally NVC, but if it is not available then repeat dermatoscopy)**

Fig. 1. Consensus on dermatoscopic related terminology and recommendation for further nailfold videocapillaroscopy (NVC).



Fig. 2. Dermatoscope overview. **A:** HEINE Delta 20 T Dermatoscope connected to a digital camera; **B:** DermLite DL3 Dermatoscope and DermLite Connection Kit for iPad mini 4.

& Co., Herrsching, Germany) connected to the digital camera via adapter to improve the quality of images with 10-16x magnification and "D2" with non-contact polarised dermatoscope with 10x lens (DermaLite, DL3 model, 3Gen, San Juan Capistrano, CA, USA) connected to an iPad (mini 4) via adapter (DermLite Connection Kit) (Fig. 2).

Equipment was assembled according to manufacturer's instructions. The distance was determined by image sharpness. In addition, a thin layer of cedar oil was applied to enhance sharpness of images. The dermatoscope's automated focusing system provided the possibility for variable magnification and one single wide view image was taken (3).

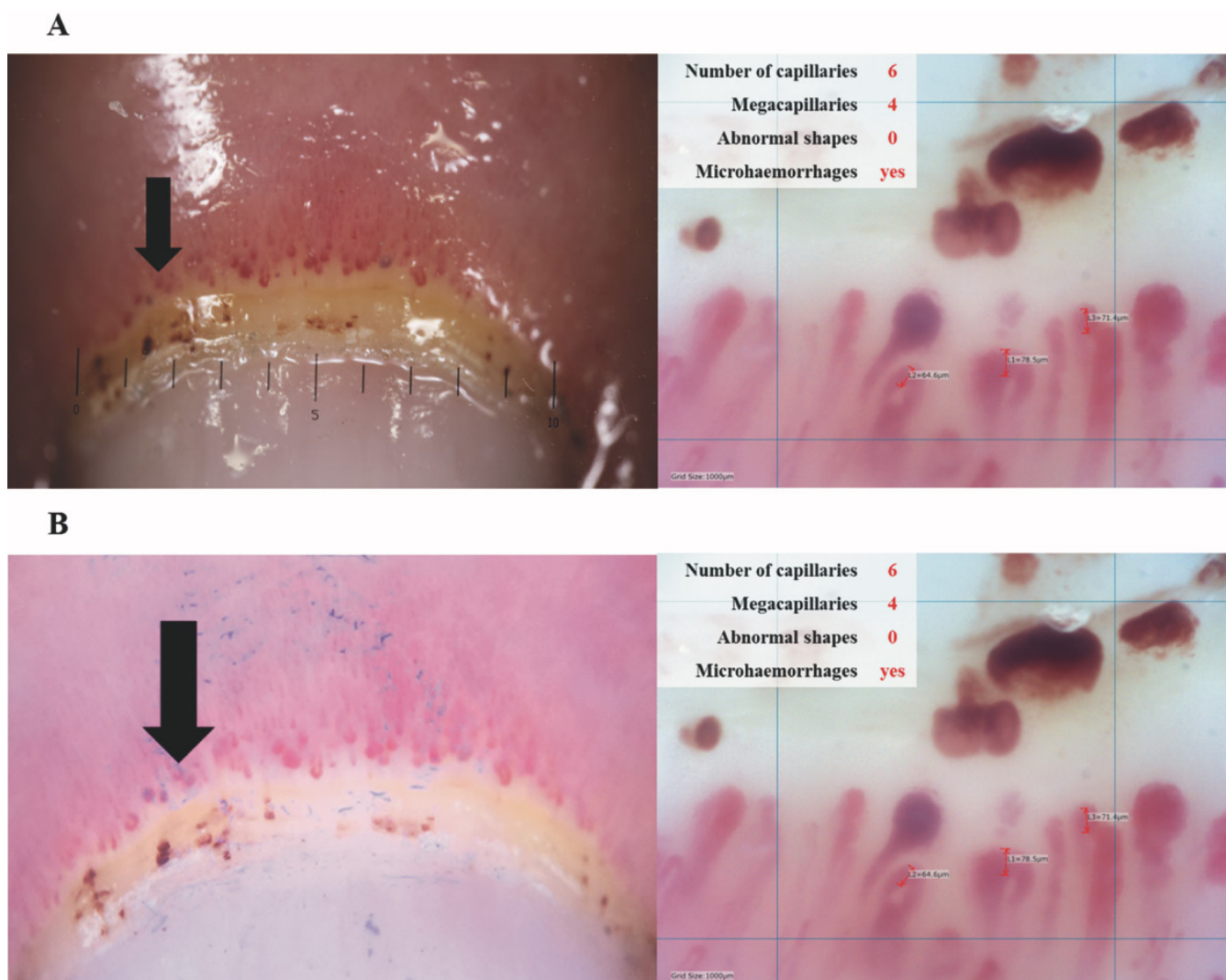


Fig. 3. Side-by-side presentation of capillaroscopic images; **A:** HEINE Delta 20 T Dermatoscope and nailfold videocapillaroscopy (NVC); **B:** DermLite DL3 Dermatoscope and NVC.

Nailfold capillaroscopy using dermatoscope and nailfold videocapillaroscopy, showing the index finger of the left hand; **(A)** dermatoscopic 'scleroderma' pattern in the area of focus (arrowhead) and in the widefield view, and **(B)** dermatoscopic 'scleroderma' pattern in the area of focus (arrowhead) and in the widefield view.

Nailfold capillaries of second to fifth finger on both hands were examined using both dermatoscopic methods and by the videocapillaroscope. Both, the widefield view and area of focus (marked by an arrowhead) were presented to the raters using PowerPoint presentation, more specifically one slide per dermatoscopic device during 11 televideoconferences (Fig. 3). On each slide, adjacent to the widefield and focused dermatoscopic image, the NVC image, taken at the area of focus of dermatoscopic image was displayed, evaluated and graded. Dermatoscopic and videocapillaroscopic images were evaluated during televideoconferences (MR, TF, MS, VS). More specifically,

the dermatoscopic images were rated primarily by TF and MS with experience in reading dermatoscopic images; and the videocapillaroscopic images mainly by VS. All four teleconference attendees always agreed on the ratings as described in the results section.

The clearest dermatoscopic image was chosen for inclusion in presentation. Most prominent dermatoscopic change was marked by arrowhead and afterwards capillaroscopy was performed at this point of focus. Concerning dermatoscopy the following approach was followed in rating. Based on clarity of image (clear/unclear) and dermatoscopic characteristics (qualitative reduction of capillary density, enlarged

capillaries at sight, haemorrhages and abnormal shapes), grade was determined in the following categories: 'normal', 'non-specific' and 'scleroderma' pattern (Fig. 1) (13, 16).

The nailfold of the second, third, fourth and fifth finger was examined on both hands in each patient using an optical probe videocapillaroscope equipped with a 200× magnification contact lens and connected to image analysis software (Inspectis AB, Solna, Sweden). Each subject remained inside the facility for a minimum of 15 min before the nailfold was examined at room temperature of about 21–22°C.

NVC was graded as per standard of EULAR study group on microcircula-

Table I. Evaluation results of dermatoscopic and nailfold videocapillaroscopy images.

Final impression	Pattern according to D1 (n=100)*		Pattern according to D2 (n=100)*		Pattern according to NVC (n=100)
	Area of focus	Wide view	Area of focus	Wide view	
Normal, n	7	2	10	4	4
Non-interpretable, n	36	37	30	23	0
Non-specific, n	48	48	46	52	13
Scleroderma, n	9	13	14	21	83

*Data provided for Heine Delta 20 T (D1) and DermLite DL3 (D2) images.
NVC: nailfold videocapillaroscopy.

tion in rheumatic diseases into scleroderma patterns or non-scleroderma patterns (normal and non-specific abnormalities) (9, 17, 18).

The institutional review board of the University of Utah, serving as the ethics committee, approved this study (IRB no. 77934). All subjects provided written informed consent prior to any evaluation.

Results

One hundred consecutive RP patients were examined using both dermatoscopic and NVC methods. Evaluation results of dermatoscopic and NVC images are shown in Table I.

Thirty-seven dermatoscopic images were interpreted as 'non-interpretable', 2 as 'normal', 48 as 'non-specific' and 13 as 'scleroderma' pattern with D1; 23 as 'non-interpretable', 4 as 'normal', 52 as 'non-specific' and 21 as 'scleroderma' pattern by the experts with D2; 0 as non-interpretable, 4 as normal, 13 as non-specific and 83 as scleroderma pattern with NVC. Overall, 'non-specific' pattern was present in 50% of cases and

30% were deemed 'non-interpretable' images, hence 80% of dermatoscopic images were defined as needing further evaluation by NVC. Furthermore, all 'normal' dermatoscopic images were verified by NVC as normal and all 'scleroderma' pattern on dermatoscopy was corroborated by 'scleroderma' pattern on NVC. All images that were read as 'scleroderma pattern' by NVC were found to be 'non-specific' or 'scleroderma' by dermatoscopy.

Discussion

Dermatoscopes are useful devices for the examination of nailfold capillaries. It has been suggested that in case of NVC is not available dermatoscopy is a low-cost mandatory alternative to NVC (19).

Recently, dermatoscopy and NVC have been compared in terms of image gradeability and capillary pattern (normal, non-specific, early, active and late) and their ability to detect SSc (12). In a recent study with 32 subjects that included healthy controls, primary RP and SSc-spectrum disorders, 27%

of dermatoscopy images were non-interpretable, which is numerically comparable to the results seen in our study (20). Both methods were of high specificity (above 80%), however sensitivity was lower for dermatoscopy (60.2% compared to 81.6%).

Dermatoscopy is often unable to evaluate nailbed capillaries in sufficient detail to define 'scleroderma' pattern, but could distinguish healthy nail beds from those with pathological changes, thus detecting cases with findings that benefit from closer follow-up.

On the other hand, NVC is well established as a useful addition to the clinical examination for distinguishing patients with secondary RP due to SSc from those with primary RP (3, 4, 9, 21, 22). At this point in time, NVC is not available to all United States rheumatologists due to limited equipment availability and cost.

In this project we report a consensus-based algorithm created by an expert team (members of the EULAR study group on microcirculation in Rheumatic diseases) to decide in which cases to further evaluate a patient and in which cases not. This study suggests that dermatoscopy indeed may be used as a screening tool, as all 'normal' and 'scleroderma' pattern dermatoscopic findings were corroborated by NVC. Furthermore, any 'non-specific' dermatoscopic findings were subsequently confirmed as definite scleroderma pattern by NVC, corroborating the need of comprehensive follow-up via established gold standard (Fig. 4).

These results confirm the validity of

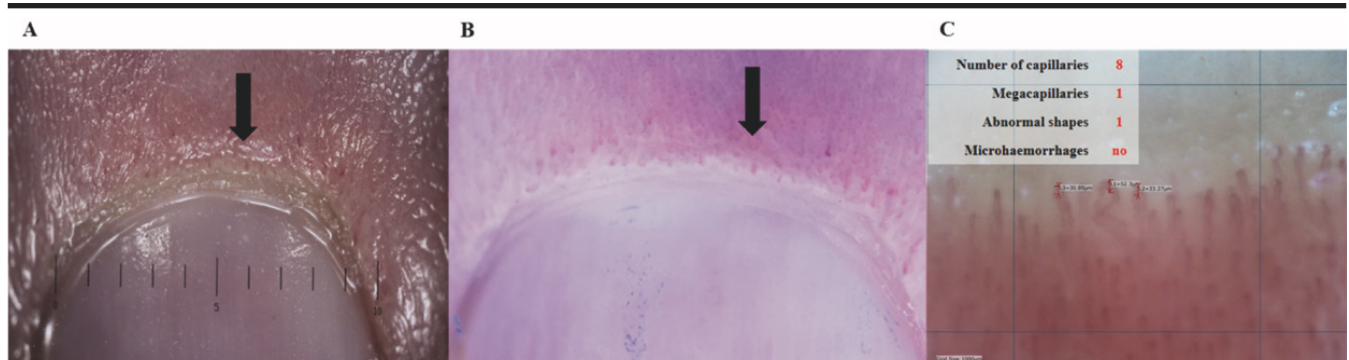


Fig. 4. Presentation of dermatoscopic 'non-specific' images. **A:** HEINE Delta 20 T Dermatoscope; **B:** DermLite DL3 Dermatoscope confirmed as **C:** 'scleroderma' pattern by nailfold videocapillaroscopy (NVC).

Capillaroscopic images showing the index finger of the left hand. Dermatoscopic images interpreted as 'non-specific' in the area of focus (arrowhead) and in the widefield view using both methods. NVC confirmed 'scleroderma' pattern.

our preliminary recommendations (Fig. 1). In further studies inter and intra rater reliability of this dermatoscopic screening algorithm will have to be evaluated.

The emergence of low-cost, easy-to-use digital imaging systems has made good quality dermatoscopy images more accessible. Viewing the nailfold dermatoscopy image on a screen enables rheumatologist to see the capillaries with increased magnification. Additionally, performance characteristics of dermatoscopy *versus* the golden standard (NVC) should be evaluated in large prospective studies, however this was not within the remit of this manuscript. By obtaining two dermatoscopic images, we aimed to check if images of poorer quality could be improved by the use of a different capture technique. D2 method connected to the iPad had less 'non-interpretable' findings confirming it as the method of higher quality. The strength of our project is in the rigorous evaluation and side-by-side image comparison by blinded image readers. The limitation is the inclusion of very small number of patients with 'normal' capillaroscopy and highly skewed population toward SSc.

Dermatoscopy has widespread use amongst dermatologists for its assistance in diagnosing malignant skin conditions and in some countries, even general practitioners are trained in its use for cancer screening (23, 24). Due to its lower cost, quicker acquisition of images and more frequent use amongst non-scleroderma specialists, dermatoscopy has a role in any clinical practice that evaluates and treats RP (24, 25). As nailfold dermatoscopy becomes more widespread capillaroscopic method, standardisation and formal training will be needed.

In this manuscript, we evaluated dermatoscopy as a possible additional screening tool in patients affected by RP. The value of this study is the not only the comparison of dermatoscopy with NVC, but also a first step toward a more uniform approach with capillaroscopy bridging US-based physicians and the European leaders in the field of capillaroscopy.

In addition, the intent of this cross-sectional study was not to give clinical practice guidelines on how frequent a patient who has RP and a scleroderma pattern or a non-scleroderma pattern is to be followed up, as this was already reported in a prospective, longitudinal study (3). In conclusion, screening RP patients with dermatoscopy provides early meaningful information but needs additional NVC study to further clarify non-interpretable and non-specific findings possibly related to non-scleroderma patterns.

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