Diagnostiek bij Raynaud-s phenomenon: benadering van de reumatoloog en nagelriem capillairmicroscopie: spoedcursus in een Fast track

Vanessa Smith

MD, PhD

Department of Rheumatology, Ghent University Hospital

Professor of Medicine, Ghent University, Belgium

Vanessa.smith@ugent.be

Agenda

I Cold hands/ Raynaud's phenomenon?

II Primary versus secondary Raynaud phenomenon?

III How to investigate a patient with Raynaud's phenomenon? And causes of secondary

IV EULAR consensus on standardised description of capillaroscopy

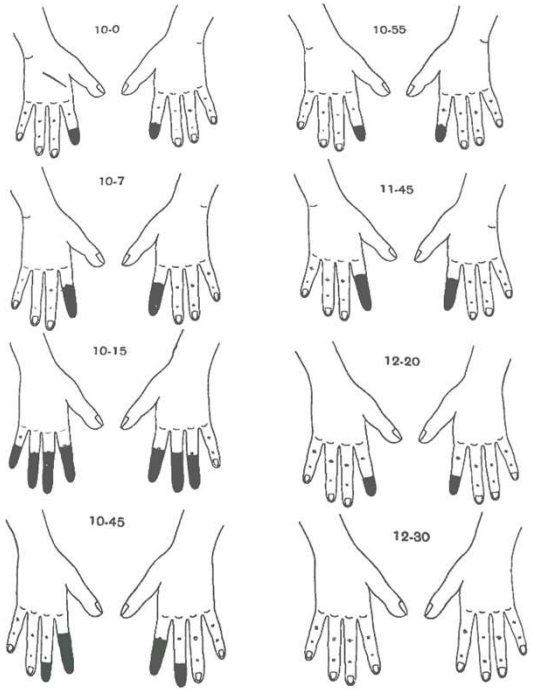
V Fast track algorithm

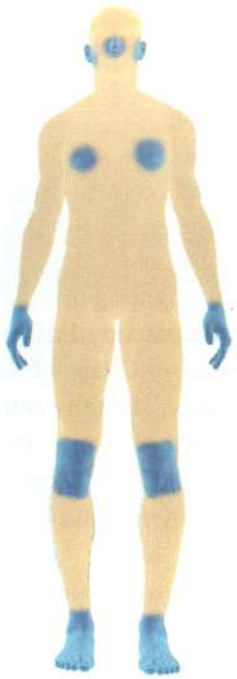
Who is Raynaud?

- Maurice Raynaud described in 1862 as first the RP:
  - Reversible vasoconstriction of digital blood flow triggered by cold resulting in a “deadly white” or “cyanotic colour” of the skin

Raynaud's Phenomenon, edited by Wigley F, Herrick A, Flavahan N. Springer Nature. 2024
Lambrecht V, et al. Reliability of the quantitative assessment of peripheral blood perfusion by laser speckle contrast analysis in a systemic sclerosis cohort. Ann Rheum Dis. 2016;75:1263-1264

Where does the Raynaud phenomenon occur on the body?





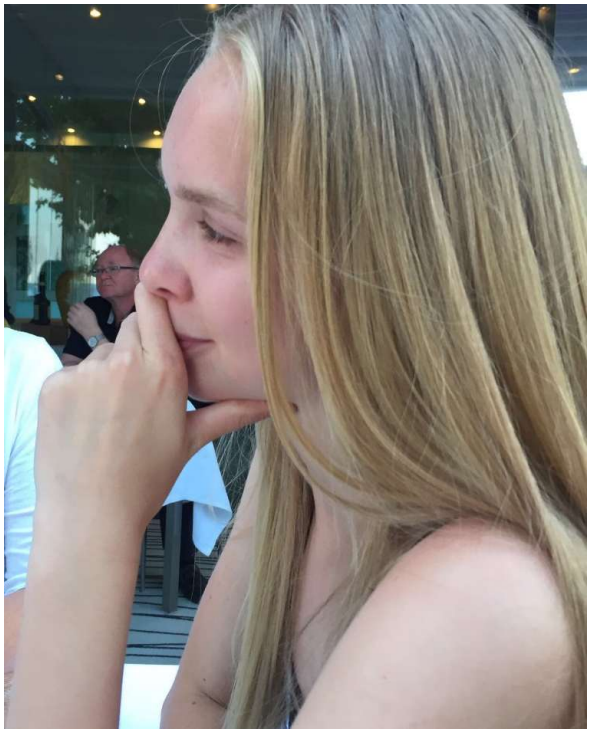
Wigley F, Herrick A, Flavahan N, eds. Raynaud's Phenomenon. Springer Nature. 2024
Chapter 6: Herrick A. Primary Raynaud's phenomenon

Types of Raynaud's phenomenon

Primary **<=>** **Secondary**

- Not related to a condition
- Occurs frequent in the general population

Primary Raynauds Phenomenon: The case of Laura



- Laura is a 15 year old healthy girl
- When she walks in the cold or when she performs ballet her hands first become white and then blue. This started when she was around 6 years old
- Her mama has the same symptoms
- Her grandmama also

Types of Raynaud's phenomenon

Primary <=> Secondary

- Not related to a condition
- Occurs frequent in the general population
- Familiar predisposition
- Young age of onset
- Lack of digital ulceration
- Absence of ANA

- Related to a condition

Capillaroscopic characteristics	Category 1				
	Non-scleroderma pattern				
	Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow			
Density (/mm)	≥7	↓			
Dimensions (µm) (figure 1)	Normal		20-50		
Abnormal morphology (figure 2)	-			+	
Haemorrhages	-				+

Types of Raynaud's phenomenon

PRP: 80-90% of all RP

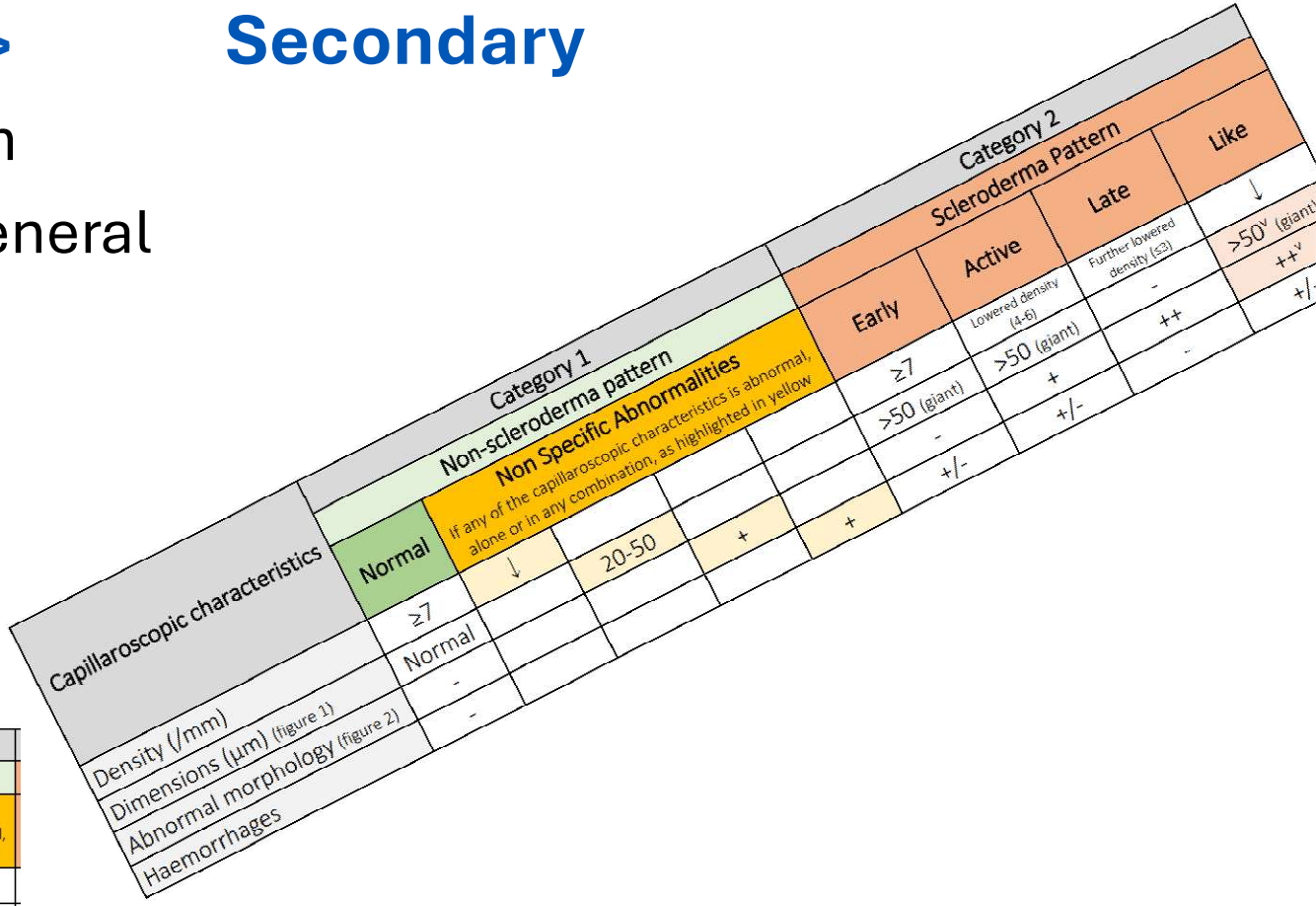
SRP: 10-20%

Types of Raynaud's phenomenon

Primary <=> Secondary

- Not related to a condition
- Occurs frequent in the general population
- Familiar predisposition
- Young age of onset
- Lack of digital ulceration
- Absence of ANA

Capillaroscopic characteristics	Category 1				
	Non-scleroderma pattern				
	Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow			
Density (/mm)	≥7	↓			
Dimensions (µm) (figure 1)	Normal		20-50		
Abnormal morphology (figure 2)	-			+	
Haemorrhages	-				+



How to investigate a patient with RP?: point of view of the rheumatologist

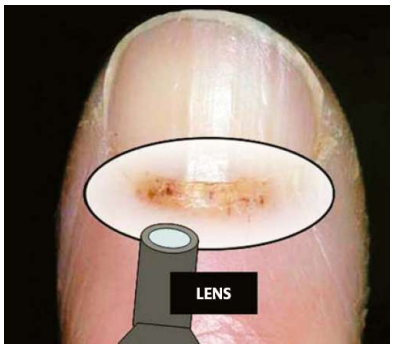
Basic investigations

- Lab:
  - Full blood count
  - ESR
  - ANA
- Nailfold capillaroscopy
- Anamnesis and Clinical examination
  - CTD

In case of unilaterality

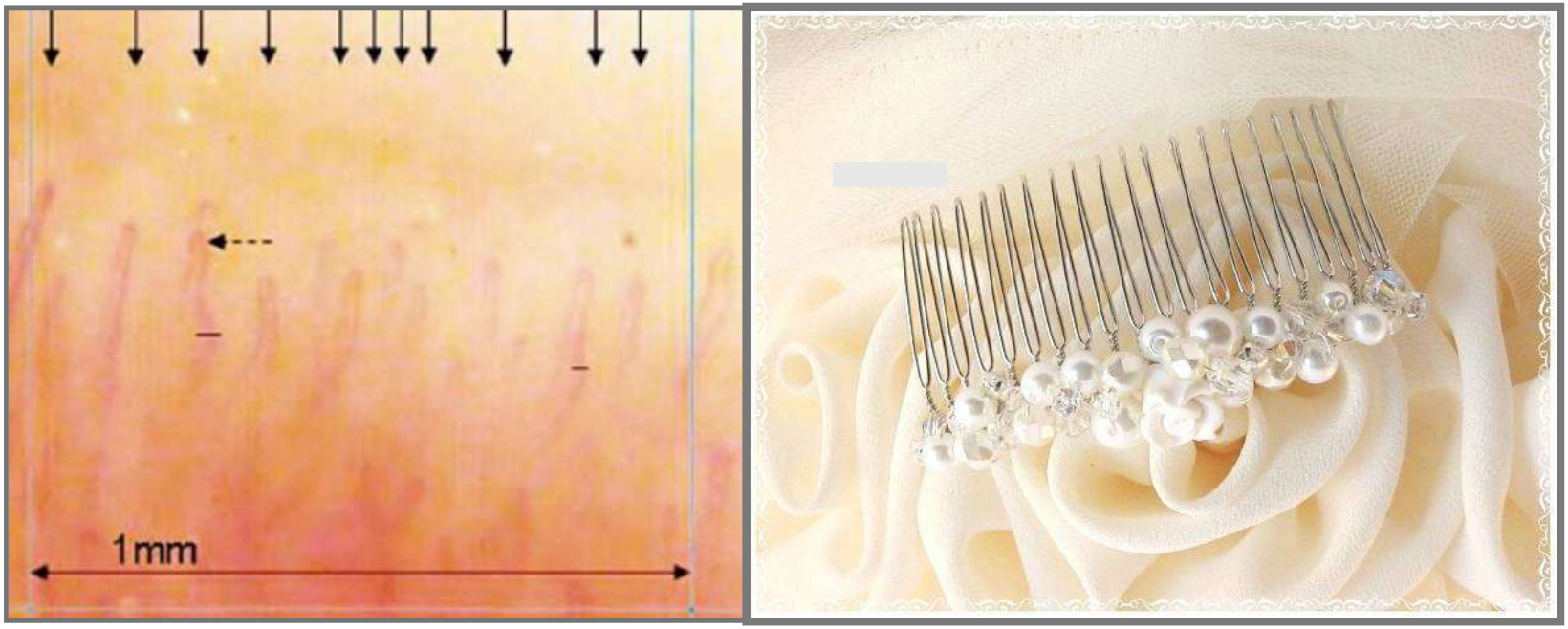
- Refer to vascular medicine
  - To confirm the macrovascular abnormality:

The nailfold videocapillaroscope



Smith V, Pizzorni C. EULAR online course on capillaroscopy 2024. Module 2, In Depth Discussion 2: “The videocapillaroscopic technique”

Criteria for primary Raynaud's phenomenon



a normal capillaroscopic pattern (or non specific abormalities)
+ negative ANA

LeRoy and Medsger. Clin Exp Rheum.1992

Smith V, et al. Best Pract Res Clin Rheumatol. 2023;37:

Criteria for secondary Raynaud's phenomenon due to SSc

Definitely enlarged – low magnification - Maricq

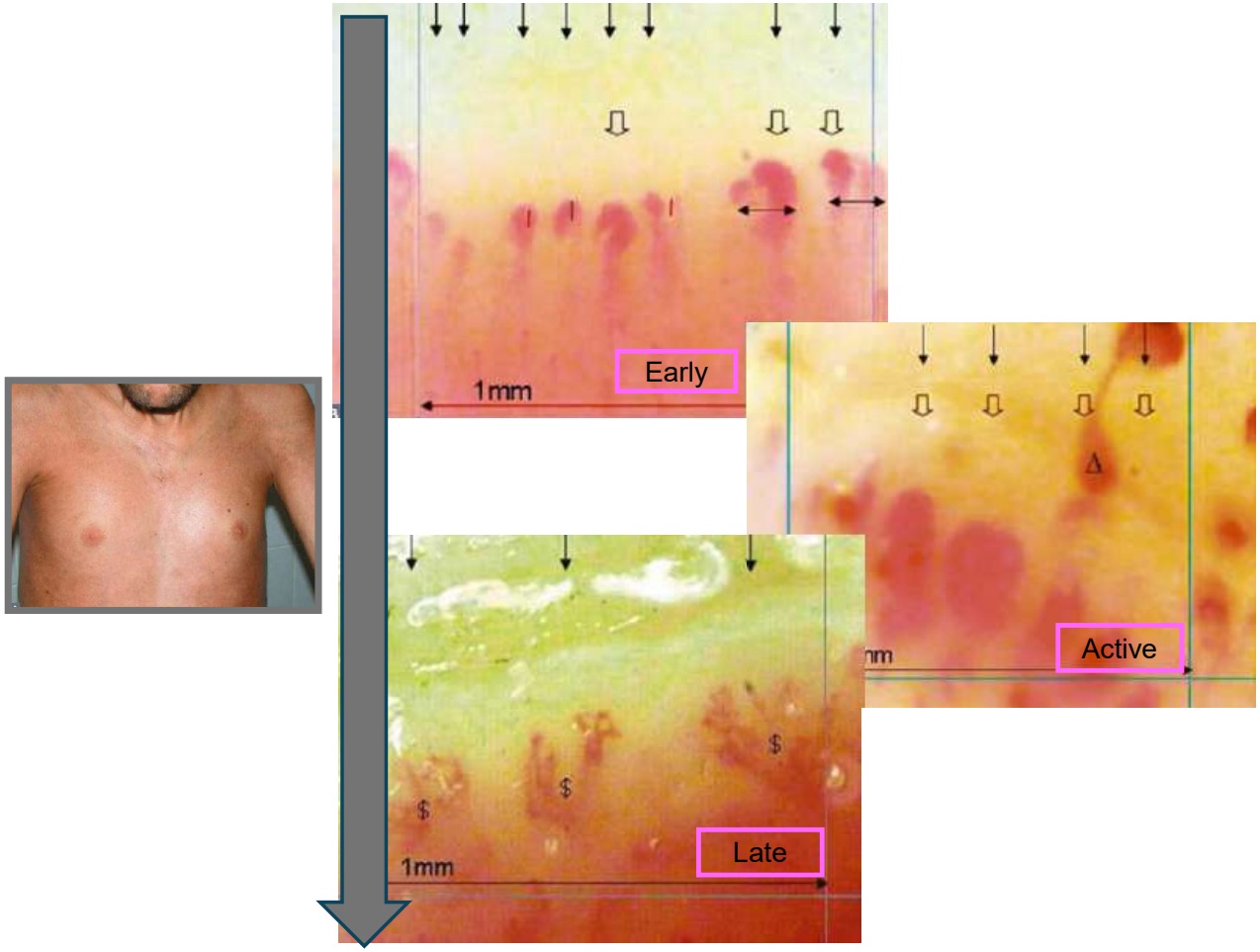
Giant capillary – high magnification - Cutolo

1. Definitely enlarged/giant capillaries are predictive of systemic sclerosis and are the first SSc-specific change

Cutolo M, et al. J Rheumatol. 2000;27:155-160

Maricq H, et al. Microvasc Res. 1986

Combination of specific changes is reflected in 3 scleroderma patterns according to Cutolo



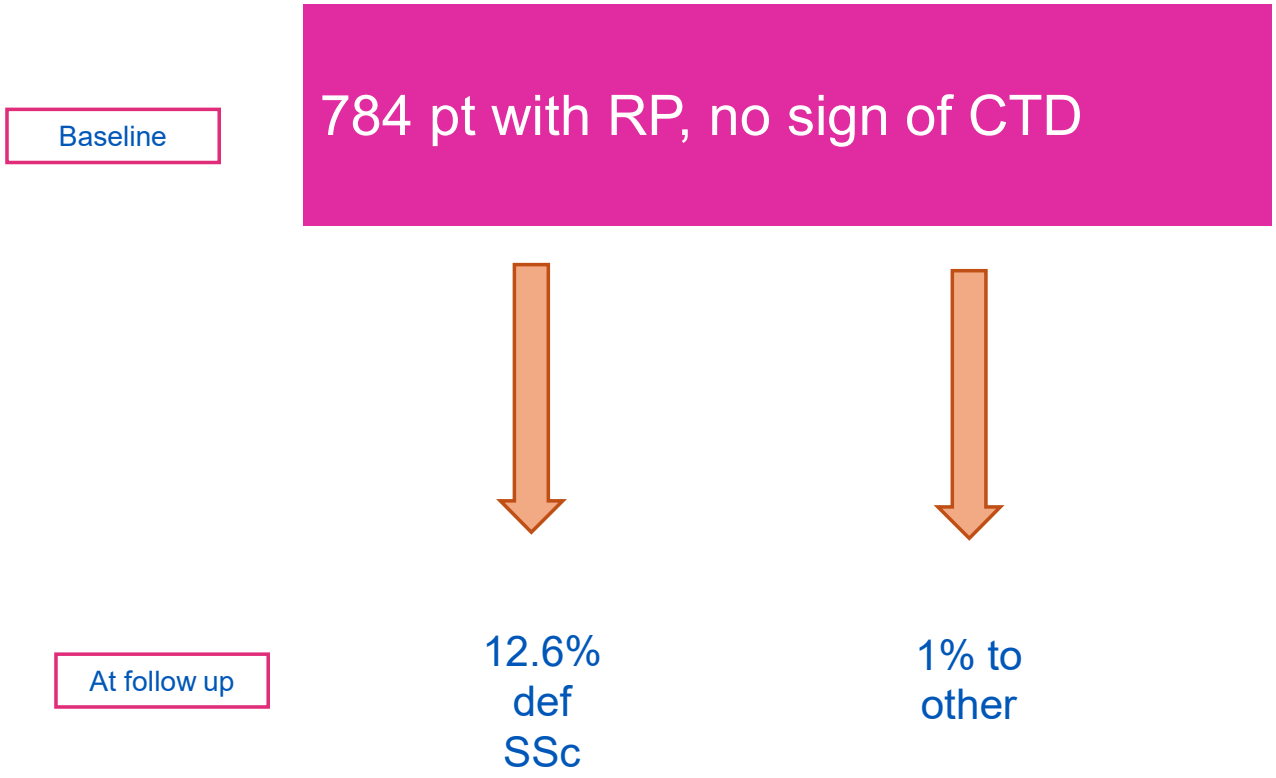
Cutolo M, et al. J Rheumatol. 2000;27:155-160

How many patients with RP Transition to secondary RP?

What auto-immune disease to they transition to?

How to detect those who will transition?

% of transition to SRP and to what auto-immune disease?

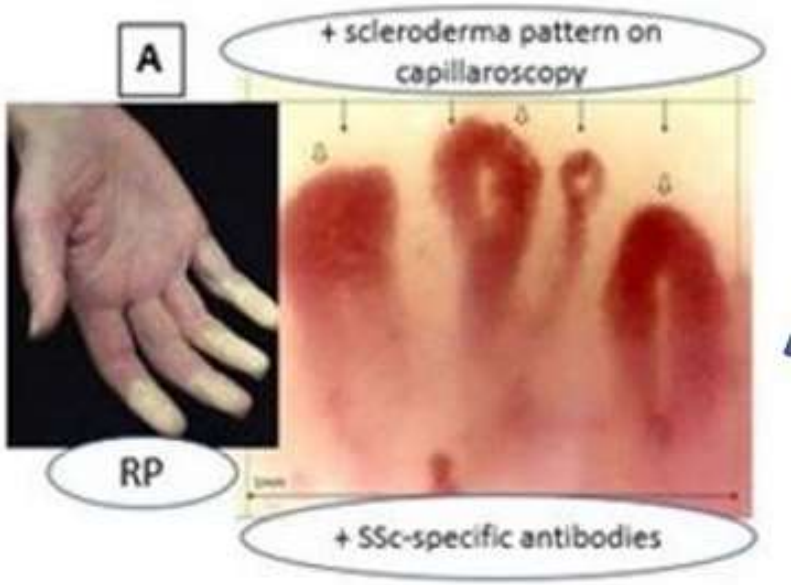


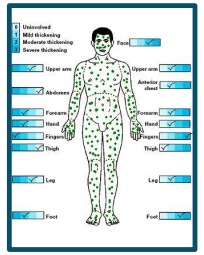
That s why the rheumatologist screens for SSc in a patient presenting with ONLY Raynaud s phenomenon

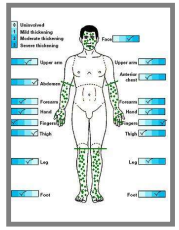
Koenig M, et al. Arthritis Reum. 2008;58:3902-3912

Two validated sets of criteria exist to inform us which RP patients will develop SSc

2001: capillaroscopy central role in criteria for classification of “early” SSc







“EARLY”

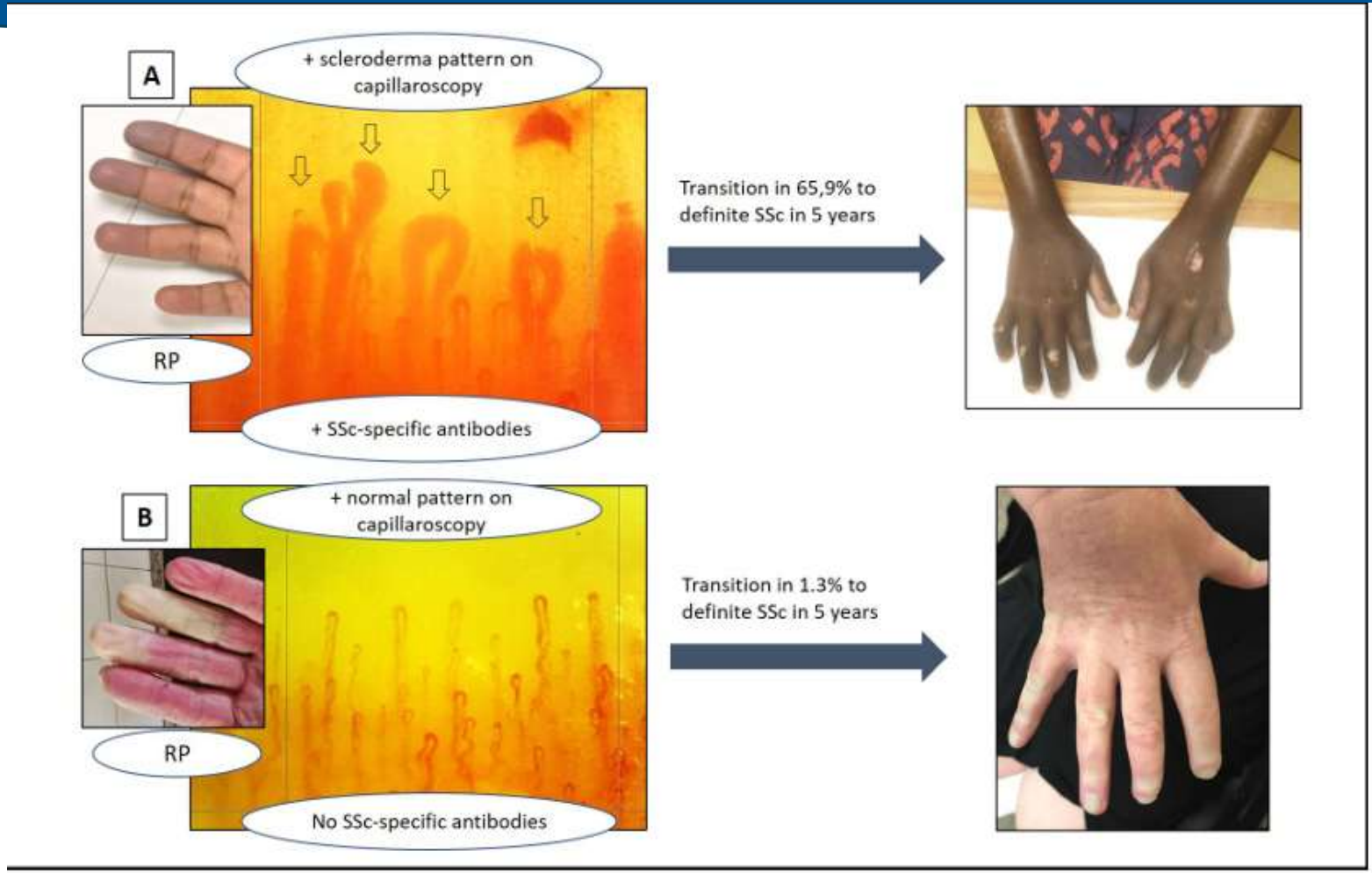
LcSc
DcSSc

LeRoy EC, et al. J Rheumatol. 2001
Koenig M, et al. Arthritis Rheum. 2008
Van Praet J, et al. Arthritis Res Ther. 2011
Vandecasteele E, et al. Eur Respir J 2017

“Early” systemic sclerosis according to leRoy is not the same as “Early” in the disease course of established SSc according to Medsger

Medsger J, et al. In: Systemic Sclerosis. Lippincot Williams and Wilkins. 2004

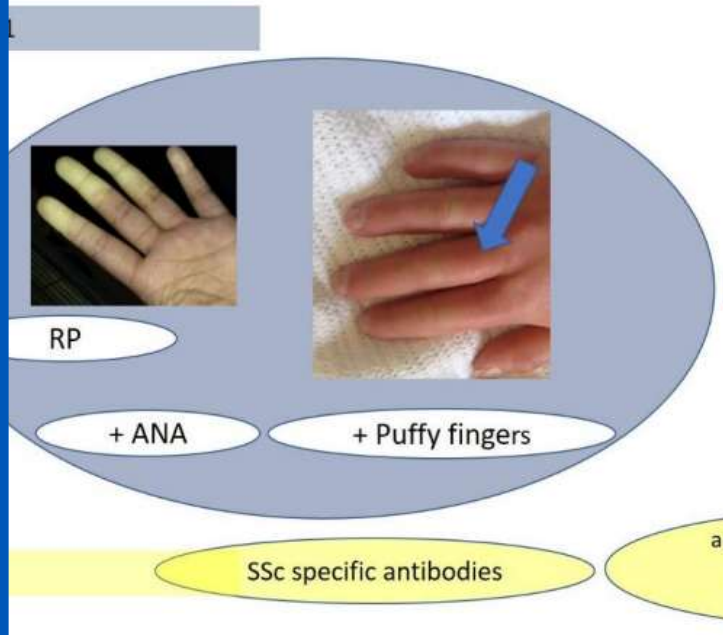
Validation of Leroy criteria



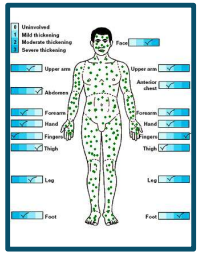
Smith V, et al. et al. Nailfold capillaroscopy. Best Practice Res Clin Rheumatol 2023; 37:101849.

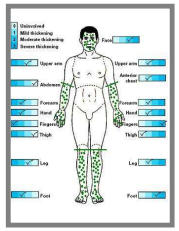
Koenig M , et al. Arthritis and rheumatism. 2008;58(12):3902-12.

2012: capillaroscopy role in criteria for classification of very “early” SSc



The presence of one or two VEDOSS criteria in patients with RP confers a progressively higher risk of fullfilling classification criteria over time





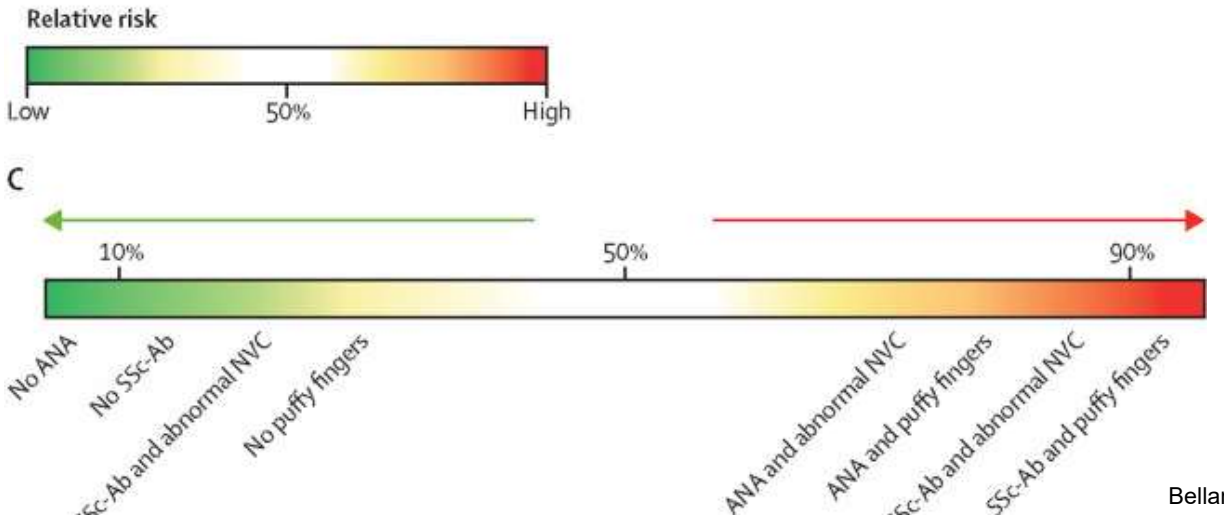
“EARLY” VERY EARLY

LcSc
DcSSc

Avouac J, et al. Ann Rheum Dis. 2012
Cosimo B, et al. Rheumatology. 2015
Bellando-Randone S, et al. Lancet Rheumatol. 2021
Ross R, et al. Arthritis Rheumatol. 2023 [Abstract]
Kersten BE, et al. Rheumatology. 2024

Validation of VEDOSS criteria

Proportion fulfilling 2013 ACR-EULAR criteria		ANA	Ssc-Ab	SSc pattern on NVC	Puffy fingers
In the presence of	ANA	58·9%	70·2%	75·0%	79·0%
	SSc-Ab	70·2%	**70·2%**	82·2%	94·1%
	SSc-Ab pattern on NVC	75·0%	82·2%	**70·1%**	69·2%
	Puffy fingers	79·0%	94·1%	69·2%	**70·8%**
In the absence of	ANA	**10·8%**	31·0%	40·4%	47·5%
	SSc-Ab	31·0%	**31·0%**	41·9%	49·6%
	SSc-Ab pattern on NVC	40·4%	41·9%	**41·5%**	50·9%
	Puffy fingers	47·5%	49·6%	50·9%	**47·9%**



Bellando-Randone S, et al. Lancet Rheumatol. 2021

Healthy- Connective tissue diseases- Systemic Sclerosis

EULAR/SCTC consensus

Consensus framework to report capillaroscopic characteristics in a standard way

Smith V, Herrick A, Ingegnoli F, Damjanov N, De Angelis R, Denton CP et al. Autoimmun Rev 2020;19:102458.

The following **capillaroscopic characteristics** are per consensus being standardly evaluated

Based on their ample combinations a capillaroscopic image can be classified as **"scleroderma pattern"** (category 2) or **"non-scleroderma pattern"** (category 1)

Capillaroscopic characteristics
Density (/mm)
Dimensions (µm)
Abnormal morphology
Haemorrhages

Category 1				
Non-scleroderma pattern				
Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow			
≥7	↓			
<20µm		20-50		
-			+	
-				+

Category 2		
Scleroderma Pattern		
Early	Active	Late
≥7	Lowered density (4-6)	Further lowered density (≤3)
>50 (giant)	>50 (giant)	-
-	+	++
+/-	+/-	-

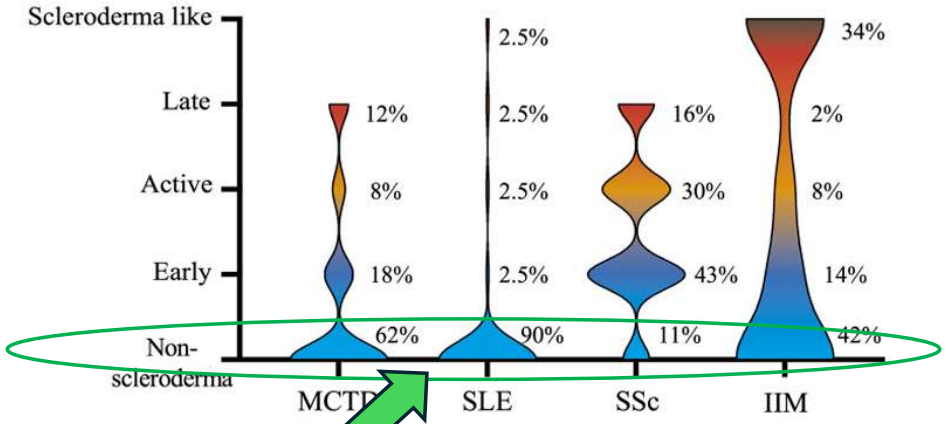
Healthy controls, CTD

Systemic sclerosis and diseases of scleroderma spectrum

Smith V, Herrick A, Ingegnoli F, Damjanov N, De Angelis R, Denton CP et al. Autoimmun Rev 2020;19:102458.

Scleroderma patterns occur in SSc and diseases of the scleroderma spectrum

FIG. 1 The prevalence and patterns of nailfold microvascular abnormalities among MCTD, SLE, SSc and IIM

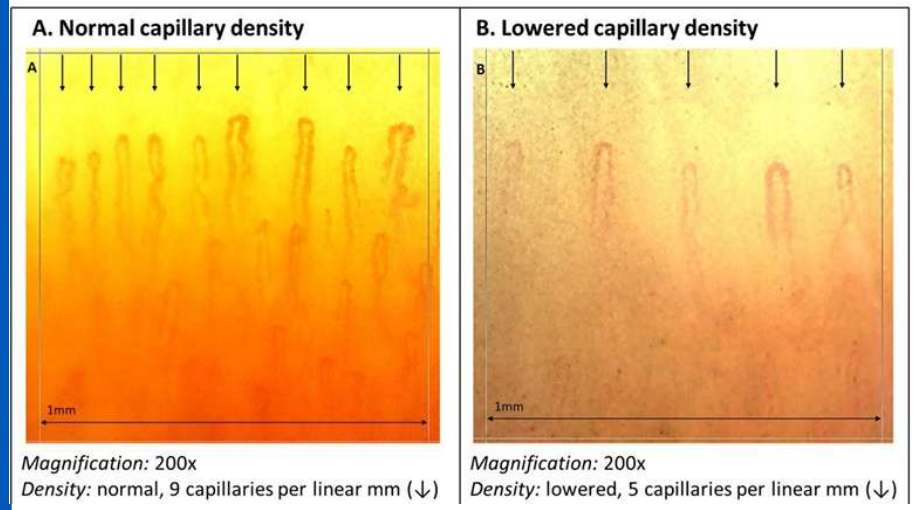


	MCTD (n=50)	SLE (n=40)	SSc (n=70)	IIM (n=50)	P-value (vs.SLE)	P-value (vs.SSc)	P-value (vs.IIM)
NVC scleroderma pattern, (%)	**38.0**	**10.0**	**88.6**	58.0	**0.003**	**<0.001**	0.07

Todokori et al.Rheumatology 2022;61:4875–4884

1st cap characteristic: Capillary density

Figure 10. Videocapillaroscopic images demonstrating capillary density



Normal

Non-specific abnormality of density

Figure 9: EULAR/SCTC study group on microcirculation in rheumatic diseases standardized capillaroscopy evaluation chart. ***Adapted from Smith V et al.(8)***

Capillaroscopic characteristics	CATEGORY 1		CATEGORY 2		
	Non-scleroderma pattern		Scleroderma Pattern		
	Normal	Non-Specific (any of the abnormalities below alone or in any combination)	Early	Active	Late
			1mm	1mm	1mm
Density (/mm)	≥ 7	W 1mm ↓ (< 7)	≥ 7	↓ (4 - 6)	↓↓ (≤ 3)
Dimension (um)	< 20	X 1mm 20 – 50	> 50 (giant)	> 50 (giant)	–
Abnormal morphology		Y 1mm	–	+	++
Haemorrhages	–	Z 1mm	±	±	–

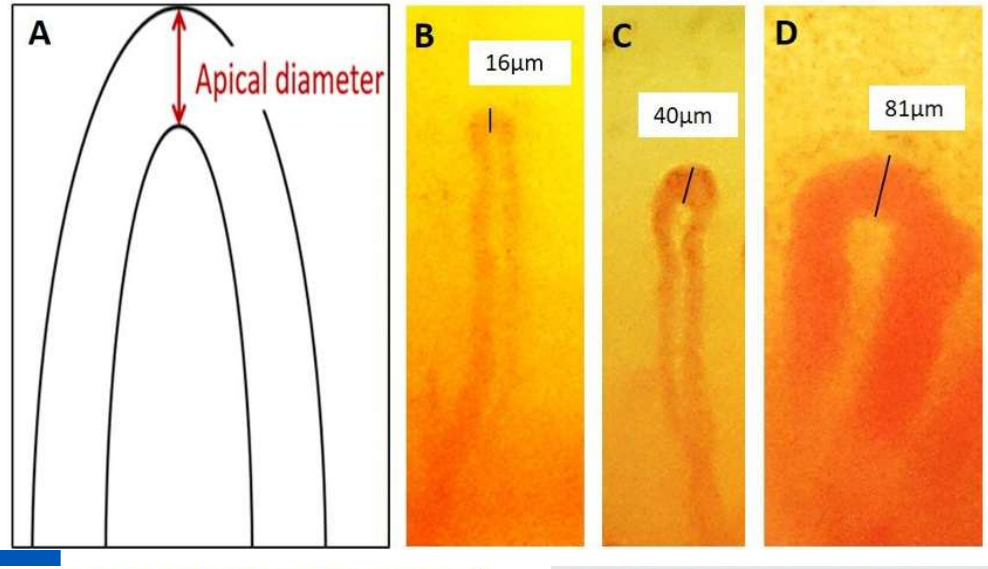
Healthy controls, CTD

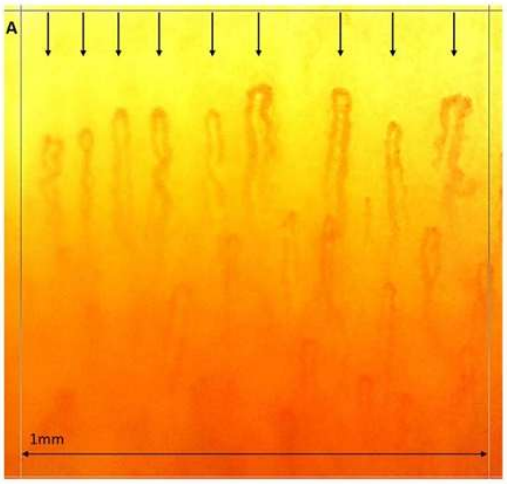
Systemic sclerosis and diseases of scleroderma spectrum,

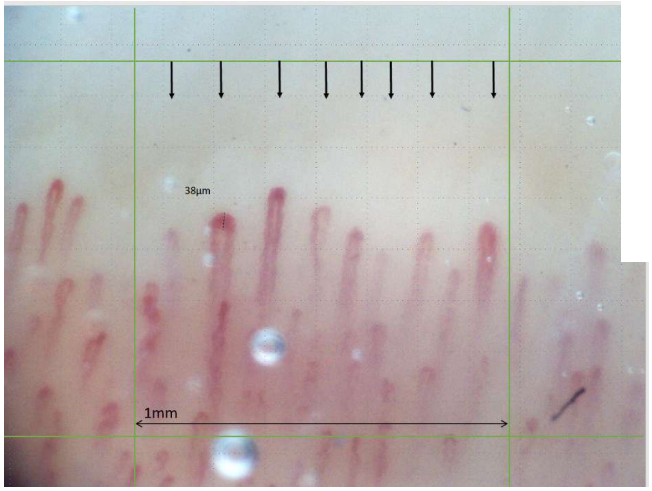
Smith V, Herrick A, Ingegnoli F, Damjanov N, De Angelis R, Denton CP et al. Autoimmun Rev 2020;19:102458.

Smith V, Cutolo M. Chapter 4: Image Interpretation. In: Nailfold Capillaroscopy in Rheumatological Diseases. Springer Nature Switzerland AG 2025. Eds: Herrick A, Murray A, Taylor C, Smith V and Cutolo M

2nd cap characteristic: Capillary dimension

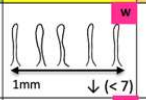
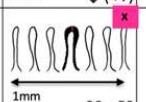
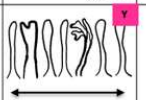
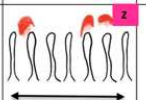






Magnification: 200x
Density: normal, 9 capillaries per linear mm (↓)

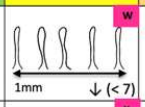
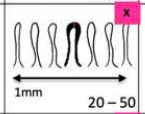
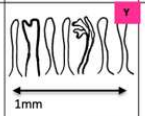
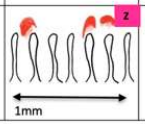
Figure 9: EULAR/SCTC study group on microcirculation in rheumatic diseases standardized capillaroscopy evaluation chart. ***Adapted from Smith V et al.(8)***

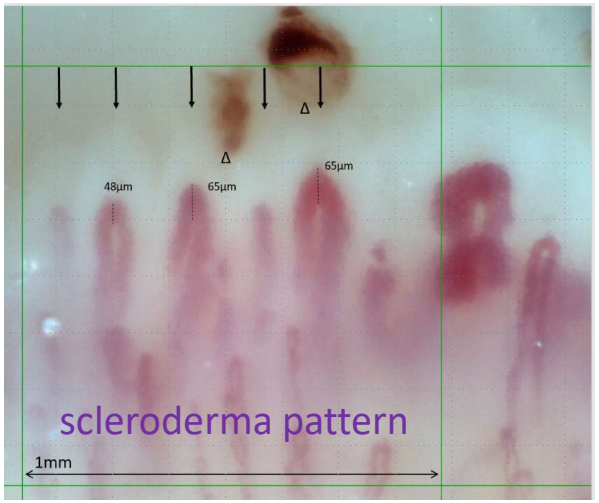
Capillaroscopic characteristics	CATEGORY 1		CATEGORY 2		
	Non-scleroderma pattern		Scleroderma Pattern		
	Normal	Non-Specific (any of the abnormalities below alone or in any combination)	Early	Active	Late
			 1mm	 1mm	 1mm
Density (/mm)	≥ 7	 W 1mm ↓ (< 7)	≥ 7	↓ (4 - 6)	↓↓ (≤ 3)
Dimension (um)	< 20	 X 1mm 20 – 50	> 50 (giant)	> 50 (giant)	–
Abnormal morphology		 Y 1mm	–	+	++
Haemorrhages	–	 Z 1mm	±	±	–

Smith V, Herrick A, Ingegnoli F, Damjanov N, De Angelis R, Denton CP et al. Autoimmun Rev 2020;19:102458.
Smith V, Cutolo M. Chapter 4: Image Interpretation. In: Nailfold Capillaroscopy in Rheumatological Diseases.

2nd cap characteristic: Capillary dimension

Figure 9: EULAR/SCTC study group on microcirculation in rheumatic diseases standardized capillaroscopy evaluation chart. ***Adapted from Smith V et al.(8)***

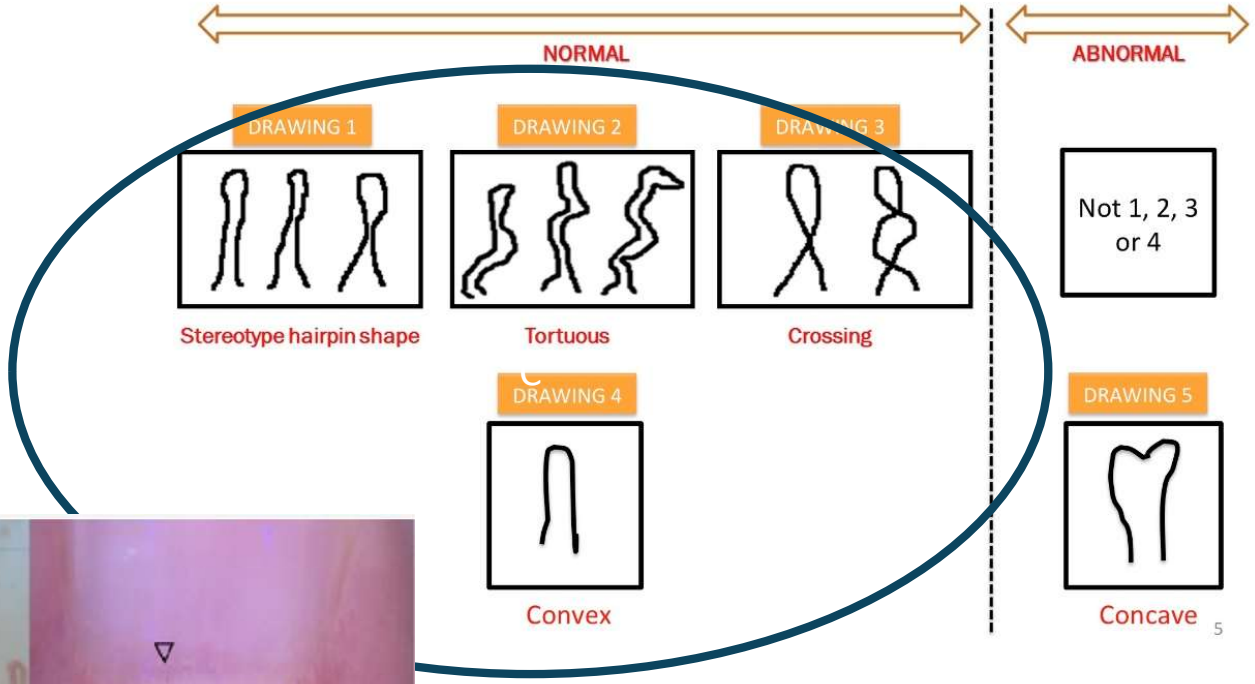
Capillaroscopic characteristics	CATEGORY 1		CATEGORY 2		
	Non-scleroderma pattern		Scleroderma Pattern		
	Normal	Non-Specific (any of the abnormalities below alone or in any combination)	Early	Active	Late
					
Density (/mm)	≥ 7		≥ 7	↓ (4 - 6)	↓↓ (≤ 3)
Dimension (um)	< 20		> 50 (giant)	> 50 (giant)	–
Abnormal morphology				+	++
Haemorrhages	–		±	±	–

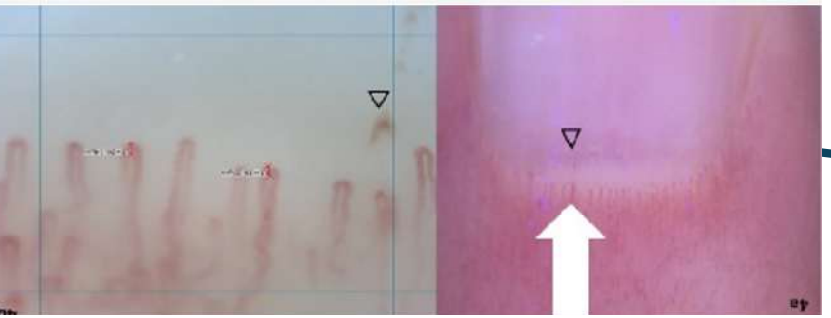


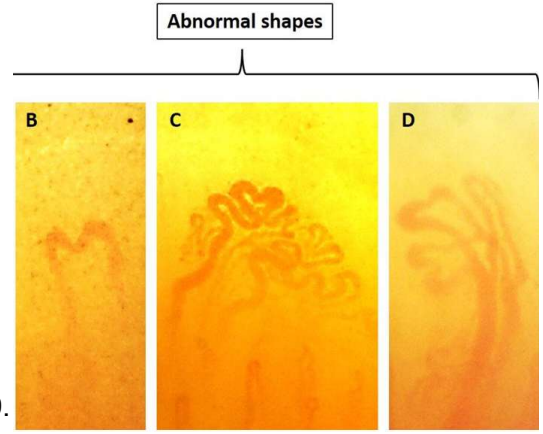
Smith V, Herrick A, Ingegnoli F, Damjanov N, De Angelis R, Denton CP et al. Autoimmun Rev 2020;19:102458.
Smith V, Cutolo M. Chapter 4: Image Interpretation. In: Nailfold Capillaroscopy in Rheumatological Diseases. Springer Nature Switzerland AG 2025. Eds: Herrick A, Murray A, Taylor C, Smith V and Cutolo M

3rd cap characteristic: Capillary morphology

Definition of normal and abnormal morphology of individual characteristics







Smith V, et al. *Rheumatology*. 2016;55(5):883-890.

Cutolo M, et al. *Rheumatology*. 2018;57(4):757-759.

A solitary change in one capillaroscopic characteristic is a non-specific abnormality

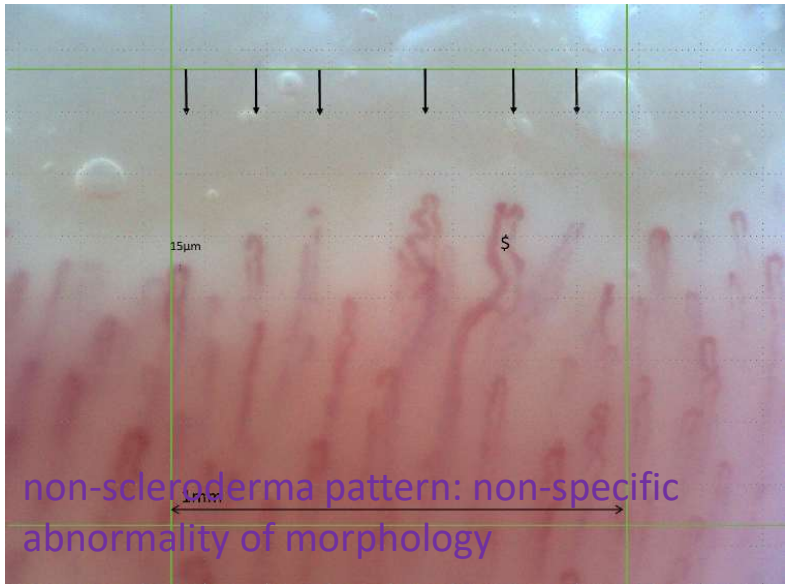


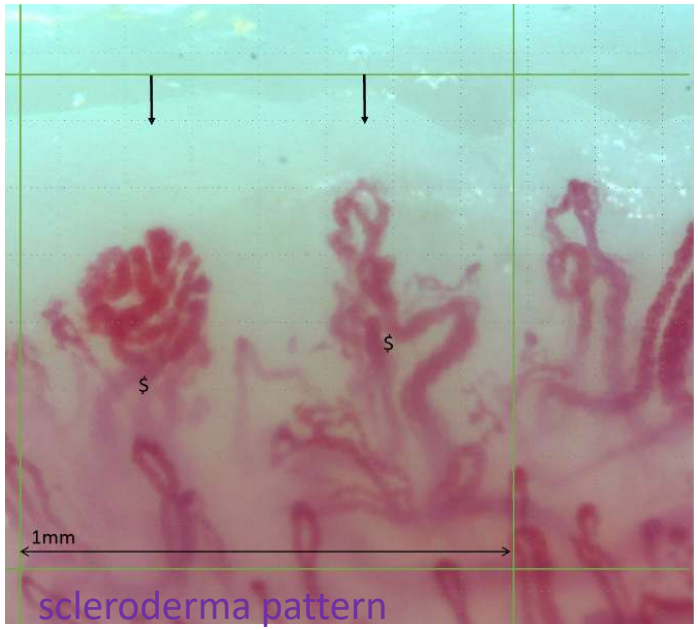
Figure 9: EULAR/SCTC study group on microcirculation in rheumatic diseases standardized capillaroscopy evaluation chart. ***Adapted from Smith V et al.(8)***

Capillaroscopic characteristics	CATEGORY 1		CATEGORY 2		
	Non-scleroderma pattern		Scleroderma Pattern		
	Normal	Non-Specific (any of the abnormalities below alone or in any combination)	Early	Active	Late
Density (/mm)	≥ 7	W 1mm ↓ (< 7)	≥ 7	↓ (4 - 6)	↓↓ (≤ 3)
Dimension (um)	< 20	X 1mm 20 – 50	> 50 (giant)	> 50 (giant)	–
Abnormal morphology		Y 1mm	–	+	++
Haemorrhages	–	Z 1mm	±	±	–

A late scleroderma pattern is the **combination** of very low density and abnormal shapes (neoangiogenesis)

Figure 9: EULAR/SCTC study group on microcirculation in rheumatic diseases standardized capillaroscopy evaluation chart. ***Adapted from Smith V et al.(8)***

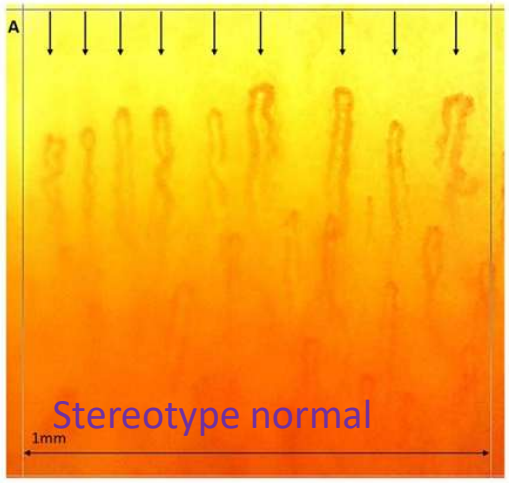
Capillaroscopic characteristics	CATEGORY 1		CATEGORY 2		
	Non-scleroderma pattern		Scleroderma Pattern		
	Normal	Non-Specific (any of the abnormalities below alone or in any combination)	Early	Active	Late
			1mm	1mm	1mm
Density (/mm)	≥ 7	W 1mm ↓ (< 7)	≥ 7	↓ (4 - 6)	↓↓ (≤ 3)
Dimension (um)	< 20	X 1mm 20 – 50	> 50 (giant)	50 (giant)	–
Abnormal morphology		Y 1mm	–	+	++
Haemorrhages	–	Z 1mm	±	±	–



Smith V, Herrick A, Ingegnoli F, Damjanov N, De Angelis R, Denton CP et al. Autoimmun Rev 2020;19:102458.

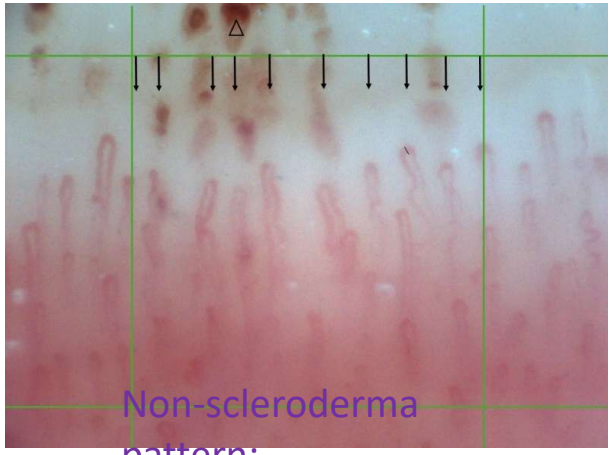
Smith V, Cutolo M. Chapter 4: Image Interpretation. In: Nailfold Capillaroscopy in Rheumatological Diseases. Springer Nature Switzerland AG 2025. Eds: Herrick A, Murray A, Taylor C, Smith V and Cutolo M

4th cap characteristic: microhaemorrhages



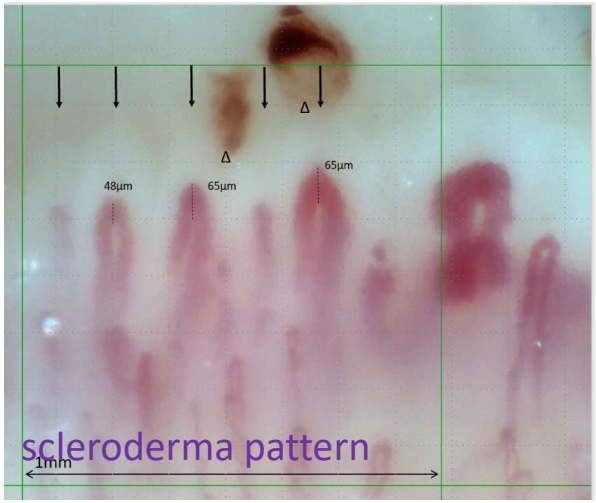
Stereotype normal

Magnification: 200x
Density: normal, 9 capillaries per linear mm (↓)
Dimension: within normal limits



Non-scleroderma pattern:

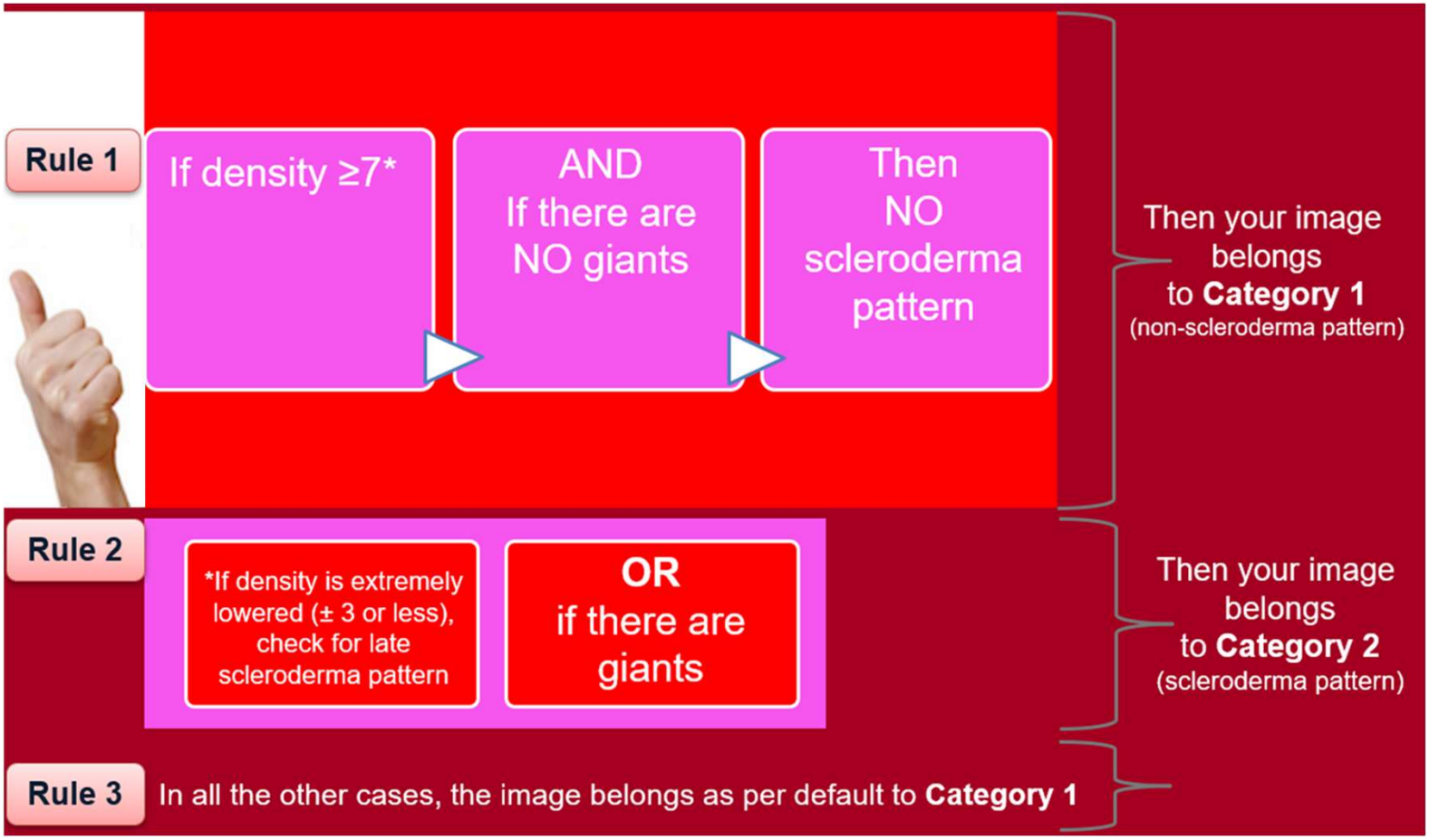
non-specific abnormality due to presence of microhaemorrhages



scleroderma pattern

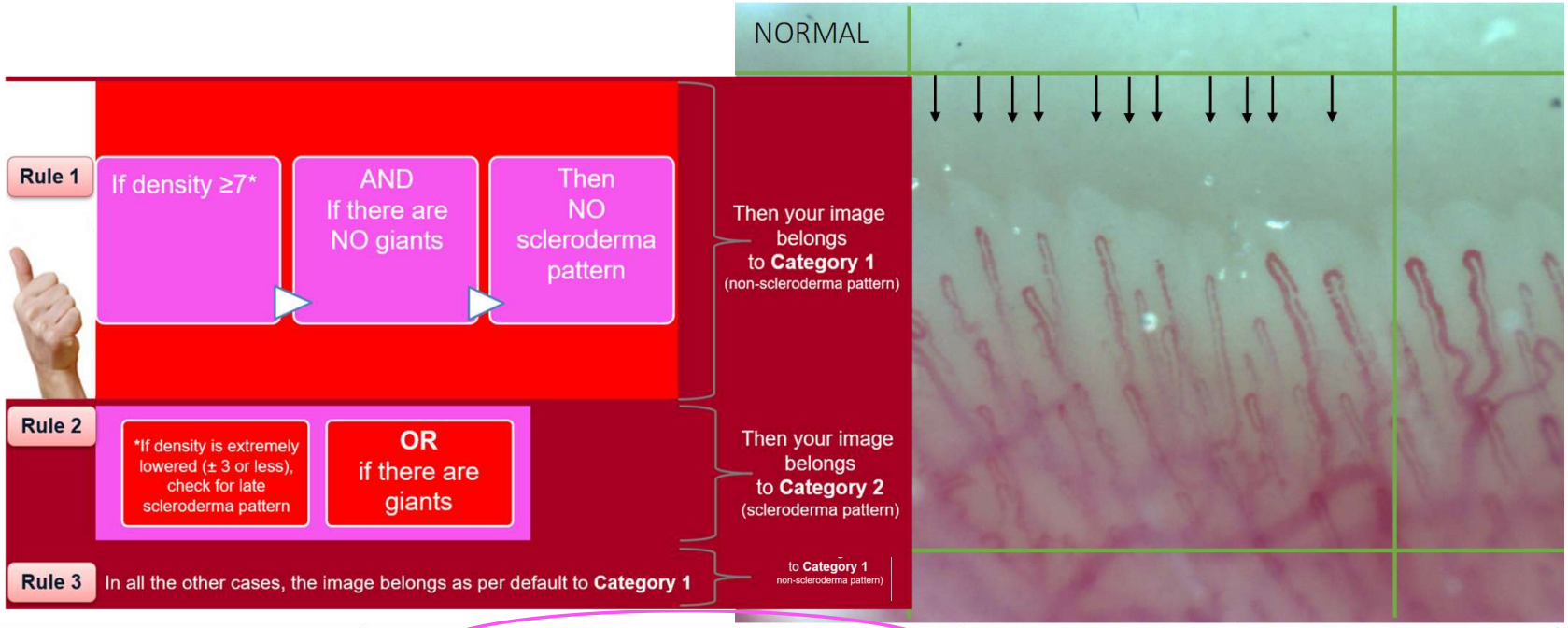
Smith V, Herrick A, Ingegnoli F, Damjanov N, De Angelis R, Denton CP et al. Autoimmun Rev 2020;19:102458.

Fast Track Algorithm

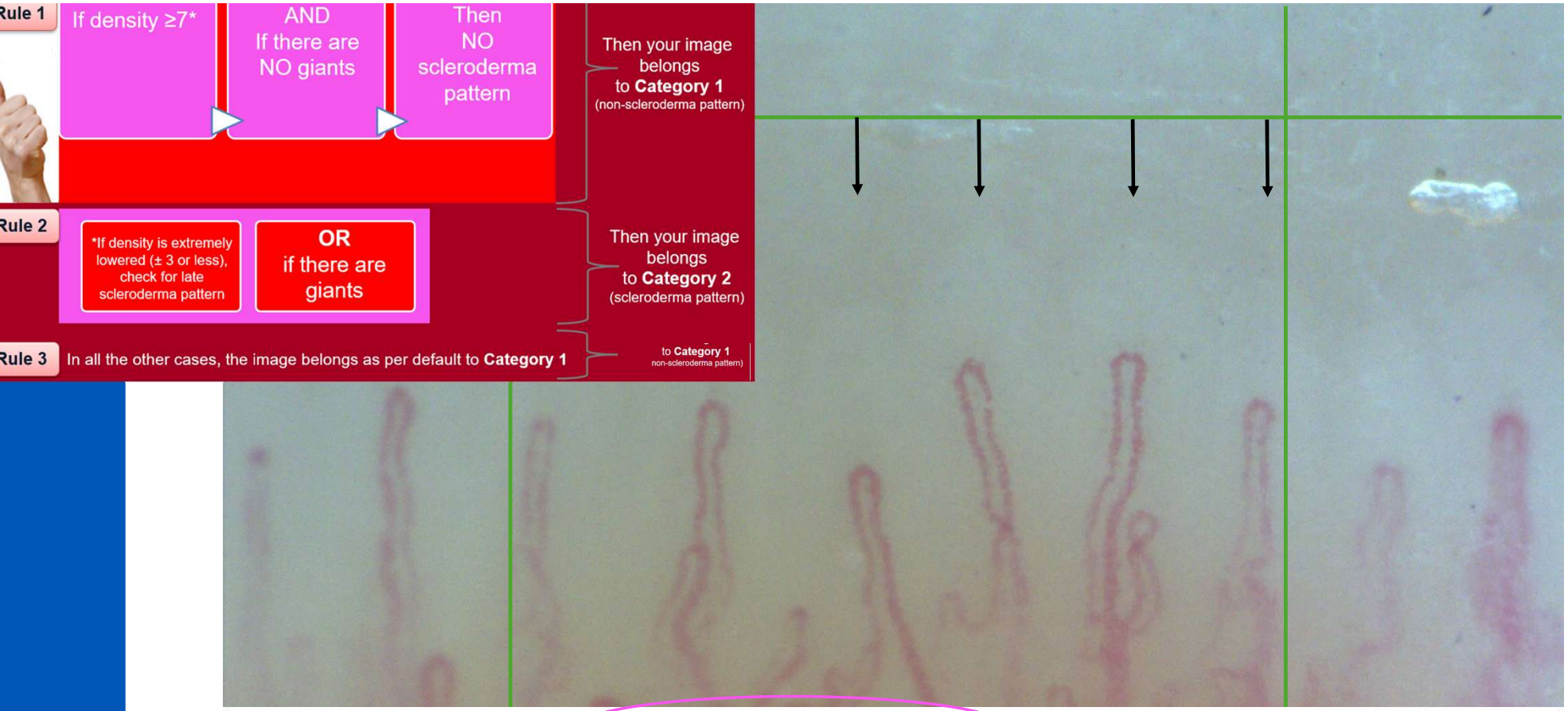


Smith V, et al. Fast track algorithm: How to differentiate a "scleroderma pattern" from a "non-scleroderma pattern". Autoimmun Rev. 2019 Sep 11:102394. (Open Access).

Example: apply the fast track algorithm

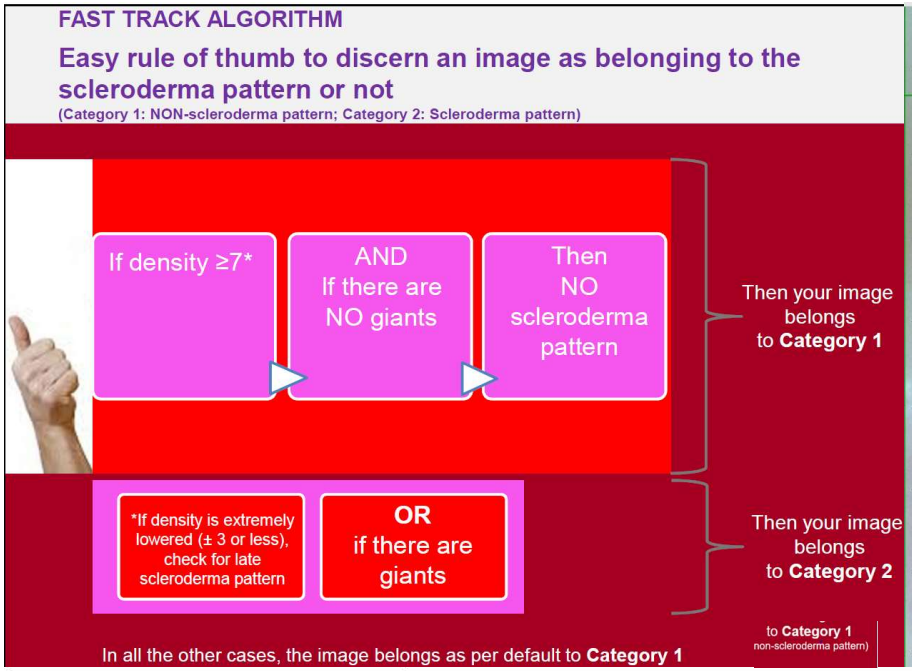


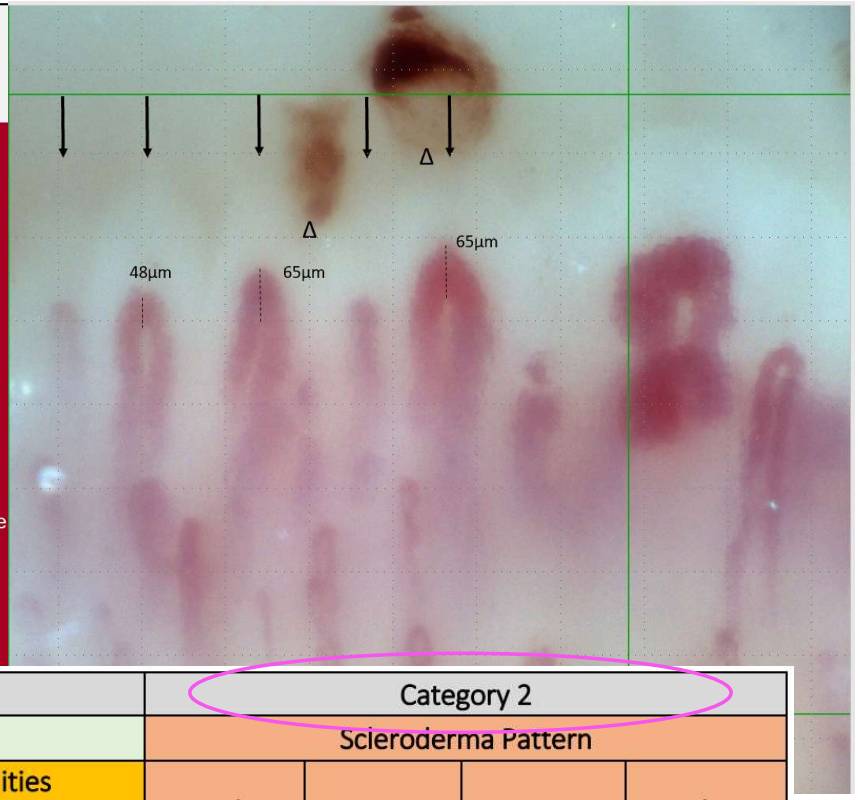
Capillaroscopic characteristics	Category 1					Category 2			
	Non-scleroderma pattern					Scleroderma Pattern			
	Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow				Early	Active	Late	Like
Density (/mm)	≥7	↓				≥7	Lowered density (4-6)	Further lowered density (≤3)	↓
Dimensions (µm) (figure 1)	rmal		20-50			>50 (giant)	>50 (giant)	-	>50[v] (giant)
Abnormal morphology (figure	-			+		-	+	++	++[v]
Haemorrhages	-				+	+/-	+/-	-	+/-



Capillaroscopic characteristics	Category 1					Category 2			
	Non-scleroderma pattern					Scleroderma Pattern			
	Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow				Early	Active	Late	Like
Density (/mm)	≥7	↓				≥7	Lowered density (4-6)	Further lowered density (≤3)	↓
Dimensions (µm) (figure 1)	Normal		20-50			>50 (giant)	>50 (giant)	-	>50[v] (giant)
Abnormal morphology (figure 2)	-			+		-	+	++	++[v]
Haemorrhages					+	+/-	+/-	-	+/-

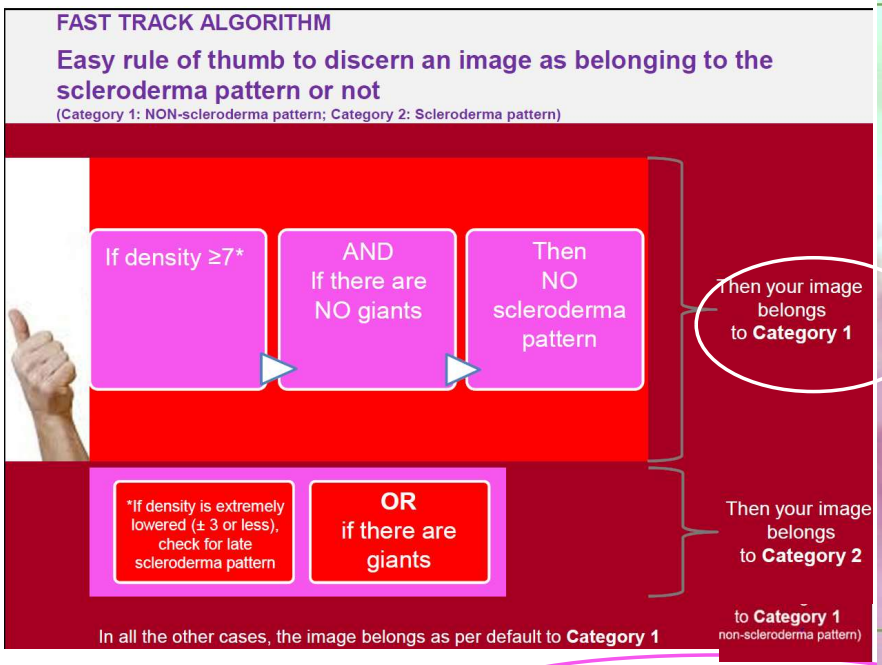
Example: apply the fast track algorithm

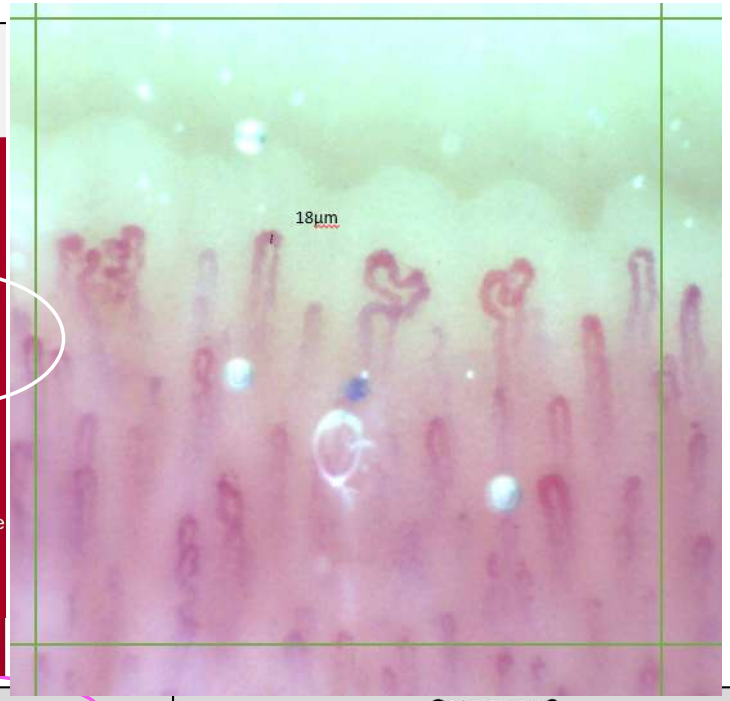




Capillaroscopic characteristics	Category 1					Category 2			
	Non-scleroderma pattern					Scleroderma Pattern			
	Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow				Early	Active	Late	Like
Density (/mm)	≥7	↓				≥7	Lowered density (4-6)	Further lowered density (≤3)	↓
Dimensions (µm) (figure 1)	Normal		20-50			>50 (giant)	>50 (giant)	-	>50[v] (giant)
Abnormal morphology (figure 2)	-			+		-	+	++	++[v]
Haemorrhages	-				+	+/-	+/-	-	+/-

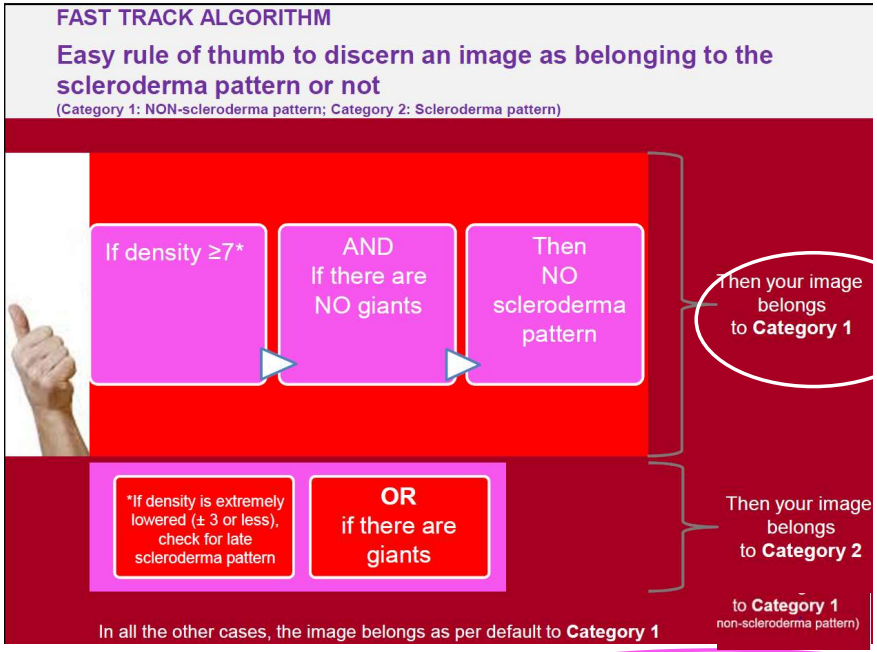
Example: apply the fast track algorithm

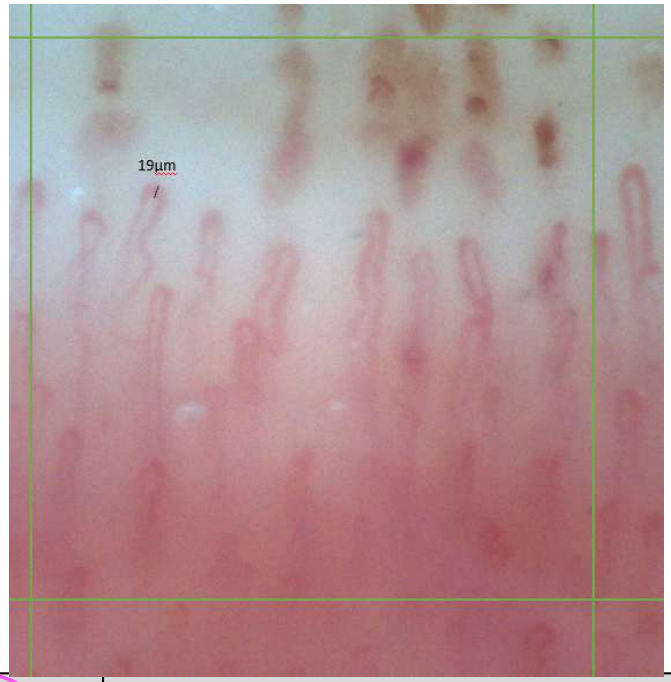




Capillaroscopic characteristics	Category 1					Category 2			
	Non-scleroderma pattern					Scleroderma Pattern			
	Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow				Early	Active	Late	Like
Density (/mm)	≥7	↓				≥7	Lowered density (4-6)	Further lowered density (≤3)	↓
Dimensions (µm) (figure 1)	Normal		20-50			>50 (giant)	>50 (giant)	-	>50[v] (giant)
Abnormal morphology (figure 2)	-			+		-	+	++	++[v]
Haemorrhages	-				+	+/-	+/-	-	+/-

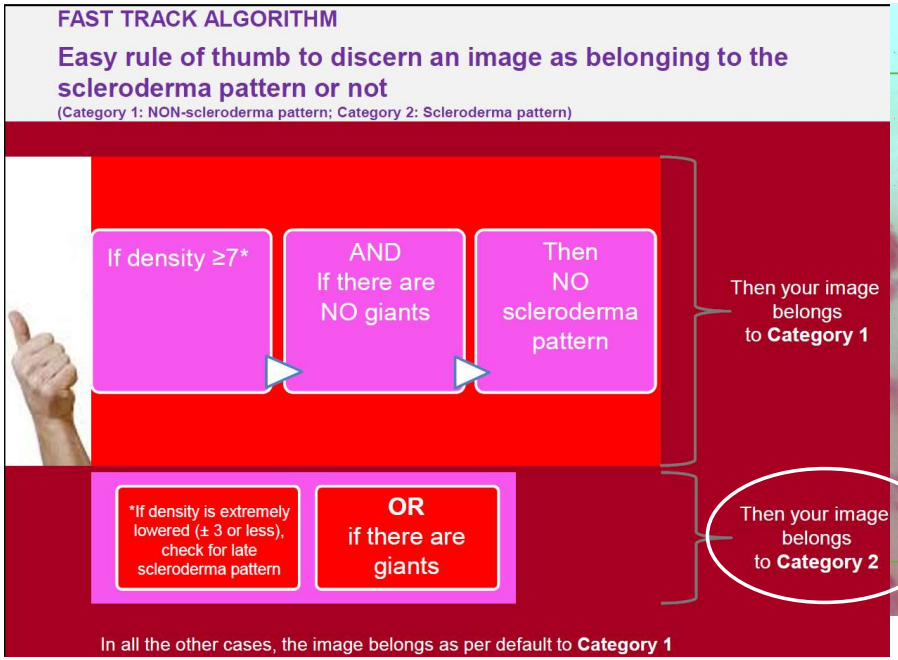
Example: apply the fast track algorithm

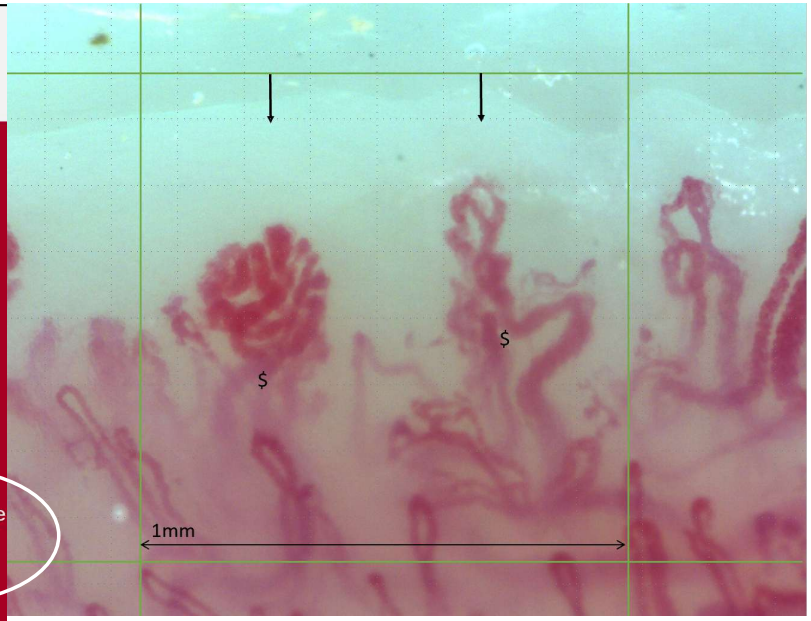




Capillaroscopic characteristics	Category 1					Category 2			
	Non-scleroderma pattern					Scleroderma Pattern			
	Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow				Early	Active	Late	Like
Density (/mm)	≥7	↓				≥7	Lowered density (4-6)	Further lowered density (≤3)	↓
Dimensions (µm) (figure 1)	Normal		20-50			>50 (giant)	>50 (giant)	-	>50[v] (giant)
Abnormal morphology (figure 2)	-			+		-	+	++	++[v]
Haemorrhages	-				+	+/-	+/-	-	+/-

Example: apply the fast track algorithm





Capillaroscopic characteristics	Category 1					Category 2			
	Non-scleroderma pattern					Scleroderma Pattern			
	Normal	Non Specific Abnormalities If any of the capillaroscopic characteristics is abnormal, alone or in any combination, as highlighted in yellow				Early	Active	Late	Like
Density (/mm)	≥7	↓				≥7	Lowered density (4-6)	Further lowered density (≤3)	↓
Dimensions (µm) (figure 1)	Normal		20-50			>50 (giant)	>50 (giant)	-	>50[v] (giant)
Abnormal morphology (figure 2)	-			+		-	+	++	++[v]
Haemorrhages	-				+	+/-	+/-	-	+/-

Interrater reliability of fast track algorithm

Table 1: Mean Cohen's kappa (95% CI) and Light's kappa for the groups of raters at the 8th EULAR course on capillaroscopy in Rheumatic Diseases (Genoa 2018).

Group of raters	Mean Cohen's kappa (95% CI)	Light's kappa
Expert raters (n=6)	1	1
Attendees (n=135)	0.96 (0.95 – 0.98)	0.92
- *"Novices" (n=68)*	0.98 (0.96 – 0.99)	0.95
- *"Moderately experienced" (n=53)*	0.96 (0.93 – 0.99)	0.91
- *"Experienced" (n=14)*	0.93 (0.85 – 1)	0.84

CI: Confidence Interval.

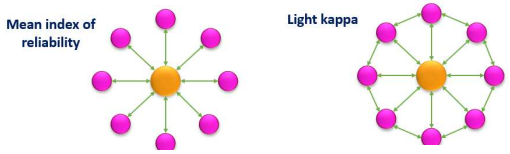


Table 2: Mean Cohen's kappa (95% CI) and Light's kappa for the groups of raters at the 8th EUSTA course on SSc (Nijmegen 2019).

Group of raters	Mean Cohen's kappa (95% CI)	Light's kappa
Expert raters (n=3)	1	1
Attendees (n=85)	0.94 (0.92 – 0.96)	0.87
- *"Novices" (n=47)*	0.93 (0.90 – 0.96)	0.85
- *"Moderately experienced" (n=29)*	0.94 (0.89 – 0.98)	0.88
- *"Experienced" (n=9)*	0.97 (0.92 – 1)	0.94

CI: Confidence Interval.

Smith V, et al. Fast track algorithm: How to differentiate a "scleroderma pattern" from a "non-scleroderma pattern". Autoimmun Rev. 2019 Sep 11:102394. (Open

Capillaroscopy and the Raynaud ‘s phenomenon

- In a healthy population and primary Raynaud ‘s phenomenon:
  - Capillaroscopic images may be stereotype normal
  - There may be non-specific abnormalities of any of the capillaroscopic characteristics
- In connective tissue diseases : Likewise
- In systemic sclerosis and diseases of the scleroderma spectrum :
  - Scleroderma patterns:
    - “Early”, “Active”, “Late” according to Cutolo: 200 magnification
    - Definitely enlarged: widefield technique
- Fast track algorithm: to fastly and reliably discern a scleroderma pattern from a non-sclerodderma pattern

Smith V. et al. Rheumatology 2016; 55: 883-890

VIENNA

2024

42

Countries

Limited to 120 participants

EULAR LIVE COURSE on Capillaroscopy and Microcirculation in Rheumatic Diseases

since 2004

14th EULAR Course on Capillaroscopy and Microcirculation in Rheumatic Diseases

Barcelona, Spain

Saturday, 7 June 2025 – Monday, 9 June 2025

Next course: may 30th- June 1st 2026, London

Registration process: January 2026, EULAR site

Thank you kindly for your attention!!!

European Reference Networks

UZ GENT

UNIVERSITEIT GENT

EULAR Study Group on Microcirculation in Rheumatic Diseases (EULAR SG MC/RD): reflections after ten years

Interested to join us?
Please mail: vanessa.smith@ugent.be

Next study Group:hybrid

OCTOBER 8th 2025 at 18 o clock

European Reference Networks

vanessa.smith@ugent.be

UZ GENT