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DOI: 10.1007/s00296-017-3808-0

#### **Document Version**

Accepted author manuscript

#### Link to publication record in Manchester Research Explorer

#### Citation for published version (APA):

Ingegnoli, F., Ughi, N., Dinsdale, G., Orenti, A., Boracchi, P., Allanore, Y., Foeldvari, I., Sulli, A., Cutolo, M., Smith, V., Herrick, A. L., Hij, A., Sulli, A., Nitsche, A., Vacca, A., Balbir-Gurman, A., Abdessemed, A., Vargas, A., Valenzuela, A., ... The Eular Study Group On Microcirculation In Rheumaticdiseases (2017). An international SUrvey on non-iNvaSive techniques to assess the mIcrocirculation in patients with RayNaud's phEnomenon (SUNSHINE survey). *Rheumatology International*, *37*(11), 1879-1890. https://doi.org/10.1007/s00296-017-3808-0

#### Published in:

Rheumatology International

#### Citing this paper

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Running header: survey on techniques to assess Raynaud's phenomenon

## An international SUrvey on non-iNvaSive tecHniques to assess the mIcrocirculation in patients with RayNaud's phEnomenon (SUNSHINE survey)

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#### ABSTRACT

Objectives. To canvas opinion concerning the role of non-invasive techniques in the assessment of patients with Raynaud's phenomenon (Rp) in clinical and research settings: four nailfold capillaroscopy methods (videocapillaroscopy [NVC], dermoscopy. stereomicroscopy, digital USB microscopy), four laser Doppler methods (laser Doppler flowmetry. imaging, anemometry/velocimetry, laser Speckle Contrast Analysis), thermographic imaging, and upper limb arterial Doppler ultrasound.

**Methods.** Emails with a link to the survey were sent to physicians from the European Scleroderma Trials and Research group (EUSTAR), the EULAR Study Group on Microcirculation in Rheumatic Diseases (SG\_MC/RD) and members of the pediatric rheumatology Email board. The main descriptive analysis related to physicians looking after adult patients, with some analysis also of opinions from paediatric rheumatologists.

**Results.** 106 'adult physicians' responded (a response rate of 25.8%), of whom 68.9% were European, and 81.1% practising for more than 10 years. Nineteen paediatricians responded. The most widely available technique was NVC (72.7%). Nailfold capillaroscopy was most frequently performed by the physician him/herself, using different types of equipment relating to availability. Most rheumatologists reported high levels of appropriateness for NVC in both clinical and research settings for global assessment and differential diagnosis of Rp. Other techniques were less used.

**Conclusions.** Of all the different techniques, nailfold capillaroscopy was the one most used in both clinical and research settings by adult physicians, the majority of whom use NVC in their everyday practice. The low proportion of clinicians using other techniques suggests that these are currently mainly research tools, available only in specialist centres.

## Key words

Nailfold capillaroscopy, videocapillaroscopy, dermoscopy, laser Doppler flowmetry, laser

Doppler imaging, anemometry/velocimetry, laser Speckle Contrast Analysis,

thermographic imaging, upper limb arterial Doppler ultrasound, Raynaud's phenomenon,

systemic sclerosis, connective tissue disease

Compliance with Ethical Standards:

- \* Disclosure of potential conflicts of interest: none
- \* Research involving human participants and/or animals: not applicable
- \* Informed consent: not applicable

#### Funding statement: none

#### INTRODUCTION

Raynaud's phenomenon (Rp) is common, with an estimated prevalence in the general population of 3 to 5% [1]. While clinical assessment and laboratory testing provide important information for the differential diagnosis between primary and secondary forms, imaging investigations are considered a valuable addition [2], in both clinical and research settings. The added value of magnified visualization of the nailfold microcirculation (capillaroscopy) is highlighted in the 2013 classification criteria for systemic sclerosis (SSc) [3, 4], meaning that ideally all rheumatologists should be familiar with the technique.

Different diagnostic imaging techniques may be applied in patients with Rp and SScspectrum disorders to study the structure and function of the finger microcirculation [5, 6]. Among the available techniques, nailfold capillaroscopy is widely applied either with highly specialized equipment such as videocapillaroscopy (NVC), or simple in-office dermatoscopes. Thermographic imaging and laser Doppler techniques may also be valuable in the assessment of Rp, but the extent of their use among specialists in clinical practice is unknown and an expert committee suggested that thermographic imaging and laser Doppler flowmetry were 'inappropriate' due to 'difficulties in implementation and questionable utility' [7]. The concurrent use of multiple techniques tends currently to be restricted to tertiary referral centers and for research purposes.

Despite growing interest in the use of non-invasive imaging techniques in the assessment of Rp, current usage of these different techniques to assess microcirculation in Rp is unknown. We therefore surveyed physicians in specialties routinely involved in the management of Rp. Here we report the analysis of responses from this international SUrvey on non-iNvaSive tecHniques to assess the mIcrocirculation in patients with RayNaud's phEnomenon (SUNSHINE survey). Our goal was to obtain an insight into current opinion and utilisation of the specific techniques that may be used in the

assessment of patients with Rp in both clinical and research practice. Specifically, opinion regarding their potential role in screening, in clinical monitoring and as outcome measures was evaluated.

#### METHODS

#### Survey Design

The SUNSHINE survey (see Appendix 1) was designed on the basis of a review of the literature and from the contributions of experts in the field. The survey comprised 27 questions, 11 of which included basic demographic and background information regarding respondents' current practice and monitoring of Rp. The other 16 questions focussed on the non-invasive techniques: NVC, nailfold dermoscopy, nailfold stereomicroscopy, nailfold digital USB microscopy, laser Doppler flowmetry, laser Doppler imaging, laser Doppler anemometry/velocimetry, Laser Speckled Contrast Analysis (LASCA), thermographic imaging, upper limb arterial Doppler ultrasound (US). In particular, participants were asked about their self-assessed knowledge regarding the different techniques (1 question), their current usage and the availability of the different techniques in their practice (5 questions), and their opinion as to the appropriateness of the techniques (for global assessment, differential diagnosis, and monitoring) in clinical (5 questions) and in research settings (5 questions) (see appendix 1).

#### Survey Sample and Administration - adult physicians

The SUNSHINE survey was devised to evaluate opinions of the members of the European League Against Rheumatism (EULAR) Study Group on Microcirculation in Rheumatic diseases (SG\_MC/RD) and the EULAR Scleroderma Trials and Research (EUSTAR), using their 2015 mailing lists. It was conducted between October and December 2015 using an internet-based program (Google forms). A call for survey completion was sent after nearly one month. At the beginning of the survey participants were all explicitly asked if they were willing to complete the survey and informed that their consent and the completion of the survey would have permitted to listed them in the manuscript as part of SUNSHINE Study Group unless denied.

From the 456 email addresses, we excluded all those which were not specifically namedpersons and duplicates, giving a total sample of 420 (Figure 1-A). Of the 120 responses, 9 were from individuals who responded twice, 4 were ineligible (2 respondents reported they were not sufficiently skilled to participate in the survey, as per their response to Question 1, and 2 were paediatricians), and 1 questionnaire was returned blank.

All the 106 eligible responders completed the questionnaire: no partial questionnaires were returned due to the design of the survey in which skipping items were not permitted. Of the 309 non-respondents, 5 were estimated ineligible from information regarding eligibility from web-based public data (Figure 1-A).

This yielded a raw eligibility [(305+106)/420] 97.8%. Response rate was [106/(106+305)] 25.8%, the cooperation rate was [106/(106+1)] 99.1%. Outcome rates were calculated according to the American Association for Public Opinion Research 2015 [8].

The distributions of variables collected in the survey were summarized by means of absolute numbers and percentages and plotted by bar charts.

#### Survey Substudy - paediatricians

To provide information regarding the management of paediatric Rp, the survey was extended into a substudy involving paediatric rheumatologists. The same internet-based

survey was sent to a paediatric rheumatology email board. As this mailing list was not sufficiently detailed in terms of number and characteristics of the email addresses/members, outcome rates were not calculated and the substudy was managed separately. Of 20 respondents, 3 were ineligible because the participants reported they were not sufficiently skilled (Question 1). The 2 paediatricians previously excluded from the EULAR SG\_MC/RD and EUSTAR mailing lists were added to this substudy (Figure 1-B).

#### RESULTS

#### **Demographic characteristics**

Among specialists taking care of adult patients, the characteristics of the respondents and non-respondents are shown in Figure 2. Respondents were mainly rheumatologists (83.0%) in University hospitals (90.6%) in European countries (68.9%) and were mainly practicing for more than 10 years (81.1%).

More than 50% of the respondents reported that they looked after > 30 patients per year with primary and/or secondary Rp. The area of specialization was deemed relevant to the survey, but the number of participants with specializations other than rheumatology turned out to be too low to allow proper analysis (Figure 2). The following analysis is confined to rheumatologists' opinions (88 respondents), to ensure uniformity.

eTable 1 shows how often rheumatologists monitor their patients with primary and secondary Rp in relation to the number of patients under their care per year. Overall, patients with primary or secondary Rp are monitored regularly, but the frequency of visits is highly variable.

#### **Overall view**

As shown in figure 3A, the nailfold capillaroscopic techniques were those associated with the highest levels of self-assessed knowledge.

Specifically, for NVC the level of knowledge was judged as either good or satisfactory in 90.9% (80/88). NVC is also the most often performed (60.2% "Routinely – more than once/month"), performed by rheumatologists themselves (61.4%) and routinely available in the place of work (72.7%) (Figure 4). In contrast, fewer than 50% of rheumatologists reported a good or satisfactory level of knowledge of techniques other than capillaroscopy. Regarding use and availability, very few rheumatologists (fewer than 10%) sometimes or routinely used any of the techniques other than NVC, and these were seldom available (less than 30%) either at the workplace or in another hospital, except for dermoscopy and upper limb arterial Doppler ultrasound (over 50% among rheumatologists) (Figure 4).

#### **Clinical and research settings**

Respondents were asked to self-assess their knowledge for each technique. Only respondents whose self-assessed level of knowledge was at least good or satisfactory were considered. Therefore this analysis included a different number of respondents for each technique.

*Clinical setting.* More than 85% of rheumatologists judged all nailfold capillaroscopy techniques as 'appropriate' or 'very appropriate' in the global assessment, differential diagnosis, and monitoring of primary and Rp secondary to either SSc or other connective tissue diseases (Figure 5). The use of NVC was consistently assessed as appropriate or very appropriate by more than 95% of respondents, and the use of nailfold dermoscopy, stereomicroscopy, and USB microscopy by more than 88%. For thermography and upper limb arterial Doppler US, only their use for the global assessment of Rp was judged

appropriate or very appropriate (respectively 76.5% and 67.6%), while for all the other indications proportions were substantially lower (range 13.3%-35.3% and 38.9%-51.3% respectively) (Supplementary materials, eTable 2).

*Research setting.* Only NVC was consistently judged as appropriate or very appropriate in the global assessment (98.7%), differential diagnosis (98.7%) and monitoring primary and secondary Rp either in SSc or other connective tissue diseases (87.3%, 98.7% and 87.2% respectively) (Figure 5). Opinions about the use of nailfold dermoscopy, stereomicroscopy, and USB microscopy were less uniform, and heterogeneous answers were observed for thermography and Doppler US (Supplementary materials, eTable 2).

#### Survey Substudy on Paediatric Rheumatologists

The characteristics of the respondents among paediatric physicians are shown in Figure 2. In the online appendix, eTable3 summarizes how often paediatric rheumatologists monitor Rp.

As shown in Figure 3B, both NVC and dermoscopy have the highest levels of selfassessed knowledge (good or satisfactory in 72.2% and 66.7%, 13/18- 12/18, respectively). However, only dermoscopy was performed sometimes or routinely by paediatric rheumatologists themselves, and available at workplace in more than 50% of the responders (Supplementary materials, eTable 4).

Among paediatric rheumatologists whose opinion was taken into account for analysis (good or satisfactory knowledge range 33.3%-72.2%, 6/18 - 13/18 all the nailfold capillaroscopy techniques showed consistent ratings of appropriateness (appropriate or very appropriate >80%) for each item both in clinical and research settings (eTable 5). Ratings about the techniques other than capillaroscopy were derived from a minority of the responders (eTable 6) range 5.5% - 33.3%, 1/18 – 6/18) and were inconsistent.

#### DISCUSSION

The SUNSHINE survey gives a real-life overview about knowledge and availability of noninvasive techniques to assess the microcirculation among rheumatologists who take care of patients with Rp, and therefore provides useful background information for clinicians and researchers writing management guidelines or planning collaborative studies.

Our data show that the level of self-assessed knowledge varies between different techniques. Among adult rheumatologists, capillaroscopy was most widely used, probably because rheumatologists are especially interested in the early differential diagnosis between primary and secondary Rp. The widespread us of capillaroscopy is not surprising since the value of the morphologic assessment of nailfold capillary abnormalities has long been recogniszed, evidenced by the proposal for classification of Rp in 1992 [9], and recently further corroborated by the inclusion of abnormal nailfold capillaries into the 2013 classification criteria for SSc [3]. The level of knowledge and availability of NVC was higher than other capillaroscopic techniques. Studies comparing different capillaroscopic techniques are sparse and limited to NVC, dermoscopy and stereomicroscopy in patients with SSc-spectrum disorders [10-12]. A clinician's choice of technique is likely to be guided by her/his personal experience. Rheumatologists tend to favour NVC, whereas dermatologists may prefer to use dermoscopy (data from four respondents, not shown). This applies both in research and clinical settings.

Regarding the techniques other than capillaroscopy, the low numbers of evaluable responses (i.e. responses from individuals knowledgeable in the technique) combined with the inconsistent opinions about the appropriateness of use suggest that these are currently little used and confined to specialist centers. Data from paediatric rheumatologists were influenced by the small sample size and so few conclusions can be drawn. However, it can be seen that NVC and dermoscopy are the techniques most used by paediatric

rheumatologists and these results underscore the importance of recent efforts to develop recommendations for assessment and monitoring of Rp in children [13].

Our survey has several limitations. First, the nonresponse bias may have affected the representativeness of these data. Our response rate was low as expected for internet surveys conducted among physicians and comparable with similar studies [14]. Second, although respondents were from 115 different centers from all over the world, the majority of respondents were rheumatologists from Europe and university hospitals and so results may not be generalizable to other countries/settings/specialties. However, since EUSTAR centers are those mainly represented in this survey, the results are representative of those centres likely to be participating in multicentre research projects initiated by EUSTAR and EULAR study group on microcirculation (SG\_MC/RD). Finally, data were mainly obtained from self-assessment and this subjectivity reflects attitudes and perception from specialists' experience.

Despite these limitations, the survey benchmarks current clinical and research practice in the assessment of the microcirculation. We have shown that capillaroscopy, particularly NVC, is the technique with which the rheumatologists are most familiar, and most widely used in everyday practice. Knowledge and experience with other non-invasive imaging techniques is extremely limited. This finding needs to be taken into account when developing recommendations on the assessment of the microcirculation in patients with Rp in both clinical and research settings. Our findings suggest that if objective measures of finger temperature and blood flow (i.e. thermography, laser Doppler methods) are to be proposed as outcome measures of disease progression or treatment response in multicentre trials, then clinician education and training in these different methods is warranted, as is done by the EULAR courses on capillaroscopy which include these different methods (www.eular.org-education).

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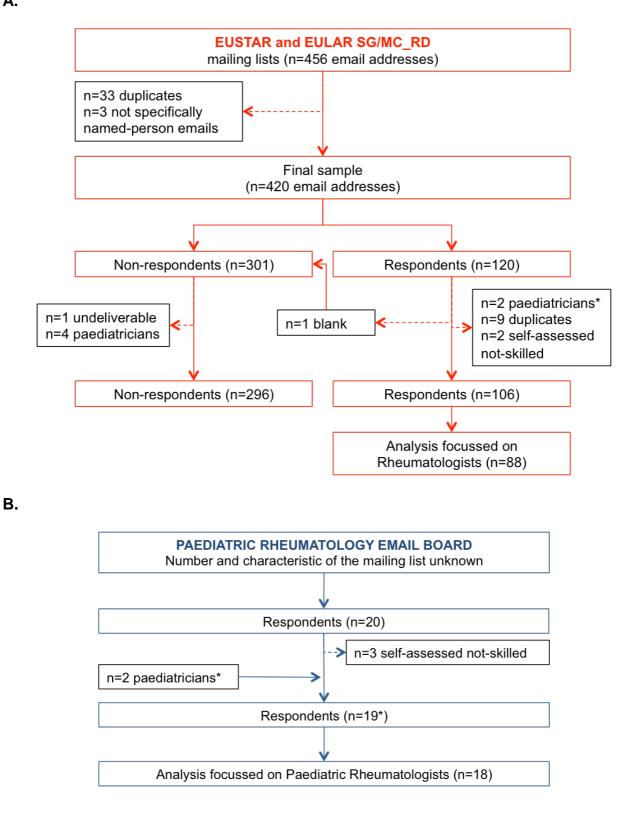
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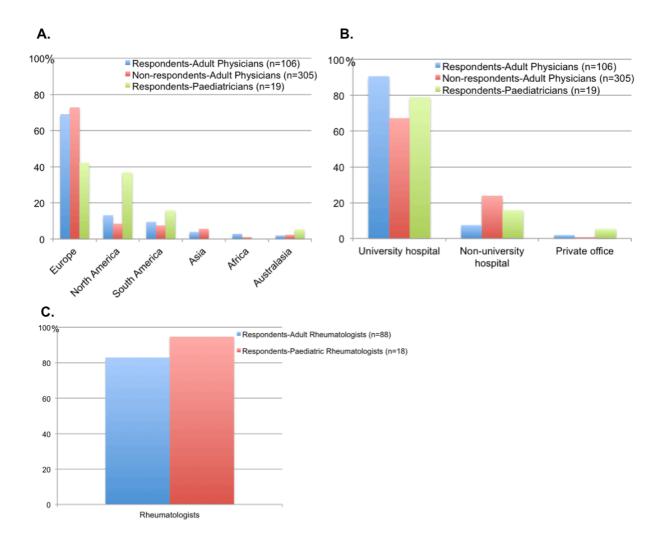
Figure 1. Flowchart of SUNSHINE survey in medical professionals who take care of adult patients (A) and children (B).

### Α.



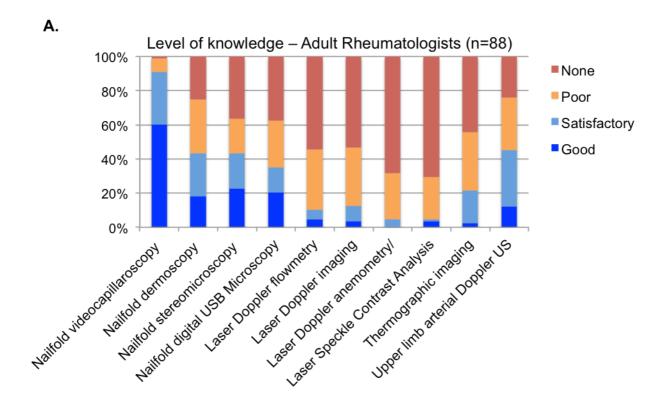
\*2 paediatricians from the EUSTAR and EULAR SG/MC\_RD were included in the final analysis focused on paediatric opinions.

**Figure 2.** Characteristics of respondents and non-respondents by international representation (A), work setting (B), and primary speciality (C).

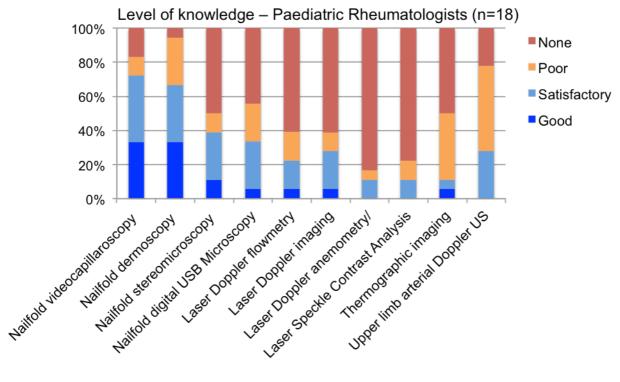


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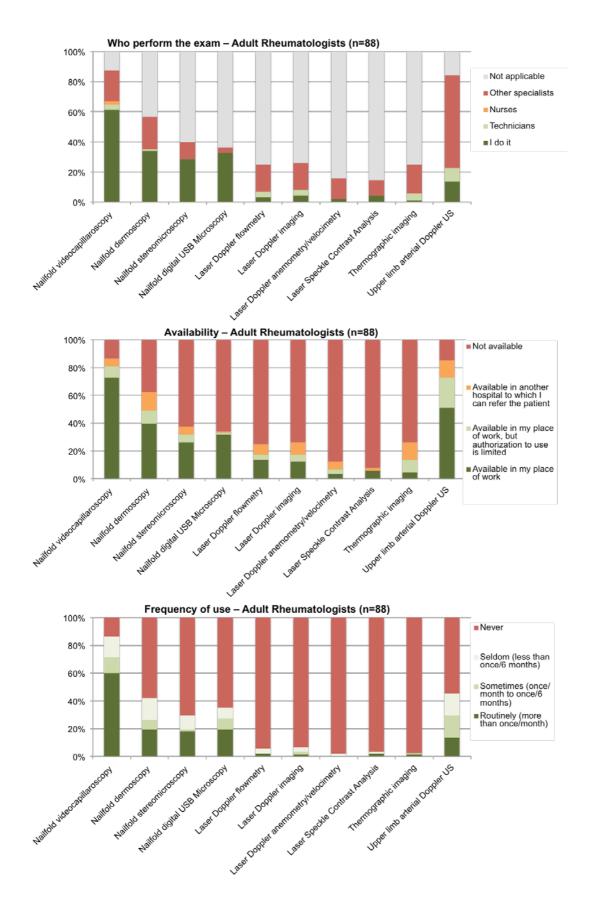
Other specialities among respondents: 9 Internal medicine, 4 Dermatology, 2 Immunology, 1 Cardiology, 1 Internal Medicine and Angiology, 1 Internal Medicine and Immunology; non-respondents: 21 Internal Medicine, 16 Dermatology, 4 Immunology, 4 Angiology, 1 Gastroenterology, 1 Epidemiology, 1 Psichology, 1 Biology, 1 Biostatistician, 2 Nurses; Paediatricians: 1 Immunology. **Figure 3.** The self-assessed level of knowledge on different techniques by adult rheumatologists (n= 88) (A) and paediatric rheumatologists (n= 18) (B).



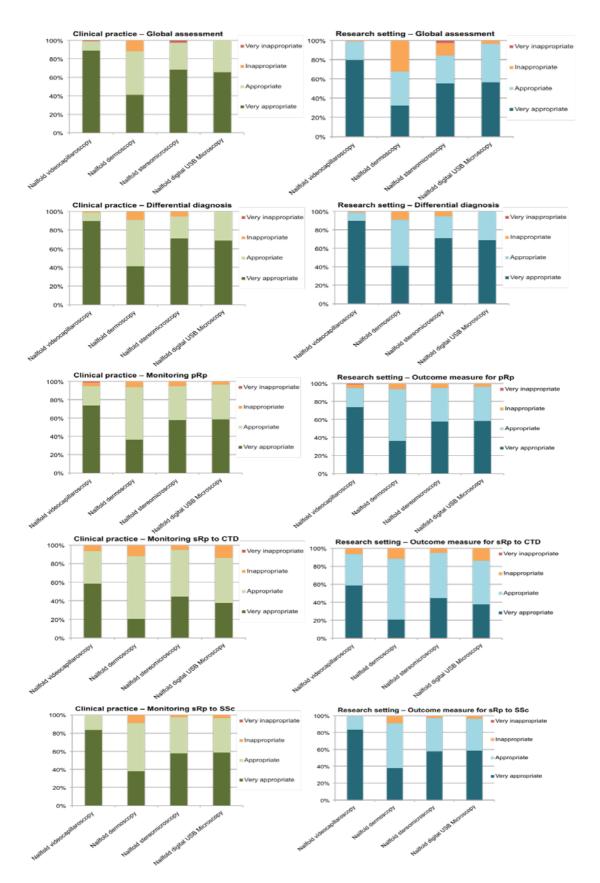
В.



**Figure 4.** Overall view on the real-world usage and availability of non-invasive techniques to assess the microcirculation in patients with Raynaud's phenomenon.



**Figure 5.** Opinion of adult rheumatologists on the appropriateness of use of nailfold capillaroscopy techniques in clinical practice and in a research setting.



#### **Supplementary Online Content**

**Appendix 1.** Questions of the **SU**rvey on non-i**N**va**S**ive tec**H**niques to assess the mIcrocirculation in patients with Ray**N**aud's ph**E**nomenon (SUNSHINE) survey.

**eTable 1**. Summary of how often rheumatologists taking care of adults monitor their patients with primary and secondary Raynaud's phenomenon in relation to the number of patients under their care per year.

**eTable 2.** Results from rheumatologists take care of adults on the role of imaging techniques other than capillaroscopy in the management of Rp in clinical practice and research setting.

**eTable 3**. Summary of how often paediatric rheumatologists monitor their patients with primary and secondary Raynaud's phenomenon in relation to the number of patients under their care per year.

**eTable 4.** Overall view on the real-world usage and availability of imaging techniques by paediatric rheumatologists.

**eTable 5.** Results from paediatric rheumatologists on the role of capillaroscopic techniques in the management of Rp in clinical practice (A) and research setting (B).

**eTable 6.** Results from paediatric rheumatologists on the role of imaging techniques other than capillaroscopy in the management of Rp in clinical practice and research setting.

**Appendix 1**. Questions of the **SU**rvey on non-i**N**va**S**ive tec**H**niques to assess the mIcrocirculation in patients with Ray**N**aud's ph**E**nomenon (SUNSHINE) survey.

#### **Demographic Questions**

#### How many years have you been practicing as a clinician?

1-10 11-20 21-30 >30

#### Which region of the world do you work in?

North America South America Asia Australia Africa Europe What best describes your predominant type of practice? Private office Non-university hospital University hospital What is your area of specialization? Rheumatology Dermatology Angiology Vascular Surgery Cardiology Pulmonology Other How many patients with primary Raynaud's phenomenon (including both new diagnosis and follow-up) do you see each year?

None <30 31-60 61-100 >100

How often do you usually monitor the microcirculation in patients with <u>primary</u> Raynaud's phenomenon after the first assessment?

Never

Only if required on the basis of clinical progression

Once, independently of clinical progression

Periodically, independently of clinical progression (less than once a year)

Periodically, independently of clinical progression (twice a year)

Periodically, independently of clinical progression (more than twice a year)

How many patients with Raynaud's phenomenon secondary <u>to connective tissue</u> <u>diseases other than systemic sclerosis</u> (new diagnosis and follow-up) do you see each year?

None <30 31-60 61-100 >100

How often do you usually monitor the microcirculation in patients with Raynaud's phenomenon secondary to <u>connective tissue diseases other than systemic</u> <u>sclerosis</u> after the first assessment?

Never

Only if required on the basis of clinical progression

Once, independently of clinical progression

Periodically, independently of clinical progression (less than once a year)

Periodically, independently of clinical progression (twice a year)

Periodically, independently of clinical progression (more than twice a year)

How many patients with Raynaud's phenomenon secondary to systemic sclerosis

(new diagnosis and follow-up) do you see each year?

None <30 31-60 61-100 >100

How often do you usually monitor the microcirculation in patients with Raynaud's

#### phenomenon secondary to systemic sclerosis after the first assessment?

Never

Only if required on the basis of clinical progression

Once, independently of clinical progression

Periodically, independently of clinical progression (less than once a year)

Periodically, independently of clinical progression (twice a year)

Periodically, independently of clinical progression (more than twice a year)

#### **Overview of the techniques**

The following questions aim to evaluate knowledge and availability of different techniques to assess microcirculation in your practice.

Please familiarize yourself with all the items on this page before answering to ensure the similarities and differences are noted.

#### How would you define the level of your knowledge of the following techniques?

	1 None	2 Poor	3 Satisfactory	4 Good
Nailfold videocapillaroscopy				
Nailfold dermoscopy				
Nailfold stereomicroscopy				
Nailfold USB digital microscopy				
Laser Doppler flowmetry				
Laser Doppler imaging				
Laser Doppler anemometry/velocimetry				
Laser Speckle Contrast Analysis (LASCA)				
Thermographic imaging				
Upper limb arterial Doppler ultrasound				

#### How often do you perform the following techniques in your clinical practice?

	1	2	3	4
	Never	Seldom	Sometimes	Routinely
		(less than once/6 months) (o	nce/month to once/6 month	s)(more than once/month)
Nailfold videocapillaroscopy				
Nailfold dermoscopy				
Nailfold stereomicroscopy				
Nailfold USB digital microscopy				
Laser Doppler flowmetry				
Laser Doppler imaging				
Laser Doppler anemometry/velocimetry				
Laser Speckle Contrast Analysis (LASCA)				
Thermographic imaging				
Upper limb arterial Doppler ultrasound				

#### Are the following techniques available in your practice?

	Not available	Available in my place of work	Available in another hospital to which I can refer the patient	Available in my place of work, but authorization to use is limited
Nailfold videocapillaroscopy				
Nailfold dermoscopy				
Nailfold stereomicroscopy				
Nailfold USB digital microscopy				
Laser Doppler flowmetry				
Laser Doppler imaging				
Laser Doppler anemometry/velocimetry				
Laser Speckle Contrast Analysis (LASCA)				
Thermographic imaging				
Upper limb arterial Doppler ultrasound				

#### Which is the level of accessibility of the following technologies in your practice?

(i.e.: the technology is available but authorization to use is limited for any reason)

(				/
	1	2	2 3	
	Not accessible	Seldom	Sometimes	Routinelv
		(less than once/6 months) (		
Nailfold videocapillaroscopy	П	П	П	П
Nailfold dermoscopy	_	-		
1,2				
Nailfold stereomicroscopy				
Nailfold USB digital microscopy				
Laser Doppler flowmetry				
Laser Doppler imaging				
Laser Doppler anemometry/velocimetry				
Laser Speckle Contrast Analysis (LASCA)				
Thermographic imaging				
Upper limb arterial Doppler ultrasound				

#### If one or more of these techniques are available, who performs the exam?

	l do it	Technicians	Nurses	Other specialists	Not applicable
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Namou COD digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					
Leser Deppler enoments (halo simple)					
Laser Doppler anemometry/velocimetry					
Laser Speckle Contrast Analysis (LASCA)					

Thermographic imaging

Upper limb arterial Doppler ultrasound

## Are there other techniques that you use, or would consider using, in the assessment of Raynaud's phenomenon?

□ Yes □ No

If yes, please specify and explain why

#### **Clinical Setting**

The following questions are designed to evaluate the appropriateness of different techniques to assess the microcirculation in Raynaud's phenomenon in a routine clinical setting (i.e. diagnosis and monitoring).

How would you rate the appropriateness of the following items for the <u>global</u> <u>assessment of microcirculation</u> in primary and secondary Raynaud's phenomenon in a routine clinical setting?

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	l lack sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					
Laser Doppler anemometry/velocimetry					
Laser Speckle Contrast Analysis (LASCA)					

Thermographic imaging

Upper limb arterial Doppler ultrasound

How would you rate the appropriateness of the following items for <u>the differential</u> <u>diagnosis of primary and secondary</u> Raynaud's phenomenon in a routine clinical setting?

	inappropriate			appropriate	to answer
		Inappropriate	Appropriate		confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					
Laser Doppler anemometry/velocimetry					
Laser Speckle Contrast Analysis (LASCA)					

Thermographic imaging

Upper limb arterial Doppler ultrasound

## How would you rate the appropriateness of the following items for monitoring

## primary Raynaud's phenomenon over time in <u>clinical settings</u>?

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	l lack sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					
Laser Doppler anemometry/velocimetry					
Laser Speckle Contrast Analysis (LASCA)					

Thermographic imaging

Upper limb arterial Doppler ultrasound

How would you rate the appropriateness of the following items for monitoring the clinical course of patients with Raynaud's phenomenon <u>secondary to a connective</u> <u>tissue disease other than systemic sclerosis</u> in <u>clinical settings</u>?

I lack

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					
Laser Doppler anemometry/velocimetry					
Laser Speckle Contrast Analysis (LASCA)					

Thermographic imaging

Upper limb arterial Doppler ultrasound

# How would you rate the appropriateness of the following items for monitoring the clinical course of patients with Raynaud's phenomenon <u>secondary to systemic</u> <u>sclerosis</u> in <u>clinical settings</u>?

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	l lack sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					

Laser Doppler anemometry/velocimetry

Laser Speckle Contrast Analysis (LASCA)			
Thermographic imaging			

Upper limb arterial Doppler ultrasound

#### **Research Setting**

The following questions are designed to evaluate the appropriateness of different techniques to assess the microcirculation in Raynaud's phenomenon in a research setting (i.e. outcome measure in clinical trials).

How would you rate the appropriateness of the following items for the <u>global</u> <u>assessment of microcirculation</u> in primary and secondary Raynaud's phenomenon in a research setting?

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	l lack sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					
Laser Doppler anemometry/velocimetry					
Laser Speckle Contrast Analysis (LASCA)					

Thermographic imaging

Upper limb arterial Doppler ultrasound

# How would you rate the appropriateness of the following items for the differential

# diagnosis of primary and secondary Raynaud's phenomenon in a research setting?

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	l lack sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					
Laser Doppler anemometry/velocimetry					
Laser Doppler anemometry/velocimetry					
Laser Speckle Contrast Analysis (LASCA)					

Thermographic imaging

Upper limb arterial Doppler ultrasound

# How would you rate the appropriateness of the following items as an outcome

### measure in patients with primary Raynaud's phenomenon in research settings?

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	l lack sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Neilfold LICD digital microscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					

Laser Doppler anemometry/velocimetry			
Laser Speckle Contrast Analysis (LASCA)			

Thermographic imaging

Upper limb arterial Doppler ultrasound

# How would you rate the appropriateness of the following items as an <u>outcome</u> <u>measure</u> in patients with Raynaud's phenomenon <u>secondary to a connective tissue</u> <u>disease other than systemic sclerosis</u> in <u>research settings</u>?

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	l lack sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					
Nailfold dermoscopy					
Nailfold stereomicroscopy					
Nailfold USB digital microscopy					
Laser Doppler flowmetry					
Laser Doppler imaging					
Laser Doppler anemometry/velocimetry					
Laser Speckle Contrast Analysis (LASCA)					

Thermographic imaging

Upper limb arterial Doppler ultrasound

How would you rate the appropriateness of the following items as an <u>outcome</u> <u>measure</u> in patients with Raynaud's phenomenon <u>secondary to systemic sclerosis</u> in <u>research settings</u>?

	Very inappropriate	Inappropriate	Appropriate	Very appropriate	l lack sufficient knowledge or experience to answer confidently
Nailfold videocapillaroscopy					

Nailfold dermoscopy			
Nailfold stereomicroscopy			
Nailfold USB digital microscopy			
Laser Doppler flowmetry			
Laser Doppler imaging			
Laser Doppler anemometry/velocimetry			
Laser Speckle Contrast Analysis (LASCA)			

Thermographic imaging

Upper limb arterial Doppler ultrasound

eTable 1. Summary of how often rheumatologists taking care of adults monitor their patients with primary and secondary Raynaud's

phenomenon in relation to the number of patients under their care per year.

primary Rp										
	No. patients/year									
Frequency of monitoring	None	<30	31-60	61-100	>100					
Never	2 (100%)	0 (0%)	1 (3.9%)	1 (7.1%)	0 (0%)					
Only if required on the basis of clinical progression	0 (0%)	18 (58.0%)	12 (46.1%)	3 (21.4%)	4 (26.7%)					
Once, independently of clinical progression	0 (0%)	3 (9.7%)	2 (7.7%)	1 (7.1%)	0 (0%)					
Periodically, independently of clinical progression (less than once a year)	0 (0%)	4 (12.9%)	6 (23.1%)	4 (28.6%)	6 (40.0%)					
Periodically, independently of clinical progression (twice a year)	0 (0%)	3 (9.7%)	5 (19.2%)	5 (35.8%)	3 (20.0%)					
Periodically, independently of clinical progression (more than twice a year)	0 (0%)	3 (9.7%)	0 (0%)	0 (0%)	2 (13.3%)					
Rp secondary to CTDs										
Never	0 (0%)	1 (4.2%)	2 (7.1%)	0 (0%)	2 (8.7%)					
Only if required on the basis of clinical progression	0 (0%)	9 (37.5%)	10 (35.7%)	7 (53.8%)	5 (21.7%)					
Once, independently of clinical progression	0 (0%)	1 (4.2%)	2 (7.1%)	1 (7.7%)	1 (4.4%)					
Periodically, independently of clinical progression (less than once a year)	0 (0%)	5 (20.8%)	5 (17.9%)	3 (23.1%)	8 (34.8%)					
Periodically, independently of clinical progression (twice a year)	0 (0%)	5 (20.8%)	7 (25.1%)	1 (7.7%)	2 (8.7%)					

Periodically, independently of clinical progression (more than twice a year)	0 (0%)	3 (12.5%)	2 (7.1%)	1 (7.7%)	5 (21.7%)
Rp secondary to SSc					
Never	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (3.3%)
Only if required on the basis of clinical progression	0 (0%)	2 (12.5%)	5 (18.5%)	3 (20.0%)	9 (30.0%)
Once, independently of clinical progression	0 (0%)	1 (6.3%)	2 (7.4%)	2 (13.3%)	3 (10.0%)
Periodically, independently of clinical progression (less than once a year)	0 (0%)	3 (18.7%)	8 (29.7%)	5 (33.3%)	11 (36.7%)
Periodically, independently of clinical progression (twice a year)	0 (0%)	6 (37.5%)	9 (33.3%)	4 (26.7%)	1 (3.3%)
Periodically, independently of clinical progression (more than twice a year)	0 (0%)	4 (25.0%)	3 (11.1%)	1 (6.7%)	5 (16.7%)

RP: Raynaud's phenomenon, CTD: connective tissue disease; SSc: systemic sclerosis

**eTable 2.** Results from rheumatologists take care of adults on the role of imaging techniques other than capillaroscopy in the management of Rp in clinical practice (A) and research setting (B).

#### Α.

	Laser Doppler flowmetry	Laser Doppler imaging	Laser Doppler anemometry/ velocimetry	Laser Speckle Contrast Analysis (LASCA)	Thermographic imaging	Upper limb arterial Doppler ultrasound
Global assessment						
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)
Inappropriate	2 (22.2%)	2 (22.2%)	1 (50.0%)	1 (25.0%)	4 (23.5%)	11 (29.7%)
Appropriate	4 (44.5%)	4 (44.5%)	1 (50.0%)	1 (25.0%)	10 (58.8%)	17 (46.0%)
Very appropriate	3 (33.3%)	3 (33.3%)	0 (0%)	2 (50.0%)	3 (17.7%)	8 (21.6%)
Differential diagnosis				· ·		
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (11.8%)	2 (5.4%)
Inappropriate	5 (55.6%)	4 (44.4%)	2 (100%)	2 (50.0%)	10 (58.8%)	16 (43.3%)
Appropriate	4 (44.4%)	5 (55.6%)	0 (0%)	1 (25.0%)	3 (17.6%)	13 (35.1%)
Very appropriate	0 (0%)	0 (0%)	0 (0%)	1 (25.0%)	2 (11.8%)	6 (16.2%)
Monitoring pRP						
Very inappropriate	1 (12.5%)	1 (12.5%)	0 (0%)	0 (0%)	2 (13.3%)	10 (27.8%)
Inappropriate	3 (37.5%)	3 (37.5%)	2 (100%)	2 (50.0%)	11 (73.4%)	12 (33.3%)
Appropriate	2 (25.0%)	2 (25.0%)	0 (0%)	0 (0%)	2 (13.3%)	10 (27.8%)
Very appropriate	2 (25.0%)	2 (25.0%)	0 (0%)	2 (50.0%)	0 (0%)	4 (11.1%)
Monitoring sRP to CTI	D					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (13.3%)	8 (22.2%)
Inappropriate	4 (50.0%)	3 (37.5%)	2 (100%)	2 (50.0%)	11 (73.4%)	14 (38.9%)
Appropriate	3 (37.5%)	4 (50.0%)	0 (0%)	1 (25.0%)	2 (13.3%)	11 (30.6%)
Very appropriate	1 (12.5%)	1 (12.5%)	0 (0%)	1 (25.0%)	0 (0%)	3 (8.3%)

Monitoring sRP to SS	C					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5.9%)	5 (13.5%)
Inappropriate	3 (33.3%)	3 (37.5%)	2 (100%)	2 (50.0%)	10 (58.8%)	15 (40.6%)
Appropriate	4 (44.5%)	3 (37.5%)	0 (0%)	0 (0%)	6 (35.3%)	12 (32.4%)
Very appropriate	2 (22.2%)	2 (25.0%)	0 (0%)	2 (50.0%)	0 (0%)	5 (13.5%)

# В.

	Laser Doppler flowmetry	Laser Doppler imaging	Laser Doppler anemometry/ velocimetry	Laser Speckle Contrast Analysis (LASCA)	Thermographic imaging	Upper limb arterial Doppler ultrasound
Global assessment	· · · · ·			· · ·		
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5.9%)	4 (10.8%)
Inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (47.0%)	10 (27.0%)
Appropriate	5 (55.6%)	2 (22.2%)	0 (0%)	0 (0%)	7 (41.2%)	15 (40.6%)
Very appropriate	4 (44.4%)	7 (77.8%)	2 (100%)	4 (100%)	1 (5.9%)	8 (21.6%)
Differential diagnosis				· ·		·
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (6.7%)	4 (11.1%)
Inappropriate	0 (0%)	1 (11.1%)	0 (0%)	0 (0%)	6 (40.0%)	13 (36.1%)
Appropriate	6 (75.0%)	3 (33.3%)	0 (0%)	0 (0%)	7 (46.6%)	11 (30.6%)
Very appropriate	2 (25.0%)	5 (55.6%)	1 (100%)	4 (100%)	1 (6.7%)	8 (22.2%)
Outcome measure for	<sup>r</sup> pRP			· ·		·
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (6.3%)	8 (22.2%)
Inappropriate	0 (0%)	1 (11.1%)	1 (50.0%)	0 (0%)	5 (31.2%)	13 (36.1%)
Appropriate	5 (62.5%)	5 (55.6%)	0 (0%)	1 (25.0%)	9 (56.2%)	12 (33.4%)
Very appropriate	3 (37.5%)	3 (33.3%)	1 (50.0%)	3 (75.0%)	1 (6.3%)	3 (8.3%)
Outcome measure for	sRP to CTD					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5.9%)	5 (13.2%)
Inappropriate	0 (0%)	1 (11.0%)	0 (0%)	0 (0%)	8 (47.0%)	12 (31.5%)
Appropriate	5 (55.6%)	4 (44.5%)	0 (0%)	1 (25.0%)	7 (41.2%)	16 (42.1%)

Very appropriate	4 (44.4%)	4 (44.5%)	1 (100%)	3 (75.0%)	1 (5.9%)	5 (13.2%)
Outcome measure for	sRP to SSc					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (6.3%)	5 (13.2%)
Inappropriate	0 (0%)	0 (0%)	1 (50.0%)	0 (0%)	7 (43.7%)	10 (26.3%)
Appropriate	5 (62.5%)	4 (50.0%)	0 (0%)	1 (25.0%)	6 (37.5%)	16 (42.1%)
Very appropriate	3 (37.5%)	4 (50.0%)	1 (50.0%)	3 (75.0%)	2 (12.5%)	7 (18.4%)

eTable 3. Summary of how often paediatric rheumatologists monitor their patients with primary and secondary Raynaud's phenomenon

in relation to the number of patients under their care per year.

primary Rp						
	No. patients/year					
Frequency of monitoring	None	<30	31-60	61-100	>100	
Never	0 (0%)	0 (0.0%)	0 (0.0%)	0 (0%)	0 (0%)	
Only if required on the basis of clinical progression	0 (0%)	5 (38.5%)	1 (25.0%)	0 (0%)	0 (0%)	
Once, independently of clinical progression	0 (0%)	1 (7.7%)	2 (50.0%)	0 (0%)	0 (0%)	
Periodically, independently of clinical progression (less than once a year)	0 (0%)	1 (7.7%)	1 (25.0%)	0 (0%)	0 (0%)	
Periodically, independently of clinical progression (twice a year)	0 (0%)	4 (30.7%)	0 (0%)	0 (0%)	0 (0%)	
Periodically, independently of clinical progression (more than twice a year)	0 (0%)	2 (15.4%)	0 (0%)	0 (0%)	1 (100.0%)	
Rp secondary to CTDs						
Never	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Only if required on the basis of clinical progression	0 (0%)	4 (25.0%)	0 (0%)	0 (0%)	0 (0%)	
Once, independently of clinical progression	0 (0%)	1 (6.2%)	0 (0%)	0 (0%)	0 (0%)	
Periodically, independently of clinical progression (less than once a year)	0 (0%)	3 (18.8%)	0 (0%)	0 (0%)	0 (0%)	

Periodically, independently of clinical progression (twice a year)	0 (0%)	3 (18.8%)	0 (0.0%)	0 (0%)	0 (0%)
Periodically, independently of clinical progression (more than twice a year)	0 (0%)	5 (31.2%)	2 (100.0%)	0 (0%)	0 (0%)
Rp secondary to SSc					
Never	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Only if required on the basis of clinical progression	0 (0%)	3 (16.7%)	0 (0%)	0 (0%)	0 (0%)
Once, independently of clinical progression	0 (0%)	1 (5.5%)	0 (0%)	0 (0%)	0 (0%)
Periodically, independently of clinical progression (less than once a year)	0 (0%)	3 (16.7%)	0 (0%)	0 (0%)	0 (0%)
Periodically, independently of clinical progression (twice a year)	0 (0%)	3 (16.7%)	0 (0%)	0 (0%)	0 (0%)
Periodically, independently of clinical progression (more than twice a year)	0 (0%)	8 (44.4%)	0 (0%)	0 (0%)	0 (0%)

RP: Raynaud's phenomenon, CTD: connective tissue disease; SSc: systemic sclerosis

eTable 4. Overall view on the real-world usage and availability of imaging techniques by paediatric rheumatologists.

Frequency o	of use									
<b>i</b>	Nailfold video capillaroscopy	Nailfold dermoscopy	Stereo microscopy	Nailfold digital USB Microscopy	Laser Doppler	Doppler imaging	Anemometry	LASCA	Thermo graphic imaging	Upper limb arterial Doppler ultrasound
Never	9 (50.0%)	4 (22.2%)	13 (72.1%)	16 (88.9%)	17 (94.4%)	17 (94.4%)	18 (100%)	18 (100%)	17 (94.4%)	9 (50.0%)
Seldom	3 (16.7%)	4 (22.2%)	3 (16.7%)	2 (11.1%)	1 (5.6%)	0 (0%)	0 (0%)	0 (0%)	1 (5.6%)	4 (22.2%)
Sometimes	4 (22.2%)	1 (5.6%)	1 (5.6%)	0 (0%)	0 (0%)	1 (5.6%)	0 (0%)	0 (0%)	0 (0%)	5 (27.8%)
Routinely	2 (11.1%)	9 (50.0%)	1 (5.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Availability			I				I	I	I	
Not available	8 (44.4%)	2 (11.1%)	14 (77.7%)	18 (100%)	15 (83.3%)	15 (83.3%)	16 (88.8%)	18 (100%)	15 (83.3%)	2 (11.1%)
Available in my place of work	7 (38.9%)	12 (66.7%)	2 (11.1%)	0 (0%)	1 (5.6%)	1 (5.6%)	0 (0%)	0 (0%)	0 (0%)	7 (38.9%)
Avalilable in another hospital	3 (16.7%)	1 (5.5%)	1 (5.6%)	0 (0%)	2 (11.1%)	2 (11.1%)	1 (5.6%)	0 (0%)	2 (11.1%)	2 (11.1%)
Authorization limited	0 (0%)	3 (16.7%)	1 (5.6%)	0 (0%)	0 (0%)	0 (0%)	1 (5.6%)	0 (0%)	1 (5.6%)	7 (38.9%)
Who perforn	n the exam									
I do it	4 (22.2%)	12 (66.6%)	2 (11.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Technicians	1 (5.6%)	1 (5.6%)	1 (5.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (11.1%)	5 (27.8%)
Nurses	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other spec	5 (27.8%)	3 (16.7%)	2 (11.1%)	0 (0%)	3 (16.7%)	3 (16.7%)	1 (5.6%)	0 (0%)	0 (0%)	9 (50.0%)
Not applicable	8 (44.4%)	2 (11.1%)	13 (72.2%)	18 (100%)	15 (83.3%)	15 (83.3%)	17 (94.4%)	18 (100%)	16 (88.9%)	4 (22.2%)

LASCA: Laser Speckle Contrast Analysis

**eTable 5.** Results from paediatric rheumatologists on the role of capillaroscopic techniques in the management of Rp in clinical practice (A) and research setting (B).

## Α.

	Nailfold video capillaroscopy	Nailfold dermoscopy	Nailfold stereo microscopy	Nailfold digital USB Microscopy
Global assessment				
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	0 (0%)	0 (0%)	0 (0%)	1 (20.0%)
Appropriate	4 (30.8%)	3 (27.3%)	4 (57.1%)	4 (80.0%)
Very appropriate	9 (69.2%)	8 (72.7%)	3 (42.9%)	0 (0%)
Differential diagnosis				
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	2 (15.4%)	2 (18.2%)	1 (14.3%)	0 (0%)
Appropriate	5 (38.5%)	3 (27.3%)	2 (28.6%)	2 (50.0%)
Very appropriate	6 (46.2%)	6 (54.5%)	4 (57.1%)	2 (50.0%)
Monitoring pRP	· · · ·		· · ·	
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	1 (7.7%)	2 (18.2%)	0 (0%)	1 (25.0%)
Appropriate	3 (23.1%)	6 (54.5%)	3 (42.9%)	2 (50.0%)
Very appropriate	9 (69.2%)	3 (27.3%)	4 (57.1%)	1 (25.0%)
Monitoring sRP to C	TD			
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	1 (7.6%)	2 (18.2%)	0 (0%)	1 (25.0%)
Appropriate	6 (46.2%)	5 (45.4%)	4 (57.1%)	3 (75.0%)
Very appropriate	6 (46.2%)	4 (36.4%)	3 (42.9%)	0 (0%)
Monitoring sRP to SS	Sc	· · · ·	· · · ·	
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	1 (7.7%)	2 (16.6%)	0 (0%)	1 (20.0%)
Appropriate	5 (38.5%)	5 (41.7%)	3 (42.9%)	3 (60.0%)
Very appropriate	7 (53.8%)	5 (41.7%)	4 (57.1%)	1 (20.0%)

В.

	Nailfold video capillaroscopy	Nailfold dermoscopy	Nailfold stereo microscopy	Nailfold digital USB Microscopy				
Global assessment								
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)				
Inappropriate	0 (0%)	2 (18.2%)	0 (0%)	0 (0%)				
Appropriate	2 (15.4%)	7 (63.6%)	3 (42.9%)	3 (75.0%)				
Very appropriate	11 (84.6%)	2 (18.2%)	4 (57.1%)	1 (25.0%)				
Differential diagnosis								
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)				
Inappropriate	0 (0%)	3 (27.3%)	0 (0%)	0 (0%)				
Appropriate	2 (15.4%)	6 (54.5%)	3 (42.9%)	2 (66.7%)				
Very appropriate	11 (84.6%)	2 (18.2%)	4 (57.1%)	1 (33.3%)				
Outcome measure in	pRP		· · ·	-				
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)				
Inappropriate	2 (15.4%)	3 (27.3%)	0 (0%)	0 (0%)				
Appropriate	4 (30.8%)	7 (63.6%)	4 (57.1%)	3 (100%)				
Very appropriate	7 (53.8%)	1 (9.1%)	3 (42.9%)	0 (0%)				
Outcome measure in	sRP to CTD							
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)				
Inappropriate	0 (0%)	3 (27.3%)	0 (0%)	0 (0%)				
Appropriate	4 (30.8%)	7 (63.6%)	5 (71.4%)	3 (100%)				
Very appropriate	9 (69.2%)	1 (9.1%)	2 (28.6%)	0 (0%)				
Outcome measure in	Outcome measure in sRP to SSc							
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)				
Inappropriate	0 (0%)	3 (27.3%)	0 (0%)	0 (0%)				
Appropriate	3 (23.1%)	7 (63.6%)	5 (71.4%)	3 (100%)				
Very appropriate	10 (76.9%)	1 (9.1%)	2 (28.6%)	0 (0%)				

**eTable 6.** Results from paediatric rheumatologists on the role of imaging techniques other than capillaroscopy in the management of Rp in clinical practice (A) and research setting (B).

## Α.

	Laser Doppler flowmetry	Laser Doppler imaging	Laser Doppler anemometry/ velocimetry	Laser Speckle Contrast Analysis (LASCA)	Thermographic imaging	Upper limb arterial Doppler ultrasound
Global assessr	ment					
Very	0 (00()	0 (00()	0 (00()	0 (00()	0 (00()	
inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	2 (50.0%)	3 (60.0%)	0 (0%)	0 (0%)	1 (50.0%)	1 (25.0%)
Appropriate	2 (50.0%)	2 (40.0%)	1 (100%)	1 (100%)	1 (50.0%)	3 (75.0%)
Very appropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Differential diag	gnosis					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	2 (50.0%)	3 (60.0%)	0 (0%)	0 (0%)	1 (50.0%)	3 (60.0%)
Appropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)
Very appropriate	2 (50.0%)	2 (40.0%)	1 (100%)	1 (100%)	1 (50.0%)	0 (0%)
Monitoring pRF	<b>.</b>					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	1 (25.0%)	2 (40.0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)
Appropriate	2 (50.0%)	2 (40.0%)	1 (100%)	1 (100%)	1 (50.0%)	3 (60.0%)
Very appropriate	1 (25.0%)	1 (20.0%)	0 (0%)	0 (0%)	1 (50.0%)	0 (0%)
Monitoring sRF	o to CTD					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)
Appropriate	2 (66.7%)	2 (50.0%)	1 (100%)	1 (100%)	1 (50.0%)	3 (60.0%)
Very appropriate	1 (33.3%)	1 (25.0%)	0 (0%)	0 (0%)	1 (50.0%)	0 (0%)
Monitoring sRF	P to SSc					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Inappropriate	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)
Appropriate	1 (33.3%)	1 (25.0%)	1 (100%)	1 (100%)	0 (0%)	3 (60.0%)
Very appropriate	2 (66.7%)	2 (50.0%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)

# В.

	Laser Doppler flowmetry	Laser Doppler imaging	Laser Doppler anemometry/ velocimetry	Laser Speckle Contrast Analysis (LASCA)	Thermographic imaging	Upper limb arterial Doppler ultrasound		
Global assessr	Global assessment							
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Inappropriate	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)		
Appropriate	2 (66.7%)	2 (50.0%)	1 (100%)	1 (100%)	1 (50.0%)	1 (20.0%)		
Very appropriate	1 (33.3%)	1 (25.0%)	0 (0%)	0 (0%)	1 (50.0%)	2 (40.0%)		
Differential diag	gnosis							
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Inappropriate	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)		
Appropriate	2 (66.7%)	2 (50.0%)	1 (100%)	1 (100%)	1 (50.0%)	1 (20.0%)		
Very appropriate	1 (33.3%)	1 (25.0%)	0 (0%)	0 (0%)	1 (50.0%)	2 (40.0%)		
Outcome meas	sure for pRP		l .					
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Inappropriate	1 (25.0%)	3 (60.0%)	1 (100%)	2 (100%)	1 (50.0%)	3 (60.0%)		
Appropriate	2 (50.0%)	1 (20.0%)	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)		
Very appropriate	1 (25.0%)	1 (20.0%)	0 (0%)	0 (0%)	1 (50.0%)	0 (0%)		
Outcome meas	sure for sRP	to CTD						
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Inappropriate	0 (0%)	2 (40.0%)	1 (100%)	1 (100%)	0 (0%)	2 (40.0%)		
Appropriate	3 (75.0%)	2 (40.0%)	0 (0%)	0 (0%)	2 (100%)	2 (40.0%)		
Very appropriate	1 (25.0%)	1 (20.0%)	0 (0%)	0 (0%)	0 (0%)	1 (20.0%)		
Outcome meas	sure for sRP	to SSc						
Very inappropriate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Inappropriate	0 (0%)	2 (40.0%)	1 (100%)	1 (100%)	0 (0%)	2 (40.0%)		
Appropriate	2 (66.7%)	2 (40.0%)	0 (0%)	0 (0%)	2 (100%)	2 (40.0%)		
Very appropriate	1 (33.3%)	1 (20.0%)	0 (0%)	0 (0%)	0 (0%)	1 (20.0%)		