Reliability of nailfold capillary density measurement as a possible outcome measure for systemic sclerosis-related microangiopathy

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Introduction

- Nailfold videocapillaroscopy allows non-invasive imaging of the digital microcirculation, and is particularly useful in patients with systemic sclerosis (SSc) who present with a heterogeneous range of abnormalities in their capillary architecture (see Figure 1).
- The qualitative assessment of capillaroscopy images is subjective and requires experience and training.
- Custom computer software for image annotation can be used to enable quantitative measurements to be made by trained observers, allowing tracking of changes over time; important for the use of capillaroscopy as an outcome measure in clinical trials.
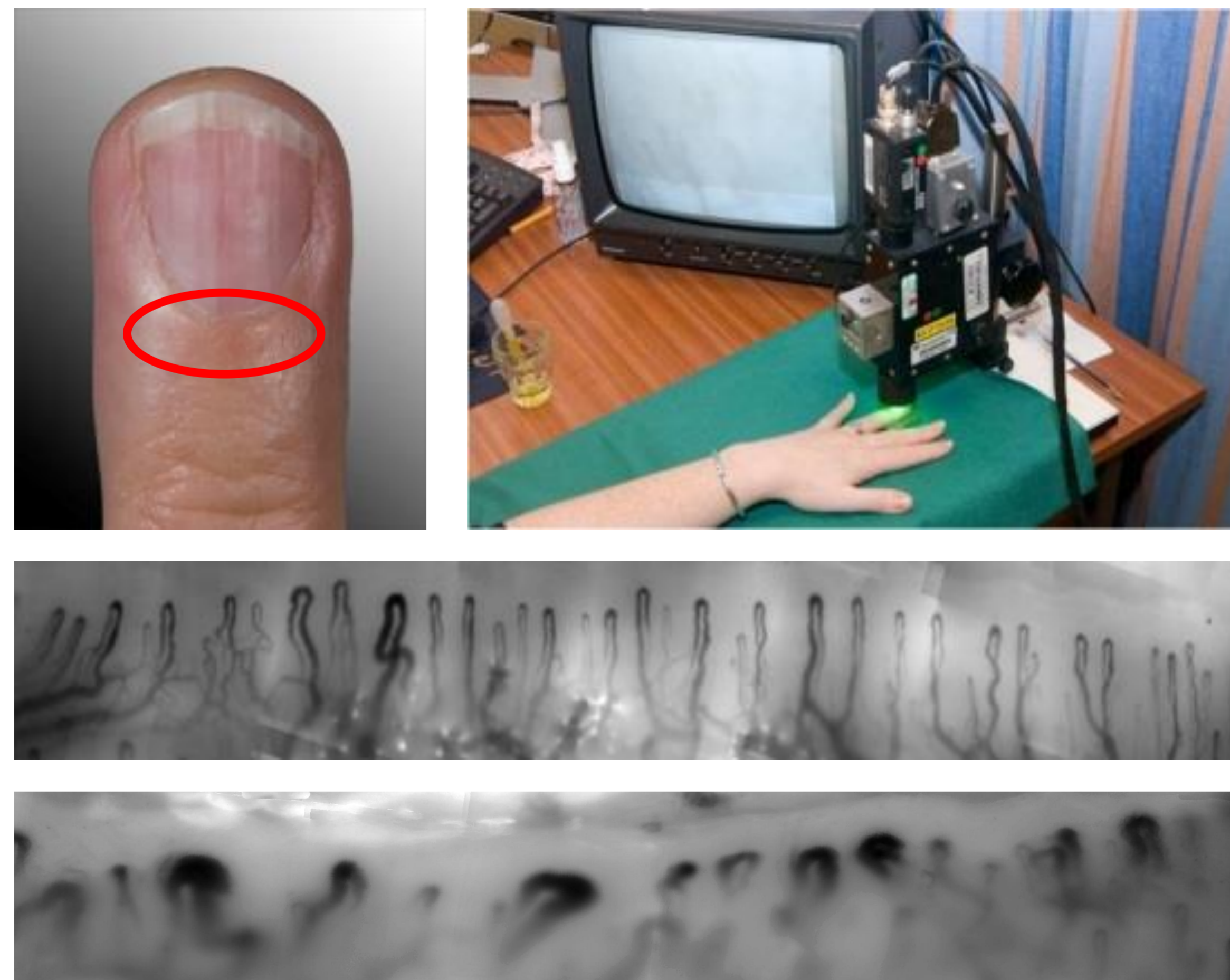

Figure 1. Nailfold capillaroscopy. Top left: area of finger imaged. Top right: a finger under the microscope. Middle: example normal capillaroscopic mosaic. Bottom: example abnormal capillaroscopic mosaic

Objectives

To assess the intra and inter-rater reliability of capillary density measurement. The capillary density is known to be reduced in patients with SSc[1].

Method

- 124 patients (102 SSc, 22 PRP) and 50 healthy controls underwent high-magnification (300x) videocapillaroscopy mosaic imaging of all 10 digits, using a microscope system from KK Technology (Honiton, UK)[2].
- Custom software (Figure 2) allowed the location of distal vessels to be identified. Vessel density is then calculated as the number of distal vessels divided by the distance between the left-most and right-most vessels.
- Sets of images sampled over disease categories were randomly assigned to at least 2 from a panel of 10 capillaroscopy experts. At least 6 images were assessed from each subject.
- Intra-rater reliability was assessed by having each rater perform repeat assessments on a sub-group of images.
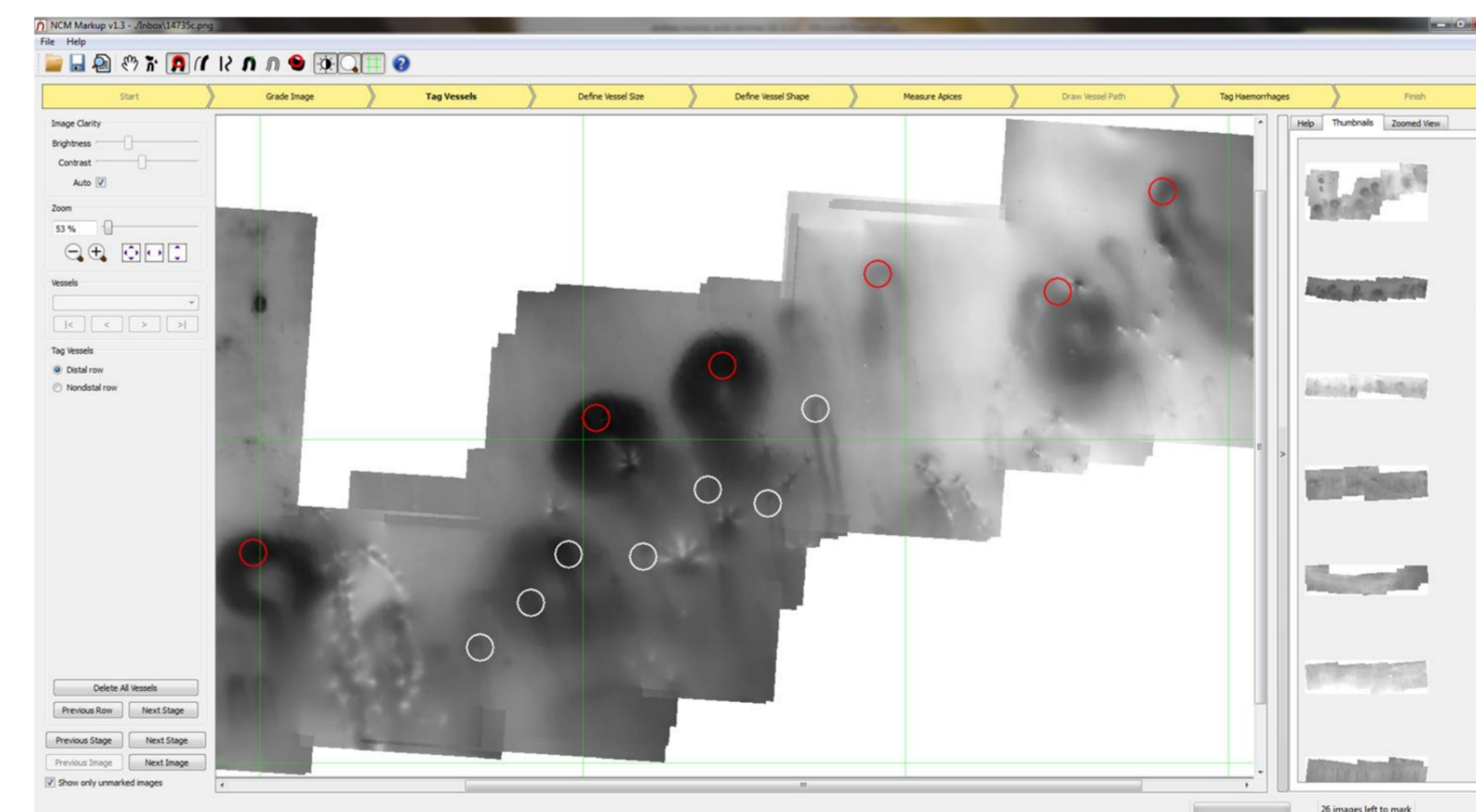

Figure 2. Capillaroscopy image mark-up software interface. Vessels are marked by clicking at their apex (red circles: distal vessels, white circles: non-distal vessels. Image measurement tools are on the left, a queue of images to be marked is on the right.

Statistical methods

- The probability of raters marking sufficient (2 or more) distal vessels (hereafter referred to as "vessel mark-up") in an image was assessed using a logistic mixed-effects model.
- Conditional on an image evaluation having sufficient distal vessels marked, distal vessel density was assessed using a linear mixed-effects model.
- Intra and inter-rater reliability was estimated with intra-class correlation coefficients from fitted model variance components.

Results

- 3463 image evaluations were performed. Each rater assessed a median (range) of 112 (87, 1406) unique images from 14 (9, 174) subjects.
- Same-rater repeat evaluations were performed on (median, across raters) 17% of images, and 904 images from 116 patients were evaluated by at least 2 raters.
- Raters marked sufficient distal vessels in 79% of evaluations, with mean vessel density calculated in these cases (Table 1). Density was unmeasurable in 21% of cases.

	Control	PRP	SSc	Intra-rater reliability [95% C.I.]	Inter-rater reliability [95% C.I.]
Vessel mark-up (odds ratio vs. control group [95% C.I.])	1 [-]	3.80 [0.37, 5.23]	0.23 [0.14, 1.41]	0.91 [0.89, 0.92]	0.51 [0.39, 0.76]
Mean vessel density (vessels/mm), difference [95% C.I.] compared to control group	9.84, -	9.58, -0.26 [-1.12, 0.63]	6.62, -3.22 [-3.88, -2.63]	0.89 [0.87, 0.91]	0.56 [0.47, 0.64]

Table 1. Sufficient vessel markup odds ratios and mean vessel density with corresponding intra/inter-rater reliability.

Conclusion

- Differences in vessel mark-up rates between groups are most likely due to differences in capillary architecture (capillary loss/damage in SSc patients).
- The high intra-(compared to inter-) rater reliability suggests that density could serve as an outcome measure in prospective studies if the same rater examines images.
- Research on the impact of training on inter-rater reliability, and into more objective (automated) analysis methods is required to further develop this promising outcome measure.

1. Cutolo M et al. Nature Rev Rheumatol 2010;6:578-87
2. Anderson ME et al. J Rheuamtol 2005;32(5):841-8

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