Automatically Extracted Quantitative Biomarkers for Assessing Connective Tissue Disease Using Nailfold Capillaroscopy

M Berks[1], G Dinsdale[2], A K Murray[2], T Moore[2], C J Taylor[1] and A L Herrick[2]

[1] Centre for Imaging Science, University of Manchester, UK; [2] Centre for Musculoskeletal Research, University of Manchester, MAHSC, UK

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Introduction

- Nailfold capillaroscopy provides high magnification images of the microvasculature in human fingers
- Measuring the number, size and shape of individual capillaries can help detect change indicative of connective tissue disease[1]
- Taking such measurements manually is a time consuming task subject to high-levels of inter-observer variability
- We have developed fully automated software to measure the spatial density, width and tortuosity of capillaries[2]

Objective

- To assess how well the automated biomarkers differentiate between:
  - Healthy controls (HC)
  - Subjects with primary Raynaud's phenomenon (PRP)
  - Patients with systemic sclerosis (SSc)
  - Patients with an undifferentiated connective tissue disease (UCTD)

Method

- We analysed 85 HC, 46 PRP, 402 SSc and 44 UCTD nailfold images (see Figure 1)
- The software:
  1. Detects all vessels, measuring orientation and width
  2. Extracts measures that characterize the size and shape of each distal capillary
  3. Computes a single value of density, width and tortuosity for each image
- For each biomarker 1-way ANOVA, followed by Tukey's range test, was used to check for differences between the means of each subject group

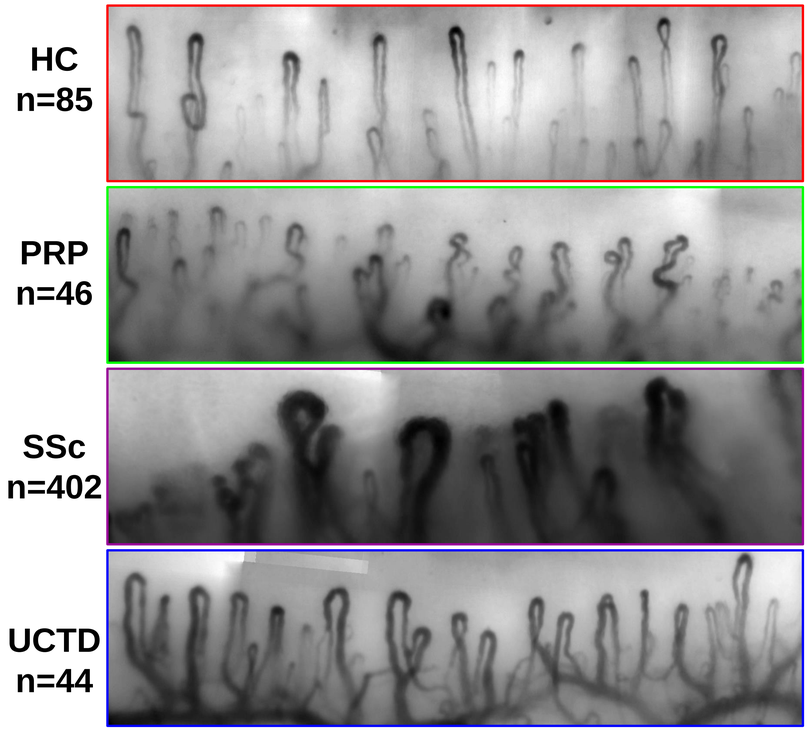

Figure 1: Example nailfold images for each subject group

Biomarker type	Subject group means (95% confidence intervals)				Groups with Tukey's test p<0.01
	HC	PRP	SSc	UD	
Capillary density (per mm)	12.6 (12,13.3)	13.4 (12.5,14.2)	9.02 (8.74, 9.3)	11.5 (10.6,12.3)	HC v SSc PR v SSc UD v SSc PR v UD
Mean apical width (μm)	10.5 (11.0,10.1)	11.2 (11.9,10.5)	14.3 (14.7, 14)	12.5 (13.4,11.7)	HC v SSc PR v SSc UD v SSc HC v UD
Mean capillary tortuosity (no units)	4.42 (4.38,4.46)	4.33 (4.27,4.39)	4.55 (4.53,4.57)	4.41 (4.35,4.47)	HC v SSc PR vSSc UD v SSc

Table 1: Group-wise means and confidence intervals for each automatically measured capillaroscopy biomarker. Pair of groups with significantly different means are listed in the rightmost column

Results

- See Table 1 and Figure 2 for group means, 95% confidence intervals and the results of Tukey's test
- ANOVA tests showed significant group-wise differences for all biomarkers (all p <0.001)
- Images from patients with SSc had significantly lower capillary density and higher width and tortuosity than all other subject groups
- No significant differences were observed between healthy controls and PRP
- Images from patients with UCTD generated biomarkers that lay in between healthy controls/PRP and SSc

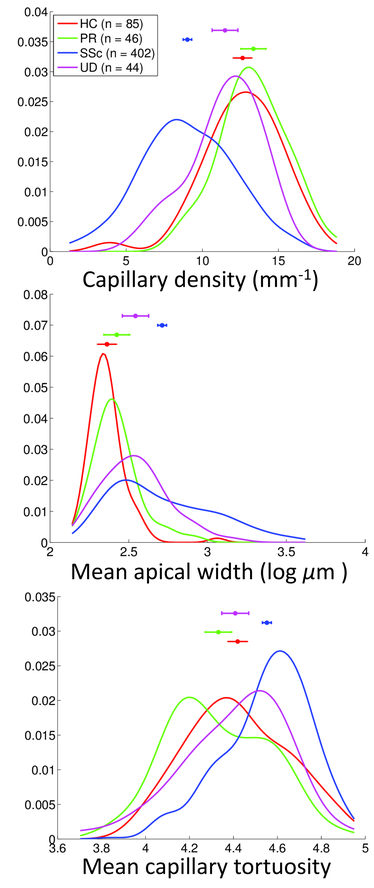

Figure 2: Distributions of capillary biomarkers for each subject group. Horizontal bars show group means and 95% confidence intervals

Conclusion

- These highly promising results suggest our software produces clinically useful biomarkers of connective tissue disease.
- Automatic analysis is potentially a major step forward, enabling large datasets of images to be assessed quickly and efficiently, obviating the inherent subjectivity of manual assessment

1. Murray et al, *Non-invasive Imaging Techniques in the Assessment of Scleroderma Spectrum Disorders*, Arthritis Care and Research, 61(8), 2009
2. Berks et al, *An Automated System for Detecting and Measuring Nailfold Capillaries*, proc. of MICCAI, 8673, 658-665, 2014

michael.berks@manchester.ac.uk/graham.dinsdale@manchester.ac.uk