**FINAL REPORT ON ‘NAILFOLD CAPILLAROSCOPY – VALIDATION OF ITS USE AS A CLINICAL TOOL, FURTHER EXPLORATION OF ITS USE AS A RESEARCH TOOL’ (GRANT REFERENCE MU3)**

**LAY SUMMARY**

Nailfold capillaroscopy allows the small blood vessels (capillaries) of the finger nailfold to be examined directly and non-invasively. These blood vessels are almost always abnormal in people with scleroderma (also termed ‘systemic sclerosis’)-spectrum disorders. However, separating out normality from abnormality can be very subjective, relying heavily on the opinion of the reviewing clinician. Our main objective was to assess both qualitative (subjective) and quantitative (objective) methods of scoring capillaries, in order to make recommendations to: (a) the practicing rheumatologist about the reliability of the different scoring methods, and (b) the research community about how capillaries should be scored/measured in studies of disease progression and treatment response.

To achieve our objective, we collected nailfold images using the high-magnification microscope technique known as videocapillaroscopy (magnification 300x) from all 10 fingers (including thumbs) from 173 participants: 101 patients with scleroderma, 22 with primary Raynaud’s phenomenon and 50 healthy control subjects. Ten capillaroscopy experts from 7 centres in 4 European countries evaluated the images. Using specially-designed computer software, each nailfold image was assessed for the following variables:

1. **Overall grade** (‘normal’, ‘early’ changes, ‘active’ changes, ‘late’ changes, ‘non-specific’ changes, or ‘ungradeable’)
2. **Capillary density** (number of capillaries per millimetre)
3. **Average capillary width**
4. **The presence of ‘giant’ (very large) capillaries.**

Each observer (expert) analysed an average of around 130 images each. There was some variation between observers in whether or not they felt that the different images could be assessed, although once this was accounted for, reliability was high for the overall image grade, density and width. In other words, for these three variables there was good agreement in measurements both between and within observers (good ‘within observer’ agreement means that if the same observer performs measurements on the same image twice, then the results are similar each time).

Our conclusion was that overall image grade, density and width all have the potential to be used as outcome measures in research studies including clinical trials. This means that if, for example, researchers want to examine if a drug has beneficial effects on nailfold capillaries, then these three measurements could be used to assess changes in capillaries over time.

A second part of the research was to compare images taken with two different capillaroscopy techniques, the high magnification videocapillaroscopy already mentioned above, and lower magnification dermoscopy (magnification 10x). This data is currently being analysed. As a final point,
we would like to highlight that in undertaking this project, we collected a very large number of nailfold images, and these will be a very useful resource for future research.

TECHNICAL REPORT

Most of the objectives of our project have been achieved as follows:

1. Determining inter- and intra-observer reliability of videocapillaroscopy. This was our main objective. This work has now been published (Dinsdale et al. Microvascular Research 2017) and represents the most comprehensive study of reliability of videocapillaroscopy in the literature.

2. Determining reproducibility of measurement over a short follow-up period of 1 week. This work has been completed and has been submitted for publication to Microvascular Research (copy of submitted paper attached). We have shown that at least with a single observer, both image analysis and acquisition are reproducible. This therefore is further confirmation that overall image grade, vessel density and mean vessel width provide reliable outcome measures for clinical studies including randomised controlled trials.

We are currently in the process of analysing the data comparing overall image grade obtained by videocapillaroscopy versus dermoscopy, and hope to complete this within the next 3 months. Also, we are currently undertaking some additional analysis to answer the question 'How many fingers have to be studied to give the 'correct' answer as to whether a patient does or does not have abnormal capillaries?' Although this was not one of our initial objectives, many clinicians ask this question, and so we are using our dataset to try to answer it.
LIST OF PUBLICATIONS

Full papers


Conference abstracts


Presentations (posters appended to this document)


POSTER: British Microcirculation Society (BMS) annual meeting, Manchester, UK, April 2015. Reliability of nailfold capillary density measurement as a possible outcome measure for systemic sclerosis-related microangiopathy. Presenter: G Dinsdale.


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