Micro magnetic resonance angiography of the finger in systemic sclerosis


Objective. To characterize vascular lesions in SSC disease with high-resolution magnetic resonance angiography (Micro-MRA) of the finger.

Methods. Eight SSC subjects and eight age- and sex-matched healthy controls were recruited for this study. Among the SSC subjects, the mean ± s.d. age was 54.5 ± 4.9 yrs, and the mean ± s.d. duration of disease was 8.3 ± 8.4 yrs. The numbers of SSC subjects that had telangiectasia, calcinosis and impaired finger flexion were 3, 2 and 3, respectively. The 2D time-of-flight micro-MRA was performed on a 3T clinical MRI scanner using a custom-designed finger coil with an in-plane resolution of 0.16 × 0.21 mm² and slice thickness of 1.2 mm. The data for the proper palmar digital artery lumen area, the number of visible dorsal digital veins and a semi-quantitative vascular score, which evaluates the overall integrity of digital vessels, were independently evaluated by two experienced reviewers who were blinded to the status of the subject.

Results. Micro-MRA detected significant differences in the digital vasculature between SSC subjects and healthy volunteers. The SSC subjects had a significantly decreased digital artery lumen area (0.13 ± 0.06 vs 0.53 ± 0.26 mm², P < 0.001), a reduced number of digital veins (0.63 ± 1.06 vs 3.13 ± 0.99, P = 0.001) and a lowered overall vascular score (1.75 ± 1.04 vs 3.5 ± 0.53, P = 0.001). The study also found that both the digital artery lumen area (Pearson’s r = −0.72, P = 0.044) and vascular scores (Spearman’s ρ = −0.75, P = 0.047) of the SSC subjects were inversely correlated with the duration of the disease.

Conclusions. Micro-MRA can be used to identify and quantitatively characterize the vascular disease in SSC fingers. The parameters derived from micro-MRA could potentially be used as prospective biomarkers for clinical evaluation.

Key words: Systemic sclerosis, Scleroderma, Vascular disease, Micro magnetic resonance angiography, Finger imaging.

Introduction

Systemic sclerosis (SSc or scleroderma) is an autoimmune CTD that, if severe, is frequently fatal. RP is often seen as a prodromal feature of the disease, suggesting that the vasculopathy may even be the central injury leading to organ damages [1–3]. The vascular lesions include occulsive intimal lesions of the small and large arteries and capillary rarefaction [4, 5]. Subjects sometimes have severe ischaemia in the peripheral circulation, with ulcers, gangrene and loss of digits.

An understanding of the vascular abnormalities in the fingers of SSC subjects is of importance in early diagnosis, as well as for better understanding of disease pathogenesis. RP, which is characterized by paroxysmal blanching and cyanosis of digits [6], is found in 95% [3] of the SSC subjects and has been found to be one of the earliest manifestations of the disease [4, 7]. The typically moderate-to-severe RP of SSc is likely caused by features of the abnormal digital vasculature, such as the fibrotic intimal hyperplasia found in the digital artery and arterioles. The vascular lesions of SSc have been primarily found in digital arteries and less frequently in the ulnar artery, superficial arch and common digital arteries [8, 9].

MR1 has been used to study the vascular conditions in SSC fingers [10–12]. MR1 has been demonstrated to visualize vessels, avascular areas and venous flow. However, the relatively low spatial resolution (>0.4 mm) in previous studies has made it difficult to quantify the vascular conditions of digital artery. In this study, we report our initial experience in high-resolution (0.16 × 0.21 mm²) magnetic resonance angiography (micro-MRA) for finger vascular imaging in SSC subjects, and describe a methodology for the quantitative characterization of finger angiograms.

Methods and materials

Study population

Eight SSc patients (two males, six females, mean ± s.d. age 54.5 ± 4.9 yrs, mean ± s.d. disease duration 8.3 ± 8.4 yrs) who had volunteered to participate in the MRI study were enrolled between November 2006 and October 2007. Four of them had disease durations of <5 yrs. Seven of the subjects were diagnosed with dcSSc and the other was diagnosed as having lcSSc. The characteristics of the subjects with SSc are summarized in Table 1. The skin score of the subjects were determined using modified Rodnan skin score system.

The control group included eight age- (within 2 yrs difference from the patients) and sex-matched healthy subjects (two males, six females, mean ± s.d. age 53.9 ± 5.0 yrs). The study was approved by the local institutional review board, and informed consent was obtained from all participants.

Finger coil

All MR images were acquired on a 3T whole-body scanner (Philips Achieva R2.1.1, Best, The Netherlands). Due to the high-resolution requirements, a custom-made radio frequency (RF) receive-only finger coil was utilized to acquire images of the fingers. The coil has a diameter of 25 mm to accommodate possible flexion contractures in impaired fingers. The longitudinal coverage from the coil is 65 mm, so that at a minimum, the two terminal IP joints of the index finger can be covered during the scan. The signal-to-noise (SNR) performance of this dedicated finger coil was compared with that of a standard manufacturer’s wrist coil by imaging a tube filled with water. The scanning parameters...
were: turbo spin echo (TSE) sequence, repetition time (TR)/echo time (TE) 2326/9 ms, field-of-view (FOV) 100 × 30 mm², acquisition matrix 382 × 112, slice thickness 1 mm, number of signal averages (NSA) 1.

The wrist coil was selected because it provides the highest SNR among all commercially available coils for small object imaging. The signal level was determined from the signal intensity of the water phantom; and the noise level was determined from the s.d. of a region of interest of the air. The SNR was calculated as described previously [13].

### Imaging protocol

All subjects were scanned in the supine position, with the coil positioned at the centre of the magnet. Scans were performed on the right index finger in all subjects. In the imaging protocol, a series of longitudinal proton density (PD) weighted images of the index finger were first obtained as the reference for the subsequent scans (Fig. 1). The imaging parameters were: TSE sequence, TR/TE 2326/9 ms, FOV 100 × 30 mm², acquisition matrix 256 × 135, in-plane resolution 0.16 × 0.21 mm², slice thickness 1.2 mm, 32 slices, sequentially acquired from distal to proximal, NSA 1 and scan time 3 min 30 s. To distinguish arterial and venous blood flow, the same 2D TOF sequence was performed twice with and without inflow saturation. A saturation band was placed proximally at the distance of 8 mm from the slice package and thus allowing saturation of arterial inflow of blood.

The digital arteries were identified as vessels that demonstrated the signal disappearance on images obtained with inflow saturation, as shown in Fig. 2.

### Image review

A primary MR image reviewer (J.W.) and a peer reviewer (B.C.), both with more than 4 yrs experience in vascular MRI and blinded to the status of the subject, independently reviewed all MR images. Images were displayed and analysed using a custom-written image-processing software package, CASCADE [14].

Evaluation of finger angiograms included three criteria. To quantitatively characterize the state of the arterial circulation, we measured the proper palmar digital artery lumen area (arrow in Fig. 2). Another supplying artery, radial artery of the index finger (arrowhead in Fig. 2), was not quantified because of its small size. Measurements were obtained from lumen contours of the proper palmar digital artery outlined using the semi-automated edge-detection tool provided by CASCADE. To ensure accurate comparison between subjects, the digital artery lumen area was measured at the location of the DIP joint as the average from three consecutive slices. To characterize venous circulation, the number of visible dorsal veins was counted. The use of this semi-quantitative index instead of vascular area measurements was motivated by individual anatomical appearance of the venous vasculature in the finger. Similar to lumen area measurements, the number of veins was counted as the average from three adjacent slices at the location of the DIP joint. The overall integrity of the subject’s finger vasculature was assessed by using a 5-point categorical scale (vascular score). The evaluation was performed using the reconstructed maximal intensity projections (MIPs) of digital vessels. All MIP images were reconstructed and displayed in nearly the same orientation using CASCADE software. The vascular scoring system is based on the previously defined ones [15, 16] but was further modified for finger imaging applications. The following scoring criteria were used: 0—no visible vessels; 1—barely visible spotted vessels; 2—poorly visible vessels with considerable discontinuities; 3—visible vessels with minor discontinuities; 4—clearly continuous visible vessels with well-defined boundaries. Example images of different vascular scores are shown in Fig. 3. Primary reviewer’s measurements were used for clinical evaluation.

### Statistical analysis

The Pearson’s correlation coefficients and 95% CIs were calculated to assess inter-reader agreement for lumen area measurement and vein number count. Bland–Altman plots were

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**Table 1. Characteristics of the subjects with SSc**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± s.d. (yrs)</td>
<td>54.5 ± 4.9</td>
</tr>
<tr>
<td>Female/male</td>
<td>6/2</td>
</tr>
<tr>
<td>Cutaneous subtype, diffuse/limited</td>
<td>7/1</td>
</tr>
<tr>
<td>Disease duration, mean ± s.d. (yrs)</td>
<td>8.3 ± 8.4</td>
</tr>
<tr>
<td>RP, n (%)</td>
<td>8 (100)</td>
</tr>
<tr>
<td>Skin score, mean ± s.d.</td>
<td>23.6 ± 9.6</td>
</tr>
<tr>
<td>Telangiectasia, n (%)</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>Calcinosis, n (%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>Impaired finger flexion, n (%)</td>
<td>3 (37.5)</td>
</tr>
</tbody>
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**Fig. 1.** PD-weighted longitudinal image of the finger and the scheme of positioning the MRA slice package (dotted rectangle). The package centre is positioned at the DIP joint (arrow), which is used as a landmark for subsequent image analysis.

**Fig. 2.** Comparison of angiography images without (a) and with (b) arterial signal saturation for digital artery identification. The palmar digital artery (arrow) and radial digital artery (arrowhead) can be identified when they appear only on the image (a) but not on the image (b).
also generated for these variables to assess systematic errors across the range of values by plotting the difference of paired sets of measurements vs their mean [17]. Cohen’s-κ and 95% CI were used to assess agreement for vascular score rating.

Two-tailed Mann–Whitney U-test was used to compare the digital artery lumen area, number of dorsal veins and vascular scores between SSc subjects and normal controls. Pearson’s (for the digital artery lumen area and number of dorsal veins) or Spearman’s (for the vascular score) correlation was used to analyse associations between clinical variables and vascular measurements.

A P-value of 0.05 was considered significant for all statistical tests. Statistical analyses were conducted with SPSS R12.0 (SPSS Inc., Chicago, IL, USA) software.

Results

**Finger coil**

The phantom SNR comparison revealed that the SNR of the finger coil exceeded the wrist coil by ~2 times at the centre and over 4 times in the peripheral region (Fig. 4). In addition, a more uniform SNR profile across the longitudinal direction was obtained from the finger coil.

**Inter-reader agreement evaluation**

Excellent inter-reader agreements were achieved for both lumen area measurements ($r = 0.97$; 95% CI 0.92, 0.99) and number of dorsal veins ($r = 0.90$; 95% CI 0.74, 0.97). The corresponding Bland–Altman analysis (Fig. 5) showed no significant bias between the measurements from two reviewers.

Very good inter-reader rating agreement was also achieved for vascular score evaluation (Cohen’s-κ = 0.75; 95% CI 0.49, 1.0).

**MR image review results**

Dramatically different visual appearance of the digital vasculature was found between SSc subjects and healthy controls (Fig. 6). The vessels from the SSc subjects generally demonstrated a poorer visibility and more discontinuities. Proper palmar digital arteries were identified in all subjects, except one SSc subject. It is also noteworthy that the radial artery of the index finger was visible in all healthy volunteers but in only four out of eight SSc subjects. The number of dorsal veins was always less in SSc subjects (Fig. 6a and b). Vascular measurements from micro-MRA and the corresponding statistical test results are summarized in Table 2. The proper palmar digital artery lumen area, the dorsal vein count and the overall vascular score were significantly reduced in SSc subjects as compared with controls.

For the SSc subject group, the scatter plot between the duration of the disease (in years) and the subject’s proper palmar digital artery lumen area is shown in Fig. 7a. A strong correlation (Pearson’s $r = -0.72$, $P = 0.044$) was found between the two parameters. Similarly, a strong correlation was observed between the duration of disease and the vascular score (Spearman’s $\rho = -0.75$, $P = 0.047$); the scatter plot is shown in Fig. 7b.

Fig. 3. Example MIP images of the finger vasculature illustrating vascular scores 1 (a), 2 (b), 3 (c) and 4 (d).

Fig. 4. SNR comparison between the wrist coil (dotted line) and the finger coil (solid line).

No significant correlation was found between number of veins and disease duration (Pearson’s $r = -0.20$, $P = 0.64$). No significant correlation was found between the modified Rodnan’s skin score and vascular measurements.

Discussion

Results of this study indicate significant involvement of digital vasculature in SSc. Our findings are consistent with previous invasive imaging studies that utilized digital subtraction angiography (DSA) [18] and contrast-enhanced MRA [12] to assess vascular conditions in the hands of SSc patients. Particularly, high prevalence of stenoses and occlusions was identified among SSc subjects in all studies. At the same time, previous studies did not attempt to characterize vascular abnormalities with quantitative measurements, but relied on qualitative descriptions.

A strong correlation was observed between the duration of the disease and lumen area/vascular score measurements from the SSc subjects. This suggests that the digital vascular lesions of SSc progress with time. This observation is in good agreement with previous findings stating that vascular lesions can be progressive in subjects with RP [19]. The correlation between vascular parameters and overall modified Rodnan’s skin score was also analysed, but no significant correlation was found. This could be explained by two reasons. First, the overall skin score is the sum of skin conditions at different locations, but the vascular parameters measured in this study only focus on digital vascular lesions. Second, the two parameters were measured based on two relatively independent pathological progresses (fibrosis and vascular changes). The proper palmar digital artery lumen area and visible dorsal veins may correlate well with disease duration, since the luminal narrowing may be progressive. Skin thickening, on the other hand, has a peak of severity and then softens, and the natural history of skin involvement is different between the subsets of SSc. Skin thickening could also be more closely associated with capillary rarefaction or with small-vessel malformation, which...
could not be measured directly by this technique. A further study that looks at disease progression will be helpful in understanding the physiological reason behind this observation.

The finger coil used in this study is critical to achieving the resolution and image quality needed for micro-MRA. The high spatial resolution required to accurately characterize digital arteries necessitates the use of a small volume coil for the highest intrinsic signal-to-noise ratio. The multi-loop solenoid coil provides the volume coverage necessary for whole finger imaging while maintaining a high SNR. The SNR of the finger coil is up to 4 times higher than that of the wrist coil, which is otherwise the most sensitive coil provided by the manufacturer for clinical applications. With this SNR improvement, an in-plane resolution of 0.16 x 0.21 mm² and a slice thickness of 1.2 mm can be achieved for quantitative measurements on small vessels.

Non-invasiveness and the lack of ionizing radiation make MRA a safer tool than DSA [18] for the clinical assessment of SSc disease. In this study, it is noteworthy that with the extra SNR brought by the new finger coil, vascular details in the SSc fingers were revealed without the use of a gadolinium-based contrast agent. Compared with previous contrast-enhanced applications [10–12], this non-contrast approach added another layer of safety assurance for clinical application in SSc subjects. This assurance is an advantage to subjects with SSc-associated kidney disease, who may be at a higher risk for the development of nephrogenic systemic fibrosis, a recently identified potential complication, which needs to be considered when administering gadolinium-based contrast agents to individuals with impaired kidney function [20].

This study is limited by the enrolment of a relatively small number of SSc and control subjects. Since SSc is a rare disease, the recruitment of subjects for the study is slow. Despite this, significant differences and correlations were still observed based on the vascular measurements. This demonstrates that the digital vascular MRI is a powerful tool for SSc finger imaging. As the
number of subjects becomes larger, we will be able to expand our analysis of SSc into disease subtypes, and look at correlations of the MR scores based on skin involvement, presence of particular organ involvement and autoantibodies present in serum.

The MRI technique demonstrated in this study is of likely utility in other rheumatological and vascular disease assessments. For example, primary Raynaud’s disease is also a disorder with considerable vascular involvement, but which does not typically progress to the severe obliterative vasculopathy seen in SSc. Additional disorders that can present severe distal digital vascular manifestations include vasculitis and APS. Whether this technique may be useful in discriminating among these sometimes overlapping conditions and assisting in diagnostic or treatment decisions has yet to be determined, but represents an important opportunity for further research.

Conclusion
The results of this study demonstrate that non contrast-enhanced micro-MRA can identify and quantitatively characterize the digital vascular involvement in SSc. Quantitative variables derived from finger micro-MRA can likely be used as prospective biomarkers in clinical research focused on SSc treatment.

**Rheumatology key messages**
- Micro MRA can identify and quantitatively characterize vascular lesions in SSc fingers.
- The severity of vascular lesions in SSc fingers is correlated with the duration of the disease.

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**References**