Computer-aided image analysis aids early diagnosis of connective-tissue diseases

Chia-Hsien Wen, Wei-Duen Liao, Tsu-Yi Hsieh, Der-Yuan Chen, Jong-Liang Lan, and Kuan-Ching Li

Automated classification of individual blood-vessel abnormalities may improve the efficiency of a common test for autoimmune diseases.

Systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) are autoimmune diseases of connective tissue. If left untreated, SLE and SSc can harm the heart, joints, skin, lungs, blood vessels, liver, kidneys, and nervous system, but their progression can be kept under good control if they are detected and treated early. Most SLE or SSc patients develop Raynaud’s phenomenon (RP), a blood-vessel disorder typically causing discoloration of the fingers and toes. RP deforms the capillaries (tiny blood vessels) of the nailfold, the skin overlapping the base and sides of a nail. SLE and SSc can therefore be detected early by checking nailfold capillaries for signs of RP. However, it is tedious and inefficient for a physician to check the huge number of capillaries individually.

RP can be detected by assessing the morphology, topology, and other related features of nailfold capillaries.1–4 Until now, a computer-based system has been used only to store and retrieve frames of nailfold video acquired for analysis. We have implemented a computer-based diagnosis-support system that extracts features of the capillaries to assist physicians in detecting these connective-tissue diseases.

RP generally emerges in both SLE and SSc and deforms normal nailfold capillaries into giant/enlarged ones or disorganization (see Figure 1). Our system selects many subimages, showing a single capillary from a patient’s nailfold images (see Figure 2). It then measures the area, perimeter, and diameter of each capillary. SLE or SSc are diagnosed and distinguished by considering the averages of these attributes for all imaged capillaries. Disease progression may be diagnosed by detecting the progression of RP2 and so the system subsequently assesses each individual capillary as either normal, giant/enlarged, or disorganization, using the criteria given in Table 1.

To test the consistency of diagnoses made by both the system and physicians, we considered 33 patients. Among them, there are 24 cases of SLE and nine suffering from SSc, as previously diagnosed by a team of rheumatologists. We captured color nailfold-capillary images (excluding thumbs) from each patient using a CCD (Leica MZ 12), each at 720 × 480-pixel resolution and 12.5 × magnification. External illumination was controlled by the operator to obtain clear image quality. We manually partitioned these images into subimages, each containing a single capillary, for later analysis.

During image analysis, the system transforms color subimages into monochrome ones and enhances them to minimize any noise. It captures the profile of each capillary using the $k$-means clustering method. Figure 2 shows processing stages.
Table 1. Criteria used for classifying capillaries of patients in Taiwan as either normal, giant/enlarged, or disorganization. Capillary type is determined when at least two of the three criteria are met.

<table>
<thead>
<tr>
<th>Type of capillary</th>
<th>Diameter/µm</th>
<th>Area/µm²</th>
<th>Perimeter/µm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;11</td>
<td>&lt;87.5</td>
<td>&lt;38.5</td>
</tr>
<tr>
<td>Disorganization</td>
<td>11–25.5</td>
<td>87.5–267.5</td>
<td>38.5–68.5</td>
</tr>
<tr>
<td>Giant/enlarged</td>
<td>&gt;25.5</td>
<td>&gt;267.5</td>
<td>&gt;68.5</td>
</tr>
</tbody>
</table>

Table 2. Average and diagnostic values of capillary attributes investigated based on patients in Taiwan.

<table>
<thead>
<tr>
<th>Disease type</th>
<th>Diameter (D) /µm</th>
<th>Area (A) /µm²</th>
<th>Perimeter (P) /µm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average value</td>
<td>Diagnostic value</td>
<td>Average value</td>
</tr>
<tr>
<td>SSc</td>
<td>27</td>
<td>D &gt; 22.67</td>
<td>405</td>
</tr>
<tr>
<td>SLE</td>
<td>14</td>
<td></td>
<td>130</td>
</tr>
<tr>
<td>Healthy</td>
<td>8</td>
<td>D &lt; 10</td>
<td>65</td>
</tr>
</tbody>
</table>

Table 3. Experimental results in diagnosing disease progression. Based on previous diagnosis of rheumatologists, there are 12, 15, and 6 patients in early, active, and late pattern, respectively.

<table>
<thead>
<tr>
<th>Test result</th>
<th>Early pattern</th>
<th>Active pattern</th>
<th>Late pattern</th>
<th>Total</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original diagnosis</td>
<td>11</td>
<td>1</td>
<td>0</td>
<td>12</td>
<td>91.6%</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>11</td>
<td>2</td>
<td>15</td>
<td>73.3%</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>66.6%</td>
</tr>
</tbody>
</table>

of each subimage, aimed at capturing the profile of the given capillary. It then averages the values of the three attributes of all capillaries and determines the patient’s disease according to the criteria in Table 2. Diagnostic values for SSc are derived from the average values of SSc and SLE so that the SSc diagnostic value is more than the SSc average value minus one third of the difference between the SSc and SLE averages. Similarly, the healthy diagnostic value is set to less than the healthy average plus one third of the difference between the SLE and healthy average values. A patient’s disease type is determined when at least two of the three criteria are met. Evaluation is performed to test SSc and healthy status in sequence. If a case is neither SSc nor healthy, it is classed as SLE.

Finally, the system applies the decision rule shown in Figure 3 to deduce disease progression, based on the number of capillaries classified and recognized in each category. The experimental results obtained suggest that our system correctly diagnoses SLE 79.16% of the time. SSc diagnoses appear 100% accurate. Additionally, the proportions of correct diagnoses of disease progression as early, active, or late pattern are 91.6, 73.3, and 66.6%, respectively (see Table 3).

In summary, we have developed a pilot computer-based system for early diagnosis of SLE and SSc by evaluating nailfold-capillary microscopy images. The results are proof of principle of the system, although further refinement to improve diagnostic accuracy is required. At present, images of individual capillaries are extracted manually from nailfold images because we have not found any suitable extracting algorithm. Future work will focus on how to extract images automatically and how to improve the system’s effectiveness, for example, by obtaining higher-quality, higher-resolution images using a higher-magnification CCD, thus permitting more precise recognition of capillary features. We also intend to combine capillary

Continued on next page
image research with other methods, such as antibody examination, to improve the accuracy of the diagnosis.

This research is sponsored in part by the National Science Council (NSC) of Taiwan (grants NSC98-2410-H-126-010-MY2 and NSC96-2221-E-126-004-MY3) and also by the Taichung Veterans General Hospital (TCVGH) and Providence University (PU) Collaborative Project (grants TCVGH-PU988107 and TCVGH-PU988106). Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the NSC, TCVGH, or PU.

Author Information

Chia-Hsien Wen
Department of Computer Science and Information Management
Providence University
Taichung, Taiwan

Chia-Hsien Wen is an associate professor and chair of the Department of Computer Science and Information Management. Prior to joining Providence University in 2005, he was director of the Computing Center at Taichung Veterans General Hospital (TCVGH). His research interests include medical image processing, medical informatics, and machine learning.

Tsu-Yi Hsieh, Der-Yuan Chen and Jong-Liang Lan
Division of Allergy, Immunology, and Rheumatology
Taichung Veterans General Hospital (TCVGH)
Taichung, Taiwan

Tsu-Yi Hsieh graduated from China Medical College and completed both his residency and his rheumatology specialist training at TCVGH. He is the attending physician of the Division of Allergy, Immunology, and Rheumatology, as well as executive coordinator of Evidence-based Medicine and head of Clinical Competence at TCVGH.

Der-Yuan Chen graduated from Yang-Ming Medical College and completed his residency at TCVGH. He received his rheumatology training there and completed a PhD degree at Yang-Ming Medical University. He is the current head of the Division of Allergy, Immunology, and Rheumatology.

Jong-Liang Lan graduated from Taipei Medical College and completed his residency and training in rheumatology at Taipei Veterans General Hospital. He subsequently became the first head of the Division of Allergy, Immunology, and Rheumatology. He has also been president of both the Rheumatism Association and the Chinese Society of Immunology. He is currently deputy superintendent at TCVGH.

Wei-Duen Liao and Kuan-Ching Li
Department of Computer Science and Information Engineering
Providence University
Taichung, Taiwan

Wei-Duen Liao received Master and Bachelor degrees from the Department of Computer Science and Information Management at Providence University in 2008 and 2006, respectively. He is currently a research assistant.

Kuan-Ching Li is currently a professor and chair of the Department of Computer Science and Information Engineering. His research interests include peer-to-peer, cluster and grid computing, parallel software design, and life-sciences computing.

References