博士論文の要約

学位論文題名

Assessment of Automatic Software for Detecting Radiographic Joint Space Narrowing Progression in Rheumatoid Arthritis

（関節リウマチにおける単純 X 線写真を用いた

関節裂隙狭小化進行の自動検出ソフトウェアの評価）

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Introduction

Rheumatoid arthritis (RA) is an autoimmune and chronic inflammatory joint disease that can cause cartilage, bone damage, and disability [1]. The estimated prevalence of RA is more than 700 thousand in Japan [2]. The ratio of male to female RA patients is 1:4, with the incidence between 30 and 50 [3, 4]. After the onset of RA, joint destruction progresses rapidly, and daily life becomes difficult due to joint pain and deformity.

The progression of joint space narrowing (JSN) over time is one of the parameters used to evaluate joint destruction in RA patients. The gold standard for its assessment is the modified Sharp/van der Heijde score (SHS) or the Genant-modified Sharp score (GSS) [5, 6]. This is evaluated visually by a physician. However, it is difficult to objectively and quantitatively assess the progression of slight JSN [7]. In addition, recent advances in anti-rheumatic drugs, such as biological agents have reduced the progression of symptoms, and in some cases, the progression of JSN is only a few millimeters per year [8]. Therefore, the objective and quantitative evaluation of JSN plays an important role in clinical trials in RA drug development and evaluation of efficacy in drug therapy.

This study verified whether a newly developed in-house software could automatically and quantitatively evaluate the slight progression of JSN on plain radiographs, which is difficult to evaluate visually.

Fully Automatic Software for Detecting Radiographic Joint Space Narrowing Progression in Rheumatoid Arthritis: Phantom Study and Comparison with Visual Assessment

Okino T., Ou Y., Ikebe M., Tamura K., Sutherland K., Fukae J., Tanimura K., Kamishima T., *Japanese Journal of Radiology*, 2022, 1-11.

Introduction

We have developed in-house software equipped with partial image phase-only correlation (PIPOC), which can automatically calculate the displacements of multiple areas with sub-pixel accuracy. To validate the software, we conducted a phantom assessment. We then assessed JSN progression by the GSS and synovial vascularity (SV) by quantitative power Doppler ultrasonography (PDUS). The purpose of this study was to evaluate the in-house software with PIPOC in terms of detecting slight radiographic progression in finger JSN using the GSS and the PDUS assessments as well as in phantom finger JSN.

Materials and methods

In the phantom assessment, the software's performance on radiographic images was compared to the joint space width (JSW) difference using a micrometer as ground truth. The JSW was changed at intervals of 0.1 and 0.01 mm. The delta (Δ) JSWs, or changes from JSN = 1.2 and 1.65 mm for 0.1 mm and 0.01 mm intervals, respectively, were used to evaluate the process of JSN by the PIPOC method. The phantom was made of titanium medical apatite (TMA) [9]. TMA is a recently introduced material that is easier to model than hydroxyapatite, and its CT value (Hounsfield units) is equivalent to that of subchondral and cancellous bones. The phantom mimics the metacarpophalangeal joint.

We have developed in-house software equipped with PIPOC. The analysis procedure was performed following five steps (Fig. 1). First, the software detects the approximate area of the joints to speed up the detection in the following steps. Second, the software detects joints using a machine learning algorithm. Third, the software with full image phase-only correlation corrects the detection error to avoid a mismatch in subsequent steps. The software focuses only on the phase component of the images and extracts the peak of the joint edge. Fourth, a dividing line is drawn in the gully to calculate the movement of the proximal and distal bones separately in order to avoid mutual interference. And finally, the PIPOC is used to calculate the relative movement of the proximal and distal bones. The bone movement can be obtained by calculating the peak position of the Dirac delta function in the phase difference spectrum. Thus, the JSN between the baseline and follow-up images can be quantified according to the bone movement difference between proximal and distal bones. From these steps, we can calculate the progression of JSN according to the vertical movements of the proximal and distal bones. We describe the details of the PIPOC algorithm in a previous study [10].

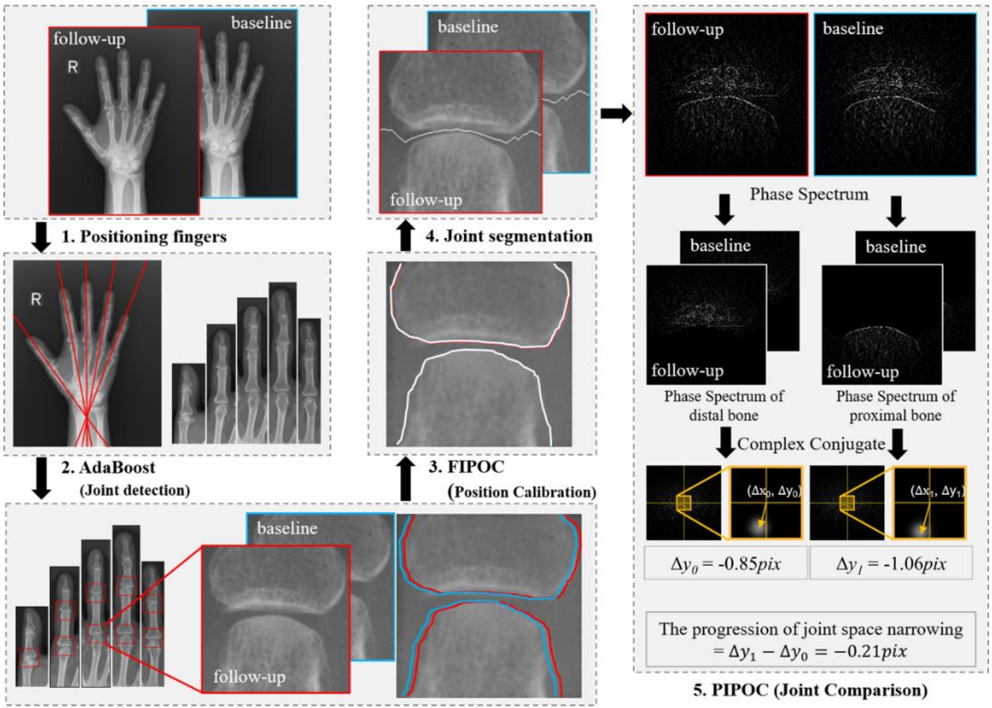

Fig. 1 The algorithm flow of in-house software equipped with PIPOC

FIPOC, full image phase-only correlation; PIPOC, partial image phase-only correlation

In the clinical assessment, 15 RA patients with long-term sustained clinical low disease activity (CLDA) were included. The software measured the radiological progression of the metacarpophalangeal (MCP) and the proximal interphalangeal (PIP) joints between the baseline and the 52nd week. The cases were also evaluated with the GSS, a conventional visual scoring method. We also quantitatively assessed these joints' SV on PDUS (0, 8, 20, and 52 weeks). Differences in parameters were examined using the Mann–Whitney U test.

Results

In the phantom assessment, the mean error, the standard deviation (SD) and the smallest detectable difference (SDD) for JSW measurements at 0.1 mm and at 0.01 mm intervals are 0.001, 0.023, 0.044, and -0.037, 0.028, 0.055 mm, respectively. There were significant correlations between true JSW and measured JSW differences ranging from 1.2 to 2.2 mm at 0.1 mm intervals ($R^2 = 0.996$; $p < 0.001$), and from 1.65 to 1.75 mm at 0.01 mm intervals ($R^2 = 0.553$; $p = 0.009$).

In the clinical assessment, the JSW change of the joints with GSS progression detected by the software was significantly greater than those without GSS progression (Mann-Whitney U test, $p = 0.004$). The JSW change of joints with positive SV at baseline was significantly higher than those with negative SV ($p = 0.024$).

Conclusion

Our in-house software equipped with PIPOC can automatically and quantitatively detect slight radiographic changes of JSW in clinically inactive RA patients.

Subtle Radiographic Progression at Six Months Can Be Detected Using Automated Quantitative Software in Rheumatoid Arthritis While Receiving Tocilizumab

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Introduction

This study aimed to investigate whether the in-house software equipped with PIPOC can detect subtle JSN progression six months after baseline and predict the prognosis of bone destruction at 12 months in RA patients under tocilizumab (TCZ) treatment. JSN progression at baseline, six, and 12 months was assessed by GSS and compared with the automated results.

Materials and methods

The study included 39 RA patients who were treated with Tocilizumab. Bilateral hand radiographs were acquired at baseline, six, and 12 months. The mean and SD between baseline and follow-up were 6.3 (±0.8) months and 13.3 (±2.1) months, respectively. Radiological progression of the MCP and the PIP joints was evaluated according to the GSS at 0, 6, and 12 months. Automatic measurements were performed with the software.

To ensure the homogeneity of the subjects, we targeted the joints with GSS = 0 at baseline for the software analysis. The following statistical analyses were performed using the Mann-Whitney U tests. We compared the 0-12-month GSS/PIPOC with and without JSN progression according to the 0-6-month GSS/PIPOC assessment. The GSS (+)/PIPOC (+) were defined as joints with JSN progression according to the GSS assessment and the software analysis, respectively. Otherwise, joints were defined as the GSS (-)/PIPOC (-), non-progressive JSN. We then compared the 0-6-/0-12-month PIPOC between the 0-6-/0-12-month GSS (-) and GSS (+).

The relationships between the 0-6-month and the 0-12-month PIPOC for each joint were investigated using linear regression tests. The joints within 1.5 mm of the JSW difference were included in the linear regression tests. The relationships for each joint were indicated according to the coefficient of determination (R^2) [11].

Results

The success rate of the software for JSW measurement was 96.8% (449/464). The 0-12-month GSS/PIPOC with the 0-6-month GSS (+)/PIPOC (+) group was significantly more JSN progression than the 0-6-month GSS (-)/PIPOC (-) group ($p < 0.001$ and $p = 0.001$, respectively). The 0-12-month JSW change by the software was significantly greater in joints with 0-12-month GSS (+) than with 0-12-month GSS (-) ($p = 0.020$). The linear regression tests showed significant correlations between the 0-6-month and the 0-12-month PIPOC in the left 2nd and 3rd MCP joints ($R^2 = 0.554$ and 0.420, respectively).

Conclusion

In conclusion, subtle radiographic JSN progression in RA patients under TCZ treatment is detectable by our automatic software equipped with PIPOC. Our results suggested that the software can predict subsequent joint destruction with only short-time observations at six months from baseline.

Summary

The main results of this study were as follows.

First, this study clarified the accuracy to which automated in-house software is able to precisely measure JSW. The potential for clinical application was demonstrated in terms of both phantom validation and comparison of visual evaluation. In the phantom assessment, the software could detect changes in JSN with the smallest detectable difference of 0.044 mm. In the clinical assessment, the software was comparable to the conventional scoring method regarding the detectability of JSN progression in RA patients. The in-house software equipped with PIPOC can automatically and quantitatively detect slight radiographic changes of JSW in clinically inactive RA patients.

Second, this study revealed whether in-house software could detect subtle JSN progression and predict the subsequent joint destruction with only short-term observation in RA patients undergoing potent biological disease-modifying anti-rheumatic drugs (DMARDs) treatment with TCZ. In the assessment by the software and the conventional scoring method, JSN progression at 0-12 months was significantly greater in the JSN progression group than in the non-progression group at 0-6 months. In addition, there was a significant correlation in the software measurement between 0-6-month and 0-12-month JSN progression in the left 2nd and 3rd MCP joints. The results suggest that the software can detect subtle JSW changes at six months and predict JSN progression at 12 months.

In conclusion, the automated software used in this study, which can automatically and quantitatively detect slight radiographic RA lesions, is expected to be a powerful tool for the prevention and early detection of the disease and for making appropriate medication decisions and inducing remission.

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