Longitudinal evaluation for COVID-19 chest CT disease progression based on Tchebichef moments

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Abstract
Blur is a key property in the perception of COVID-19 computed tomography (CT) image manifestations. Typically, blur causes edge extension, which brings shape changes in infection regions. Tchebichef moments (TM) have been verified efficiently in shape representation. Intuitively, disease progression of same patient over time during the treatment is represented as different blur degrees of infection regions, since different blur degrees cause the magnitudes change of TM on infection regions image, blur of infection regions can be captured by TM. With the above observation, a longitudinal objective quantitative evaluation method for COVID-19 disease progression based on TM is proposed. COVID-19 disease progression CT image database (COVID-19 DPID) is built to employ radiologist subjective ratings and manual contouring, which can test and compare disease progression on the CT images acquired from the same patient over time. Then the images are preprocessed, including lung automatic segmentation, longitudinal registration, slice fusion, and a fused slice image with region of interest (ROI) is obtained. Next, the gradient of a fused ROI image is calculated to represent the shape. The gradient image of fused ROI is separated into same size blocks, a block energy is calculated as quadratic sum of non-direct current moment values. Finally, the objective assessment score is obtained by TM energy-normalized applying block variances. We have conducted experiment on COVID-19 DPID and the experiment results indicate that our proposed metric supplies a satisfactory correlation with subjective evaluation scores, demonstrating effectiveness in the quantitative evaluation for COVID-19 disease progression.

KEYWORDS
blur, COVID-19 CT image, disease progression, objective evaluation, Tchebichef moments

1 | INTRODUCTION

Recently, a novel coronavirus rapidly spread worldwide.1-8 The clinical manifestations are pneumonia with fever, cough, and dyspnea. The infectious disease caused by the coronavirus is called COVID-19 by the World Health Organization (WHO). In the confirmed COVID-19 diagnosis of every suspected case, real-time reverse transcription polymerase chain reaction (RT-PCR) of viral nucleic acid is considered as the gold standard. However, it is time-consuming and it tends to generate high false negative rates via subject judgement.9,10 Recent literatures reported that chest computed tomography (CT) have relatively high sensitivity for the diagnosis of...
COVID-19. Moreover, in accordance with diagnosis and treatment plan of novel coronavirus pneumonia (version 7) published by the National Health Commission of China, CT has been regarded as an important tool in diagnosing, monitoring, and evaluating progress of COVID-19.

Up to now, some CT image visual analysis approaches of COVID-19 have been presented. The most visual analysis methods are generally based on descriptive analyses and statistical analysis. Descriptive analysis is a subjective qualitative analysis method, which potentially causes the delay of COVID-19 patient isolation and treatment. Statistical analysis methods could quantify CT manifestations of the patients, and illuminate the relationship between the degree of inflammation and the clinical manifestations of the patient. In recent years, artificial intelligence (AI) technology has been developed for processing medical images. AI-based methods are introduced into the automatic quantification of the infection for COVID-19 patients. For instance, Shan et al. used VB-Net neural network to segment COVID-19 infection regions for lung infection quantification. Li et al. proposed deep learning-based methods to differentiate COVID-19 from community-acquired pneumonia and other lung diseases. Tang et al. trained random forest model to realize automatic severity assessment of COVID-19 based on quantitative CT images features. Gozes et al. used deep learning algorithms to measure opacities burden, and then obtain corona score, which evaluate the progress of patients over time. The above methods were exploited on the basis of training network, and obtain fairly high performances achieving radiologist level.

In this article, we mainly focus on evaluating the progress of COVID-19 in each patient quantitatively by comparing the CT images acquired from same patient but different stages. With the case of confirmed and suspected patients of COVID-19 increase explosively, the number of radiologists is severely limited due to time costly acquisition. So, quantitative assessment of COVID-19 disease progression without manual reading is eagerly designed. Subjective assessment score is the ground-truth, which plays an important role in evaluating the performance of objective assessment metric. COVID-19 disease progression CT image database (COVID-19 DPID) is directly used for the check and comparison of same patient COVID-19 progress. Radiologist subjective ratings and manual contouring are obtained, where the slice of maximum lesions are manually sketched. It saves the doctor's time. COVID-19 disease progression is assessed applying the subjective research, which can assess and compare the CT images acquired from same patient over time. Considering that subtle changes of CT image are generally ignored, and inconsistent manual reading affect treatment. Thus, objective quantitative assessment metric is recommended for assessing COVID-19 disease progression.

Reportedly, ground-glass opacities (GGO) is the cardinal hallmark for COVID-19, which is manifested as hazes areas with slightly increased density in lungs without obscuration of bronchial and vascular margins. Typically, blur causes edge extension, which bring shape changes in infection regions. The CT manifestations of COVID-19 are characterized by different blur areas, which are irregular shapes in essence. Tchebichef moments (TM) have been demonstrated effective in shape representation, infection regions are mainly characterized by extension of edge. Typically, blur leads to edge extension, which subject to shape changes in infection regions. Intuitively, quantitative assessment disease progression can be conducted by shape changes. The shape changes can be caught by TM. In other words, disease progression of same patient over time is represented as different blur degrees of infection regions image since different blur degrees cause the change of TM magnitudes of infection regions, blur of infection regions can be captured by utilizing TM. Based on the above consideration, this paper proposes an objective quantitative evaluation method for COVID-19 disease progression based on TM. The main contributions are as follows:

1. We construct COVID-19 disease progression CT image database (COVID-19 DPID). Subjective ratings and manual contouring infection regions are the key to the subjective image database. It can measure the performance of objective quantitative evaluation metrics.

2. We first time propose a TM model in assessing disease progress of COVID-19. The images are first preprocessed, including lung segmentation, CT slice registration of the same patient over time, fusing each slice of same patient at same times point, and a fused image with region of interest (ROI) is obtained. Then, the gradient of a fused ROI image is calculated to denote the shape since the gradient is more efficient in blur representation. The gradient image of fused ROI is separated into same size blocks, a block energy is calculated as quadratic sum of non-direct current moment values is obtained by calculating a block energy. Finally, the TM energy with variance normalized is obtained as the objective assessment score.

3. We propose a new objective quantitative evaluation method for COVID-19 disease progression by applying the TM mentioned earlier. We compare and test the performance of the proposed method on subjective rating COVID-19 DPID. Experimental results
demonstrate that our method effectively in the quantitative evaluation for COVID-19 disease progression.

2 | TCHEBICHEF MOMENTS

TM have been demonstrated effective in field of image blur assessment. Although they have only appeared within the recent years since the pioneering work by Li et al.\textsuperscript{23} The TM used in image analysis can be found in Mukundan et al.\textsuperscript{22} In this paper, we focus on ROI of CT image. TM extract features from the ROI to calculate the blur degree of ROI.

2.1 | Definition

TM captures features efficiently, due to its outstanding capability in shape representation. The definition of the nth order TM with N-point kernel is as:

\[
T_n(x;N) = n! \sum_{k=0}^{n} (-1)^{n-k} \binom{N-1-k}{n-k} \binom{n+k}{n} (x)_k
\]

(1)

To satisfy numerical stability, generally, Tchebichef kernel is weighted:

\[
\tilde{T}_n(x;N) = \frac{\omega(x;N)}{\rho(n;N)} T_n(x;N)
\]

(2)

where \(\omega(x;N) = \frac{1}{N+1}\) is weight, \(\rho(n;N) = \frac{(2n)!}{(2n+1)} \binom{N+n+1}{2n+1}\) is norm. So, the definition of the \((m+n)\)th order TM with the weighted kernels based on \(M \times N\) image \(f(x,y)\) is as:

\[
T_{mn} = \sum_{x=0}^{M-1} \sum_{y=0}^{N-1} \tilde{T}_m(x;M) \tilde{T}_n(y;N) f(x,y)
\]

(3)

where \(m \in \{0, 1, 2, \cdots, M-1\}, n \in \{0, 1, 2, \cdots, N-1\}\).

2.2 | The relevance of ROI blur and TM

Blur leads to attenuation of image. Accordingly, it brings magnitudes change of TM.\textsuperscript{22,23} We believe that it exists relationship between ROI Blur and TM. Figure 1 gives an example of intuitive understanding with this kind of the relationship. ROI of first CT images for same patient, and the subsequent two times CT scans versions, along with their gradient images according to Equation (4). It is observed from the Figure 1 that blur degrees affect edge extension, as the blur increases, the edge becomes wider, the blur decreases, and the edge becomes narrower. This is more obvious in the structured regions of the image. Comparing the three images acquired from same patient, the blur is more serious in the first image. It denotes deterioration of disease progression. Especially, edge extension is more obvious in gradient transformation. By calculating the gradients, we easily obtain the shape of the image, and the extent of blur can be better represented using the gradient image. So, ROI shape is easily acquired, and the ROI blur degree is better expressed via the gradient of ROI.

3 | EVALUATION METHOD FOR COVID-19 DISEASE PROGRESSION

3.1 | Subjective assessment

From January 23, 2020 to February 14, 2020, 70 consecutive patients are applied to structure the subjective image database, which is shown in Table 1. From Table 1, we can see that it contains 34 males and 36 females, with a median age 40.5 years, where 23 patients were scanned on a Discovery PET/CT 690 scanner with a 64-row multidetector-row CT system (GE Healthcare, Milwaukee, WI, United States) in the Affiliated Hospital of Xuzhou Medical University. Forty-seven patients were scanned on a Brilliance 16 scanner with a 16-row multidetector-row CT system (Brilliance 16; Philips Healthcare, Cleveland, Ohio, United States) in Xuzhou Hospital for Infectious Disease. Non-enhancement plain scans were performed in all patients. Unequal section thickness, only one CT scans are all removed. Three times CT scans on same patient are kept. Thus, COVID-19 DPID includes 55 cases and 165 CT images.

Subjective CT visual quantitative assessment was based on each of the five lung lobes for percentage of the lobar involvement. According to diagnosis and treatment plan of COVID-19 issued by the China National Health Commission (7th), the severity is divided into four types: mild, common, severe, critical. For the same patient over time, two senior radiologists review original CT slice independently blinded to the clinical information. They are asked to manual contouring and giving ranking score 0–5, where 4–5 indicates restore health, 3–4 means mild, 2–3 is common, 1–2 means severe, and 0–1 indicates critical. There are 14 mild images, 38 common images, 51 severe, and 62 critical images in COVID-19 DPID. The ROI are obtained by contouring the slice of maximum lesions. If subjective scores and manual contouring are inconsistent, the third senior radiologist is required to confirm. The mean opinion score (MOS) is as final
subjective scores. The different scores of subjective quantitative evaluations provide us to easily evaluate the performance of objective strategies.

3.2 Objective assessment

The schematic of the proposed objective assessment method is given in Figure 2. The detailed assessment metric mainly consists of image preprocessing, calculating gradient, calculating block energy of TM, and obtaining objective assessment score. The proposed evaluation method is summarized in following steps.

3.2.1 Image preprocessing

Original chest CT images are preprocessed, including lung automatic segmentation, longitudinal registration, and CT slice fusion. Specifically, to accurately locate the lung, automatic lung segmentation is first performed in the Thoracic VCAR revision 2.0 image analysis software package (GE General Electric Company) on a GE Advantage Workstation. Then, due to quantitative comparison of CT images acquired from same patient over time during the treatment, it is necessary for lung slice longitudinal registration. ANTsPy registration tools available at https://antspy.readthedocs.io/en/latest/index.html. Where symmetric normalization algorithm is used for slice registration. It is an optimization method of mutual information based on affine and deformable transformation. Considering that single lung slice may not be enough to provide clinical needs to radiologists, fusion of each lung slice provides an effective resolving approach by integrating information of each slice into a fused image, which aids radiologists to diagnosis, together with subjective assessment contain manual contouring and giving ranking score. Guided filtering (GF) has been widely employed in image fusion, considering that GF-based image fusion can fuse multiple images, we use this kind fusion method to fuse each slice on same patient at one time scan. Finally, the ROI of fused slice image is obtained.

3.2.2 Calculating gradient

The ROI of fused slice image is represented by $F(x, y)$, $x \in \{1, 2, 3, \cdots, M\}$, $y \in \{1, 2, 3, \cdots, N\}$. The gradient image is denoted as:

![TABLE 1 General information of COVID-19 DPID database](image)

| Cases | Median age | Scans times | Images number | CT type                   |
|-------|------------|-------------|---------------|--------------------------|
| 70    | 40.5 years | 3           | 165           | 64-row multidetector-row 16-row multidetector-row |

![FIGURE 1 Region of interest (ROI) of three times computed tomography (CT) scans images (A)-(C) for same patient during the treatment and their corresponding gradient image (D)-(F)](image)
\[ g = \frac{|g_x| + |g_y|}{2} \]  
(4)

\[ g_x = [-1 0 1] \times F, g_y = [-1 0 1]' \times F \]  
(5)

where \(^{\text{\textprime}}\) and \(*\) represent the transpose and convolution, respectively. \(F(x, y)\) and its gradient image is separated into same size blocks \((Q \times Q)\). Image block and gradient block are represented by \(\{B^e_x\}\) and \(\{B^e_y\}\), respectively. Where \(i \in \{1, 2, 3, \ldots K\}, j \in \{1, 2, 3, \ldots L\}, K = \left\lceil \frac{M}{Q} \right\rceil, L = \left\lceil \frac{N}{Q} \right\rceil, \lfloor \cdot \rfloor \) is the floor operator.

### 3.2.3 Calculating block energy of TM

Next, the variances of the blocks are represented by \(\{\mu^2\}\).

The TM of the image blocks in \(\{B^e_x\}\) are calculated and indicated by:

\[
T_{ij} = \begin{pmatrix}
T_{00} & T_{01} & \ldots & T_{0n} \\
T_{10} & T_{11} & \ldots & T_{1n} \\
M & M & O & M \\
T_{m0} & T_{m1} & \ldots & T_{mn}
\end{pmatrix}
\]  
(6)

where, \(m, n \in \{0, 1, 2, 3, \ldots Q - 1\}\). The energy of Tchebichef moments (ETM) is calculated and represented as follows:

\[
E_{ij} = \sum_{p=0}^{m} \sum_{q=0}^{n} (T_{pq})^2 - (T_{00})^2
\]  
(7)

where \((T_{00})^2\) is 0-order moment, which is removed. To measure edges and shapes, we keep alternating current values.

From Equation (7), we can see that if image blurred degree is serious, the value of \(E_{ij}\) will decrease accordingly.

### 3.2.4 Objective assessment score

Consideration that ROI image has different components, its variances are different accordingly. Image energy is normalized by applying the sum of block variances. The objective assessment score is defined as
\begin{align}
O_{\text{score}} = \frac{\sum_{i=1}^{K} \sum_{j=1}^{L} E_{ij}}{\sum_{i=1}^{K} \sum_{j=1}^{L} v_{ij}}
\end{align}

4 | EXPERIMENTAL RESULTS

4.1 | Experimental settings

The performance of the proposed objective assessment metric is assessed on COVID-19 DPID database, including 55 patient images, 3 CT scans over times during the treatment. AOI of these CT images are acquired by radiologists’ manual rough contouring. Spearman rank order correlation coefficient (SRCC) and Kendall rank order correlation coefficient (KRCC) are as the evaluation metrics. SRCC and KRCC are two most popular rank correlation indicators, which can predictive consistency between MOS values and objective assessment scores. Generally, the larger values of SRCC and KRCC denote better assessment metric. In implementation, parameters are fixed according to experiments.

4.2 | Results and analysis

To demonstrate how the presented metric performs on ROI images, we test it using three images of same patient over time during the treatment. We give experimental results for eight patients and their individual over time during the treatment in the COVID-19 DPID database. From Figure 3, it is known that the proposed objective metric can acquire scores of disease progress consistent with subjective assessment.

To prove the availability of the proposed evaluation metric, we assess the overall performance based on COVID-19 DPID database. For each patient, we compute the SRCC, KRCC values between MOS values and predicted scores, which are shown in Table 2. In COVID-19 DPID database, there are two groups, Group 1:19 patients with the Affiliated Hospital of Xuzhou Medical University; Group 2:36 patients with Xuzhou Hospital for Infectious Disease. We compute the SRCC and KRCC values of all 55 patients image sets. The average performances over all patient image sets are given in the Table 1. For comparison, we also provide the scores predicted by two existing blur metrics, namely, MLV²⁷ and LPC.²⁸ We calculate the SRCC and KRCC values of all 55 patients image sets for three image blur metrics.
(including the two existing models described above and proposed metric). Table 3 summarizes the blur scores predicted by different metrics. From Table 3, we can see that proposed metric acquires the satisfactory effect on the average values of SRCC and KRCC. It shows effectiveness in the disease progression assessment of COVID-19 CT image.

5 | CONCLUSION

Blur is a key property in the perception of COVID-19 CT image manifestations. Establishing calculational models to assess COVID-19 disease progression is thus of great significance. This paper proposed an objective evaluation method for COVID-19 disease progression based on TM. It is basically based on the observation that blur causes the shape changes of infection regions, shape changes can be captured by applying TM. For this purpose, we first create a COVID-19 disease progression CT image database. Radiologist subjective ratings and manual contouring are obtained by subjective experiments. Then the images are preprocessed, including lung automatic segmentation, longitudinal registration, CT slice fusion. Next, we calculate the gradient image of a fused ROI, a block moment energy is calculated as quadratic sum of non-direct current moment values. The objective assessment score is obtained by TM energy normalized applying block variances. Finally, we have verified proposed objective assessment method on COVID-19 DPID. Experimental results indicate that our proposed metric supplies a satisfactory correlation with subjective evaluation scores, and it outperforms the state-of-the-art image blur metrics.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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