Predicting Pain Progression in Knee Osteoarthritis Subjects by Learning Image Biomarkers from Structural MRI

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Introduction

Recent studies suggest that there are distinct subgroups of knee osteoarthritis pain trajectories. While some patients suffer progressively worsening pain, others can stabilize the pain for a long-term period [1-2]. Establishing a direct relationship between image-based biomarkers and pain progression will be valuable as a prognostic tool. [3] The goal of this study consists of two parts: 1) to identify the distinct pain trajectories 2) to investigate the association between MRI image biomarkers learned using the 3D convolutional neural network and the identified pain trajectories.

Methods

Datasets: A total of 4,796 subjects' KOOS pain score for both knees over 10-year study were obtained from the Osteoarthritis Initiative. 3D Double Echo Steady State (DESS) images of the knee for the subjects at baseline were used for the image biomarker discovery. Data processing overall pipeline is described in Figure 1.

Modeling pain trajectory: We temporally smoothed individual's pain curve by fitting a regression model using the orthogonal polynomials as the basis in order to reduce the inherent noise in the dataset and to handle missing data. The estimated parameters were used as input into the Bayesian Gaussian mixture model. Silhouette approach was used to choose the optimal model. The parameters from regression were re-fitted against the selected Gaussian mixture model's means to obtain the posterior probabilities of the cluster membership. Deep learning architecture and training details: 3D extension of the DenseNet 121 architecture [5, 6]. The training dataset images were augmented. The network was trained to learn the posterior probabilities of pain trajectory membership. Mean squared error function was used as the loss function for regression.

Results

Pain trajectory clustering analysis: A total of 24 candidate models of varying number of components and different types of covariance were optimized. The Gaussian Mixture of three components with tied covariance was selected as the optimal clustering model. The clustering analysis based on the GMM model identified three pain trajectories: stable, worsening, progressively worsening. The distribution of age and gender were very similar across the clusters, while the Kellgren-Lawrence grades and OA status were more severe in the progressively worsening cluster.

Training results: The mean squared error scores were 0.0148, 0.1556, 0.1549 for training(n=5,470), validation(n=1,368), and test(n=1,710) set, respectively. The mean absolute error scores were 0.0174, 0.1661, 0.1654 for training, validation, and test set, respectively. The accuracy results were 0.9853, 0.8041, 0.7830 for training, validation, and test set, respectively.

Pain curve prediction: We evaluated the model's performance by comparing the simulated pain trajectories with the posterior probabilities of fitted GMM to the ones with the posterior probabilities the deep learning learned from MRI images. We simulated 1,000 sets of a random sample to obtain the confidence intervals and measured the overlap over the union of the intervals. The results were 0.8489, 0.5935, 0.5991 for the train, validation, test set, respectively.

Discussion

We built a deep learning model that relates imaging biomarkers to temporal information of the knee pain. With our design we can provide, not only the point estimate but also the uncertainty incorporated into the problem. As the analysis was focused on the relationship between image biomarker and pain, other clinical and demographic patient information was not examined.

Reference

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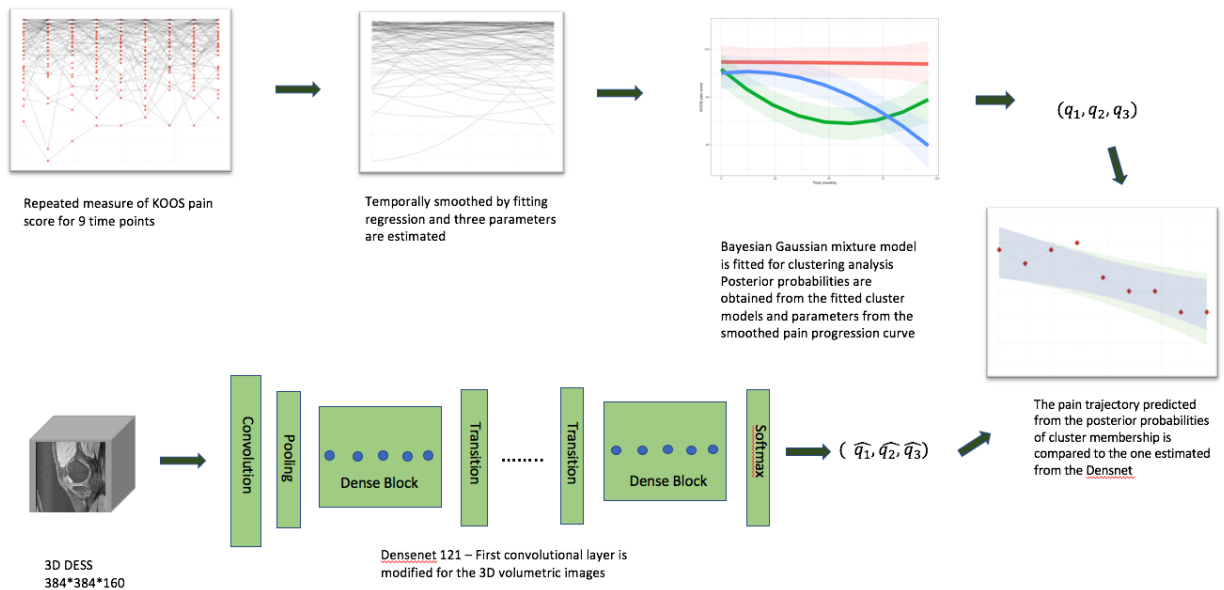
Figure 1. The pipeline of this study is shown above. The repeated measures of KOOS pain score were temporally smoothed. The regression parameters were used to identify the patterns of pain progression. Each parameter estimates from each pain curve then re-parameterized as the posterior probabilities relative to the identified Gaussian mixtures. The Deep learning architecture was trained to learn these posterior probabilities from the 3D DESS images. Finally, the pain curve identified in the clustering analysis and one that predicted from the DenseNet are compared and evaluated.