Prediction of Kellgren-Lawrence Grade of Knee Osteoarthritis by Deep Residual Networks Using MR Image with Segmented Image and Slice Position

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Abstract: This research explores the application of deep learning techniques, specifically employing a residual neural network, to predict Kellgren-Lawrence grade (KLG) in osteoarthritis patients using magnetic resonance images (MRI). Taking advantage of the characteristics of images, the proposed model integrates the MRI slice number and the use of segmented images. Unlike conventional approaches, we adopt a one-to-one image processing strategy, so our model takes each slice individually as input and returns a prediction for each of them to enhance the model’s ability to focus on specific slices and increase the results’ interpretability. Furthermore, results on real-world data corroborate the idea that the segmented image can provide more accurate prediction by allowing our network to focus on the crucial parts of the knee. The empirical results show the model’s promising performance in predicting KLG, demonstrating its potential for accurate and detailed diagnosis of osteoarthritis. This research contributes to advancing studies on the early prediction of osteoarthritis by proposing an effective and interpretable deep-learning framework for osteoarthritis assessment.

1 INTRODUCTION

Osteoarthritis is a debilitating joint disease that poses a significant health challenge worldwide. It is characterized by the degeneration of articular cartilage, subchondral bone changes, osteophyte formation, and joint space narrowing. An accurate and timely disease progression assessment is crucial for effective clinical management. Indeed, treating knee osteoarthritis (KOA) may involve surgical methods, e.g., ostectomy, arthroscopic interventions, knee arthroplasty, or conservative therapies. However, surgical interventions are considered almost exclusively in the case the disease is in its advanced stage. Instead, for milder degrees of such a pathology, it is common to prefer pharmacological and non-pharmacological approaches Vaishya et al. (2016).

Among the various grading systems utilized to evaluate osteoarthritis severity, the Kellgren-Lawrence grade (KLG) grading system Kellgren and Lawrence (1957) has stood the test of time as a widely accepted and validated method. More specifically, it consists of a four-values scale, going from the value 1 for the mildest state of osteoarthritis to the value 4 for the most severe. Traditionally, radiographic imaging, particularly X-rays, has been employed to determine KLGs Ahmed and Mstafa (2022). While effective, this approach has limitations, as it provides a static and two-dimensional view of the joint, often missing to distinguish the subtleties of early-stage osteoarthritic changes Roemer et al. (2018). In recent years, there has been a paradigm shift toward leveraging advanced medical imaging techniques, such as magnetic resonance imaging (MRI), to provide a more comprehensive and nuanced understanding of the disease Guida et al. (2021). The use of MRI as a substitute for X-rays is justified by its ability to provide a more complete picture of the entire articulation. Indeed, structural abnormalities detected...
by MRI, such as cartilage damage, osteophytes, and bone marrow lesions, were commonly present in the knees of middle-aged patients without radiographic evidence of KOA Kinds et al. (2013). Among the MRI findings, synovitis had the most pronounced effect on knee pain and could be a therapeutic target in patients with early KOA. So, although MRI is a more expensive technique than X-rays, from a medical point of view, they are essential in analyzing this problem Roemer et al. (2018).

This paper delves into the promising domain of osteoarthritis assessment using MRI images, specifically focusing on predicting KLGs. MRI offers a unique advantage by allowing for multi-planar imaging, detailed visualization of cartilage, bone, and soft tissues, and, most importantly, the ability to capture dynamic aspects of the joint. By harnessing the power of deep learning techniques Goodfellow et al. (2016), this research aims to develop a robust and accurate predictive model that can streamline the KLG grading process, ultimately improving diagnostic precision and facilitating early interventions in osteoarthritis management.

The main contributions of the paper are:

- The design of a novel approach, namely MMRI-SE-ResNet, for predicting KLG uses the segmented image and the slice number along with the MR images as input and outputs one prediction for each slice and aggregates the results;
- An empirical demonstration over a real-world dataset shows that the proposed approach gives better results than the existing baselines using MRI to predict the KOA status of a patient.

The objective of this research is to contribute to the advancement of non-invasive osteoarthritis assessment, thus enhancing the quality of life for individuals affected by this joint disorder.

The paper is structured as follows. In Section 2, we review the most related works to ours. Section 3 provides the formalization of the problem of predicting the OA status of patients. Section 4 describes the proposed novel methodology and highlights the most innovative elements designed for the analysed problem. Section 5.2 proposes a set of experiments on real-world data and Section 6 draws conclusions and delineates some future lines of research.

2 RELATED WORKS

The problem of diagnosing the severity of osteoarthritis has been analyzed over the years by many researchers. As outlined before, this has been done in the past by using X-ray images, which are generally already available and less expensive. Examples of this approach can be found in the work by Shamir et al. (2008); Antony et al. (2017). The studies present in this line of research model the problem as a multiclass classification and solve the problem by relying on classical supervised ML techniques. However, the obtained results are not impressive, especially because they fail systematically to distinguish between the 1 and 2 KLGs of the disease. This is due to the limited information that can be extrapolated from 2D X-ray images. Instead, Thomas et al. (2020) developed an automated model for detecting the severity of KOA from radiographs achieving 71% accuracy and 70% average F1 score. However, this study requires a specific standardized protocol to acquire images that would otherwise jeopardize the results. This makes it hard to be applied to other real-world cases.

With the advent of deep learning, new approaches have been applied also to the estimation of KLG using X-ray images. For instance, Chen et al. (2019) proposed two deep convolutional neural networks to automatically measure the KOA severity with an ordinal loss function that assigns larger penalties to misclassification with a larger distance between the prediction and the real severity of the disease. They reached a multiclass classification accuracy of 69.7%. In the work by Tiulpin et al. (2018) a deep Siamese CNN architecture has been applied to predict the severity of the OA disease using X-ray images. They exploited the symmetry existing in the problem, i.e., the symmetries between the left and right knees to get an average multiclass accuracy of 66.71%.

Another line of work is the one taking as input information the MRI of the knee to segment, and find correlations between the MRI and the KLG, without explicitly predicting the KLG. More specifically, the work developed by Kimura et al. (2022) uses the MRI image to get an automatic segmentation of the different parts of the knee. From this representation, this work analyses the characteristics of the parts of the knee affected by osteoarthritis, e.g., their volume, to highlight the differences between the OA degrees of severity. Among the other works using MRI for OA analysis, we cite the work by Harada et al. (2011), who tried to find the correlation between cartilage volume and KLG, and Schiratti et al. (2021), who implemented a deep learning method to predict, from MR images and clinical variables including body mass index, further cartilage degradation measured by joint space narrowing at 12 months. However, this last work cannot be applied as a baseline diagnostic tool since it makes use of longitudinal data.

Finally, the work by Guida et al. (2021) is the first,
to the best of our knowledge, to use a 3D convolutional neural network that combines the information about MRI to classify osteoarthritis severity degree by taking into account all the slices simultaneously reaching the $83\%$ of accuracy in a binary classification setting using a dataset of 1100 patients. We will compare this work with ours in the experimental part to evaluate its performance in our specific scenario.

3 PROBLEM FORMULATION

3.1 Evaluating Osteoarthritis

We will focus on analyzing how the classification problem can be tackled from already segmented images. For this purpose, we will make use of the classification system proposed by Kellgren and Lawrence, which is now widely used and considered a standard in the literature, e.g., Mohammed et al. (2023). This metric is prescribed to rank the severity of patients according to an integer numerical value, described as follows Kohn et al. (2016):

- Grade 0 (none): absence of radiographic changes of osteoarthritis;
- Grade 1 (doubtful): doubtful joint space narrowing and possible osteophytic lipping;
- Grade 2 (minimal): osteophytes and possible joint space narrowing;
- Grade 3 (moderate): multiple moderate osteophytes, definite joint space narrowing, sclerosis, and possible deformity of bony extremities;
- Grade 4 (severe): large osteophytes, marked joint space narrowing, severe sclerosis and definite deformity of the bony ends.

It is worth mentioning that patients with grades equal to or larger than 2 are commonly required to proceed with further analyses and controls. This implies that the most crucial patients to discriminate against are those with disease grades 0 or 1 versus 2 or larger grades. Indeed, an incorrect prediction may lead to an unnecessary further control (patients with grade 0 or 1 classified as 2 and above) or suggest no control to patients having the disease (patients with grade 2 and above classified as 0 or 1). Therefore, the patients can be naturally divided into two classes, which will be formally defined later in the paper.

3.2 Data-Driven Estimation

The problem we will analyze is a classic problem of supervised learning and, in particular, classification. We assume to have a dataset $\{X_i\}_{i=1}^N$ of $N$ MRI scans $X_i$, where each scan is represented as a sequence $X = [X_1, \ldots, X_s]$ of $S$ slices. Each slice $X_{i,s} \in \{0, \ldots, 255\}^{D \times D}$ for $s \in [1, S]$, is a raw image, i.e., an 8-bit grayscale images of size $D$ whose pixels take value from 0 to 255.

For each MRI scan, we are given as a corresponding target $y_i \in \{0, 1\}$ the absence or presence of the disease, i.e., a binary classification problem. In this case, values 0 and 1 for the KLGs correspond to a negative outcome of the examination, and instead, larger values, i.e., 2 to 4 grades, represent a positive outcome. The goal of our approach is, given a new MRI scan $X$, to provide a prediction of the class corresponding to the low and high KLGs $\hat{y}_i$ (1 for the presence of OA and 0 otherwise) for input $X_i$ that maximizes the accuracy over the entire learning space:

$$\max_{\gamma \in \mathcal{Y}} \mathbb{E}_{X,y} \mathbb{I} \{y = \hat{y}\},$$

where $\mathcal{Y}$ is an appropriate hypothesis space, the expected value is taken over the joint distribution of the pairs $(X, y)$ and $\mathbb{I} \{\cdot\}$ is the indicator function.

4 PROPOSED APPROACH

4.1 Input of the Model

Let us define first the segmentation $Z_{i,s}$ of an MRI slice $X_{i,s}$ that will be used for the definition of the input of our model. Formally, the segmentation $Z_{i,s} \in \{0, \ldots, C-1\}^{D_x \times D_y}$, with $C = 4$ represents a mask of the original MRI slice $X_{i,s}$. In the matrix $Z_{i,s}$, each element indicates the specific knee element to which the corresponding element in $X_{i,s}$ is associated. More specifically, the correspondence of the numbers with different elements of the segmentation is the following: 0 background, 1 femur, 2 femoral cartilage, 3 tibia, and 4 tibial cartilage. An example of the segmented elements on the knee is presented in Figure 1.

The final proposed model uses a tuple $(X_{i,s}, Z_{i,s}, s)$ as input, i.e., a combination of the raw image $X_{i,s}$, segmented image $Z_{i,s}$, and slice number $s$. Our model
wants to show how the combination of the segmented image and the slice number can significantly increase prediction accuracy for the OA state \( \hat{y} \) for the analysed problem. A visual representation of the network, whose details will be described in the following, is presented in Figure 2.

We remark that differently from the previously designed methods for evaluating the KLG, in this work, we are treating each slide independently from each other. This is in contrast with previous approaches that provide a single prediction per patient, e.g., Guida et al. (2021) in which they used a 3D convolutional neural network to process the MRI. In our model, the final outcome for a patient is provided by integrating all the information provided by the different slices (details are provided below).

### 4.2 The MMRI-ResNet

For capturing the difference between slice positions, we propose to use a Squeeze and Excitation network (Hu et al., 2018) (SE-ResNet) to capture the relationship between the various feature channels and to allow injecting the information of slice position \( s \) and add a fusion mechanism to provide a single outcome per patient. This architecture has been chosen due to the fact that the original formulation of this network has shown excellent performance in generic image recognition tasks in the past Russakovsky et al. (2015). From now on, we will refer to the newly defined network as Multi MRI SE-ResNet (MMRI-Se-ResNet), an architecture that will make use of \( S \) different networks that are specifically crafted to deal with the MRI images working in parallel. Figure 2 provides a visual representation of MMRI-Se-ResNet.

In the following, we review the models we design and highlight the significant contribution that has been introduced to SE-ResNet. As shown in Figure 3, our version of the SE-ResNet, namely the MRI-ResNet starts using a 2D convolution of the original MRI slice, and this operation is followed by a sequence of blocks denoted as \( R' \). These blocks are copies of a modified version of the Residual block originally used in the ResNet. The output from this block sequence is subsequently fed into an average pooling layer and subsequently into a linear layer.

Since the \( R' \) blocks have a crucial role in our network and represent the element that has been modified from the ones used in the original SE-ResNet, we provide a detailed description of its elements. Moreover, we divide its flow into two parts: the former which is in common with the residual block in the SE-ResNet, and the latter which has information about the slice number plugged. Specifically, the first part is composed as follows:

- 2D batch normalization layer;
- Dropout layer;
- 2D convolutional layer;
- 2D batch normalization layer;
- Leaky ReLU as activation function;
- Leaky ReLU as activation function.

Instead, the second part, shown in Figure 4, is composed as follows:

- global average pooling;
- linear layer to which an input feature corresponding to our slice number is concatenated;
- Leaky ReLU activation function;
- linear layer to which an input feature corresponding to our slice number is concatenated;
- Sigmoid activation function.

The final output consists of a scaled version of the original input, where the scaling factor is determined by the second element of the residual block (right flow in Figure 4).

The final return of the network model provides, for each slice, the probability \( \hat{p}_{i,s} \) that this slice does or does not belong to a patient with OA. So, in the end, the number of predictions equals the number of slices we took as input. The final prediction is obtained by averaging these probabilities and applying a threshold of \( \tau = 0.5 \), formally:

\[
\hat{y} = \mathbb{1} \left\{ \frac{\sum_{i=1}^{S} \hat{p}_{i,s}}{S} \geq \tau \right\}.
\]

This method was preferred to majority voting because it considers not only the fact of having classified a slice positively or negatively but also the degree of confidence with which it did so.

The objective of our model is to minimize the binary cross-entropy loss function \( L_{BCE} \) with weighted loss due to an unbalanced dataset. Formally, the loss is defined as follows:

\[
L_{BCE} = - \frac{1}{NS} \sum_{i=1}^{N} \sum_{s=1}^{S} w_{y_i} \cdot l_{BCE}^{i,s}
\]  (2)
where the cross-entropy loss for a single image is 
\[ L_{BCE}^i = y_i \cdot \ln \hat{p}_{i,s} + (1 - y_i) \cdot \ln (1 - \hat{p}_{i,s}) \],
the weights are 
\[ w_{y_i} = 1 - \frac{N_0}{N_1} \] if \( y_i = 0 \), and 
\[ w_{y_i} = 1 = \frac{N_0}{N_1} \] if \( y_i = 1 \),
and \( N_0 \) and \( N_1 \) are the number of occurrences for the negative class and the positive class, respectively. The use of the weights as defined above is a common tool to deal with unbalanced classes (Wang et al. (2020)).

We remark that our proposal is based on a two-step prediction that allows greater interpretability of the results. Indeed, we have information about the contribution that each slice provides to the final outcome in the probability of the slice \( \hat{p}_{i,s} \). This makes it easier to understand which parts one should focus on most when deciding the treatment. Our model offers a notable advantage w.r.t. the X-rays-based ones that do not provide information on the most relevant areas that determined the outcome. In general, in medical engineering, interpretability is preferred over simplistic black-box models that merely process inputs and outputs without any explanatory capability.

5 EXPERIMENTS

In the following, we applied the proposed methodology to a real-world dataset of OA patients and compared its performance with some baseline methods. Moreover, we also show how the different elements of the proposed approach impact the final performances.

5.1 Dataset

The Osteoarthritis Initiative (OAI) Nevitt et al. (2006); Ambellan et al. (2019) provided the dataset we worked on. It consists of 507 patients with or at risk of KOA. From the initial dataset, only \( N = 479 \) patients were analyzed since the remaining ones do not have information about the KLG. Each MRI consists of 160 slices, each having dimension 384 × 384. The corresponding segmented images \( Z_{i,s} \) were obtained by manual segmentation performed by experts in the field of radiomics.

Before feeding the data to the model we applied some pre-processing steps. First, following the suggestions provided in Guida et al. (2021), it was decided to exclude the slices with indexes in \( \{0, \ldots, 9\} \cup \{70, \ldots, 89\} \cup \{150, \ldots, 159\} \). Indeed, these slices very often consist of a completely dark background, thus not providing any meaningful information to the model. Therefore the final input had \( S = 120 \). Moreover, due to the fact that MRI scans are generally performed on large areas, each scan has been cropped to the central area resulting in a slice with \( D = 224 \).
Table 1: Evaluation metrics overview for binary classification of KLG. The proposed model is the best for the evaluation metrics analyzed. 95% confidence intervals are provided in square brackets.

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<td>$\hat{s}a$</td>
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<td>63.97 [±2.54]</td>
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<td>$\hat{a}$</td>
<td>62.94 [±5.65]</td>
<td>71.29 [±2.58]</td>
<td>68.71 [±3.90]</td>
<td>76.78 [±1.29]</td>
<td>78.39 [±3.32]</td>
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<td>$\hat{F}1$</td>
<td>55.36 [±7.99]</td>
<td>69.41 [±3.07]</td>
<td>64.54 [±5.05]</td>
<td>74.86 [±1.99]</td>
<td>76.45 [±3.10]</td>
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The slice number as input, i.e., requiring as input the tuple $(X_{i,s}, s)$:
- MMRI-SE-ResNet-Z, a version of MMRI-SE-ResNet making use only of the raw and segmented MRI, i.e., using the tuple $(X_{i,s}, Z_i)$ as input.

Notice that the last three methods will share the structure of the network (i.e., the layers number, dimension, and topology) except for the required input. Training for the 3D Conv has been conducted using the parameters suggested in Guida et al. (2021) for training. Conversely, the other methods have been trained using the Adam optimizer with default parameters, a learning rate of 0.001, a batch size of 256, and a number of epochs of 75. We applied dropout with a rate of 0.25 and early stopping with the patience of five epochs to prevent overfitting. The models have been optimized in terms of the 3D and 2D convolutional layer size. The choice of the final sizes has been done using a 5-fold cross-validation approach.

The performance metrics to compare the different methods we evaluated are the following:

- $\hat{s}a$ per-slice accuracy percentage (when available), which has been obtained by comparing the binary value returned for each individual slice with the one of the patient and averaging over all slices:
  \[ \hat{s}a := \frac{\sum_{i=1}^{N} \sum_{s=1}^{S} \mathbb{I}\{\hat{y}_{i,s} = y_i\}}{SN} \cdot 100, \]
  where $\hat{y}_{i,s} := \mathbb{I}\{\hat{y}_i \geq \tau\}$ are the predictions provided by a specific method for slice $s$ and $y_i$ is the patient KLG true value;

- $\hat{a}$ accuracy, the average accuracy percentage we get for the methods, formally:
  \[ \hat{a} := \frac{\sum_{i=1}^{N} \mathbb{I}\{\hat{y}_i = y_i\}}{N} \cdot 100, \]
  where $\hat{y}_i$ is the prediction for a specific patient;

- $\hat{F}1$ macro F1 score percentage, formally:
  \[ \hat{F}1 := \frac{\hat{F}_{1,y_0} + \hat{F}_{1,y_1}}{2} \cdot 100, \]
  where $\hat{F}_{1,y_0}$ and $\hat{F}_{1,y_1}$ are the empirical F1 scores (Taha and Hanbury, 2015) for the positive and negative classes, respectively.

We test our model using a hold-out approach. 70% of the samples were used for training, 20% for validation, and 10% for testing. The experiments have been repeated 5 times using a random split between the three sets. The 95% confidence intervals for the measured performances have been reported in the results in square brackets.

5.3 Results

Table 1 shows the performances of the different methods and their characteristics. Our approach significantly outperforms the baseline ones in terms of accuracy $\hat{a}$ and macro F1 score $\hat{F}1$. In particular, it is able to provide an increased accuracy of $\approx 15\%$ and $\approx 7\%$ w.r.t. 3D Conv and Se-ResNet, respectively. Similar improvements are provided in terms of macro F1 score ($\approx 21\%$ and $\approx 7\%$, respectively).

The MMRI-SE-ResNet-S and MMRI-SE-ResNet-Z models provide intermediate results between the baselines and the MMRI-SE-ResNet in terms of per-slice accuracy $\hat{s}a$ and accuracy $\hat{a}$. However, the use of the segmentation seems to provide a larger improvement than the one given by the slice number. Conversely, if we look at the macro F1 score, using MMRI-SE-ResNet-S reduces the score w.r.t. the original SE-ResNet, from 69.41% to 64.54% on average. Instead, the introduction of the information about the segmentation provided in MMRI-SE-ResNet-Z significantly improves the macro F1 score of the method. Finally, using both modifications (i.e., using the slice number and the segmentation) to the network results in being the best choice.
5.4 Testing the Significance of the MRI

Based on the previous results, we want to analyse if the different slices coming from multiple areas of the knee provide significantly different information to the MMRI-ResNet method. To do that we trained two models: one using data corresponding to slices $X_{s,t}$ with $s \in \{20, \ldots, 70\} \cup \{100, \ldots, 140\}$, and one using the data $X_{s,t}$ with $s \in \{10, \ldots, 60\} \cup \{110, \ldots, 150\}$. We tested such models to predict the outcome $y_i$ on slides coming from $s \in \{90, 99\}$. The results provide a per-slide accuracy of 70.1%, and 43.5%, respectively. This shows how the information of a model using slices that are closer to the test set is more significant than those of the model trained on slices that are not close to the test. Therefore, we need to include all the information about the different slices in our model to have a general picture of the phenomenon.

5.5 Discussion

Table 1 shows that segmented images significantly improve KLG prediction. We believe that including this input is crucial in our setting. Indeed, this allows the network to focus only on those areas that are the most significant to estimate the OA degree.

Let us compare the methods using per-slide prediction and 3D Conv. The results suggest that the ability to have separate predictions for each slice improves significantly the accuracy of the overall patient status. This strengthens the idea that the per-slice approach is valid in this setting. This phenomenon is especially true in settings in which the data are scarce. Indeed, as reported by Guida et al. (2021), 3D Conv achieved 83% accuracy using a larger cohort of 1100 patients, but, the accuracy decreased to 62.94% in our setting (479 patients).

Finally, we remark that in a medical setting, the macro F1 score indicates that models are effective at correctly identifying positive instances (high recall) and minimizing the number of false positives (high precision). In our case, the proposed MMRI-ResNet model provides an improvement on average of such an index of 1.59% w.r.t. the other analysed models. Therefore, it suggests that our method is a good choice when an automatic prediction is required.

6 CONCLUSIONS

In this paper we propose a novel architecture to solve the problem of predicting the presence of OA in knees using MRI scans. The resulting neural network-based model, namely MMRI-SE-ResNet, has been designed on the basis of an existing architecture, i.e., SE-ResNet, by including information about the segmentation of the knee extending the network architecture. The application of the above-mentioned method on a real-world dataset provided an overall prediction accuracy of 78.39% and a macro F1 score of 76.45, outperforming the existing method present in the literature. In general, the idea of processing the slices individually obtains better results than an approach that considers all the slices simultaneously.

The contribution of using the segmented image is significant in the prediction. Moreover, the use of slice numbers, which indicate the position of the slice in the knee, in combination with the segmentation provides a marginal improvement.

There are several works that we aim to pursue. Currently, the predictions of each slice are averaged to generate the final prediction, however, they might be of different interest depending on the specific pathology of the patient. This is usually supported by some a priori medical evidence, that could be exploited to focus more on some specific slides, e.g., modifying the weighting scheme using such information.

Using standardized images from OAI introduces biases due to consistent positioning and focus. This may lead to a lack of variation in patient presentation, potential overfitting to specific protocols, and challenges in generalizing to diverse clinical scenarios. To address these limitations another interesting study would use external validation over data coming from different clinical centers to validate the results we got in this study. At the same time, using those data as a training source would allow us to assess the limit of the method when applied to larger datasets.

Similar techniques could be applied also to distinguish the 5 KLGs, by considering a multiclass classification problem. An interesting development could extend our architecture for this setting.

Finally, the developed model is promising for effective application in the diagnosis and prediction of OA in different parts of the body, e.g., hands Hau- gen and Bøyesen (2011). This is possible due to the similarities in the scoring systems for both knee and hand joints, and the compatibility of MRI acquisition techniques.

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