Application of machine learning on the modelling of diffusion Magnetic Resonance Imaging signal

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Abstract—The modelling of diffusion Magnetic Resonance Imaging (dMRI) signals is very important for medical clinical application. However, the traditional method is to use a fixed mathematical model to make assumptions about the diffusion-weighted (DW) signals of all regions of human organ, which is unreasonable. In this paper, Convolutional Neural Network (CNN), a machine learning based method is used for learning the different characteristics of the signals, and finally intelligently give multi-model predictions for different regions of human livers. The performance of the proposed method is verified on both simulation and real liver data. The results show that the multi-model predicted by CNN method has high performance in distinguishing normal liver from diseased liver, and has great clinical application prospects.

1. INTRODUCTION

Diffusion Magnetic Resonance Imaging (dMRI) is an MRI imaging technology, which adds diffusion gradient to the MR sequence in order to obtain the information of irregular movement of water molecules in the human body. Specifically, the water molecule movement information in the tissue is called diffusion information, and the water molecule movement information in the blood vessel is called pseudo-diffusion or perfusion. The diffusion and perfusion information is very useful in the clinical application, such as the diagnosis of liver cirrhosis \cite{1} and brain tumor \cite{2}.

To obtain the diffusion or perfusion information form the diffusion-weighted (DW) signals, the signal model should be assumed, which is to describe the relations between the diffusion or perfusion parameter and DW signals. Therefore, the reasonable assumption of signal model is the key point. In previous studies, many models have been used, such as monoexponential model\cite{3}, bi-exponential model (the intravoxel incoherent motion imaging (IVIM) model)\cite{4}, multi-exponential model and other models. Among them, the IVIM bi-exponential model is the most common model used in DW signals analysis and achieved good clinical effects on some organs. However, different tissues, areas and diseases will lead to different internal environment, the movement of water molecules should be different. In the traditional way, only one model to describe the full regions of interest (ROI) was not appropriate, which also affects its further application.
Currently, the assumptions of the signal model rely on empiricism. Different signal models have different characteristics, and it is difficult to accurately describe these characteristics in this empirical way. To solve this problem, this paper proposed a CNN method to learn the characteristics of different DW signal model, and then using the learned CNN to dynamically predict the signal model of each pixel in the ROI. Finally, we obtain the diffusion and perfusion information form the predicted model by using a fitting method [5]. The CNN predicted model parameters will then compared with IVIM bi-exponential model parameters to evaluate its clinical application value.

2. METHODS

2.1. Multi-Model DW Signal Simulation

1. Monoexponential model

\[ S_n = S_0 e^{-b ADC} \]  

Where \( b \) is the diffusion sensitivity factor, which affects the DW signal strength. \( S_n \) is the DW signal measured at the \( b \)-value \( b_n \). ADC is the apparent diffusion coefficient assuming that perfusion information does not exist, which present the diffusion information.

2. Stretched exponential model

\[ S_n = S_0 e^{-(b ADC)^\alpha} \]

In Equation (2), \( \alpha \) ranges from 0 to 1 and the model changes between exponential and non-exponential.

3. IVIM bi-exponential model

\[ S_n = S_0((1 - F)e^{-b D^*} + Fe^{-b D}) \]

Where \( D^* \) is the pseudo-diffusion or perfusion coefficient, which present the perfusion information. \( D \) is the diffusion coefficient similar as ADC in Equation (1). \( F \) is the perfusion fraction.

4. IVIM-DKI model

\[ S_n = S_0((1 - F)e^{-(b ADC)^\frac{1}{6}b^2 ADC^k} + Fe^{-b D^*}) \]

In Equation (4), the first exponential part is DKI (Diffusion Kurtosis Imaging) model, which represent the non-Gaussian diffusion behavior of water molecules. The second exponential part is Gaussian perfusion model of IVIM bi-exponential model. The parameter \( k \) is a measure of the degree of non-Gaussian diffusion of water molecules.

5. GIVIM model[6]

\[ \frac{S(b)}{S_0} = (1 - F)e^{-b D} + F \int_0^\infty \frac{\exp(-(D' - \bar{D})^2 / 2\sigma^2)}{\sqrt{2\pi}}e^{-b D'}dD' \]

This equation is a generalized IVIM model and assumed the perfusion is composed of infinite perfusion components. Also assumption that the perfusion fraction density function obeys a Gaussian distribution. \( D' \) is the continues pseudo-diffusion variable. \( \bar{D} \) and \( \sigma^2 \) represent the mean and standard deviation of perfusion fraction density function, respectively.

To simulate the liver DW signals, we first set the value ranges of different model parameters according to the previous studies: ADC = [0, 4] x 10^{-3} mm^2/s, \( b \) = [0, 1], \( D \) = [0, 4] x 10^{-3} mm^2/s, \( D^* \) = [0, 150] x 10^{-3} mm^2/s, \( F \) = [0, 1], \( k \) = [0, 2], \( \bar{D} \) = [0, 150] x 10^{-3} mm^2/s and \( \sigma^2 \) = [0, 25] x 10^{-3} mm^2/s. The parameters of different models are uniformly sampled within their parameter ranges, and DW signals are generated according to the corresponding models. The \( b \)-value distribution is 0, 10, 20, 40, 60, 80, 100, 200, 300, 400, 600 and 800 s/mm^2. Finally, 1.33 million samples were obtained, 80% of them were
used as training set, and the rest were validation set. The test set generated by a random way, which means the parameter sampled randomly instead of uniformly. All the samples were added with Rician noise of different signal-to-noise ratios (SNRs): SNR 5, SNR 10, SNR 20, SNR 30, SNR 40, SNR 50, SNR 60, SNR 70, SNR 80 and SNR 100. Samples with different SNRs are mixed together to form a training set, which leads to the training set have more noise features.

2.2. Construct and Train the CNN Network

The CNN network we proposed is a multilayer network, including several convolutional layers, Pool layers, full connection layers and 1 inception model (The combination of several layers, such as convolutional and Pool layers). The input layer is a n-dimensional vector \( M(b) \) representing the normalized DW signal of model \( M \) acquired at different b-values:

\[
M(b) = \begin{pmatrix}
M(b_1) \\
M(b_2) \\
\vdots \\
M(b_n)
\end{pmatrix}
\]  

Figure 1. The architecture of CNN model. Different colours means different operations. For example, in the convolutional layer, ‘1x3 conv, 32’ mean that the kernel size is 1x3, the number of output channel is 32.

The output layer is a 5-dimensional vector \( R \), the value is 1, 2, 3, 4 and 5. Different dimensions represent different model categories. For each convolution layer, the 1-D convolution kernel was used and the stride was 1. Each convolution layer follows a batch normalization and activation operation (Prelu). For each Pooling layer, MaxPool function was used for pooling operation. In the full connection layer, the dropout (p=0.5) was used for reducing the effect of over-fitting. The detailed network structure is depicted in Fig. 1.
For the training, cross entropy loss function was used for learning the network parameters. The batch size is set to 2100, the optimizer used in this paper is Adam with learning rate of 0.001. To reduce the effect of over-fitting, early stop was performed in the training process.

The performance of the proposed CNN method for the model prediction of DW signals will then be verified on both simulation and real liver data. The simulation data is the test set mentioned above. And the real DW liver data is composed of 10 healthy and 10 diseased livers. The acquisition protocol is as follows: diffusion gradient amplitude = 50 mT/m, field of view (FOV)=400×300 mm², matrix size=128×96, slice thickness=8 mm, repetition time (TR)=2000 ms, echo time (TE)=55 ms, b-values=(0, 10, 20, 40, 60, 80, 100, 200, 300, 400, 600, 800 s/mm²). To obtain the diffusion or perfusion parameter in the DW signal model, such as the diffusion parameter \( D \) and perfusion parameter \( D^* \) or \( F \), a fitting method called nonlinear least squares (LSQ) was applied in this paper.

3. RESULTS AND DISCUSSIONS

3.1. Simulation Results
The results of the DW signal model prediction on simulation data were shown in Fig. 2. In this figure, Acc_average represents the average classification accuracy of the 5 model types. Acc_mono represents the accuracy of the monoexponential model. The same, Acc_Stretched represents Stretched exponential model, Acc_IVIM the bi-exponential model, Acc_IVIM_DKI the IVIM_DKI model and Acc_GIVIM the GIVIM model. The results show that CNN network performed well in the signal model prediction. The average classification accuracy of the five models is about 87%. Among them, the simpler model such as monoexponential model and the stretch exponential model have the higher classification accuracy (above 95%), even for relatively complex models, such as bi-exponential models, GIVIM model and IVIM_DKI model, the classification accuracy of is still above 75%. At the same time, because the CNN training data set is a mixed noisy data set, the signal model prediction based on CNN has good resistance to noise. The good performance of CNN on simulation data provides the guarantee for the application on real liver data.

3.2. Real Liver Results
The CNN signal model prediction method also performed on the real liver data. An example of DW signal model prediction performed on a healthy and diseased liver was shown in Fig. 3. The first row represent the dMRI b0 image of liver, the second row is model map predicted by CNN. The numbers in different colours correspond to five different model categories: 1= monoexponential model, 2= Stretched exponential model, 3= IVIM bi-exponential model, 4= IVIM_DKI model and 5= GIVIM model. The first column is normal liver, the second column is diseased liver. As we see, IVIM_DKI model is the most numerous of all models, followed is the GIVIM model. This means that the traditional bi-exponential IVIM model is not sufficient to interpret the liver's perfusion and diffusion environment. Due to the existence of a large number of non-Gaussian diffusion, the number of IVIM_DKI model increased. At the same time, only one exponential can’t describe the complex perfusion environment, which leads to the increasing of the number of GIVIM models. In addition, normal liver compared to diseased liver, the distribution of the signal model has also been changed. For these two examples of livers, the number of GIVIM models of diseased livers has decreased compared to healthy livers. This shows that the occurrence of liver disease causes changes in the internal environment of the organs, and corresponding changes in diffusion and perfusion. As the result, the DW signal model has been changed. Therefore, signal model prediction based on CNN can provide information in the discovery of liver disease.
Figure 2. The accuracy of signal model prediction on simulation test data

Figure 3. Comparison of DW signal models predicted by CNN between normal liver and diseased liver

To further illustrate the performance of signal model prediction in the liver, Fig. 4 summarized the signal model parameters of the two livers in Fig. 3, which obtained by LSQ fitting method. In this figure, the first two rows indicate the IVIM bi-exponential model parameters and the last two rows represent the parameters of CNN predicted model. In addition to the bi-exponential model, the model predicted by CNN also contains several other types. Therefore, more parameters of CNN predicted model can describe the difference of diffusion or perfusion information between healthy and diseased livers compared to only IVIM bi-exponential model. As we see, the parameters obtained by the CNN prediction model can not only distinguish the normal and diseased liver in the bi-exponential model parameters, but also other model parameters. This shows that this method based on CNN for DW signal model prediction has great potential in the application of liver diseases.

Figure 4. Model parameter maps of the two livers in Fig. 3
To systematically analyze the performance of the DW signal model prediction method based on CNN, Fig. 5 summarized the CV (coefficient of variation) of model parameters of healthy and diseased livers. The CV is defined by the ratio of the standard deviation to the mean of model parameters, which represents the homogeneous of model parameter in ROI (The lower CV indicates that the parameters are more evenly distributed in the ROI). In this figure, Bie_h means the CV of bi-exponential model parameters, and CNN_h indicates the CV of CNN predicted model parameters. P value is calculated by t-test for assessing the difference of CV between healthy and diseased livers (P<0.05 indicates significant difference). Whether it is diffusion parameters or perfusion parameters, the CV of the diseased group parameters is higher than that of the normal group parameters, showing higher parameter distribution heterogeneity. Among them, only the parameters of model predicted by the CNN method can significantly distinguish the normal and diseased liver in the CV of the diffusion parameter (ADC or D) and the pseudo diffusion coefficient (D* or D_D). However, any parameter of the traditional IVIM bi-exponential model cannot significantly distinguish diseased liver from healthy liver on CV. Changes in the internal environment of the organ will cause changes in the signal model. The signal model prediction method based on CNN can learn the characteristics of different signal models, so as to capture the information of changes in the environment within the organization.

![Figure 5. Comparison of the CV of DW signal model parameters between healthy and diseased livers](image)

4. CONCLUSION

Based on the results and discussions presented above, the conclusions are obtained as below:

1. The diffusion MRI signal modeling by CNN method can more comprehensively describe the diffusion and perfusion information in the liver compared to traditional IVIM bi-exponential model.
2. The signal model prediction based on CNN can better distinguish the normal and diseased livers.
3. Methods based on machine learning, such as CNN, have great potential in the medical application of diffusion MR (Magnetic Resonance) imaging.

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