Fusing Medical Image Features and Clinical Features with Deep Learning for Computer-Aided Diagnosis

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Abstract. Current Computer-Aided Diagnosis (CAD) methods mainly depend on medical images. The clinical information, which usually needs to be considered in practical clinical diagnosis, has not been fully employed in CAD. In this paper, we propose a novel deep learning-based method for fusing Magnetic Resonance Imaging (MRI)/Computed Tomography (CT) images and clinical information for diagnostic tasks. Two paths of neural layers are performed to extract image features and clinical features, respectively, and at the same time clinical features are employed as the attention to guide the extraction of image features. Finally, these two modalities of features are concatenated to make decisions. We evaluate the proposed method on its applications to Alzheimer’s disease diagnosis, mild cognitive impairment converter prediction and hepatic microvascular invasion diagnosis. The encouraging experimental results prove the values of the image feature extraction guided by clinical features and the concatenation of two modalities of features for classification, which improve the performance of diagnosis effectively and stably.

Keywords: Computer-Aided Diagnosis · Deep Learning · Fusion of Multi-modal Features · Alzheimer’s Disease · Hepatic Microvascular Invasion.

1 Introduction

In recent years, there has been remarkable progress on Computer-Aided Diagnosis (CAD), especially with the help of deep learning technologies [5]. Some studies have shown that the inclusion of CAD system in the diagnostic process can improve the performance of image diagnosis by reducing inter-observer variation [10][13] and providing quantitative support for clinical decisions, such as biopsy recommendations [2].

Medical images are really important for diagnosis. But they are not just the information that we should consider in the diagnosis. The clinical information is also important and necessary in practical clinical diagnosis. So, it is better to fuse medical image and clinical information in CAD system. The main methods
of fusing these two modalities of information in CAD can be divided into three categories. The first category is to concatenate original clinical data with image features. Pacheco et al. [9] proposed a method to detect skin cancers by concatenating clinical data with image features to improve the accuracy. Mobadersany et al. [7] proposed a method to predict the cancer patient’s survival, which uses VGG19 network and Cox proportional hazards model to extract features from pathological images. Then the genomic biomarkers data and image features are combined with a fully connected layer. Zhen et al. [19] used convolutional neural networks (CNNs) to classify liver tumors with enhanced MR images, unenhanced MR images and clinical data. Liu et al. [6] developed a deep learning system to provide diagnosis for skin diseases based on concatenating skin photographs’ features and associated medical histories. Ning et al. [8] proposed a method to diagnose coronavirus diseases based on concatenating CT features, clinical features and laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) clinical status and use penalized logistic regression to classify hybrid features. Tognetti et al. [14] proposed a deep learning architecture to classify atypical melanocytic skin lesions by concatenating dermoscopic image features and clinical data. Yamamoto et al. [16] proved that the integration of clinical data can improve the performance of diagnosis of osteoporosis from hip radiographs. Sandhu et al. [11] proved that concatenating clinical, demographic data and imaging features can improve the performance of diagnosis of non-proliferative diabetic retinopathy (NPDR). The second category is to transform original clinical data into a matrix and combine it with the image. Sharma et al. [12] proposed a preprocessing method that transforms 1D clinical data vector to 2D graphical image, which allows 2D CNNs to diagnose breast cancers based on the overlapping of transformed clinical data and image data. The third category is to employ clinical information and medical image in two independent stages. Yin et al. [17] proposed a method that firstly according to the clinical manifestation of the patient, then the MRI images of the patients who could not be given a clear diagnosis were put into a convolution neural network (CNN) to be tested and finally conclude. The combination of two types of information improved the accuracy of Parkinson’s Disease diagnosis by 7%.

The medical images and clinical information are not only complementary but also correlated. Some clinical features can be reflected in images, and some others cannot be. The existing methods mainly consider the complementary relationship between these two types of information. In this paper, we propose a new deep neural network to employ both complementary and correlated relationship between the medical images and clinical information for improving the accuracy of medical diagnosis. It is composed of two correlated paths of neural layers for extracting clinical features and image features and a fully connected layer for merging two modalities of features to make decisions for diagnosis. In image feature extraction, we embed clinical features as the attention to guide the finding of more discriminative image features. We evaluate the proposed approach on its applications to Alzheimer’s Disease (AD) diagnosis, Mild Cognitive Impairment (MCI) converter prediction and hepatic microvascular invasion diagnosis.
The main contributions of this paper are summarized as follows.

1. We proposed a new deep network architecture that fuses medical images and clinical information to perform medical diagnosis, in which clinical features are employed as the attention to guide image feature extraction and two modalities of features are merged for the final diagnosis. The reasonability of our design for this architecture is confirmed by ablation studies.

2. The proposed deep network for medical diagnosis is applied to AD diagnosis, MCI converter prediction, and hepatic microvascular invasion diagnosis. It yields beneficial results in these three tasks, which proves the effectiveness and the robustness of our method.

2 The Proposed Approach

2.1 The Whole Architecture

We propose a new deep neural network that fuses medical image and clinical information to achieve a more accurate diagnosis. The architecture of our deep network is illustrated in Fig. 1, which has two correlated computation paths for feature extraction, one for extracting image features and the other for extracting clinical feature. As shown in the right part of Fig. 1, we construct 2 fully connected layers to extract the features from clinical data. These clinical features are inserted into the image feature extraction module shown in the left part of Fig. 1 as the attention to guide the extraction of image features. Considering that clinical features can correlate with different-scale image features, we implement residual block with clinical attention for the last three blocks of ResNet since the semantic hierarchy of first block is too low. Finally, two modalities of features are merged to make decisions for diagnosis through a fully connected layer.

2.2 Residual Block with Clinical Attention

As described before, some clinical features can be reflected in images. For example, in the diagnosis of Alzheimer’s Disease (AD), the Neuro Filament L (NFL) is in direct proportion to the extent of brain shrinkage. In order to utilize the correlated clinical features to help finding the attentive features in medical images, we insert a clinical feature attention module into the residual block of ResNet50 deep network. The core part of ResNet50 is the residual block. We modify it to make clinical features guide the image feature extraction for improving the accuracy of diagnosis. The modified residual block is called Residual Block with Clinical Attention (RBCA) and is shown in Fig. 2.

The inputs of RBCA are medical image features and clinical features. For different diagnostic tasks, different clinical features could be reflected in different scales of image features. In order to deal with this problem of scale selection, we let the original image features concatenated with the image features processed by the clinical features and let the neural network learn to choose truly useful
Fig. 1: The proposed deep architecture of fusing medical images and clinical information for medical diagnosis

Fig. 2: Residual Block with Attention: (a) the whole structure, (b) the clinical attention module in (a)
features from the combination of them. Considering this doubles the dimension of features and increase the model complexity greatly, we reduce the dimension of inputted image features by a half with $1 \times 1$ convolution. The operations above can keep our representation sparse and make RBCA scale insensitive.

Then the reduced image features are processed by clinical features in Clinical Attention Module (CAM), the detail of which is shown in Fig. 2(b). At first, to align these two modalities of information by channel, we use a convolution layer with the kernel size of 1 to process clinical features. Let $T'$ be the processed clinical feature vector, $I$ be the inputted image features, $C$ be the number of channels of $I$ and $T'$, $H$ and $W$ be the height and the width of image feature map, respectively. Each dimension of $I$ is multiplied with correspond element of $T'$ to do the similarity measure between each dimension of image features and each dimension of clinical features. Let $I'$ be the resultant feature map. To get the similarity between each channel of image features and clinical features, we use global average pooling to average each resultant feature map. Let $H_{GP}(\cdot)$ be the global average pooling function, then we have

$$H_{GP}(i'_c) = \frac{1}{H \times W} \sum_{j=1}^{H} \sum_{k=1}^{W} i'_c(j, k),$$

where $i'_c(j, k)$ is the value at position $(j, k)$ of $c$-th feature $i'_c$. Such channel statistic can be viewed as a collection of the local descriptors, whose statistics contribute to express the whole image [4].

Finally, the CAM outputted features and the reduced image features are concatenated to pass through two layers of convolution to obtain the final result. In this way, the more discriminative features in the image will be enhanced and play more influence in the diagnosis.

### 2.3 Decision Making Based on Combined Features

In the last subsection, we employ the clinical features that can be reflected in images for improving the extraction of image features. However, there are also some useful clinical features that cannot be reflected in the image, such as Tau in the diagnosis of AD. It means that we should concatenate the clinical features with the image features to do the final classification. In this paper, the merged features pass through a fully connected layer and Softmax function to obtain the classification possibilities for each category. Then the category with the highest probability is taken as the classification result.

As described in Section 2.1, there are some other works of combining clinical data and medical images for diagnosis. However, they usually use the original clinical data. The number of attributes in original clinical data is usually much smaller than the image features. For example, in our experiments of AD diagnosis, original clinical data has only 237 attributes while the dimension of image features are 2048. This makes the clinical information drowned in the sea of image features and could be neglected in the classification. To solve this problem,
we extract high dimensional deep features from clinical attributes. The number of extracted clinical features is close to that of image features.

### 2.4 Learning Algorithm

As we are dealing with classification problem, we choose the popular loss function of categorical Cross-Entropy (CE) to perform learning. Based on the CE loss, we apply the Back Propagation (BP) algorithm with stochastic gradient descent to update the parameters of our model.

### 3 Experiments

We conduct three groups of experiments on three diagnostic tasks to demonstrate the effectiveness of our proposed approach. In the training of our model, we use He initialization and Adam optimization and set the learning rate as 0.0001 and the number of training epochs as 100. The algorithm is implemented in PyTorch framework and runs over a GPU server with Nvidia RTX 2080Ti.

In the experiments, we conduct ablation studies to demonstrate the reasonability of the design of our approach. Our main contributions on the deep architecture for AD diagnosis exist in two aspects, guiding the image feature extraction by employing clinical features as the attention and concatenating two modalities of features in the final classification. In order to confirm whether these two new operations are really effective, we perform diagnosis by using each of four following options of our deep architecture and compare their performance:

1. Only Image: only image features are employed
2. Image + Clinical: In the classification, image features and clinical features are used, but image feature extraction is not guided by clinical features
3. Full Model: our full model including two new operations

Furthermore, we conduct 5-fold cross validation on these three tasks.

### 3.1 AD Diagnosis

AD is characterized as a genetically complex and irreversible neurodegenerative disorder and often found in persons aged over 65. AD versus Normal Cognitive (NC) is a typical problem within AD diagnosis. We evaluate our proposed method for AD diagnosis on AD Neuroimaging Initiative dataset (ADNI 1 1.5T). From ADNI 1 1.5T, we construct a 2D MRI dataset with 5640 slices.

* Data used in preparation of this article were obtained from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: [http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf](http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf)
4530 of them are used for training and 1110 of them for testing. The patients in the training set and the test set have no intersection. Inspired by [18], we selected 10 slices from the coronal position of every MRI image, with y-value range between 130 and 140, because these slices are corresponding with informative part of brain for AD diagnosis. We resize each slice to $256 \times 256$. As for the clinical data, we choose a part of the biospecimen data by a senior doctor with 14 years’ experiences in AD diagnosis. Total 237 clinical data are obtained, which are listed in supplement material.

The results of AD diagnosis are reported in Table 1. We can see that the clinical data is very valuable for AD diagnosis. Introducing clinical features lead to better performance on all the criterions, even they are only concatenated with image features. However, the images also contain many useful information for diagnosis, which cannot be reflected in clinical features. By appending our attention from clinical information and combining two modalities of features to utilize some clinical information that are necessary for diagnosis but cannot be reflected in images, the classification accuracy based on only images can be improved greatly, as shown in the comparisons between the results in the last two rows in Table 1.

![Table 1: The results of ADNI1 dataset](image)

| Task           | Approach   | ACC       | Sensitivity | Specificity | PPV       | NPV       |
|----------------|------------|-----------|-------------|-------------|-----------|-----------|
| AD vs. NC      | Image Only | 66.73%    | 54.29%      | 73.68%      | 53.05%    | 74.64%    |
|                | Image+Clinical | 92.70%    | 86.18%      | 95.74%      | 90.35%    | 93.74%    |
|                | Full Model  | 95.52%    | 92.41%      | 96.96%      | 93.25%    | 96.53%    |

3.2 MCI Converter Prediction

Recently, an increasing number of studies on AD research begin to address classification of MCI to AD conversion (MCI-AD) and MCI non-conversion (MCI-NC) patients based on the high-resolution brain imaging data. We also choose a part of MRI images of MCI patients from ADNI2, with a dataset of 800 slices, 640 of them are used for training and 160 of them for testing. These images are used for the classification of MCI versus MCI-AD converter. The image data selection method and preprocessing are the same with ADNI1. For ADNI2, total 234 clinical data are obtained, which are also listed in supplement material. The results of MCI converter prediction are reported in Table 2. We can observe the same phenomenon as those in the first experiment, i.e. concatenating clinical features with image features can improve the accuracy of MCI converter prediction, and using clinical features as the attention can extract better image features and further improve the accuracy of prediction.
Table 2: The results of ADNI2 dataset

| Task                        | Approach       | ACC   | Sensitivity | Specificity | PPV   | NPV   |
|-----------------------------|----------------|-------|-------------|-------------|-------|-------|
| MCI vs. MCI-AD converter    | Image Only     | 67.41%| 42.92%      | 82.33%      | 79.25%| 71.25%|
|                             | Image+Clinical | 70.63%| 50.42%      | 83%         | 75.67%| 73.67%|
|                             | Full Model     | 74.06%| 55.73%      | 86.13%      | 78.06%| 77.38%|

3.3 Hepatic Microvascular Invasion

Liver cancer is the second leading cause of cancer-related deaths worldwide and hepatocellular carcinoma (HCC) represents the most common primary liver cancer [115], hence the diagnosis of hepatic microvascular invasion is quite an important task. We used 1394 2D liver CT images from 139 patients of hepatic microvascular invasion to conduct our third group of experiments. Total 29 preoperative clinical data are obtained, which are also listed in supplement material. This dataset is used for the diagnosis of hepatic microvascular invasion (HMI). The results of hepatic microvascular invasion diagnosis are shown in Table 3. Again, concatenating image and clinical features improve the accuracy of hepatic microvascular invasion diagnosis and introducing clinical attention module into image feature extraction can further improve the performance of the hepatic microvascular invasion diagnosis.

Table 3: The results of HMI dataset

| Task                        | Approach       | ACC   | Sensitivity | Specificity | PPV   | NPV   |
|-----------------------------|----------------|-------|-------------|-------------|-------|-------|
| Hepatic Microvascular Invasion Diagnosis | Image Only     | 71.18%| 88.32%      | 34.76%      | 74.23%| 48.57%|
|                             | Image+Clinical | 75.47%| 90.09%      | 46.12%      | 77.24%| 69.11%|
|                             | Full Model     | 79.17%| 88.84%      | 58.91%      | 81.76%| 78.89%|

4 Conclusions

This paper has proposed a deep network architecture to fuse medical image and clinical information for Alzheimer’s Disease (AD) diagnosis, MCI versus MCI-converter prediction and liver tumor benign/malignant diagnosis, in which clinical features are used as the attention for image feature extraction and combined with the image features to perform classification. To our best knowledge, this is the first work of utilizing clinical data as the attention by deep learning to guide the image feature extraction in computer-aided diagnosis. Our approach yields a good performance on the ADNI1 dataset, ADNI2 dataset and our private dataset. The ablation studies confirm that 1) the clinical information is very valuable and necessary for medical diagnosis; 2) the better image features can be obtained under the guidance of clinical features, and 3) two modalities of features are complementary and should be combined for improving the accuracy of diagnosis.
References

1. El-Serag, H.B., Rudolph, K.L.: Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology 132(7), 2557–2576 (2007)

2. Giger, M.L., Karssemeijer, N., Schnabel, J.A.: Breast image analysis for risk assessment, detection, diagnosis, and treatment of cancer. Annual review of biomedical engineering 15, 327–357 (2013)

3. He, K., Zhang, X., Ren, S., Sun, J.: Delving deep into rectifiers: Surpassing human-level performance on imagenet classification. In: Proceedings of the IEEE international conference on computer vision. pp. 1026–1034 (2015)

4. Hu, J., Shen, L., Sun, G.: Squeeze-and-excitation networks. In: Proceedings of the IEEE conference on computer vision and pattern recognition. pp. 7132–7141 (2018)

5. Litjens, G., Kooi, T., Bejnordi, B.E., Setio, A.A.A., Ciompi, F., Ghafoorian, M., Van Der Laak, J.A., Van Ginneken, B., Sánchez, C.I.: A survey on deep learning in medical image analysis. Medical image analysis 42, 60–88 (2017)

6. Liu, Y., Jain, A., Eng, C., Way, D.H., Lee, K., Bui, P., Kanada, K., de Oliveira Marinho, G., Gallegos, J., Gabriele, S., et al.: A deep learning system for differential diagnosis of skin diseases. Nature Medicine 26(6), 900–908 (2020)

7. Mobadersany, P., Yousefi, S., Amgad, M., Gutman, D.A., Barnholtz-Sloan, J.S., Vega, J.E.V., Brat, D.J., Cooper, L.A.: Predicting cancer outcomes from histology and genomics using convolutional networks. Proceedings of the National Academy of Sciences 115(13), E2970–E2979 (2018)

8. Ning, W., Lei, S., Yang, J., Cao, Y., Jiang, P., Yang, Q., Zhang, J., Wang, X., Chen, F., Geng, Z., et al.: Open resource of clinical data from patients with pneumonia for the prediction of covid-19 outcomes via deep learning. Nature biomedical engineering 4(12), 1197–1207 (2020)

9. Pacheco, A.G., Krohling, R.A.: The impact of patient clinical information on automated skin cancer detection. Computers in biology and medicine 116, 103545 (2020)

10. Sahiner, B., Chan, H.P., Rouhidoux, M.A., Hadjiiski, L.M., Helvie, M.A., Paramagul, C., Bailey, J., Nees, A.V., Blane, C.: Malignant and benign breast masses on 3d us volumetric images: effect of computer-aided diagnosis on radiologist accuracy. Radiology 242(3), 716–724 (2007)

11. Sandhu, H.S., Elmogy, M., Sharaferdeen, A.T., Elsharkawy, M., El-Adawy, N., Eltanboly, A., Shalaby, A., Keaton, R., El-Baz, A.: Automated diagnosis of diabetic retinopathy using clinical biomarkers, optical coherence tomography, and optical coherence tomography angiography. American journal of ophthalmology 216, 201–206 (2020)

12. Sharma, A., Kumar, D.: Classification with 2-d convolutional neural networks for breast cancer diagnosis. arXiv e-prints pp. arXiv–2007 (2020)

13. Singh, S., Maxwell, J., Baker, J.A., Nicholas, J.L., Lo, J.Y.: Computer-aided classification of breast masses: performance and interobserver variability of expert radiologists versus residents. Radiology 258(1), 73–80 (2011)

14. Tognetti, L., Bonechi, S., Andreini, P., Bianchini, M., Scarselli, F., Cevenini, G., Moscarella, E., Farnetani, F., Longo, C., Lallas, A., et al.: A new deep learning approach integrated with clinical data for the dermoscopic differentiation of early melanomas from atypical nevi. Journal of Dermatological Science (2020)

15. Wang, H., Naghavi, M., Allen, C., Barber, R.M., Bhatta, Z.A., Carter, A., Casey, D.C., Charlson, F.J., Chen, A.Z., Coates, M.M., et al.: Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249
causes of death, 1980–2015: a systematic analysis for the global burden of disease study 2015. The lancet **388**(10053), 1459–1544 (2016)
16. Yamamoto, N., Sukegawa, S., Kitamura, A., Goto, R., Noda, T., Nakano, K., Takabatake, K., Kawai, H., Nagatsu, H., Kawasaki, K., et al.: Deep learning for osteoporosis classification using hip radiographs and patient clinical covariates. Biomolecules **10**(11), 1534 (2020)
17. Yin, D., Zhao, Y., Wang, Y., Zhao, W., Hu, X.: Auxiliary diagnosis of heterogeneous data of parkinson's disease based on improved convolution neural network. Multimedia Tools and Applications **79**(33), 24199–24224 (2020)
18. Zhang, Y., Wang, S.: Detection of alzheimer’s disease by displacement field and machine learning. PeerJ **3**, e1251 (2015)
19. Zhen, S.h., Cheng, M., Tao, Y.b., Wang, Y.f., Juengpanich, S., Jiang, Z.y., Jiang, Y.k., Yan, Y.y., Lu, W., Lue, J.m., et al.: Deep learning for accurate diagnosis of liver tumor based on magnetic resonance imaging and clinical data. Frontiers in oncology **10**, 680 (2020)