Automatic CNS diseases real-time detection in first-trimester fetal ultrasound image via deep neural networks

nianji zhan[1], Fan Yang[2], Jingyu Ye[1], Dan Wang[3], Ying Yang[1], Sheng Zhao[3], Bin Zou[4], Jieping Song[3], Fang Chen[1], Xinlin Chen[2], Jian Guo[1], and Peiwen Chen[2]

[1]BGI-Shenzhen
[2]Affiliation not available
[3]Hubei Maternal and child Healthcare Hospital
[4]CNGB

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Abstract

Objective This paper proposed the method of real-time detection of CNS diseases using object recognition network that mainly detects abnormal planes in video and evaluates the performance and feasibility of the object recognition network in classifying disease planes. Design Central nervous system cases, random sampling. Setting Prenatal ultrasound images from Maternal and Child Healthcare Hospital, Hubei. Sample A total of 515 fetal with First-trimesters. Methods Compare the three different models was training by the same dataset, including Exencephaly plane, Holoprosencephaly plane, and two normal planes. Main Outcome Measures Compare the F1 scores of other classification networks on the original dataset and the ROI dataset and test the detection speed and accuracy in the real-time video. Results The our model achieved 92% accuracy in the test set, this result is higher than other models in the classification accuracy of the original data and ROI data is 56% and 87%, and can achieve real-time detection and location that to detect the speed of each frame in 0.04 seconds. Conclusions The aim is to detect disease planes of the CNS in real-time. But the model still has deficiencies and lacks confidence in the detection of certain disease levels, when there is the fake shadow in the disease plane, the model can easily detect erroneous results. This is unavoidable to small data sets, and the model also needs to continuously increase non-disease data to reduce the error rate. The results of this article have greatly increased our confidence and are instructive for future work.

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[1]BGI-Shenzhen, Shenzhen 518083, China

[2]Maternal and child Healthcare Hospital, Hubei 430070, China

#Correspondence: Jian Guo, BGI-Shenzhen, Building 11, Beishan Industrial Zone, Yantian District, Shenzhen 518083, China. Tel. +86 15914038192. Email: guojian@genomics.cn; Peiwen Chen. Maternal and Child Health Hospital of Hubei Province. NO.745 Wu LuoRoad, Hongshan District, Wuhan City, Hubei Province,P.R.China,430070. Email: 191287662@qq.com.

*These authors contributed equally.

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Keywords: Prenatal ultrasound, First-trimester, Exencephaly, Holoprosencephaly, Object Recognize

Introduction

As one of the congenital malformations, Central nervous system (CNS) is prone to cause physical defects of the fetus, which brings huge economic burden and mental pressure to the society and family. Previously, obstetric ultrasound examination was used primarily to screen for down syndrome and to perform some routine fetal biometrics, primarily in the mid- trimester (20-24 weeks) and late-trimester (28-32 weeks) for structural abnormalities [1]. In recent years, with the improvement of the resolution of ultrasonic instruments and the improvement of diagnostic techniques, the diagnosis scope is not only limited to the screening of down's syndrome, but also begins to be used for fetal examination in first- trimester (11-13 weeks), such as spine, heart, limbs and nervous system [2].

According to relevant studies, obstetric ultrasound examination and diagnosis of CNS malformations in early pregnancy has a very high value, and 10% to 50% of CNS diseases can be diagnosed in first trimester. To some extent, CNS malformation is one of the main causes of death in children. At present, there are many diagnostic methods for fetal congenital malformations, including villus examination, ultrasonic imaging, amniotic fluid examination, biopsy, magnetic resonance and umbilical cord blood examination. In particular, ultrasonic examination is widely used, and has the advantages of high safety, painless, clear imaging, non-invasive, simple and quick operation. However, the low prevalence of fetal central nervous system abnormalities leads to reduced practice and thus makes most obstetricians less experienced, but ultrasound may improve detection by suggesting guidelines for screening the fetal brain in a systematic manner [3]. In other words, the biggest risk of prenatal ultrasound examination may be misdiagnosis, which is prone to false positive diagnosis of malformation, because the development of fetal CNS is a complex process. During fetal development, the structure of the brain is also changing, making it difficult for ultrasound to accurately identify all structures in the brain.

In 2006, Hinton [4] et al. proposed the deep learning algorithm for the first time, whose goal is to establish a more effective feature classification network through multi-layer convolutional neural network. Since then, the theory of deep learning has been further studied, and the recognition rate and generalization ability of this algorithm are much higher than traditional algorithms. In recent years, a large number of relevant research results have been applied to various aspects of artificial intelligence, such as target tracking, speech recognition, motion posture, facial expression recognition and so on. The research of medical image analysis mainly focuses on classification, detection, segmentation and visualization.

At present, many researchers have done a lot of meaningful work on ultrasound images, and there are many different methods to analyze. Such as, a learning-based approach which combines both 3D and 2D information for automatic and fast fetal face detection from 3D ultrasound volumes[5]. R.Bharath[6] propose a Feature from Accelerated Segment Test (FAST) technique for approximate detection of fetal genitals in ultrasound images. M.Yaqub[7] propose an automatic technique to locate four local fetal brain structures in 3D ultrasound images. Pierre Chatelain [8] propose an automatic segmentation of 3d transcranial ultrasound image of the midbrain using random forest algorithm. Dong Ni [9][10] presents the first solution of automatic localization of fetal abdominal standard plane (FASP) continuous two-dimensional ultrasound image, and he also proposed a hierarchical supervised learning framework for automatic detection of abdomen standard planes from continuous two-dimensional ultrasound images. Sylvia Rueda [11] proposed is to compare and evaluate existing fetal ultrasound image segmentation methods, and make automatic measurements on this basis. Christian F. Baumgartner[12] propose a new method that name is Sononet, which can automatically detect 13 fetal standard views in freehand 2-D ultrasound data as well as provide a localization of the fetal structures via a bounding box. These researchers range from traditional methods to the latest deep learning methods, but they are all based on normal samples being analyzed, and most are conducting retrospective research. At present, most subjects that analyze ultrasound images tend to be classified. Whether it is from 3D data or 2D data, it is hoped that it can replace the manual and help the doctor find the optimal ultrasound screening plane. Therefore, disease analysis based on ultrasound images is the current trend, especially using the currently popular deep learning methods to study.

At present, the analysis of medical imaging diseases is mainly aimed at pathological image[13][14], CT [15], MRI[16] and ultrasound, as well as lesion images of other diseases. At present, ultrasound can screen out Breast Cancer[17], Thyroid Nodule[18][19], Carotid Plaque[20][21] , Colonoscopy[22] and other diseases, all of which are analyzed by deep learning, which can get better diagnosis results than professional clinicians. Very few studies will target prenatal fetal disease screening, and most fetal ultrasound image analysis is limited to normal samples for retrospective research. Xianhua Zeng[23] proposed to automatically generate diagnostic instructions on ultrasound images based on object detection. And Hosuk Ryou[24] propose to use volume data to automate the diagnosis of fetuses in first-trimester. It also proposes a three-dimensional reconstruction and visualization[25][26] of fetal ultrasound, which is helpful for multi-dimensional analysis of ultrasound data.

This paper proposes object recognition network based on One-stage, and can quickly detect video in real time. Based on the reason that the sample collection is too difficult and there are few disease examples. This article uses two diseases for analysis under the advice of experts, including Exencephaly(EX) and Holoprosencephaly (HPE). The cause of Exencephaly is the loss of a skull cap. In sonograms, the typical disease is a change in the shape of the fetal head and a loss of the skull ring. Holoprosencephaly is the most common brain disease, accounting for 50 percent of pregnancies but only 30 percent of births, because most of the affected fetuses die in utero. Therefore, this study attempts to observe fetal CNS in first trimesters by ultrasonography and disease plane, and to establish a screening model for fetal CNS malformation in first trimesters by using deep learning method, so as to provide support for clinicians to diagnose fetal CNS malformation in first-trimesters.

Method

Image data acquisition

The samples of this experiment are all from the Maternal and Child Hospital of Hubei Province. There were

515 samples, including for 104 video and 1492 for images. These data were generated on ultrasonic devices of different brands (Philips, GM, Samsung, Mindray), and there is a possibility that the same patient may have two or more samples due to the generation time. The research was approved by the hospital review board, and each patient was informed about and consented to participate in the study.

Data augmentation: Random rotated and Random scaling

To further expand the image dataset, the original images were random rotated by [-180°, 180°] and random scaling by 50% - 70%. The augment images can also improve the detection performance of the neural network.

Yolo-v3 Network

Yolo-v3[27][28] networks are the third generation of the YOLO series. Compared with the two-stage network, the YOLO network transforms the detection problem into a regression problem, which does not need to set an additional Proposal region, and directly generates the boundary box coordinates and the probability of each class through regression. This greatly improves the detection speed compared to the two-stage network[29].

The network simplifies the two-stage process and solves the classification, coordinate and bounding box problems in one-stage. Loss function is one criterion for evaluating the performance of model. The Loss function in YOLO is defined as follows:

$\mathrm{Loss}_{\mathrm{yolo}} = \mathrm{loss}_{\mathrm{cls}} + \mathrm{loss}_{\mathrm{xy}} + \mathrm{loss}_{\mathrm{wh}} + \mathrm{loss}_{\mathrm{confidence}}(1)$

Except the loss function for $\mathrm{Error}_{\mathrm{wh}}$ is the MSE (Mean Square Error), the other part of the loss function is the Binary Cross Entropy.

In order to improve the detection speed, the network evenly divides each image in the training set into SXS (S = 7) grids. During training, the network detects which grid the center of the target ground truth falls on. Each grid predicts B boundary boxes and their confidence scores, as well as C class conditional probabilities. The definition of confidence is as follows:

$$\mathrm{Confidence} = p_r(Obj) \times \mathrm{IoU}_{\mathrm{pred}}^{\mathrm{truth}}$$

Confidence refers to whether a small region is being used to identify a target and the accuracy of the bounding box that corresponds to that region. If the center of the ground truth is inside the small region, the $p_r(Obj)$ equal to 1, otherwise it is 0. IoU is the proportion of the overlap area between bounding box and ground truth to the total coverage area. In Faster R-CNN, IoU is only used to obtain $p_r(Obj)$, but not really used for regression calculation. In YOLO, IoU participates in regression, so as to obtain more accurate target position.

The model uses the convolutional layer instead of the full connection layer in the output layer.

The methods of batch normalization, high resolution classifier, dimension clustering, direct location prediction, and multi-scale training are also introduced to improve the detection accuracy. Finally, multi-scale prediction is used to detect the final target, the model proposed in this paper predicts bounding boxes at three different scales: 52× 52, 26 × 26, and 13× 13.

It also classifies target categories to provide disease detection, so that small targets can be detected more effectively.

The detection models were trained and tested on an NVIDIA GeForce GTX 1080Ti server. During the training, adjust the input image to 416x416 pixels. Considering the memory limitations of the server, we set the batch size to 16. This model can effectively improve the accuracy and prevent overfitting by using transfer learning. The steps are as follows:

1. The model used pre-training weights to train the parameters of the output layer for 50 Epoch and fixed the parameters of other layers.

2. Un-fixed the parameters of all layers and we use own data for training.

The data set is divided into training, verification, testing according to the ratio of 9:1. The test data using ultrasonic video and non-trainable images, which not been data enhanced. All data is divided according to samples, and there is no crossover in the enhanced image. Table 1 shows the training set and the test set.

For classification problems, samples can be divided into four categories according to the combination of true and predicted categories: true positive (TP), false positive (FP), true negative (TN) and false negative (FN). However, it is necessary to change the calculation method of evaluation criteria for multi-classification model.

$F1 = \frac{2*P_{\text{precision}}*R_{\text{Recall}}}{P_{\text{precision}}+R_{\text{Recall}}}$

For multi-classification models, Macro Average algorithm is used to calculate F1 score. Precision and recall of all categories need to be calculated separately. For each category, P and R are calculated as follows:

$P_{\text{precision}} = \frac{\text{TP}}{TP+FP}$

$$R_{\text{Recall}} = \frac{\text{TP}}{TP+FN}$$

Therefore, the formula of F1 score of the model is to calculate the mean value of F1 score of each N class. The formula is as follows:

$$F1_{\text{All}} = \frac{F1_{cls-1}+F1_{cls-2}+F1_{cls-3}+\ \ +F1_{cls-N}}{N}$$

Another indicator IoU is used to evaluate the accuracy of the final object detection box. The IoU evaluates the performance of the model by calculating the overlap rate between the predicted boundary box and the ground truth boundary box, as shown below:

$$IoU = \frac{S_{\text{overlap}}}{S_{\text{union}}}$$

Where S_{overlap} represents the area of the intersection of the real box and the prediction box, and S_{union} represents the area of the union of the real box and the prediction box.

Comparison of different network

In order to evaluate the performance of our model, we used ResNet50 network[30] and Yolov3 for comparison to verify the superiority of our selected model. In reality, there is a large amount of background information in the detection target, and our main purpose is to be able to recognize the target's disease without changing the background. Therefore, we set up two different methods to analyze Resnet50 model. First, training in the original data set. Second, training the data set of background removal. As shown in figure 1, cut the original image into the area of interest. The two training methods were compared with our model.

Result and Discussion

The F1 score of yolov3 was 0.92, which is higher than the other two models. This indicates that the comprehensive recall performance and recall accuracy of yolov3 model are better than the other two models. Resnet network trained with raw data, because the background area has a lot of irrelevant information, it is easy to learn irrelevant features, which leads to bad results. The use of yolo model can resist the interference of background noise during training and achieve high recognition accuracy. The training area of interest can effectively resist the interference of irrelevant information brought by the background, and can bring better results. But the clinical situation cannot be used, because there will be a lot of irrelevant information on the clinical equipment, and the yolo network perfectly solves the problem of target positioning and classification. Figure 2(a)(b) shows the identification results of the original and enhanced data. No matter what state the target, the model can recognize the target efficiently. The data enhancement causes the background area to change together, which does not occur in reality, but it can simulate the morphological change of our area of interest, thereby increasing different actual situations.

In this paper, the model training uses the method of transfer learning. The transfer knowledge comes from the coco dataset, which is a natural image database commonly used in competitions. It is not excluded that using knowledge of natural images to learn medical images will have any impact, but without using this pre-training weight, the results obtained are very bad. Jiajun liang[31] proposed to use the pre-training weight of the placenta in the mid-trimester to migrate to the fetal plane classification, but the effect is not very significant.

Select the best model to display the test data results, as shown in Table 2b. The precision of the model is closed to 98%, which is a relatively good result for disease detection. Because of the high precision, the rate of misdiagnosis can be reduced. But we must also ensure that the model has good recall to each disease. The low recall (88%) of the model is mainly the low recognition rate of the NSP. Figure 2(c) shows the confusion matrix of the test set, there is a category of 'None' in the Figure 2(c), which means that the model does not detect anything. This is a situation that exists in target detection. The reason for the existence of 'none' is mainly because the number of NSPs is too small. As a counter-example in the model, which is also a normal plane, NSP and NAP are used to test the model's ability to detect disease, increase the difficulty of detection for the model, and make the model more convincing. It can be seen that only a few disease planes have not been detected, and I think that it is inevitable on the current small data set. If the training set can be increased in the future, the missed detection rate can be reduced. Because the test data does not appear in the training data, and from the data of the missed inspection, it is basically the image of the same sample, which also shows that the model lacks the learning of some image form. Therefore, it is necessary to increase the diversity of data in the future and improve the generalization ability of the model.

Dynamic video detection

In reality, prenatal ultrasound imaging is a dynamic process. Different fetuses will produce different data from different angles, so enhancing the data can effectively improve the generalization ability of the model. This chapter will simulate the clinical scenario and evaluate the recognition effect of the model in dynamic data. Dynamic data is a time series composed of multiple two-dimensional images, called a frame. In other words, what we need the model to do is recognize all the frames in a Dynamic data。

The dynamic data in our experiment does not participate in the training, so the generalization ability of the model can be tested in the test. To better evaluate the model's results for dynamic data, we assume that there is only one disease in a dynamic video. We determine the type of dynamic data by counting the predictive labels for all frames of the dynamic data. This is to explain our ability to detect video. In fact, the application scenario is to locate the ROI of the disease in real time and give a prediction label. Due to the prediction error, we chose the most frames of the same category as the prediction label of the video, as shown as Figure 3(a). Both samples are Ex, showing the statistical value of the prediction label of each frame, and showing the proportion of each frame of the video.

In clinical practice, normal samples contain only standard plane images, which are used as part of the medical record. Since this study is a retrospective research, dynamic videos are all disease samples. In this study, there were 76 videos included exencephaly and 28 videos with HPE. As shown in Table-2c-I and Figure 3(b) show the results of the video classification by the model. It can be seen that there are a few video classifications error. Misclassified videos actually contain very few frames that are GT, accounting for less than 10% of all frames. In fact, this is unreasonable, because in the actual situation, the disease should occupy the most frames. But these videos are not predicted as "normal" tags. The reason is that the model has a low false positive rate, but to reduce the false positive rate, the model also needs to increase the data diversity. Don't pay attention to the inevitable data problem. In other words, there will be incredible morphological changes and fake shadow caused by ultrasound, because the video is a continuous two-dimensional image. Because ultrasound images have too many shadows, it is difficult to control the quality of the image, which is one of the main obstacles to research fetal ultrasound. The YOLO model has always been based on fast detection speed, so in this article, it can achieve an average detection speed of 4.76 seconds per sample. The detection speed of each frame is close to 0.04 seconds. This is very fast and can be satisfied with the actual situation.

Conclusion

In prenatal diagnosis, CNS diseases can be detected early in pregnancy, so as to reduce the damage to the fetus, but also to reduce the social burden of a method. Inexperienced doctors are prone to misjudgments, depending on medical conditions. So, we propose object recognition network to assist in the diagnosis of CNS in first trimesters. The goal is to detect diseases of the CNS in real time. The model has obtained reliable experimental results on the constructed ultrasonic image data set. The object detection model achieved 92% F1 scores in the disease test set, and can achieve real-time detection and location that to detect the speed of each frame in 0.04 seconds. But the model still has deficiencies and lacks confidence in the detection of certain disease levels, when there is fake shadow in the disease plane, the model can easily detect erroneous results. This is unavoidable to small data sets, and the model also needs to continuously increase non-disease data to reduce the error rate. The results of this article have greatly increased our confidence and are instructive for future work.

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Disclosure of Interests

The authors declare that they have no competing interests

Contribution to Authorship

P.W.C., J.G., X.L.C., F.C. initiated this project. F.Y., D.W., S.Z., J.P.S., X.L.C., N.J.Z and Y.Y. made the diagnosis, acquired the data and labeled the data. N.J.Z., J.Y.Y., B.Z. and J.G. performed the experiments and analyzed the data and the results. N.J.Z. wrote the paper. All authors reviewed the manuscript.

Details of Ethics Approval

The procedures of the study received ethics approval on 11.01.2018 from the institutional review board of BGI (No. BGI-IRB 17039).

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