sciendo

ISSN 1335-8871

MEASUREMENT SCIENCE REVIEW

Journal homepage: https://content.sciendo.com

Deep Learning Measurement Model to Segment the Nuchal Translucency Region for the Early Identification of Down Syndrome

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Abstract: Down syndrome (DS) or Trisomy 21 is a genetic disorder that causes intellectual and mental disability in fetuses. The most essential marker for detecting DS during the first trimester of pregnancy is nuchal translucency (NT). Effective segmentation of the NT contour from the ultrasound (US) images becomes challenging due to the presence of speckle noise and weak edges. This study presents a Convolutional Neural Network (CNN) based SegNet model using a Visual Geometry Group (VGG-16) for semantically segmenting the NT region from the US fetal images and providing a fast and affordable diagnosis during the early stages of gestation. A transfer learning approach using AlexNet is implemented to train the NT segmented regions for the identification of DS. The proposed model achieved a Jaccard index of 0.96 and classification accuracy of 91.7 %, sensitivity of 85.7 %, and a Receiver operating characteristic (ROC) of 0.95.

Keywords: Fetus, Down syndrome, Nuchal translucency, Deep neural network, convolution, SegNet.

1. Introduction

Down syndrome (DS) is a genetic disorder [1] that cannot be prevented but can be detected early in pregnancy. Women of a higher maternal age are more likely to have DS. Ultrasound (US) Imaging is preferred over other modalities because of it is safe, economical, and non-invasive nature. DS [2] is examined using screening and diagnostic tests. Amniocentesis & Chorionic Villi Sampling are the two diagnostic tests performed to detect DS. Although these tests produce a high detection rate, they also carry the risk of miscarriage and fetal injury. The screening test includes a blood test such as Beta Human Chorionic Gonadotropin (Beta-HCG) and Pregnancy Associated Plasma Protein (Papp-A) as well as a US examination. These blood tests are frequently used in conjunction with the US to look for "markers" that can indicate the presence of DS. Nuchal Translucency (NT) is the most significant marker for detecting DS early in pregnancy (11-14th weeks). NT [3] refers to a fluid deposit beneath the fetal skin. It is a black area that lies between the two bright NT boundaries.

According to research findings [4], [5], increased fetal NT thickness (>3 mm) is associated with an increased risk of DS. The mid-sagittal plane is used to calibrate NT [6], and the broadest region of the translucency is used for measurement. NT [7] is calculated manually by the clinicians using an electronic caliper. This measurement is operator dependent and prone to error. As NT is of small size [8], [9], a slight variation caused in the estimation leads to an incorrect assessment of the fetus. Thus, computerized methods [10], [11] are proposed to overcome the problems faced in manual measurements and to provide a better detection rate.

Giuseppa et al. [12] devised an automated method for determining the thickness of NT. This method employs wavelet and multi-resolution analysis to assist clinicians in predicting DS in the early stages of gestation. Lee et al. [13] presented a method for locating NT edges and accurately measuring their thickness. This method emphasized the semi-automatic method, in which the NT boundary is highlighted with a diffusion filter and its thickness is calibrated with dynamic programming. Using wavelet analysis and neural networks, Sciortino et al. [3] proposed a non-supervised method for tracing and calibrating the thickness of NT. For accurate NT estimation, the fetal position should be in the mid-sagittal region.

Measurement of NT is an important step in computer-aided diagnosis (CAD) for early detection of DS. Conventional segmentation methods face a lot of challenges like fuzzy edges, Intensity homogeneity, more time consumption, and

DOI: 10.2478/msr-2022-0023

high probability error in extracting the NT region. Automatic detection of DS would resolve these obstacles and provide a fast and better diagnosis of the fetus. Deep learning (DL) [14] is a useful technique for constructing networks that can effectively mimic higher-order systems and achieve human-like performance. DL is an effective approach for segmenting complex medical images. DL-based methods can learn efficient traits directly from the datasets. Especially, the development [15] of the Convolutional Neural Network (CNN) has further enhanced the state-of-the-art in semantic segmentation of medical datasets. CNN [16] has proven to perform exceptionally well for image segmentation and classification tasks. The Semantic Segmentation model (SegNet) [17], [18] is the well-known CNN architecture for image segmentation and it is computationally efficient and developed for pixel-wise semantic segmentation. Image classification plays a significant task to classify the disease by learning its feature from the Segmented model.

Kei Otsuka [24] presented a transfer learning-based technique for segmenting medical images using SegNet. The SegNet algorithm classified the images of trained blood smears into three categories: background, blood parasites, and blood cells. Thus, SegNet model will significantly boost the performance of image recognition, segmentation, and categorization in the area of computer vision.

This study proposes a novel methodology for semantic segmentation of NT and categorization of DS in the early stages of pregnancy using CNN architecture.

SUBJECT & METHODS

A. Details of subjects

The US fetal image was provided by the Mediscan Fetal care Research Foundation, Chennai, India. The dataset contained images of 100 fetuses between 11-14 weeks of gestation. There were 50 healthy and 50 DS fetuses in the database. The size of the image is 1136x852. The protocol [23] for accurate measurement of NT was outlined by the Fetal Medicine Foundation (FMF). The dataset also has information on the Crown Rump Length and maternal age which was measured by the clinician as shown in Table 1.

Table.1. Patient's clinical information.

Characteristics	Healthy	DS
Number	50	50
Average Maternal age	27.368 (Range 20-28 yrs)	29.710 (Range 28-40 yrs)
Average Crown Rump length (mm)	65.657 (Range 52-84 mm)	69.421 (Range 54-84 mm)
Gestational weeks	11-14th	11-14th

B. Schematic flow of the method

The schematic flow of the methods for detecting DS is explained below in Fig.1.

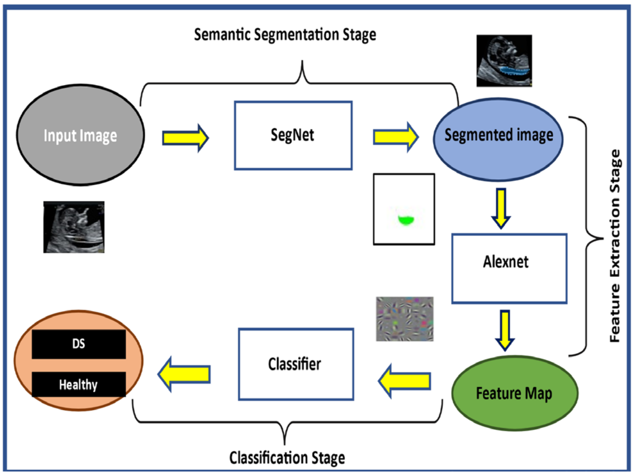

Fig.1. Schematic of the presented model.

C. Data pre-processing

US Images are prone to inherent noise, poor quality, and size variation. Speckle [20] is the granular noise observed in the US images which degrade the quality of the active images. Image processing is a primary step to extract useful details from the images by removing noise and distorted pixels. The US images are subjected to pre-processing techniques such as filtering and resizing. Filtering [21] reduces noise, enhances the image, and preserves fine edge features. The filtration of an image is accomplished using a wiener filter as shown in Fig.2.a). The images are then transformed to grayscale and resized before being given to the system as input. As a result, the pre-processing method aids in normalizing all images so that they are independent of their origin and the image size influence on system performance is avoided.

D. Semantic segmentation using DL model

Segmentation of the NT region from US fetal images is an important step for the early identification of DS. This model is built on SegNet, which is one of the most widely used DL architectures. SegNet [17], [22] is a semantic segmentation model for pixel-wise image segmentation and classification. The SegNet model semantically segments the selected region of interest and categorizes the images into two grades. SegNet is also known as binary [23] segmentors to distinguish the classes.

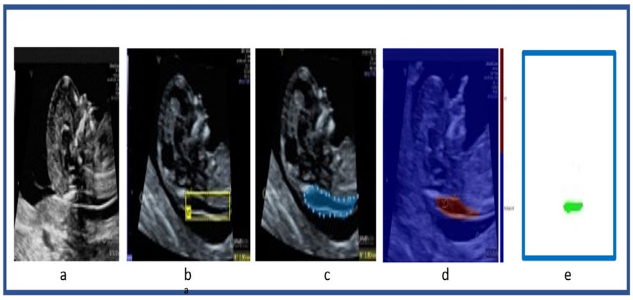

Fig.2. Definition of labeling. a) speckle free image b) selection of NT region c) Manual labeling of an NT area using Pixel labeler d) pixel labeled images e) Final segmented output.

The network architecture of SegNet is shown in Fig.3. and explained as follows:

i. Encoder, decoder network, and a pixel-wise classification layer are the main components of Semantic segmentation.
ii. SegNet consists of 13 convolutional layers of Visual Geometric Group (VGG-16) and the depth of the encoder-decoder is 5 as seen in Fig.4.
iii. The layers of the encoder network include convolution layers of 64 filters, the dimension of each is 3×3, along with batch normalization and a Rectified Linear Unit (ReLU) non-linearity, then performs max-pooling 2×2 window stride size 2 to the result, while storing the indices of values extracted from each feature map.
iv. The decoder creates the target mask by using the pooling indices from the max-pooling of the corresponding encoder.
v. The last decoder output feature maps are given to a soft-max layer to classify the pixels according to their classes. Replaced the Fully Connected (FC) layers with Conv layers of semantic segmentation.

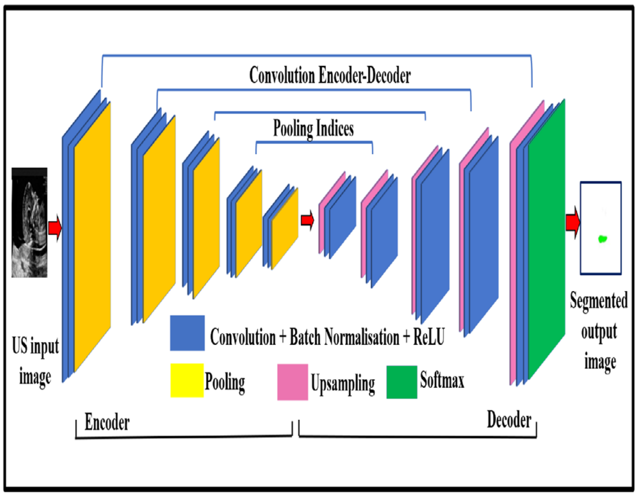

Fig.3. Layout of the SegNet architecture.

The layers of the encoder are very similar to VGG-16 convolution layers [24]. The input size of SegNet is 300×300×3, with 64 convolution filters of size 3×3 are used to convolve the input with a stride [1 1] and padding [1 1 1 1], to extract the feature map. It is also followed by the batch normalization layer to normalize the third dimension and ReLU is used to convert the negative value to zeros. The first layer has a convolutional layer, normalization layer and, ReLU layer along with a max-pooling layer of 2×2 windows and a stride of 2 to downsample the feature map. The second convolution layer uses the same filter size and reduces the dimensions to 128. The third convolution layer is further downsampled to 256 using max pooling. The fourth convolution layer is further downsampled to 512. The fifth convolution layer is downsampled to 512. The segmentation mask is developed by using the pooling indices from the max-pooling of the corresponding encoder. The output of the last decoder is loaded into the classification layer (Softmax layer) to classify the pixel. The SoftMax layer classifies the image into two classes: NT and background.

The proposed methodology uses semantic segmentation to segment and classifies every pixel in a US image as seen in Fig.2.b). This model prepares pixel label data for training, creating, and assessing the VGG-16 based SegNet into-NT and background. Before the training phase, each pixel is labeled/annotated as either NT or background as shown in Fig.2.c). Every pixel belonging to the NT will take the value 0. On the other hand, pixels in the background will take the value 255 as shown in Fig.2.d). Both the US fetal images and their corresponding segmented ground truth labels are used as input to train the VGG-16 based SegNet model.

This method solves handcrafted problems and achieves better results. Thus, the proposed method trains and assesses a VGG-16-based SegNet to segment the NT region from the US images for the early identification of DS as shown in Fig.2.e). The architecture layout involved in our model is shown in Fig.4.

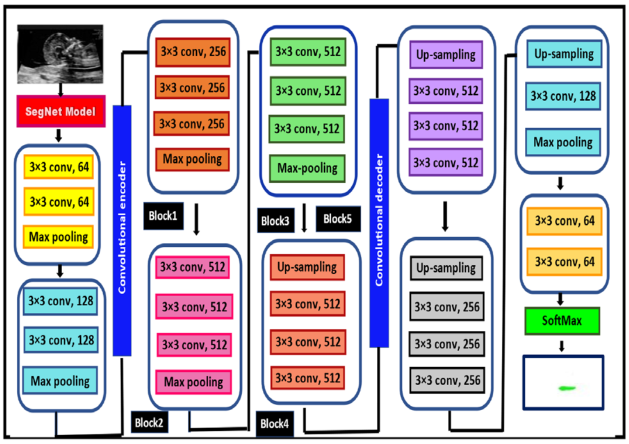

Fig.4. Layers of VGG 16 based SegNet.

E. Deep learning training network of SegNet

The input images are resized to 300×300 to minimize the time required for training and memory consumption. The class weights are calibrated using median frequency balancing and delivered to the pixel classification layer to formulate a weighted cross-entropy loss function. The stochastic gradient descent with momentum (SGDM) is used as an optimization algorithm for training the network. The network training parameters are tabulated in Table 2.

Table 2. Training parameters of SegNet.

Parameter	Value
Probability	0.5
Initial Learning rate	0.001
Epoch	5
Cross- entropy	Loss function
Optimizer	SGDM

F. Quality metrics of segmentation

The performance of SegNet is evaluated using these measures.

i. *Global accuracy*: The percentage of pixels correctly categorized in the dataset is measured by global accuracy, it is necessary to obtain high global accuracy which yields overall smooth segmentation.

ii. *Mean intersection over union (mIoU)*: it is also referred to as Jaccard Index. The mIoU of the image is computed for multi-class segmentation by averaging the IoU of each class. The mIoU score ranges from 0 to 1, with higher values indicating a better result. The mathematical expression between boundaries X and Y is as shown in (1).

$$J\,(X, Y) = \frac{X \cap Y}{X \cup Y}. \tag{1}$$

G. Image categorization using CNN

i. *Network architecture*: Deep learning-based classification approach using AlexNet is proposed for the early detection of DS. AlexNet is made up of five convolutional layers, three sub-sampling layers, and three fully-connected layers. In this method, the semantically segmented NT images are annotated and loaded into the AlexNet model. The segmented NT image is then trained using the AlexNet model to categorize the images into two classes DS and healthy fetus as shown in Fig.5. Convolution layers consists of kernels or filters to compute convolution operations. These convolution operations are performed by moving the kernels over the inputs in steps called strides. For each kernel, a multiplication operation was executed between the input and the kernel with the bias summed to the result. The convolved results produce the feature map. The feature map is sent to an activation function to provide input for the subsequent layers. The property vectors obtained from the convolution and pooling layers are fed to the FC classification layer.

ii. *Pre-processing*: To ease our classification, images are resized to the desired size 224×224 as required for our deep learning architecture. The dataset is augmented for faster resizing and transformation/combination to alter the dataset. The input images are resized to reduce the training time and also for memory requirement.

iii. T*raining & testing*: The networks are trained using the 'MaxEpochs' as 5, mini-batch size of 128, and Adaptive Descent with momentum (ADAM) stochastic optimizer was used for fast convergence rate compared to other optimizers. The proposed model is tested and, the result is achieved in terms of Area Under the Curve (AUC) and overall accuracy. This would support the clinicians in providing valuable second opinions and also assist them in screening DS without user intervention.

iv. *Performance evaluation*: The following metrics were used to study the performance of the architecture. The confusion metric computes the overall performance of the model in terms of sensitivity, specificity, precision, and accuracy. The Receiver operating characteristic (ROC) graph illustrates the relationship between false and true positive rates (FPR & TPR) for the classification problem. The True Positive (TP) indicates the occurrence of the accurately classified healthy images and the True Negative (TN) indicate the accurately classified DS images. The False Positive (FP) and True Negative (TN) indicates the DS are wrongly categorized as healthy and healthy NT images categorized as DS. AUC-ROC graph value must lie between 0-1.

Sensitivity = TP / (TP + FN).
Specificity = TN / (TN + FP).
Positive Predictive Value = TP / (TP + FP).
Negative Predictive Value = TN / (TN + FN).

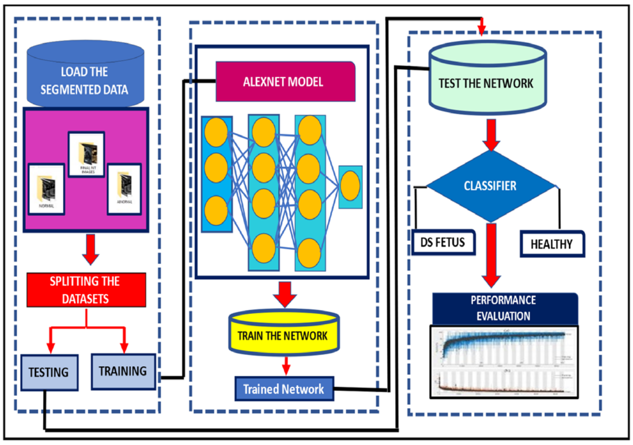

Fig.5. Process flow classification.

RESULTS

i. Seg*mentation*: In this study, we introduced a Deep Learning-based technique for automatically segmenting the NT region. A semantic segmentation network using the VGG-16 model was implemented to segment the NT region. The performance of the network was tested on 50 DS and 50 healthy fetuses. SegNet model performed exceptionally well and achieved an accuracy of 0.9818 and Jaccard index to 0.96

ii. *Classification*: The segmented NT images were further trained using the AlexNet model to distinguish between the DS and the heathy fetus. The performance of the Image classification model was evaluated using a confusion matrix and achieved overall 91.7 % accuracy, 85.7 % specificity, and 100 % sensitivity as displayed in Table 3. The AUC- ROC curve predicted value is 0.95. The proposed method would potentially be helpful for clinicians in the classification of DS.

Table 3. Performance evaluation of the classification model.

	DS	Healthy	
DS	41.7 %(TP)	0 % (FN)	100 % sensitivity
Heathy	8.3 % (FP)	50 % (TN)	85.7 % Specificity
	83.3 % Precision	100 % Negative Predictive	91.7 % Accuracy

DISCUSSION

This study proposed a DL model for the automated detection of the DS. The segmentation of NT from the US image is a crucial step in detecting DS. Manual Selection of NT is difficult and leads to erroneous estimation. Traditional NT segmentation methods face issues with weak edges and other artifacts. They are also are subject to border leakage because of their discontinuous intensities in the NT contour and speckle noise. These problems are resolved in this proposed approach by using DL techniques.

The proposed methodology efficiently segmented the NT contour using SegNet architecture and achieved high accuracy. The AlexNet model was then used to train the segmented NT feature to categorize the images into DS and Healthy fetus. It was trained and tested on 100 US fetal images. This classification model performed well and produced favorable outcomes. This would ultimately provide a second opinion to physicians and assist them in predicting the syndrome at the early stage of gestation.

Automatic analysis of US fetal images faces similar challenges in detecting DS and remains a significant research subject. There are a few shortcomings in this model; they include a prominent Collection of medical images and obtaining labeled data from experts is a tedious process and time-consuming. The limited availability of datasets is one of the major drawbacks of Deep Learning. In the future, Unsupervised learning can be investigated to classify DS. Further advancement in this field would certainly be a boon to the physicians for early prediction. As a result, we reported an automatic segmentation and classification of DS using DL in our study.

The limited availability of datasets is one of the major drawbacks of Deep Learning. Our reported network was based on transfer learning, learns from a small dataset, and still demonstrates superior performance for the detection of DS. This automatic detection of DS using Deep Learning overcomes the problems of variability and reproducibility. This methodology is simple, consumes less time, and further improves the detection rate of DS. This will also support the physician both to identify automatically the NT region and classify the syndrome at the early stage. This makes the whole process is non-invasive, easier for the operator, and, at the same time, more robust by removing the issue of intra-observer and inter-observer Thus, this automated system is capable of detecting the NT from US images and classifies DS effectively.

CONCLUSION

In this paper, we developed a novel methodology using DL for the early diagnosis of DS. Fetal US images were pre-processed to remove the speckle noise and resized for faster computation. The contours of NT were semantically segmented from US fetal images using VGG-16 based SegNet architecture and effectively classified using AlexNet Model. Thus, the CAD will certainly be a great tool for clinicians in screening for DS, enhances the detection rate, and provides a valuable second opinion for early diagnosis of DS. This technology helps to identify the individuals who are at higher risk for this condition and allows termination at the early stages of gestation.

ACKNOWLEDGMENT

The authors would like to extend their sincere thanks to Dr. Suresh, MEDISCAN Fetal Care Research Foundation, Chennai for providing us with the datasets required for the research work, we are also grateful to Dr. Mala Raj, Gynecologist, and Dr. Gayathri, consultant sonologist, Firm Hospitals for their constant support and guidance

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Received November 22, 2021
Accepted April 19, 2022