Deep Learning-Based Lesion Segmentation in Paediatric Epilepsy

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ABSTRACT

In this research, our goal is to implement a Convolutional Neural Network (CNN) to segment Focal Cortical Dysplasia (FCD). FCD is a common lesion responsible for paediatric medically intractable focal epilepsy. MRI features of FCD can be subtle and may be missed by a radiologist. Recent advances in deep learning techniques in different fields have motivated us to develop a deep learning-based model to detect and segment the lesion responsible for FCD. We proposed a Fully Convolutional Network (FCN) for the task of FCD detection and localization. Our proposed model has four blocks of two convolutional layers followed by a pooling layer, as feature extraction part. Then, we have added three up-sampling blocks which include one convolutional layer and one up-sampling layer. The convolutional layers' kernels are 3×3 and we are utilizing $4x$ and $2x$ upsampling layers in the decoder part. We are using skip layers as well, to get a more refined up-sampled output. We are adding the respective down-sampled feature map from the encoder part. To train and evaluate the model leave-one-out technique has been utilized where one test subject is left out of training in each experiment. We have identified 13 out 13 healthy subjects as healthy. The model has identified the lesion in 15 out of 17 MR-positive FCD subjects with 73 percent lesion coverage. For MR-negative cases, 11 out of 13 subjects were identified with lesion coverage of 64 percent. Based on our experiments, FCN holds the potential to assist specialists in detecting and localizing the lesion.

Keywords: Epilepsy, Focal Cortical Dysplasia (FCD), Fully Convolutional Network (FCN), Segmentation, Magnetic Resonance Imaging (MRI)

1. INTRODUCTION

Paediatric epilepsy has devastating consequences on children's quality of life. It is one of the most common neurological disorders in children.[1,2] Drug-resistant epilepsy is a specific type of neurological disorder, which can lead to detrimental effects on children's cognition and psychosocial development.[3–5] Surgical treatment with complete resection of the lesion responsible for medically intractable epilepsy may be the only treatment option to achieve seizure-free outcome for these patients.[6,7] In case of surgery, a precise pre-surgery evaluation of the lesion and its location is critical where Magnetic Resonance Imaging (MRI) plays an essential role. One of the lesions responsible for paediatric epilepsy is Focal Cortical Dysplasia (FCD).

As mentioned FCD is one of the most common lesions responsible for drug-resistant epilepsy specially in children. The MRI features of FCD are frequently subtle and may not be detected by visual assessment. The detection of a lesion on MRI varies in the literature and range from 30% to 85% of patients with drug-resistant epilepsy.[8] Epileptic patients with normal MRI are considered to have MR-negative focal epilepsy (also known as non-lesional epilepsy or cryptogenic epilepsy or MRI-occult epilepsy). Up to 72% of patients with MR-negative epilepsy have FCD reported on histopathology.[9–13] Patients who have MR-negative epilepsy have poorer seizure-free epilepsy surgery outcome,[14] and may have increased use of invasive electroencephalography (EEG) monitoring for surgical planning. Therefore, it is critical to improve our ability to detect FCD, as discovering a previously undetected lesion can increase the success of surgery in curing focal drug-resistant epilepsy, and change pre-surgical planning of epilepsy surgery. Visual assessment of MRI is subjective and highly dependent on the expertise of the observer. Thus there is a need for a more advanced and objective tool for analyzing

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the MRI data to improve detection of FCD. Machine learning algorithms offer the potential to detect subtle structural changes, which may not be identifiable on visual inspection of MRI.

Recently, Deep Neural Networks (DNN) have emerged and been successful in many fields, such as computer vision and natural language processing.[15,16] Deep neural network methods also have been applied in various fields of medicine, including identifying lesions on medical imaging.[17] In general, DNN works on vector shaped inputs, however a more specific type of these models has been proposed to work on images as input and learn kernels or filters in order to extract features, then performs classification or regression to get the desired output. These deep networks are called "Convolutional Neural Networks (CNN)".[18]

In this study, we apply a slightly modified CNN known as Fully Convolutional Network (FCN). FCN takes an input image and produces the same size output, and it is used in the image-to-image translation problems such as segmentation. We will implement and train an FCN which takes MRI slices and generates a segmentation map indicating the location of the FCD lesion. We will use peadiatric T1 MRIs to train and evaluate the proposed FCN.

2. LITERATURE REVIEW

Due to the importance of FCD detection for pre-surgery evaluation, numerous works[19–27] have been proposed to help neuroradiologists. There is a few studies[19,24,27] concentrated on paediatric FCD detection.

Most of mentioned studies are based on extracting MRI features which are fed into a classifier, including voxel-based morphometric analysis[20,21] or surface-based algorithms to detect FCD.[22–24,27,28] Most common features of FCD extracted and utilized in these algorithms are cortical thickness, gray-white junction, sulcal depth, and cortical fold. A challenging part of these approaches is the time-intensive task of feature extraction which requires domain experts. Also, the feature construction part includes several data processing steps where errors in processing are propagated throughout the algorithm. We have chosen state-of-the-art deep learning approach using CNN to overcome some of the limitations of classical computer aided tools to identify FCD, which does not require feature extraction and could learn optimal features automatically without human intervention.

More recently, a few studies have utilized deep learning approaches to detect FCD.[25,26,29–31] Wang et al.[30] have used patch-wise CNN which uses five convolutional layers and one max pooling layer as feature extraction part and two fully connected layers to identify FCD, and found that their model successfully classified 9 out of 10 FCD cases. These studies have used CNN to classify subjects as lesional or non-lesional but have not evaluated the performance of CNN for localizing the lesion. Feng et al.[29] have used CNN with two convolutional layers, two pooling layers and two fully connected layers. The authors reported subject-wise recall or detection rate of 83% to 100%, and dice coefficient of 53% to 71% for localizing FCD. Aminpour et al.[19] proposed a whole slice and patch-wise network applied on T1 MRI slices and patches. The patch-wise network has three blocks of three convolutional layers followed by three fully connected layers. The authors have reported sensitivity of 100% for MR-positive cases and 85% for MR-negative cases.

Gill et al.[26] trained two networks on three dimensional patches extracted from T1 and FLAIR MRI data from a single site and evaluated on independent data from seven sites. Two networks have similar architecture, consisting of three blocks of convolution and max-pooling layers with 48, 96 and 2 feature channels and $3 \times 3 \times 3$ kernels. The first network is trained to recognize lesional voxels and the second network is trained to reduce the number of misclassified voxels. The authors found that the classifier showed excellent sensitivity (91%, 61/67 lesions detected) and specificity (95%, no findings in 36/38 healthy controls). Later in 2019, David et al.[25] have combined conditional generative adversarial networks (cGAN) with a CNN and showed that the addition of cGAN to CNN can improve the sensitivity of subject-wise classification from 81% to 93%, and the specificity from 71% to 96%. Previous publications based on CNN to detect FCD have been applied to adults or mixed adults and pediatric populations.

3. METHODS

Here in this research, we proposed a FCN for the task of FCD detection and segmentation. A CNN normally consists of two parts: 1) a feature extraction (encoder) part where it consists of convolutional layers along with

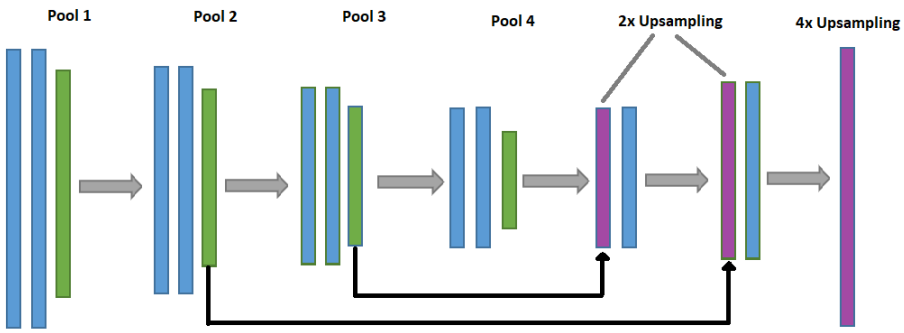

Figure 1. Two-dimensional whole-slice FCN architecture, blue rectangles are 3×3 convolutional layers, and green ones are pooling layers, purple rectangles are up-sampling layers. The black arrows represents the skip connections from pooling layers to the up-sampling layers.

downsampling layers; 2) the classification part, which is a stack of fully connected layers. However, in an FCN, the classification part is removed and replaced by an up-sampling (decoder) component.

Our network architecture is inspired by our previous lesion localization project using patch-based CNN[19] . The proposed architecture is the feature extraction part of whole slice network followed by a decoder instead of the fully connected layers. For the feature extraction part, we have four blocks of two convolutional layers followed by one Max-pooling layer. The kernels in convolutional layers are 3×3 and in pooling layers are 2×2. We apply batch normalization and ReLu activation function at the end of each convolution layer. Then, we added three up-sampling blocks which have one convolutional layer and one up-sampling layer. The convolutional layers' kernels are 3×3 and we are utilizing $4x$ and $2x$ upsampling layers to upsample the feature maps to the original size. Also, we are using skip layers, where a more refined upsampled output is constructed by adding the respective down-sampled feature map from the encoder part. Skip connection will improve the up-sampled output at each step which results in a more refined and detailed lesion segmentation. The segmentation network architecture is presented in Figure 1.

The data is presented in form of slices extracted from the MRI volumes. For each slice, we have a same size mask where the lesion is outlined by a neuroradiologist. The goal is to train models weights in order to produce the same segmentation mask for a test subject. In our early experiments, we realized that our model tends to over-fit toward the healthy pixels as the result of the smaller lesion sizes compared to healthy tissue. To overcome this problem, we sampled the number of healthy slices to match the number of lesional slices. The sampling process is random; however, it is weighted toward slices, which contain more brain tissue pixels.

The training and evaluation are done through leave-one-out technique. We are using all of the subjects except one subject as the training set and test our model on the subject that was left-out. The training and evaluation is repeated for each subject separately. The final results are reported as averaged over all the experiments. We are using Adam optimizer and cross-entropy loss function. We also apply dropout to avoid overfitting during training.

Our dataset contains T1 MRI volumes of paediatric subjects. It includes 17 FCD diagnosed MR-positive subjects, 13 MR-Negative cases and 13 healthy controls. MR-positive subjects refer to cases where traces of the lesion is identifiable in the subjects MRI and the MR-negative are cases with normal MRI. Each subject is classified as FCD if the model predicts at least one pixel as FCD. Then for the FCD predicted subjects we are reporting the region of interest's intersection (dice coefficient) with the ground truth.

4. RESULTS

To evaluate the performance of our model, we computed the number of subjects who were correctly classified by the model as well as the number of mis-classified subjects (Table 1) and then evaluated subjectwise sensitivity and subjectwise specificity. Then, we performed the same processes at pixel level to evaluate the segmentation output and compute lesional sensitivity and lesional specificity. Subjectwise sensitivity is the number of all FCD

Table 1. Confusion Matrix

		Actual	
		1-Positive	2-Negative
Prediction	1-Positive	TP	FP
	2-Negative	FN	TN

subjects correctly classified (true positive) divided by the total number of FCD subjects. Subjectwise specificity is the count of all control subjects in which no lesion is identified (true negative) divided by the total number of control subjects. Here are the definitions of sensitivity and specificity,

$$Sensitivity = \frac{TP}{TP + FN},$$

$$Specificity = \frac{TN}{TN + FP}.$$

In our experiments, we have labelled a subject as FCD using a ratio of FCD predicted pixels over healthy pixels. If this ratio is larger than one percent, we classify the subject as FCD, otherwise it is considered as healthy. Lesional sensitivity is measured as the sum of all FCD pixels labelled correctly by the model divided by the total number lesional pixels in the ground truth masks. Lesional specificity is the sum of healthy tissue pixels in FCD subjects classified as normal divided by the total number of non-lesional pixels for FCD subjects. Lesional sensitivity and lesional specificity will only be calculated for subjects which the model labelled as FCD individually and the final results were averaged over all subjects.

The collected data needed a few steps of preprocessing to make it ready for training our network. First we converted the volume file formats from DICOM to a more accessible NIFTI data type where it is used by most analysis software. Then a brain extraction step is done using the BET (Brain Extraction Tool) algorithm proposed by Smith et al. in 2002.[32] Since CNN is sensitive to the input size, we had to resize every slice in our data to a standard size. Because of the medical data nature we avoided stretching or compressing the images. Instead, we zero-padded the smaller slices while cutting background/air part of the larger slices to a size of 400 $\times$ 300. At the end, 'clean' data was presented to a neuroradiologist to segment the lesion in FCD subjects, which is used as ground truth in our training and evaluation.

The results are presented in Table 2. We successfully identified 13 out of 13 healthy control cases. In the case of the FCD subjects, the model was successful in classifying 15 of the MR-Positive cases, but failed to classify 2 subjects. In the 15 FCD labelled subjects, the model localized the lesion with an average coverage of 73 percent. We detected the lesion in 11 out of 13 MR-negative cases while localizing the lesion in the detected subject with an average coverage of 64 percent. The networks output is presented in Figure 2. Advantage of a segmentation models over patch based models[19] for localization is that in a segmentation mask, the predicted lesion location is going to be precise. However in a patch based model we will end up with an oversegmented output where a large area of healthy tissues will be labelled as lesional.

Conclusion

We discussed the problem of FCD detection and segmentation in paediatric patients. To overcome epilepsy in medically intractable cases a pre-surgery lesion detection by a radiologist is necessary. Hence, we set to develop a method based on deep learning techniques in order to help guide neuroradiologists to review this area of

Table 2. Whole-slice FCN results.

	MR-Positive	MR-Negative
Subject-wise Sensitivity	88	85
Subject-wise Specificity	100	100
Lesional Sensitivity	73	64
Lesional Specificity	99	100

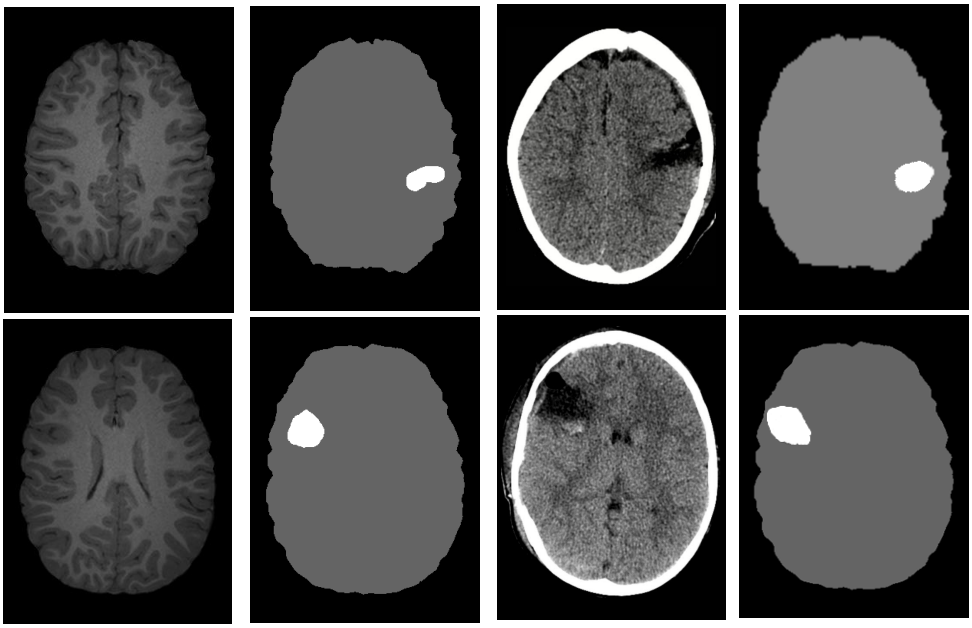

Figure 2. Whole-slice FCN output, the first column is the input slice, second column is the ground truth mask, third column is the post surgical CT scans and fourth column is the whole-slice FCN's prediction.

abnormality, and correlate the findings with the epileptogenic zone based on EEG and other functional imaging. We applied an FCN on MRI slices to segment the responsible lesion in FCD subjects. Our model successfully classified all healthy patients (13 out of 13). We identified the lesion in 15 out of 17 MR-positive subjects with a lesion coverage of 73 percent and for the MR-negative subjects, we correctly identified 11 out of 13 subjects with lesion coverage of 64 percent. These findings indicate that FCN is a promising tool to classify subtle FCD in children with focal epilepsy.

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