CNN-based MRI Regression Using U-Net

Changhee HAN[1,a)]   Florian GESSER[2,b)]   Zoltán Ádám MILACSKI[3,c)]

1.   Introduction

How can we detect dysfunction in brain such as cancer and bleeding using MRI images? In this paper, we address regressing MRI tomographic slices to detect brain dysfunction by Convolutional Neural Network (CNN)—which would lead to saving a tremendous number of potential patients clinically. In medical imaging field, machine learning has played an essential role such as in computer-assisted diagnosis, image segmentation, and image registration [1], [2], [3]; MRI brain tumor segmentation is not an exception and many machine learning techniques have been applied, such as support vector machine [4]. Especially, CNN has outperformed other methods by a large margin for the past two years [5], [6], [7], [8]. Recently, 3D CNN has performed better than 2D CNN at the cost of high computational power [9].

However, as brain disease diagnosis, brain segmentation itself has two limitations: first, diagnosing rare disease is difficult due to the lack of training data for it; second, making a large dataset containing the pathological MRI images of diverse subjects is laborious.

To tackle these limitations, we hypothesize that CNN can regress MRI tomographic slices precisely and if an MRI image shows a big error from a regression model trained on subjects without any brain dysfunction, it implies dysfunction like tumor and bleeding; at test-time, we perform multiple runs of the same input image, where in each run a different part is missing; in the end, if we combine errors between an input image and prediction, then we can infer whether it is normal or pathological. In an attempt to evaluate our approach, as a preliminary study,

we regressed 2D MRI tomographic slices from the only two adjacent previous slices using small dataset, which is a simple but challenging experimental setup.

Research Questions. In this paper, we mainly address the following two research questions:
- **(RQ1) Diagnosing rare disease:** How can we detect rare disease without enough data to recognize patterns?
- **(RQ2) Other applications:** Are there any other applications of this approach?

Contributions. Our main contributions and findings are summarized as follows:
- **Anomaly detection:** This is the first MRI regression approach for detecting rare disease. As a preliminary evaluation of our approach, our study reveals that U-Net can perform precise MRI regression almost matching the ground-truth—which would lead to saving many potential patients with rare disease.
- **MRI regression:** This research broadens the applicability of MRI regression and guides future research in anomaly detection, image completion, and denosing linking CNN and MRI regression.

Outline. The rest of the paper is structured as follows: In Section II, the particular MRI regression problem is defined. The experimental procedure of regression is presented in Section III. Section IV reports the results of the experiments. Finally, Section V presents our findings and concludes the paper with some proposed future developments.
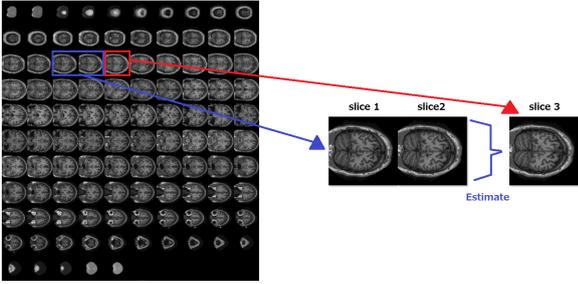
[1]   The University of Tokyo
[2]   University of Vienna
[3]   Eötvös Loránd University
[a)]   han@iba.t.u-tokyo.ac.jp
[b)]   gesserflorian@gmail.com
[c)]   zoltanmilacski@gmail.com

Fig. 1   Regressing 2D MRI tomographic slices from the only two previous slices. Reconstructing accuracy is important for real-world applications

2.   Problem Definition

We applied U-Net [10] to regress 2D MRI tomographic slices from the only two adjacent previos slices (Fig. 1). As a preliminary evaluation of our approach before the real-world applications such as anomaly detection, denoising, and image completion, three experimental setup was employed as follows to make the problem simple but challenging:

- A small dataset instead of a big dataset
- 2D MRI regression instead of 3D MRI regression
- The only two adjacent previous slices instead of all the slices

If CNN can regress MRI tomographic slices precisely and an MRI image shows a big error from a regression model trained on subjects without any brain dysfunction, it implies dysfunction like tumor and bleeding.

Dataset. As a dataset, coronal planes of T88 images from OASIS: Cross-sectional MRI Data in Young, Middle Aged, Nondemented and Demented Older Adults [11] with 176 x 176 pixels were used. All of the 20 subjects had no brain dysfunction. Each brain volume contained 208 slices and it was measured twice. For the train data, the 7072 slices of brain MRI from the 17 random patients were prepared. Similarly, for the test data, the 1248 slices of brain MRI from the rest 3 patients were prepared.

3.   Experimental Framework

We conducted an experiment with U-Net implemented in Keras. This was executed in order to see whether U-Net can regress MRI slices precisely even in such challenging and limited conditions. If MRI slices can be predicted precisely from

Proposed method. We used U-Net architecture, a convolutional network architecture for the fast and precise
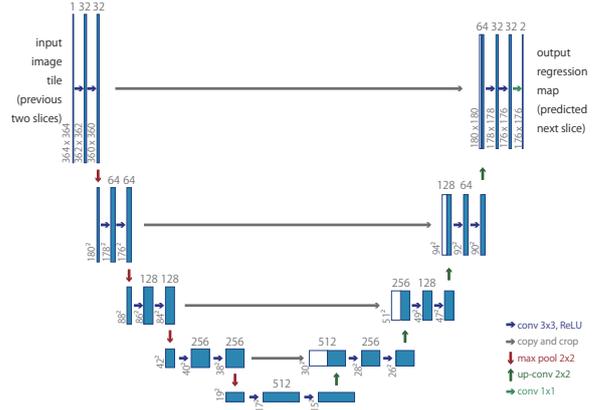

Fig. 2   U-Net architecture. The next slice is predicted from the previous two slices. The missing context in the border region of the image is extrapolated by mirroring the input image

segmentation of biomedical images with strong data augmentation; but reduced the numbers of convolutional filters to half (Fig. 2), since the image size of the dataset is quite smaller than original U-Net architecture (572 x 572 to 176 x 176). Output is a 2D MRI tomographic slice (176 x 176) regressed from the adjacent previous two slices. To predict the pixels in the border region of the image, the missing context was extrapolated by mirroring the input image. Among the 208 slices of each volume, the first and second slices were not included in output, as they don't have the previous two slices. Sigmoid activation function was used to make sure that the regressed pixels are in [0,1] range.

Pre-process. We first loaded the dataset and saved them into NumPy for faster calculation. Then, gray channels of two input slices were concatenated to estimate the next slice accordingly. For data centering and normalization, we subtracted mean from the inputs and divided them into standard deviation. Lastly, output type was changed into float, and the output was divided into 255 to scale it to [0,1] for regression.

Training and validation. Training was conducted for 100 epochs with a batch size of 16. Validation was done by spilling 10% of the train data randomly (701 out of 7004). As a loss function, mean squared error was adopted to measure the difference between the estimator and what is estimated. Adam optimizer with 1e-5 learning late was used as weights.

Testing. Using the trained model, 2D MRI tomographic
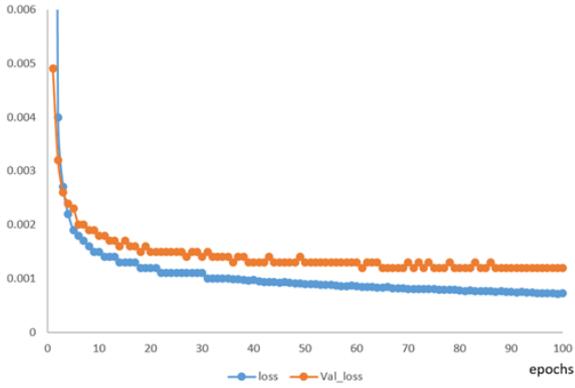
Fig. 3 Training and validation loss of regression (mean square error). The training loss keeps decreasing because of overfitting

slices were estimated from the only two adjacent previos slices. Also, in an attempt to test the ability of this method, we continuously estimated the sequential slices from the only first two slices. Towards anomaly detection, we can detect dysfunction like tumor and bleeding by comparing the errors between the predicted third slices and the ground-truth.

4. Results

This section shows how our MRI regression using U-Net works in training, validation, and testing. Our method performed the effective estimation of MRI tomographic slices owing to the high accuracy of U-Net for biomedical image.

Training and validation. Fig. 3 plots the training and validation loss at each epoch. The training loss reduced to 0.00073 after 100 epochs and the validation loss to 0.0012 after 100 epochs, which were significantly low. The training loss kept decreasing while the validation loss either started to increase or stoped decreasing after some epochs because of overfitting.

Testing. The test loss was 0.00081 between the training loss and validation loss—which achieved a significantly low value. As illustrated in Fig. 4, the third slices estimated from the only previous two slices almost matched the ground-truth. However, it seemed relatively difficult to get the precise third slices when the previous slices were really similar like the image in the second row.

When we continuously estimated the sequential slices from the only first two slices, the estimated slices matched the ground-truth to some extent for the first several slices
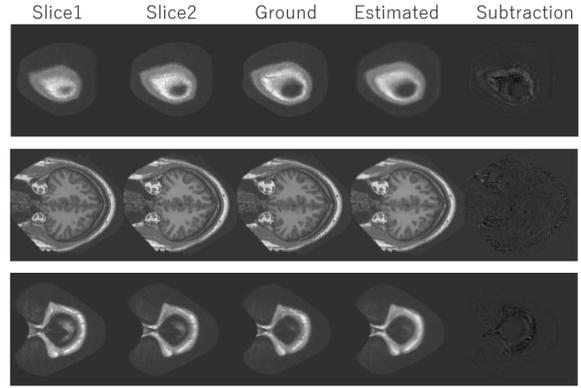
Fig. 4 Estimated slices from the previous two slices. The predicted third slices almost match the ground-truth
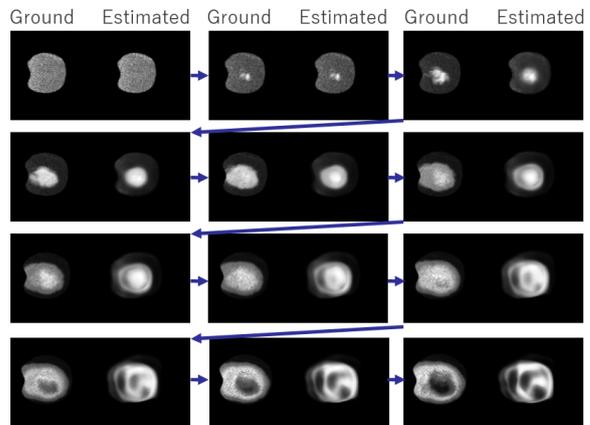
Fig. 5 Estimated sequential slices from the only first two slices. The predicted slices match the ground-truth to some extent for the first several slices

(Fig. 5).

5. Conclusion

We found that U-Net can be used to regress MRI tomographic slices precisely—almost matching the ground-truth—even in severe conditions of a small dataset, 2D MRI regression, and the only use of the two adjacent previous slices. U-Net's high capacity of handling complex biomedical images made it possible. To our knowledge, our technique is the first to tackle MRI regression using deep neural networks and their applications. As U-Net could regress MRI tomographic slices precisely, if our hypothesis is correct, it can be used for anomaly detection of brain dysfunctions, especially for diagnosing rare disease.

As our approach of MRI regression succeeded, it can be used not only for anomaly detection, but for many other biomedical applications too. For example, it can handle image completion. Because often MRI datasets are incom-

plete/corrupted and need to be completed, we can simply use regressed images. Furthermore, it can deal with denoising too. Since often MRI images contain severe noise and need to be denoised, we can denoise by removing the random voxels of an input image, making a prediction, repeating this several times, and in the end averaging over all the predictions.

Our evaluation of MRI regression was conducted in a simple but challenging experimental setup.

- A small dataset instead of a big dataset
- 2D MRI regression instead of 3D MRI regression
- The only two adjacent previous slices instead of all the slices

Future studies should explore whether our hypothesis is correct, and MRI regression can be used to many real-world applications in complex 3D MRI setup using CNN.

Taken together, our finding suggests that CNN architectures such as U-Net can handle MRI regression precisely even in severe experimental setup, and thus if our hypothesis is correct, MRI regression can have many real-world applications such as anomaly detection, image completion, and denoising. Especially anomaly detection through MRI regression can handle the two limitations of MRI segmentation: diagnosing rare disease and making a large dataset. This finding must be interpreted with caution, however, since this preliminary study was conducted to evaluate CNN-based MRI regression and the verification for such applications in 3D MRI using CNN for 3D medical imaging, such as 3D U-Net [12], V-net [13], and VoxResNet [14], was not yet done. This study proves U-net's capacity to regress MRI slices precisely; to confirm that this approach really works for real-world applications, future studies for each application or each disease are needed.

References

[1] R. F. Kenneth, K. Robert, D. S. Joseph, Machine learning, medical diagnosis, and biomedical engineering research - commentary, Biomed Eng Online, doi: 10.1186/1475-925X-13-94, 2014.

[2] N. W. Miles, Y. Yongyi, G. B. Jovan, Y. Grigori, C. S. Stephen, Machine Learning in Medical Imaging, IEEE Signal Processing Magazine, vol. 27, pp. 25–38, 2010.

[3] W. Ying, F. Yong, B. Priyanka, and D. Christos, High-dimensional pattern regression using machine learning: From medical images to continuous clinical variablesm, NeuroImage, vol. 50, pp. 1519–1535, 2010.

[4] B. Stefan, N. Lutz-P, and R. Mauricio, "Fully Automatic Segmentation of Brain Tumor Images Using Support Vector Machine Classification in Combination with Hierarchical Conditional Random Field Regularization" Proc. 14th International Conf. on Medical Image Computing and Computer Assisted Intervention (MICCAI 2011), pp. 354-361, Toronto, Canada, Oct. 2011.

[5] B. Alexander and M. Giovanni, "Deep Neural Networks for Anatomical Brain Segmentation" Proc. IEEE Conference on Computer Vision and Pattern Recognition (CVPR 2015) Workshops, pp. 20-28, Boston, The US, June 2015.

[6] M. Fausto, A. Seyed-Ahmad, K. Christine, P. Annika, R. Verena, et al., Hough-CNN: Deep Learning for Segmentation of Deep Brain Regions in MRI and Ultrasound, arXiv preprint, arXiv: 1601.07014, 2016.

[7] H. Mohammad, D. Axel, W. David, B. Antoine, et al, Brain tumor segmentation with Deep Neural Networks, Medical Image Analysis, vol. 35, pp. 18–31, 2017.

[8] A. Alansary, K. Kamnitsas, A. Davidson, R. Khlebnikov, M. Rajchl, et al., "Fast Fully Automatic Segmentation of the Human Placenta from Motion Corrupted MRI" Proc. 19th International Conf. on Medical Image Computing and Computer Assisted Intervention (MICCAI 2016), pp. 589-597, Istanbul, Turkey, Oct. 2016.

[9] K. Kamnitsas, C. Ledig, V. F. J. Newcombe, J. P. Simpson, A. D. Kane, et al, Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation, Medical Image Analysis, vol. 36, pp. 61-78, 2017.

[10] O. Ronneberger, P. Fischer, and T. Brox, "U-Net: Convolutional Networks for Biomedical Image Segmentation" Proc. 18th International Conf. on Medical Image Computing and Computer Assisted Intervention (MICCAI 2015), pp. 234-241, Munich, Germany, Oct. 2015.

[11] D. S. Marcus, T. H. Wang, J. Parker, J. G. Csernansky, J. C. Morris, and R. L. Buckner, Open Access Series of Imaging Studies (OASIS): Cross-Sectional MRI Data in Young, Middle Aged, Nondemented, and Demented Older Adults, J. Cogn. Neurosci., vol. 19, pp. 1498–1507, Sep. 2007.

[12] Ö. Çiçek, A. Abdulkadir, S. S. Lienkamp, T. Brox, O. Ronneberger, "3D U-Net: Learning Dense Volumetric Segmentation from Sparse Annotation" Proc. 19th International Conf. on Medical Image Computing and Computer Assisted Intervention (MICCAI 2016), pp. 424-432, Istanbul, Turkey, Oct. 2016.

[13] F. Milletari, N. Navab, S. A. Ahmadi, "V-net: Fully convolutional neural networks for volumetric medical image segmentation" Proc. 4th International Conf. on 3D Vision (3DV 2016), pp. 565-571, Stanford, CA, USA, Oct. 2016.

[14] H. Chen, Q. Dou, L. Yu, J. Qin, P. A. Heng, VoxResNet: Deep voxelwise residual networks for brain segmentation from 3D MR images, NeuroImage, doi: 10.1016/j.neuroimage.2017.04.041, 2017.