WHAT IS THE BEST DATA AUGMENTATION APPROACH FOR BRAIN TUMOR SEGMENTATION USING 3D U-NET?

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ABSTRACT

Training segmentation networks requires large annotated datasets, which in medical imaging can be hard to obtain. Despite this fact, data augmentation has in our opinion not been fully explored for brain tumor segmentation (a possible explanation is that the number of training subjects (369) is rather large in the BraTS 2020 dataset). Here we apply different types of data augmentation (flipping, rotation, scaling, brightness adjustment, elastic deformation) when training a standard 3D U-Net, and demonstrate that augmentation significantly improves performance on the validation set (125 subjects) in many cases. Our conclusion is that brightness augmentation and elastic deformation works best, and that combinations of different augmentation techniques do not provide further improvement compared to only using one augmentation technique. Our code is available at \url{https://github.com/mdciri/augmentation}.

Index Terms— Brain tumor segmentation, MRI, 3D U-Net, data augmentation, deep learning, artificial intelligence

1. INTRODUCTION

Deep learning is increasingly being used in medical imaging, as it often provides better results compared to traditional analysis methods \cite{1}. Compared to computer vision, it is in medical imaging more difficult to acquire a large number of training images due to ethics and data protection regulations (e.g. GDPR), and data augmentation is therefore even more important to increase the number of images for training and testing. Surprisingly, there are very few papers that investigate how important different types of augmentation (e.g. rotations, random flipping, scaling, elastic deformations) are for training convolutional neural networks (CNNs) for image classification or image segmentation, and this is especially true for 3D CNNs. Many papers that utilize CNNs only briefly mention that data augmentation was used, but do not mention details like the range of the random rotations or elastic deformations, or if the random rotations were drawn from a normal distribution or from a uniform distribution.

Nalepa et al. \cite{2} provide an overview of data augmentation for brain tumor segmentation, showing that flipping, rotation, scaling and pixel-wise (e.g. adding noise or changing the brightness) augmentation were most common, while translations and elastic deformations were less common. They also provide their own comparison of augmentation techniques, but it lacks details such how large the elastic deformations are. Furthermore, scaling was not tested, no statistical evaluation is done, and the used segmentation network seems to be 2D and not 3D. Shorten et al. \cite{3} provide a more general survey on data augmentation, but barely mention elastic deformations and brightness augmentation. A number of papers have proposed to learn the best augmentation \cite{4, 5}, but a common drawback is a much longer training time. Here we therefore provide a comparison of different data augmentation techniques for brain tumor segmentation, so that new researchers in this field know what kind of augmentation to apply.

2. DATA

The MR images used for this project are from the Multimodal Brain tumour Segmentation Challenge (BraTS) 2020 \cite{6, 7, 8, 9}. The BraTS 2020 training dataset contains MR volumes of shape $240 \times 240 \times 155$ from 369 patients, and for each patient four types of MR images were collected: native (T1), post-contrast T1-weighted (T1Gd), T2-weighted (T2), and T2 Fluid Attenuated Inversion Recovery (FLAIR). The BraTS 2020 validation dataset contains the same type of MR images from 125 patients, without the ground truth annotations. The images were acquired from 19 different institutions with different clinical protocols. The training set was segmented manually, by one to four raters, following the same annotation protocol, and their annotations were approved by experienced neuro-radiologists; whereas no segmentation was provided for the validation set. Moreover, all data were co-registered to the same anatomical template, interpolated to the same resolution (1 mm$^3$) and skull-stripped.
3. METHODS

In this project we used a standard 3D U-Net architecture which is trained with 4 MR images (T1, T1Gd, T2, FLAIR) to perform a 4 class segmentation: background, whole tumour (WT), tumour core (TC), and enhancing tumour (ET). Although more advanced segmentation networks have been proposed, a standard U-Net won the BraTS 2020 challenge. Our network is trained on sub-volumes of $128 \times 128 \times 128$ voxels. The U-Net has 4 encoder and decoder steps: each step is made by two 3D convolutions: for the encoder a 3D convolution layer with stride 1 followed by another one but with stride 2; whereas for the decoder a 3D Transpose convolution with stride 2, concatenated with the respective encoded step output, followed by a 3D convolution with stride 1. Each convolution has kernel size $4 \times 4 \times 4$, He normalization and same padding. The first 3D convolution uses 64 filters which are doubled at each encoder step, vice versa for the decoder. Adam is used as the network’s optimizer with learning rate $\lambda = 10^{-4}$, and the loss chosen is the generalized Dice loss. The augmentation techniques used for this projects are:

- **Patch extraction**: from each original volume a sub-volume of shape $128 \times 128 \times 128$ is extracted around its centre. In this way each sub-volume mostly contains brain tissue and not the surrounding background.
- **Flipping**: random flipping of one of the three different axes with 1/3 probability.
- **Rotation**: rotation applied to each axis with angles randomly chosen from a uniform distribution with range between $0^\circ$ and $15^\circ$, $30^\circ$, $60^\circ$, or $90^\circ$.
- **Scale**: scaling applied to each axis by a factor randomly chosen from a uniform distribution with range $\pm 10\%$ or $\pm 20\%$.
- **Brightness**: power-law $\gamma$ intensity transformation with its parameters gain ($g$) and $\gamma$ chosen randomly between 0.8 - 1.2 from a uniform distribution. The intensity ($I$) is randomly changed according to the formula: $I_{\text{new}} = g \cdot I^\gamma$.
- **Elastic deformation**: elastic deformation with square deformation grid with displacements sampled from a normal distribution with standard deviation $\sigma = 2$, $5$, $8$, or $10$ voxels, where the smoothing is done by a spline filter with order 3 in each dimension.

Moreover, in order to report a robust evaluation, 3-fold cross validation is applied to each model, and these 3 models are ensembled by averaging their softmax layers outputs.

Successively, the authors ranked all the augmentation approaches as in the BraTS 2020 challenge and handled the ties as in [15] to determine which of of these augmentation techniques and parameters yield the best performance on the validation set. There will be shown two rankings: one for all the different augmentation techniques and one including also their combinations. Furthermore, the techniques with higher rank are also combined between each other with a probability of 0.5 for each patch.

Each model is trained, with one or more augmentation techniques, over 200 epochs with early stopping after 25 epochs in case the validation loss does not decrease. The segmentation networks were trained with Nvidia Tesla V100 and Nvidia Quadro RTX 8000 graphics cards. In the end, all the trained models were evaluated on the 125 subjects of the BraTS 2020 challenge validation set. The metrics (Dice score and Haudsford distance 95 percentile) reported in Table 2 are calculated for each class by the CBICA Image Processing Portal while the rank scores were calculated by us.

4. RESULTS

First of all, we want to investigate whether augmentation significantly increases the Dice scores. Hence, we applied a non-parametric permutation test to the Dice scores from the 125 validation subjects. As the Dice scores are from the same 125 validation subjects in all cases, we used a paired t-test to test if the mean Dice difference is significantly different from zero. In non-parametric statistics, a paired t-test can be performed with a sign flipping test, where the sign of each pairwise difference is randomly flipped a large number of times, to obtain the null distribution. We used 100,000 sign flips per test and the p-values are given in Table 1. Brightness augmentation and elastic deformations with a $\sigma = 2$ result in significantly higher Dice scores for all 3 tumor classes, scaling with $\pm 20\%$ significantly improves the Dice scores for 2 classes, while flipping and $90^\circ$ rotation only significantly improve one tumor class.

Table 2 shows the average and standard deviation for the Dice score and Hausdorff distance 95 percentile on the three different brain tumour classes over the 125 subjects in the validation set, for each tested augmentation approach. Here too, looking at the ranking, is it possible to say that brightness and elastic deformations with a $\sigma = 2$ are the two best augmentation techniques for this dataset, having $1^{st}$ and $2^{nd}$ position in the ranking respectively. Moreover, the other most important techniques are scaling with $\pm 20\%$, rotation with random angle chosen between $0^\circ$ - $90^\circ$, and flipping with having $4^{th}$, $7^{th}$, and $8^{th}$ rank position respectively. Hence, four more training were done combining these techniques and the results are also shown in Table 2. In the end, a second ranking was performed including these four new models to the others.

5. DISCUSSION

The aim of this paper is not to propose a new archtecture with high image segmentation performance, but to investigate how different augmentation techniques affect the network’s learning. Our results show that data augmentation significantly im-

[1] https://ipp.cblca.upenn.edu
proves the performance on the validation data in many cases compared to only using patch extraction as baseline technique (see Table 1). A possible explanation why data augmentation has not been fully explored for brain tumor segmentation is that the BraTS training set is rather large (369 subjects for the 2020 version), and several papers suggest that data augmentation would not help much [17, 18, 19]. Since all subjects in BraTS have been registered to a common space, augmentation is important to show the network brains from different angles, while augmentation may not be as important for a dataset where the brains have not been registered.

In Table 2 we reported also the rank for our tested approaches. It is clear that augmentation improves the training performance because patch augmentation, which is our baseline, has the lowest rank in both cases (13th and 17th). Augmentation techniques have to be chosen smartly in order to create new training images that still represent and/or look like the original ones. For this particular dataset:

- elastic deformation generates realistic tumors and achieves its best scores with $\sigma = 2$, which is also the technique with the best rank position. Anyway, even using a value of $\sigma = 5$ or 8, the scores are still suitable, achieving the 6th and 3rd rank position respectively, whereas $\sigma = 10$ it is too high and it deforms the brains excessively;
- $\gamma$ correction (brightness) augmentation is the second best form of augmentation here, which is probably explained

| Table 1. Non-parametric $p$-values for comparing different types of data augmentation, obtained through a sign flipping test using the 125 validation subjects. ET = enhancing tumor, WT = whole tumor, TC = tumor core. The $p$-values have been multiplied with 36 (36 one sided tests) as Bonferroni correction for multiple comparisons. |
| Comparison | p-value for Dice score ET | WT | TC |
|------------|--------------------------|----|----|
| Flipping + PE $>$ PE | 0.0082 | 1.0 | 0.19116 |
| Brightness + PE $>$ PE | 0.00036 | 0.00036 | 0.00036 |
| Scale $\pm 10\%$ + PE $>$ PE | 0.00036 | 1.0 | 1.0 |
| Scale $\pm 20\%$ + PE $>$ PE | 1.0 | 0.00036 | 0.00396 |
| Rotation $0^\circ$- $15^\circ$ + PE $>$ PE | 1.0 | 1.0 | 1.0 |
| Rotation $0^\circ$- $30^\circ$ + PE $>$ PE | 1.0 | 1.0 | 1.0 |
| Rotation $0^\circ$- $60^\circ$ + PE $>$ PE | 0.4676 | 0.2422 | 1.0 |
| Rotation $0^\circ$- $90^\circ$ + PE $>$ PE | 0.00036 | 1.0 | 1.0 |
| Elastic deformation 2 + PE $>$ PE | 0.00036 | 0.00036 | 0.00036 |
| Elastic deformation 5 + PE $>$ PE | 0.00036 | 1.0 | 0.44208 |
| Elastic deformation 8 + PE $>$ PE | 0.00036 | 0.00071 | 0.13464 |
| Elastic deformation 10 + PE $>$ PE | 0.00036 | 1.0 | 1.0 |

by the fact that the BraTS 2020 dataset contains data from 19 different sites. Moreover, according to Nalepa et al. [11], only Isensee et al. [11] used gamma correction in their comparison of the BraTS 2018 participants:

- random scaling and rotation create bigger and/or smaller tumors that are distributed everywhere in the training volumes’ space. This is probably the reason why greater scaling and rotation ranges result in better scores;
- flipping is very easy to implement technique, but it does not increase significantly the network’s performance.

Moreover, Table 2 shows that the best combination is the one with elastic deformation and brightness, followed by the one with scaling, but it is interesting to notice that combining different augmentation techniques does not improve the network’s performance. Indeed, the models trained with only elastic deformation or brightness augmentation are higher ranked than the ones trained on multiple augmentation techniques (see column ‘Rank score (2)’). This may be due to the fact that each augmentation technique is applied with a probability 0.5, so, if more augmentation techniques are applied, less original images are shown to the network during the training. Indeed, the percentage of original images used during the training is 50%, 25%, 12.5%, 6.25%, and 3.125% combining 1, 2, 3, 4 and 5 different techniques respectively. Combining different types of augmentation can potentially be done differently, to always guarantee that for example 20% of the shown patches are always the original ones.

To summarize, the authors recommend everyone who is going to use this type of dataset in the future to apply, at least, elastic deformation and brightness adjustment as augmentation techniques, and in case they would like to use more augmentation techniques, to be sure that the network considers a suitable percentage of original images during its training.

6. COMPLIANCE WITH ETHICAL STANDARDS

This research study was conducted retrospectively using human subject data made available in open access by Brain Tumor Segmentation (BraTS) Challenge 2020 requiring only citation of the source references. Ethical approval was not required as confirmed by the license attached with the open access data.

7. ACKNOWLEDGMENTS

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Table 2. Average and standard deviation for the Dice score and Hausdorff distance 95 percentile on the three different brain tumour classes over the 125 subjects in the BraTS20 Challenge validation set, for each tested augmentation approach. The predictions are calculated by ensemble 3 models trained in a 3-fold cross-validation, and post-processed as in [12]. The values reported here were calculated by the CBICA Image Processing Portal. In the last two columns we report the rank of each model. ET = enhancing tumor, WT = whole tumor, TC = tumor core.

| Augmentation technique | Parameter range | Dice score [%] | | | Hausdorff distance 95 [mm] | | | Rank score | Rank score (2) |
|-----------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Patch Extraction      |                | ET 70.46 ± 28.02 | WT 86.74 ± 10.01 | TC 72.56 ± 22.34 | ET 41.86 ± 113.38 | WT 10.73 ± 9.39 | TC 22.90 ± 64.71 | 7.6213 (13th) | 10.1033 (17th) |
| Fliping               |                | ET 72.45 ± 26.88 | WT 87.15 ± 10.28 | TC 74.43 ± 20.92 | ET 35.68 ± 105.28 | WT 13.59 ± 31.92 | TC 13.04 ± 33.20 | 6.622 (8th) | 8.9533 (11th) |
| 0.8 - 1.2             |                | ET 75.76 ± 28.40 | WT 87.94 ± 10.68 | TC 76.49 ± 22.91 | ET 38.40 ± 109.57 | WT 10.40 ± 11.08 | TC 18.70 ± 56.20 | 4.25 (2nd) | 5.8013 (2nd) |
| Scaling               | ±10%           | ET 75.42 ± 28.99 | WT 86.98 ± 9.43  | TC 73.50 ± 23.66 | ET 38.38 ± 109.57 | WT 10.67 ± 9.57  | TC 16.63 ± 46.38 | 5.8733 (3rd) | 8.024 (8th) |
| 0.8 - 20%             |                | ET 71.89 ± 27.53 | WT 88.24 ± 7.98  | TC 75.43 ± 21.34 | ET 36.22 ± 105.30 | WT 8.68 ± 10.48  | TC 12.66 ± 34.22 | 5.279 (4th) | 7.2673 (6th) |
| Rotation              | 0° - 15°       | ET 71.23 ± 27.80 | WT 86.70 ± 10.82 | TC 72.19 ± 23.08 | ET 38.85 ± 109.42 | WT 13.68 ± 33.72 | TC 19.30 ± 56.31 | 7.3513 (12th) | 9.7666 (16th) |
| Elastic Deformation   | 0° - 30°       | ET 71.60 ± 27.49 | WT 86.86 ± 9.37  | TC 73.93 ± 21.13 | ET 38.73 ± 109.46 | WT 10.98 ± 9.58  | TC 19.36 ± 56.34 | 7.0586 (10th) | 9.446 (13th) |
| 0° - 60°              | ET 71.92 ± 26.95 | WT 87.14 ± 9.25  | TC 72.87 ± 24.13 | ET 35.70 ± 105.28 | WT 10.56 ± 9.17  | TC 22.03 ± 64.58 | 7.3126 (11th) | 9.702 (14th) |
| 0° - 90°              | ET 74.72 ± 29.16 | WT 87.06 ± 9.39  | TC 70.44 ± 26.89 | ET 38.79 ± 109.46 | WT 10.53 ± 10.35 | TC 23.00 ± 64.71 | 6.5246 (7th) | 8.9033 (10th) |
| Elastic Deformation   | 5              | ET 75.46 ± 28.96 | WT 89.34 ± 9.49  | TC 79.01 ± 21.74 | ET 38.59 ± 109.51 | WT 6.07 ± 10.62 | TC 11.00 ± 34.20 | 2.686 (14th) | 3.6053 (16th) |
| 8                     | ET 76.32 ± 27.93 | WT 87.14 ± 10.33 | TC 73.97 ± 23.81 | ET 33.68 ± 100.93 | WT 11.17 ± 10.20 | TC 19.94 ± 56.34 | 6.388 (8th) | 6.8 (9th) |
| 10                    | ET 75.13 ± 29.70 | WT 88.06 ± 10.03 | TC 74.58 ± 25.78 | ET 41.23 ± 110.57 | WT 9.83 ± 10.18 | TC 22.27 ± 64.61 | 4.3266 (3rd) | 5.8233 (3rd) |
| Elastic Deformation   | 2              | ET 76.46 ± 29.18 | WT 86.34 ± 9.03  | TC 71.24 ± 24.45 | ET 33.03 ± 100.94 | WT 10.01 ± 9.94 | TC 20.84 ± 56.76 | 6.7053 (9th) | 9.0213 (12th) |
| Brightness +          | 0.8 - 1.2      | ET 74.1 ± 29.84  | WT 87.66 ± 9.85  | TC 73.56 ± 31.06 | ET 44.68 ± 117.18 | WT 9.14 ± 7.21  | TC 16.32 ± 46.38 | — | 6.5306 (4th) |
| Elastic Deformation + | 2              | ET 74.56 ± 29.36 | WT 87.56 ± 11.31 | TC 74.10 ± 25.55 | ET 41.48 ± 113.49 | WT 9.53 ± 9.18  | TC 20.42 ± 56.50 | — | 6.8606 (5th) |
| Brightness +          | 0.8 - 1.2      | ET 72.27 ± 29.16 | WT 87.31 ± 10.10 | TC 72.05 ± 26.51 | ET 42.58 ± 113.25 | WT 11.06 ± 12.34 | TC 20.47 ± 56.80 | — | 7.8813 (7th) |
| Scaling               | ±20%           | ET 73.16 ± 29.63 | WT 86.68 ± 9.83  | TC 69.53 ± 26.07 | ET 36.92 ± 105.21 | WT 11.26 ± 12.01 | TC 14.30 ± 33.57 | — | 9.728 (15th) |
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