Transfer Brain MRI Tumor Segmentation Models Across Modalities with Adversarial Networks

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Abstract—In this work, we present an approach to brain cancer segmentation in Magnetic Resonance Images (MRI) using Adversarial Networks, that have been successfully applied to several complex image processing problems in recent years. Most of the segmentation approaches presented in the literature exploit the data from all the contrast modalities typically acquired in the clinical practice: T1-weighted, T1-weighted contrast-enhanced, T2-weighted, and T2-FLAIR. Unfortunately, often not all these modalities are available for each patient. Accordingly, in this paper, we extended a previous segmentation approach based on Adversarial Networks to deal with this issue. In particular, we trained a segmentation model for each modality at once and evaluated the performances of these models. Thus, we investigated the possibility of transferring the best among these single-modality models to the other modalities. Our results suggest that such a transfer learning approach allows achieving better performances for almost all the target modalities.

I. INTRODUCTION

The recent popularity of Deep Learning have opened the possibility to apply these techniques in the context of healthcare. In particular, deep learning methods have been applied to a great number of tasks in healthcare in order to automatize or simplify clinical processes that would be otherwise performed manually, requiring a great amount of time and increasing the possibility of human error. In our work we focused on the task of brain cancer segmentation in Magnetic Resonance Images (MRI). In the clinical practice, different contrast modalities of a single MRI are usually acquired, each one representing biological information differently. We focus on the most commonly acquired MRI sequences for brain cancer diagnosis: (i) T1-weighted (T1), (ii) T1-weighted contrast-enhanced (T1\textsubscript{c}), (iii) T2-weighted (T2), and (iv) T2-FLAIR (FLAIR). However, in real-world scenarios, not all the sequences are always available for each patient. Moreover, MRIs could be acquired using different equipment or settings, resulting in increased data heterogeneity. Most of the Deep Learning approaches to segmentation presented in the literature\cite{1} either assume that every modality is available or focus on the modalities that are most frequently acquired, not integrating all the possible information in the model training process.

In our work, we focus on using Adversarial Networks as a segmentation model, while using transfer learning as a methodological approach. In particular, we consider a scenario in which a pre-trained segmentation model is already available for a given contrast modality. Thus, we aim to assess the advantages of fine-tuning the available model with respect to using the T1 alone. Similarly, in\cite{2} 3D FLAIR images are generated from T1 and used to train a classifier that considers both T1 and FLAIR, improving performances. Another work on cross-modality generation is\cite{6}, which uses a pair of GANs to generate modalities and subsequently uses the synthetic data to pre-train a classifier.

II. RELATED WORK

Due to the limited volumes of data that are available in healthcare with respect to the one typically used in Deep Learning, many works tried different approaches to address the problem of incomplete data. In this section we first provide an overview of some of the most commonly adopted approaches to the segmentation task with heterogeneous or missing data. Finally, we provide a brief overview to some of the most relevant works that investigated the application of Adversarial Networks to the segmentation task.

A. Image Synthesis

One commonly used approach to address the problem of MRI segmentation in the case of missing contrast modalities is to perform Image Synthesis to generate artificial data. For example, Dar et al.\cite{2} used Cycle GAN to generate missing modalities, while Sharma and Hamarneh\cite{3} developed a version that also accepts zero-values for missing modalities. In\cite{4} the authors addressed the problem of missing FLAIR sequences in White Matter hyper-intensity segmentation task by generating the FLAIR from T1 MRI while jointly producing the segmentation. Their work shows that introduction of synthetic FLAIR modalities increases the performances with respect to using the T1 alone. Similarly, in\cite{5} 3D FLAIR images are generated from T1 and used to train a classifier that considers both T1 and FLAIR, improving performances. Another work on cross-modality generation is\cite{6}, which uses a pair of GANs to generate modalities and subsequently uses the synthetic data to pre-train a classifier.

B. Hetero-Modal Models

Another investigated solution to the problem of missing modalities is to train a model that is invariant to the input con-
segmentation network is trained to perform pixel-wise classifications on images, while an adversarial network (called discriminator or critic) is trained to discriminate segmentations coming from the segmentation network and the ground truth. Their experiments run on the PASCAL VOC 2012 [21] and Stanford Background [22] datasets show an improvement in segmentation performances when an adversarial loss is used.

In the medical imaging domain, multiple works apply this method for segmentation of MRI, CT, PET and other domain specific image formats. For example, [23] applies the method to Brain MRI, studying the effectiveness of adversarial training and dilated convolution. In particular, Xue et. al. [24] propose an Adversarial Network with a Multi-Scale loss, called SegAN, achieving better performances compared to the state-of-the-art in BRATS 2013 Leaderboard (\cite{25, 26}). In our work, we use the SegAN architecture as baseline for our experiments.

III. SEGMENTATION WITH ADVERSARIAL NETWORKS

For our experiments, we only focus on whole tumor segmentation task proposed in the BRATS challenge. We considered the SegAN architecture and implement it using Tensorflow 2.0 [27]. As some details in the provided code did not correspond to the paper formulation, we experimented different variants of the SegAN architecture in order to reproduce their results. The two main modifications to the SegAN architecture proposed in the paper are:

(i) Adoption of a Dice Loss [28] in the segmentation network to mitigate the imbalance between the background and the region to annotate. The implementation is taken from the SegAN repository [1]. Since we were able to reproduce the results only when using this term, we assume the original paper used this formulation. More details can be found in section V.

(ii) Introduction of a modified input for the critic network. The SegAN architecture masks the input MRI using the proposed segmentation, coming either from the segmentation network or the ground truth, before applying it as an input for the critic. We believe that a more effective approach would be concatenating the input MRI and the segmentation, as it would allow the critic to also consider false positives (e.g. occurring in the background) and false negatives produced by the generator.

IV. EXPERIMENTAL DESIGN

A. Dataset

To address the segmentation task we use the BRATS 2015 training dataset \cite{29} which is composed of MRI of 220 high grade subjects (HG) and 54 low grade subjects (LG). Each MRI has resolution of 4 contrast modalities: T1, T1c, T2, FLAIR. Following the approach of \cite{24} we used stratified sampling for keeping the balance of HG and LG subjects within each subset. Due to the unavailability of ground truth in the testing data, we use a different splitting configuration. In particular, instead of splitting the training data in Training/Validation (9:1) splits as in \cite{24} we split the data in Training(80%)/Validation(10%)/Testing(10%), thus
obtaining a slightly smaller training dataset. The composition of the resulting datasets are 219 (Training), 27 (Validation), 28 (Testing).

B. Pre-Processing

Since BRATS2015 images have an isotropic resolution of 1mm³ per voxels we don’t perform any further spatial processing to data. Following the SegAN approach, we center-crop each MRI to a 180 x 180 x 128 volume in order to remove black regions while keeping all the relevant data. For each MRI volume, we clip voxel values to the 2nd and 98th percentile in order to remove outliers, then we apply Feature Scaling to normalize the intensity range between 0 and 1.

C. Transfer Learning

Motivated by the results of [17], we transfer both the segmentation and discriminator networks to the target domain network. To perform fine-tuning, we apply the following alternative strategies: (i) keeping all the discriminator weights fixed during training (ii) fine tuning both the segmentation and the discriminator networks with no fixed weights.

Although keeping the discriminator weights fixed during fine tuning may penalize its ability to adapt to the target domain, we believe that keeping it fixed could help to retain more knowledge from the source domain while letting the generator improve. This choice is motivated by the fact that the discriminator has been found to be the most important part of an adversarial network to transfer to the new network [17]. In fact, our results show that this strategy performs better than full fine-tuning in some scenarios. Due to the high computational cost of training and the number of modalities we considered, we couldn’t investigate more complex strategies, which are left as future work.

V. EXPERIMENTAL RESULTS

As the first step we aimed to reproduce SegAN paper results on whole tumor segmentation task using all the four contrast modalities that are available (T1, T1c, T2, FLAIR). In doing this, we tried to follow the formulation from the paper as close as possible, eventually integrating the information from the source code. We then introduced our modification to the critic input and trained our model using the four modalities.

In order to evaluate the transfer learning capabilities between modalities, we trained 4 more models using our modified architecture using as input only one contrast modality at a time. Every model we trained in our experiments uses the same initialization seed. We trained using RMSprop (lr: 2*10⁻⁵) and Early Stopping (patience = 500 epochs) on Dice Score evaluation metric to keep the best performing weights configuration on each run. In our first experiment we defined the architecture by investigating the impact of Dice Loss in the original SegAN architecture. As shown in figure 2, the absence of dice term in the segmentation network loss leads to an highly unstable training which is typical of Adversarial Networks. Due to that, we assume that the original SegAN paper implicitly made use of this term as confirmed by their code. We then trained our architecture with the modified critic input, observing an even more stable training with respect to SegAN and an increase of performances throughout all the training process. Our results for the baseline model and our proposed methods are shown in Table I.

![Fig. 2. Dice Loss on validation set of the SegAN model from the paper (blue), the SegAN with Dice Loss (green) and our proposed model (orange) with all the modalities as input. Our proposed architecture achieves better results throughout all the training process and has more stable performances than the standard SegAN. The SegAN without Dice Loss performs noticeably worse than the version from the repository, indicating that the published version may have used the dice loss.](image)

| Model            | Dice Score | Precision | Sensitivity |
|------------------|------------|-----------|-------------|
| SegAN (Paper)    | 0.85       | 0.92      | 0.80        |
| SegAN (TF2.0)    | 0.82753    | 0.91542   | 0.76507     |
| SegAN IO (Our)   | 0.86166    | 0.89635   | 0.83585     |

To perform transfer learning between modalities, we trained one network for each available contrast modality. Every model uses our proposed architecture and the same configuration of the previous experiment, except of the number of input channels (i.e. 1 instead of 4). Dice Scores for the obtained models are shown in Table II. The network achieving the best Dice Score is the one trained on FLAIR modality. This
| Modality | Dice Score | Precision | Sensitivity |
|----------|------------|-----------|-------------|
| T1       | 0.56192    | 0.56555   | 0.58940     |
| T1c      | 0.63402    | 0.67918   | 0.61699     |
| T2       | 0.75654    | 0.77593   | 0.75827     |
| FLAIR    | 0.80252    | 0.87827   | 0.75043     |

Table II: Performances of the baseline models used for training. Every model has been trained on a single contrast modality.

Fig. 3. Dice scores obtained evaluating each single-modality base model on the other modalities. Trivially, each model performs better when evaluated on the dataset for which it has been trained. However, a comparison between the performance on different modalities shows good generalization performances between some modalities, indicating that the two domains are similar. For instance, a model which is trained on T2 (bottom-left figure) can be used without fine-tuning on FLAIR MRIs with a 10 percent loss in performances.

suggests that the results of the previous experiment are mainly driven by information present in the FLAIR modality. In [12], the authors cite the FLAIR as the most contributing modality for White Matter Segmentation. The importance and relative ease of information extraction from FLAIR scans in brain is also confirmed by their common adoption in Brain imaging, suggesting that the same is valid for cancer segmentation.

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