Brain tumor segmentation with missing modalities via latent multi-source correlation representation

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\begin{abstract}
Multimodal MR images can provide complementary information for accurate brain tumor segmentation. However, it’s common to have missing imaging modalities in clinical practice. Since it exists a strong correlation between multi modalities, a novel correlation representation block is proposed to specially discover the latent multi-source correlation. Thanks to the obtained correlation representation, the segmentation becomes more robust in the case of missing modality. The model parameter estimation module first maps the individual representation produced by each encoder to obtain independent parameters, then, under these parameters, correlation expression module transforms all the individual representations to form a latent multi-source correlation representation. Finally, the correlation representations across modalities are fused via attention mechanism into a shared representation to emphasize the most important features for segmentation. We evaluate our model on BraTS 2018 datasets, it outperforms the current state-of-the-art method and produces robust results when one or more modalities are missing.
\end{abstract}

\textbf{Keywords:} Brain tumor segmentation · multi-modal · missing modalities · fusion · latent correlation representation · deep learning

\section{Introduction}

Brain tumor is one of the most aggressive cancers in the world, early diagnosis of brain tumors plays an important role in clinical assessment and treatment planning of brain tumors. Magnetic resonance imaging (MRI) is a widely used imaging technique to assess these tumors, because it offers a good soft tissue contrast without radiation. The commonly used sequences are T1-weighted, contrast enhanced T1-weighted (T1c), T2-weighted and Fluid Attenuation Inversion Recovery (FLAIR) images. Different sequences can provide complementary information to analyze different subregions of gliomas. For example, T2 and FLAIR highlight the tumor with peritumoral edema, designated whole tumor. T1 and T1c highlight the tumor without peritumoral edema, designated tumor core. An enhancing region of the tumor core with hyper-intensity can also be observed.
in T1c, designated enhancing tumor core [14]. Therefore applying multi-modal images can reduce the information uncertainty and improve clinical diagnosis and segmentation accuracy.

Segmentation of brain tumor by experts is expensive and time-consuming, recently, there have been many studies on automatic brain tumor segmentation [3, 4, 7, 12, 13], which always requires the complete set of the modalities. However, the imaging modalities are often incomplete or missing in clinical practice. Currently, there are a number of methods proposed to deal with the missing modalities in medical image segmentation, which can be broadly grouped into three categories: (1) training a model on all possible subset of the modalities, which is complicated and time-consuming. (2) synthesizing missing modalities and then use the complete imaging modalities to do the segmentation, while it requires an additional network for synthesis and the quality of the synthesis can directly affect the segmentation performance. (3) fusing the available modalities in a latent space to learn a shared feature representation, then project it to the segmentation space. This approach is more efficient than the first two methods, because it doesn’t need to learn a number of possible subsets of the multi-modalities and will not be affected by the quality of the synthesized modality.

Recently, there are a lot of segmentation methods based on exploiting latent feature representation for missing modalities. The current state-of-the-art network architecture is from Havaei, the proposed HeMIS [5] learns the feature representation of each modality separately, and then the first and second moments are computed across individual modalities for estimating the final segmentation. However, computing mean and variance over individual representations can’t learn the shared latent representation. Lau et al. [9] introduced a unified representation network that maps a variable number of input modalities into a unified representation by using mean function for segmentation, while averaging the latent representations could loss partially important information. Chen et al. [2] used feature disentanglement to decompose the input modalities into content code and appearance code, and then the content code are fused via a gating strategy into a shared representation for segmentation. While the approach is more complex and time-consuming, because it requires two encoders for each modalities, and their proposed fusion method only re-weight the content code from spatial-wise without channel-wise. Shen et al. [11] used adversarial loss to form a domain adaptation model to adapt feature maps from missing modalities to the one from full modalities, which can only cope with the one-missing modality situation.

The challenge of segmentation on missing modalities is to learn a shared latent representation, which can take any subset of the image modalities and produce robust segmentation. To effectively learn the latent representation of individual representations, in this paper, we propose a novel brain tumor segmentation network to deal with the absence of imaging modalities. The main contributions of our method are three folds: 1) A correlation representation block is introduced to discover the latent multi-source correlation representation. 2) A fusion strategy based on attention mechanism with obtained correlation repre-
representation is proposed to learn the weight maps along channel-wise and spatial-wise for different modalities. 3) The first multi modal segmentation network which is capable of describing the latent multi-source correlation representation and allows to help segmentation for missing data is proposed.

2 Method

Our network is inspired by the U-Net architecture [10]. To be robust to the absence of modalities, we adapt it to multi-encoder based framework. It first takes 3D available modalities as input in each encoder. The independent encoders can not only learn modality-specific feature representation, but also can avoid the false-adaptation between modalities. To take into account the strong correlation between multi modalities, we propose a block, named CR, to discover the correlation between modalities. Then the correlation representations across modalities are fused via attention mechanism, named Fusion, to emphasize the most discriminative representation for segmentation. Finally, the fused latent representation is decoded to form the final segmentation result. The network architecture scheme is depicted in Fig. 1.

Fig. 1. A schematic overview of our network.

2.1 Modeling the latent multi-source correlation

Inspired by a fact that, there is strong correlation between multi MR modalities, since the same scene (the same patient) is observed by different modalities [8]. From Fig. 2 presenting joint intensities of a pair of MR images corresponding respectively to FLAIR-T1, FLAIR-T2 and T1-T2, we can observe a strong correlation in intensity distribution between each two modalities. To this end, it’s reasonable to assume that a strong correlation also exists in latent representation between modalities. And we introduce a Correlation Representation (CR) block (see Fig. 3) to discover the latent correlation. The CR block consists of two modules: Model Parameter Estimation Module (MPE Module) and Linear Correlation Expression Module (LCE Module). The input modality \( \{X_i, \ldots, X_n\} \), where \( n = 4 \), is first input to the independent encoder \( f_i \) (with learning parameters \( \theta \)) to learn the modality-specific representation \( f_i(X_i|\theta_i) \). Then, MPE
Module, a network with two fully connected network and LeakyReLU, maps the modality-specific representation \( f_i(\mathbf{X}_i|\theta_i) \) to a set of independent parameters \( \Gamma_i = \{\alpha_i, \beta_i, \gamma_i, \delta_i\} \), which is unique for each moddality. Finally the correlation representation \( F_i(\mathbf{X}_i|\theta_i) \) can be obtained via LCE Module (Equation 1). Utilizing the correlation representation block, we can use the available modalities to describe the missing one, which allows the segmentation network to have strong capability to deal with missing data.

\[
F_i(\mathbf{X}_i|\theta_i) = \alpha_i \odot f_j(\mathbf{X}_j|\theta_j) + \beta_i \odot f_k(\mathbf{X}_k|\theta_k) + \gamma_i \odot f_m(\mathbf{X}_m|\theta_m) + \delta_i, (i \neq j \neq k \neq m)
\]  

(1)

**Fig. 2.** Joint intensity distribution of MR images: (a) FLAIR-T1, (b) FLAIR-T2 and (c) T1-T2.

**Fig. 3.** Architecture of correlation representation block.
2.2 Fusion based on attention mechanism

The purpose of fusion block is to emphasize the most important features from different modalities to highlight regions that are greatly relevant to brain tumor. One simple way to fuse the representation is to average over them, while it could lose some valuable information. To this end, we proposed a fusion block based on attention mechanism, described in Fig. 4. The correlation representations obtained from CR block are first concatenated as the input representation \( F = [F_1, F_2, F_3, F_4], F_k \in \mathbb{R}^{H \times W}. \) Note that, in the lowest level of the network, there are four correlation representations for the fusion block, in the other levels, the result of the previous level is also concatenated with the modality-specific representation to obtain five input representations, in the following, we just describe the fusion block in the lowest level. In the channel attention module, a global average pooling is first performed to produce a projection tensor, which represents the linearly combined representation and channel-wise representation. The fused representation representation is obtained by adding the channel-wise representation \( R \) and space-wise representation \( F \).

\[
\text{Latent multi-source correlation representation}
\]

2.3 Network Architecture and Learning Process

The detailed network architecture framework is illustrated in Fig. 5. It’s likely to require different receptive fields when segmenting different regions in an image, standard U-Net cannot get enough semantic features due to the limited receptive field. Inspired by dilated convolution, we use residual block with dilated convolutions (rate= 2, 4) (res_dil block) on both encoder part and decoder part to obtain features at multiple scale. The encoder includes a convolutional block, a res_dil block followed by skip connection. All convolutions are \( 3 \times 3 \times 3 \). Each
decoder level begins with up-sampling layer followed by a convolution to reduce the number of features by a factor of 2. Then the upsampled features are combined with the features from the corresponding level of the encoder part using concatenation. After the concatenation, we use the res_dil block to increase the receptive field. In addition, we employ deep supervision \[6\] for the segmentation decoder by integrating segmentation layers from different levels to form the final network output. The network is trained by the overall loss function: 
\[L_{total} = L_{dice} + L_1,\]
where \(L_1\) is the mean absolute loss.

3 Data and implementation details

Data and pre-processing. The datasets used in the experiments come from BraTS 2018 dataset. The training set includes 285 patients, each patient has four image modalities including T1, T1c, T2 and FLAIR. Following the challenge, there are three segmentation classes: complete tumor, tumor core and enhancing tumor. The provided data have been pre-processed by organisers: co-registered to the same anatomical template, interpolated to the same resolution (1 mm\(^3\)) and skull-stripped. The ground truth have been manually labeled by experts. We did additional pre-processing with a standard procedure. The N4ITK \[1\] method is used to correct the distortion of MRI data, and intensity normalization is applied.
to normalize each modality of each patient. To exploit the spatial contextual information of the image, we use 3D image and resize it from $155 \times 240 \times 240$ to $128 \times 128 \times 128$.

**Implementation details.** Our network is implemented in Keras. The model is optimized using the Adam optimizer (initial learning rate $= 5e^{-4}$) with a decreasing learning rate factor 0.5 with patience of 10 epochs in 50 epochs. We randomly split the dataset into 80% training and 20% testing. All the results are obtained by online evaluation platform.

Table 1. Robust comparison of different methods (Dice %) on BraTS 2018 dataset, ◦ denotes the present modality and ⚫ denotes the missing modality, ↑ denotes the improvement of CR block, bold results denotes the best score.

| Modalities | Complete | Core | Enhancing |
|------------|----------|------|-----------|
|            |          |      |           |
| F T1 T1c T2 | HeMIS Org Our | HeMIS Org Our | HeMIS Org Our |
| ◦ ◦ ◦ ⚫ | 38.6 | 31.4 | 32.3↑ | 19.5 | 14.9 | 15.7↑ | 0.0 | 6.2 | 7.2↑ |
| ◦ ◦ ⚫ ◦ | 2.6 | 29.7 | 33.5↑ | 6.5 | 49.3 | 55.9↑ | 11.1 | 50.0 | 53.5↑ |
| ⚫ ◦ ◦ ◦ | 0.0 | 3.3 | 5.3↑ | 0.0 | 4.3 | 6.3↑ | 0.0 | 4.5 | 5.3↑ |
| ◦ ◦ ◦ ◦ | 55.2 | 71.4 | 73.7↑ | 16.2 | 46.2 | 48.6↑ | 6.6 | 6.0 | 25.8↑ |
| ◦ ◦ ◦ ◦ | 48.2 | 45.1 | 48.3↑ | 45.8 | 48.1 | 50.4↑ | 55.8 | 52.0 | 52.4↑ |
| ◦ ◦ ⚫ ◦ | 15.4 | 11.4 | 29.2↑ | 30.4 | 22.6 | 54.8↑ | 42.6 | 24.8 | 53.8↑ |
| ⚫ ◦ ◦ ◦ | 71.1 | 75.9 | 80.4↑ | 22.8 | 19.4 | 31.5↑ | 2.7 | 7.7 | 10.2↑ |
| ◦ ◦ ◦ ◦ | 47.3 | 31.6 | 35.5↑ | 17.2 | 12.9 | 14.3↑ | 0.6 | 2.5 | 6.1↑ |
| ⚫ ◦ ◦ ◦ | 74.8 | 80.4 | 81.3↑ | 17.7 | 20.7 | 25.0↑ | 0.8 | 0.9 | 10.0↑ |
| ◦ ◦ ◦ ◦ | 68.4 | 80.3 | 81.5↑ | 41.4 | 65.7 | 73.4↑ | 53.8 | 62.7 | 67.5↑ |
| ◦ ◦ ◦ ◦ | 70.2 | 81.1 | 82.7↑ | 48.8 | 71.7 | 75.8↑ | 60.9 | 65.7 | 68.4↑ |
| ⚫ ◦ ◦ ◦ | 75.2 | 83.5 | 85.4↑ | 18.7 | 41.3 | 44.4↑ | 1.0 | 11.1 | 12.9↑ |
| ◦ ◦ ◦ ◦ | 75.6 | 87.5 | 87.7↑ | 54.9 | 74.2 | 77.4↑ | 60.5 | 65.4 | 67.2↑ |
| ◦ ◦ ◦ ◦ | 44.2 | 46.9 | 50.1↑ | 46.6 | 51.2 | 52.1↑ | 55.1 | 54.3 | 54.8↑ |
| ⚫ ◦ ◦ ◦ | 73.8 | 87.9 | 88.1↑ | 55.3 | 76.2 | 78.8↑ | 61.1 | 68.1 | 69.1↑ |

| Wins / 15 | 2 | 0 | 13 | 2 | 0 | 13 | 2 | 0 | 13 |

4 Experiments Results

**Quantitative Analysis.** The main advantage of our method is using the correlation representation, which can discover the latent correlation representation between modalities to make the model robust at the absence of modalities. To prove the effectiveness of our model, we use Dice score as the metric, and compare two other approaches. (1) HeMIS [5], the current state-of-the-art method for segmentation with missing modalities. (2) Org, a specific case of our model without correlation representation block. From Table 1, for all the tumor regions, our method achieves the best results in most of all cases (13/15). Compared to HeMIS, the Dice score of our method just gradually drops when modalities are
missing, while the performance drop is more severe in HeMIS. Compared to Org, the correlation representation block makes the model more robust in the case of missing modalities, which demonstrates the effectiveness of the proposed component and also proves our assumption. We can also find that, missing FLAIR modality leads to a sharp decreasing on dice score for all the regions, since FLAIR is the principle modality for showing whole tumor. Missing T1 and T2 modalities would have a slight decreasing on dice score for all the regions. While missing T1c modality would have a severe decreasing on dice score for both tumor core and enhancing tumor, since T1c is the principle modality for showing tumor core and enhancing tumor regions.

**Qualitative Analysis.** In order to evaluate the robustness of our model, we randomly select three examples on BraTS 2018 dataset and visualize the segmentation results in Fig. 6. We can observe that with the increasing number of missing modalities, the segmentation results produced by our robust model just slightly degrade, rather than a sudden sharp degrading. Even with FLAIR and T1c modalities, we can achieve a decent segmentation result.

![Fig. 6. Examples of the segmentation results compared to ground truth. Red: necrotic and non-enhancing tumor core; Orange: edema; White: enhancing tumor.](image)

### 5 Conclusion

We propose a novel multimodal brain tumor segmentation network based on the latent multi-source correlation representation and fusion using attention mechanism for making the model robust to missing data. We demonstrate our method can yield competitive results on BraTS 2018 dataset under both full and missing modalities. The comparison results also show that the important roles of FLAIR and T1c on segmenting the complete tumor and tumor core, respectively. In the future, we want to investigate more complex model to describe the multi-source correlation representation and adapt it to missing data issue.
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