MMCFormer: Missing Modality Compensation Transformer for Brain Tumor Segmentation

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Abstract

Human brain tumours and more specifically Gliomas are the most life-threatening cancers which usually arise from abnormal growth of the glial stem cells. In practice, Magnetic Resonance Imaging (MRI) with several distinctive modalities provides comprehensive information regarding the brain's structure and potential clues for malignant regions detection. Hence, the multi-modalities perspective of the MRI makes it a unique approach to be utilized in almost all clinical trials. However, the presence of artifacts usually results in missing one or more modalities. To make up for the missing information in an end-to-end manner, we propose MMCFormer, a novel missing modality compensation network. Our strategy builds upon 3D efficient transformer blocks and uses a co-training strategy to effectively train a missing modality network. To ensure feature consistency in a multi-scale fashion, MMCFormer utilizes global contextual agreement modules in each scale of the encoders. Furthermore, to transfer modality-specific representations, we propose to incorporate auxiliary tokens in the Transform module to model interaction between full and missing-modality paths. On top of that, we include feature consistency losses to reduce the domain gap in network prediction and increase the prediction reliability for the missing-modality path. Extensive experiment on the Brats 2018 dataset demonstrates the superiority of our method against the competitive approaches. The code is available at GitHub.

Keywords: Transformer, Missing Modality, Segmentation, MRI, Medical.

1. Introduction

Magnetic Resonance Imaging (MRI) is a prevalent non-invasive imaging utility commonly used in medical diagnosis and treatment that can provide a 3D visualization of the human organs, tissues, and skeletal system. However, expert annotation (e.g., identifying the brain tumour location) is mainly required for the interpretation of acquired MRI data, which is typically time-consuming and expensive. In addition, due to the restrictions and artifacts in an imaging modality, radiologist annotation is always accompanied by uncertainty.

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Therefore, Multi-modal medical imaging can be beneficial since it aggregates complementary modality-specific information and allows more accurate pathology assessment, e.g., T1, T1c, T2, and Flair modalities for MRI. However, acquiring the desired imaging modality sometimes is not feasible due to some practical constraints, such as lengthy scan time and image corruption. Hence, the missing modality issue may raise uncertainty for tumour region recognition since analyzing each modality provides unique and comprehensive information (Azad et al., 2022b; Zhao et al., 2022).

Several methods have been presented to solve the problem of automatic segmentation. Over the past decade, Convolutional Neural Networks (CNNs) have been instrumental in the development of medical image segmentation, such as UNet (Ronneberger et al., 2015), and its variants (Valanarasu et al., 2020; Zhou et al., 2018; Azad et al., 2022a), which have been widely used due to their symmetric architecture and potentiality to capture contextual semantic information while preserving multi-scale features with skip connections. Recently, the introduction of the Vision Transformer (ViT) has substantially improved the performance of all computer vision tasks due to its elegant design and the presence of an attention mechanism that effectively captures global information (Dosovitskiy et al., 2020). Since then, Transformers have been diligently deployed in medical image segmentation to compensate for CNN-based approaches' inability to capture sufficient contextual information, yielding poor performance in boundary areas. Motivated by the U-shaped architecture of UNet, Swin-UNet (Cao et al., 2021), and DS-TransUNet (Lin et al., 2022) propose pure transformer models based on Swin Transformer for image segmentation. Similarly, MISSFormer (Huang et al., 2021) employs a hierarchical symmetric encoder-decoder Transformer coupled with the enhanced Transformer block to boost the feature representations. Aside from fully-Transformer models, various approaches have been presented that employ both CNNs and Transformers together to acquire low-level and high-level features (Heidari et al., 2022; Chen et al., 2021). However, these models mandate the presence of all modalities to replicate their excellent results, otherwise, their generality would be limited in the case of a missing modality, and performance would diminish.

Several methods have been proposed for dealing with missing data in medical imaging. Early approaches dive into this problem by synthesizing the missing modality during the training process. However, reconstructing the missing modality usually requires designing a modality-specific network and limits the performance of these strategies for end-to-end training. Therefore, some methods adopt a more efficient strategy, building a uniform model for all possible missing modalities by learning full modality joint representations. HEMIS (Havaei et al., 2016) proposes to encode each modality into an embedding space using separate convolutional layers. Afterward, it calculates the embedded features' first and second-order moments (mean and variance) to establish a common representation space between modalities. During inference, any combination of inputs can be given to construct the segmentation map. The same strategy is then followed by PIMMS (Varsavsky et al., 2018), HVED (Dorent et al., 2019), and URN (Lau et al., 2019) in creating a common latent subspace and seeking to retrieve the missing information using the constructed latent representation. However, such approaches are unable to provide adequate information using only mean and variance and yield poor performance when more than one modality is absent.

In recent years, Generative Adversarial Networks (GANs) have propelled to the forefront of image synthesis investigations by generating synthetic data (Qin et al., 2022; Chang et al.,

2020; Cao et al., 2020; Sharma and Hamarneh, 2019). Nevertheless, employing GAN-based models to tackle with missing modality problem raises several difficulties. In addition to possibly generating undesirable imputation noise when synthesizing the missing modality, they can also show non-converging characteristics, require extensive and careful training, and the generator is likely to become unstable during training. Other approaches, such as the networks described by (Azad et al., 2022c; Liu et al., 2022; Wang et al., 2021), take advantage of the knowledge distillation strategy technique. They offer a co-training strategy for training the complete modality and missing modality models simultaneously in order to complement each other's feature representations and restore missing knowledge of missing modalities. However, their models rely on the CNN structure and are usually unable to effectively capture structural and shape information from full modality, resulting in less accurate prediction when facing with sever missing modalities. Besides that, these methods only perform feature recalibration between the full-modality and the missing-modality paths and lack to imitate the modality-specific information and spatial (region-based) consistency. In this paper, we argue that contextual consistency is crucial for the segmentation task and seek to model such consistency with the Transformer model. Furthermore, we propose to modify the bottleneck representation by including additional tokens to learn modality-specific representation and compensate for the missing information. We create our architecture in a pure Transformer fashion with efficient self-attention blocks and perform the co-training strategy in an end-to-end manner.

2. Proposed Method

The overall structure of the MMCFormer is depicted in Figure 1. MMCFormer is a novel pure Transformer-based approach that adopts the co-training strategy for the MRI missing modality task, where one network is assigned to train the complete modality while the other trains with the missing modality. Co-training is a multi-view algorithm that predicts every data point from two independent views (Rahate et al., 2022). These two views are trained independently and complement one another since both provide unique information. On the other hand, MRI modalities have shown that they can provide comprehensive and distinguishable features of brain structure that enable physicians to have more accurate anatomical and functional examinations. To this end, taking an input 3D modality image $X_i \in R^{H\times W\times D\times C}$ with spatial dimensions $H \times W \times D$ and C channels, we can describe the full-modality data as $X_f = \{\forall X_i, i \in M\}$, and the missing modality as $X_m = \left\{\forall X_i, i \in M^{'}\right\}$, where M indicates the set of modalities (T1, T1w, T2 and Flair) and $M^{'}$ can be any combinations of M (i.e., $M^{'} \subset M$). We define two parallel 3D efficient transformer U-Net for our co-training strategy, where each network is trained separately and simultaneously. One is trained on the complete data (X_f) to obtain comprehensive information about the full modality, the second one is trained on the incomplete data (X_m) to derive the missing modalities details. Using the co-training strategy, allows the full-modality network to distill the knowledge onto the missing one, and compensate for the lack of modality-specific information. In the next subsections, we first present our network structure, and then we will elaborate on our knowledge distillation mechanisms.

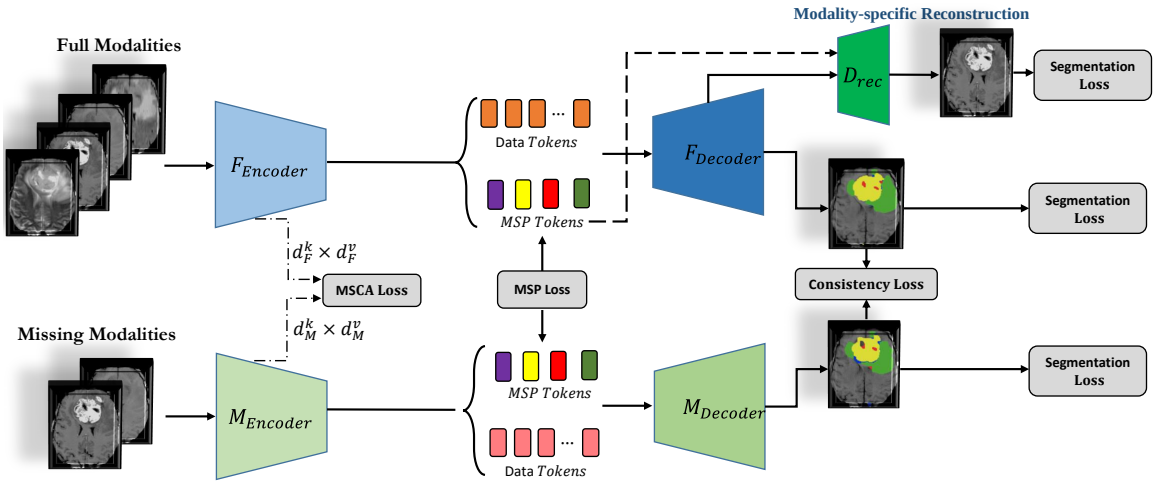

Figure 1: The overview of the proposed MMCFormer. MMCFormer deploys three feature-matching mechanisms to reduce the domain gap and ensure the knowledge distillation process from the full-modality path into a missing modality network.

2.1. Network Architecture

As stated earlier our network builds upon an efficient transformer design to reduce the computational burden for 3D data processing. More precisely, for an input image $X^{H\times W\times D\times C}$, we first perform the tokenization process by extracting n non-overlapped 3D patches and applying the parametric mapping function to embed each token into a d dimensional space. Next, following the general idea of the self-attention mechanism we create the Q, K, and V matrices using linear projections. However, instead of applying the naive self-attention module which suffers from a quadratic computational complexity, we follow the efficient self-attention strategy (Shen et al., 2021):

$$E(Q,K,V) = \rho_q(Q)\left(\rho_k(k)^T V\right) \tag{1}$$

Where ρ shows the softmax operation. It is proven that (Shen et al., 2021) the efficient self-attention module can approximate the standard self-attention operation but with much lower computational complexity, $O(d^2n)$ vs $O(n^2)$. Where d and n indicate the embedding dimension and the number of tokens, respectively. For our U-Net structure, we follow a symmetrical design and include three efficient transformer blocks in each encoder/decoder block. We use patch merging and patch expanding layers in the encoding and decoding paths, respectively. Finally, we include the skip-connection path in each scale of the network to capture multi-scale representation. The same structure is used in both full and missing-modality networks. For training, two main and three auxiliary loss functions are applied to reconstruct the segmentation map and ensure the knowledge distillation between the full modality and the missing modality paths. Our first primary loss function is Dice loss, which computes the loss between the ground truth Y and the predicted mask $Y^{'}$ to learn the segmentation map, as stated as follows:

$$\mathcal{L}_{\text{seg}} = \alpha\mathcal{L}_{\text{dice}}\left(Y_f', Y\right) + \beta\mathcal{L}_{\text{dice}}\left(Y_m', Y\right) \tag{2}$$

In the training step, we set α to 0.6, and β to 0.4. In the second step, we follow (Azad et al., 2022c) and design a consistency loss function to reduce the domain gap between the full modality and the missing one, aiming to reduce the distance between two distribution and increase the confidence of the missing modality model. Therefore, it will improve boundary area estimation in cases where the uncertainty (or entropy) of pixels is high or when the probability of a pixel belonging to a class is low. Equation 3 illustrates our consistency loss function:

$$\mathcal{L}_{Consistency}\left(S_f, S_m\right) = \sum_{i=1}^{c} \left|S_f^i - S_m^i\right| \tag{3}$$

where, S^i indicates the soft prediction map in the i_{th} channel of the network in each path. Next, we design and employ two knowledge distillation modules, namely Multi-Scale Contextual Agreement (MSCA) and Modality-Specific (MSP) tokens, to ensure the effective distillation of the semantic and contextual information associated with the full-modality model into the missing one, which we will elaborate on in the next subsection.

2.2. Knowledge Distillation Modules

MSCA: Considering a rich representation of the full-modality path, we aim to impose a hierarchical knowledge distillation module to the missing-modality path to adaptively recalibrate its feature representation and minimize the domain gap. To this end, we propose the MSCA module, which seeks to minimize the context distribution between the missing and full-modality paths in each scale of the network. In our efficient self-attention mechanism, we compute the global context (GC) using the query and value vectors as $GC = (\rho_k(k)^T V) \in R^{d\times d}$. To effectively align the correlation matrix calculated in both paths (GC_f and GC_m) we strive to minimize the distance as follows:

$$\mathcal{L}_{\text{MSCA}}\left(\mathbf{GC}_f, \mathbf{GC}_2\right) = 1 - \frac{\operatorname{tr}\left\{\mathbf{GC}_f \mathbf{GC}_m\right\}}{\|\mathbf{GC}\| \, \|\mathbf{GC}_m\|} \quad \in [0,1] \tag{4}$$

The $\mathcal{L}_{\text{MSCA}}$ becomes zero when the correlation matrices are equal and one if they have maximum difference. Using the inner product, the above equation can be reformulated as:

$$\mathcal{L}_{\text{MSCA}}\left(\mathbf{GC}_f, \mathbf{GC}_m\right) = 1 - \frac{\left\langle \operatorname{vec}\left\{\mathbf{GC}_f\right\}, \operatorname{vec}\left\{\mathbf{GC}_m\right\}\right\rangle}{\|\operatorname{vec}\left\{\mathbf{GC_f}\right\}\|_2 \, \|\operatorname{vec}\left\{\mathbf{GC_m}\right\}\|_2} \tag{5}$$

It is evident that the reformulated equation calculates the orthogonality among correlation matrices in $d * d$ dimensional space. To make it more clear the product between the correlation matrices can be written by means of the eigenvalue decomposition:

$$\mathbf{GC}_f \mathbf{GC}_m = \mathbf{U}_1 \mathbf{\Lambda}_1 \mathbf{U}_1^H \mathbf{U}_2 \mathbf{\Lambda}_2 \mathbf{U}_2^H = \mathbf{U}_1 \mathbf{D} \mathbf{U}_2^H \tag{6}$$

$$(\mathbf{D})_{ij} = \mathbf{u}_{(1),i}^H \mathbf{u}_{(2),j} \lambda_{(1),i} \lambda_{(2),j} \tag{7}$$

Where D_{ij} demonstrates (i, j) element of D. Also, $u_{(1),i}$ and $u_{(2),j}$ are the ith and jth column of U_1 and U_2, respectively and $\lambda_{(1),i}$ and $\lambda_{(2),j}$ show the corresponding eigenvalue. The value of D becomes zero whether $u_{(1),i}$ and $u_{(2),j}$ are orthogonal or either $\lambda_{(1),i}$ or $\lambda_{(2),j}$ is zero. The zero matrix for D results in $tr(GC_f GC_m)$ being zero, and as a result,

the correlation matrix becomes one. However, more overlap in the signal spaces of GC_f and GC_m brings a higher effect in the product and a decrease in the $\mathcal{L}$. Concerning this character of the $\mathcal{L}$, it is an effective approach to align the correlation of the missing modality path to the full-modality one.

Modality Specific (MSP) Module: In the MCA module, we aimed to align the feature distribution between the two networks. However, such alignment might suppress the discriminative modality-specific (MS) features that existed in the full-modality paths. Therefore, we design the MSP module to preserve discriminative features in the full path and transfer this information to the missing-modality path. For this purpose, we define four modality-specific tokens in the network bottleneck, where each token aims to preserve distinctive features of each input modality. We choose bottleneck since it contains highly condensed low-dimensional information of label maps, hence, we can exploit its useful and distinctive features to distill the modality-specific knowledge to the missing model. Thus, MSP loss is calculated using the output of full and missing tokens from the bottleneck, culminating in transferring modality-specific distinguishing features from the complete model to the incomplete one. The MSP loss is defined as:

$$\mathcal{L}_{MSP}\left(MSP_f, MSP_m\right) = \sum_{i=1}^{M} |MSP_f^i - MSP_m^i| \tag{8}$$

This soft-aligned feature representation helps the missing-modality path to reconstruct the discriminative features which are not feasible through its incomplete input modalities. We finally devise a reconstruction loss in the full-modality path to ensure that each token learns modality-specific information. To do so, we employ an auxiliary reconstruction decoder head (D_{rec}) alongside the segmentation head to perform the reconstruction task. In each step, we randomly take one of the tokens alongside the resultant feature maps from the previous decoder layer to input into the reconstruction decoder, seeking to reconstruct the modality assigned to the class token. By doing so, we can guarantee that each token learns distinctive modality information. For the reconstruction loss, we use the combination of MS-SSIM and L1 distance (Zhao et al., 2016) to better reconstruct the high-frequency information alongside the image content, which are crucial for the MRI modalities:

$$\mathcal{L}_{recon} = \theta \underbrace{\left[1 - l_M(\tilde{p}) \cdot \prod_{j=1}^{M} cs_j(\tilde{p})\right]}_{\mathcal{L}_{\text{MS-SSIM}}} + (1-\theta).G_{\sigma_G^M}.\underbrace{\frac{1}{N}\sum_{p\in P} |X_i(p) - Y'_{recon}(p)|}_{\mathcal{L}_{\ell_1}} \tag{9}$$

where Y'_{recon} is the reconstruction output. l_M and cs_j are derived from SSIM Equation 10 at scales M and j.

$$\text{SSIM}(p) = \frac{2\mu_x\mu_y + C_1}{\mu_x^2 + \mu_y^2 + C_1} \cdot \frac{2\sigma_{xy} + C_2}{\sigma_x^2 + \sigma_y^2 + C_2} = l(p) \cdot cs(p) \tag{10}$$

p stands for pixel. According to (Zhao et al., 2016), means and standard deviations are calculated using a Gaussian filter with a standard deviation σ_G, denoted G_{σ_G}. Moreover, MS-SSIM, a multi-scale form of SSIM, necessitates observing pixels at a neighbourhood of

p within a window with the same kernel size as G_{σ_G}, whereas calculating its derivative is infeasible in some boundary regions. Hence, the loss at the window is approximated by computing loss at its center pixel $\tilde{p}$.

2.3. Joint Objective

Eventually, the overall loss function $\mathcal{L}$ is formulated by:

$$\mathcal{L} = \mathcal{L}_{seg} + \lambda_0 \mathcal{L}_{con} + \lambda_1 \mathcal{L}_{MSCA} + \lambda_2 \mathcal{L}_{MSP} + \lambda_3 \mathcal{L}_{recon} \tag{11}$$

To determine the contribution of each loss to the overall loss value, we use λ coefficients, which are set experimentally. The model is trained using Adam optimization with a learning rate of 0.0001 and batch size 1 for 250 epochs. In addition, the code is developed in PyTorch, and the model is trained on a single RTX 3090 GPU.

3. Experimental Results

3.1. Dataset and Evaluation Metric

For the performance evaluation we use BraTS 2018 dataset (Menze et al., 2014; Bakas et al., 2018), which has been a common benchmarking venue for brain glioma segmentation pipelines with well-curated multi-institutional MRI data. This dataset includes 250 cases, each with four 3D MRI modalities (T1, T1c, T2, and FLAIR) rigidly aligned, resampled to $1 \times 1 \times 1$ mm isotropic resolution, and skull-stripped. The input volumetric spatial data size is 240×240 with 155 slices each. Annotations for the BraTS dataset include three tumor subregion classes: the enhancing tumor, the peritumoral edema, and the necrotic and non-enhancing tumor core. In our experiment, we follow the pre-processing step and the same input size suggested in (Azad et al., 2022c) to evaluate our network in terms of the dice similarity coefficient (DSC).

3.2. Comparative Results

In Table 1 we provided the comparative results on each combination of the missing modality scenario. It can be seen that compared to HeMIS (Havaei et al., 2016) and HVED (Dorent et al., 2019) strategies our approach produces better segmentation results, specifically in the single modality (e.g., only T1) scenario. Moreover, SMU-Net (Azad et al., 2022c) proposes to decompose the representational space into style and content vectors and then strive to minimize the distribution difference between the full and missing modality path to perform knowledge distillation. Similarly, the ACN (Wang et al., 2021) takes the same perspective and performs the knowledge distillation in terms of both style and content modules but without implicitly mentioning it. Although both approaches strive to maximize the similarity between full and missing networks, they lack to include a mechanism to preserve the modality-specific features and distill such representation to the student network. On the contrary, our approach proposes MSP tokens combined with the reconstruction head to guarantee such information preservation and performance gain. Quantitatively, compared to the U-HeMIS and HVED works our approach significantly improves the performance by a 12-49 dice score for single modality scenarios. In addition, compared to SMU-Net and

Table 1: Performance comparison on the BraTS 2018 dataset using Dice metric. HeM, HVE and MMC indicate the HeMIS, HVED and our proposed MMCFormer models, respectively.

Modalities				Complete					Core					Enhancing				
Flair	**T1**	**T1c**	**T2**	**HeM**	**HVE**	**ACN**	**SMU**	**MMC**	**HeM**	**HVE**	**ACN**	**SMU**	**MMC**	**HeM**	**HVE**	**ACN**	**SMU**	**MMC**
○	○	○	●	79.2	80.9	85.4	**85.7**	84.3	50.5	54.1	66.8	67.2	**69.1**	23.3	30.8	41.7	43.1	**49.9**
○	○	●	○	58.5	62.4	79.8	80.3	79.7	58.5	66.7	83.3	84.1	**86.4**	60.8	65.5	78.0	78.3	**79.3**
○	●	○	○	54.3	52.4	**78.7**	78.6	**78.9**	37.9	37.2	70.9	69.5	**70.9**	12.4	13.7	41.8	42.8	**42.9**
●	○	○	○	79.9	82.1	87.3	**87.5**	86.6	49.8	50.4	66.4	**71.8**	69.2	24.9	24.8	42.2	46.1	**49.0**
○	○	●	●	81.0	82.7	84.9	**86.1**		69.1	73.7	83.2	**85.0**		68.6	70.2	74.9	**75.7**	
○	●	●	○	63.8	66.8	79.6	**80.3**		64.0	69.7	83.9	**84.4**		65.3	67.0	**75.3**	75.1	
●	●	○	○	83.9	84.3	86.0	**87.3**		56.7	55.3	70.4	**71.2**		29.0	24.2	42.5	**44.0**	
○	●	○	●	80.8	82.2	84.4	**85.6**		53.4	57.2	72.8	**73.5**		28.3	30.7	46.5	**47.7**	
●	○	○	●	86.0	87.5	86.9	**87.9**		58.7	59.7	70.7	**71.2**		28.0	34.6	44.3	**46.0**	
●	○	●	○	83.3	85.5	87.8	**88.4**		67.6	72.9	82.9	**84.1**		68.0	70.3	**77.5**	77.3	
●	●	●	○	85.1	86.2	**88.4**	88.2		70.7	74.2	83.3	**84.2**		69.9	71.1	75.1	**76.2**	
●	●	○	●	87.0	88.0	87.4	**88.3**		61.0	61.5	67.7	**67.9**		33.4	34.1	42.8	**43.1**	
●	○	●	●	87.0	**88.6**	87.2	88.2		72.2	75.6	**82.9**	82.5		69.7	71.2	73.8	**75.4**	
○	●	●	●	82.1	83.3	**86.6**	86.5		70.7	75.3	83.2	**84.4**		69.7	71.1	75.9	**76.2**	
●	●	●	●	87.6	88.8	**89.1**	88.9		73.4	76.4	84.8	**87.3**		70.8	71.7	78.2	**79.3**	
Mean				78.6	80.1	85.3	**85.9**		59.7	64.0	76.8	**77.9**		48.1	50.1	60.70	**61.8**	

the ACN approaches the DSC score slightly rises by 1-3%. Visual segmentation results are presented in Figure 2 for single modality scenarios. It can be observed that the model can predict the brain tumour regions, where the such prediction was not feasible by only relying on the input data without reconstructing the missing information.

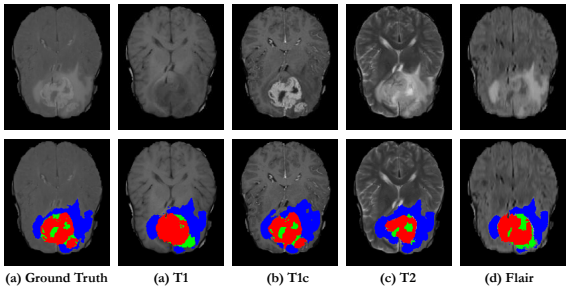

Figure 2: Segmentation results of the MMCFormer in single modality setting using Brats 2018 dataset. The WT, edema and necrotic regions are visualized with blue, red and colours.

Table 2: Contribution of each MMCFormer module on the overall performance. All experiments were done using only the T2 modality as an input for the missing modality network.

$\mathcal{L}_{\text{MCA}}$	$\mathcal{L}_{\text{MSP}}$	$\mathcal{L}_{\text{recon}}$	WT	CT	ET	Average
✗	✓	✓	83.2	68.8	48.7	66.9
✓	✗	✓	80.1	66.5	47.9	64.9
✓	✓	✗	84.0	68.5	49.2	67.2
✓	✓	✓	84.3	69.1	49.9	67.8

3.3. Ablation Study

To analyze the effect of each module on the overall performance we provide the ablation study in Table 2. It can be observed that by eliminating each module from the proposed structure the overall performance slightly decreases. The most performance drop happens when the MSP tokens are eliminated, hence, showing the importance of preserving MS features. More ablation study is provided in the appendix section.

4. Conclusion

To address missing modality in an end-to-end manner we proposed our MMCFormer model, which utilizes a co-training strategy to perform knowledge distillation from the full-modality network into a missing modality one. To preserve modality-specific features we proposed MSP tokens in conjunction with the reconstruction head to distill more discriminative

features to the student network. We also included a context agreement module to refine the feature representation in each scale of the co-training strategy.

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Appendix A. Details on Network Architecture

The MMCFormer framework employs a pure Transformer-based hierarchical U-Net structure that builds upon a 3D efficient Transformer. As shown in Figure 3(a), there are two paths incorporated in the proposed model, namely the full-modality and the missing-modality paths. Both paths use the same structure but with different input data. In each path, the input image $X \in R^{H\times W\times D\times C}$ is first processed by a patch embedding module, which creates overlapping patch tokens of size $4 \times 4 \times 4$. These tokens are then processed by the encoder, which consists of three stacked encoder blocks. Each block contains two successive 3D efficient Transformer layers and a patch merging layer that merges $2 \times 2 \times 2$ patch tokens to reduce the spatial dimension while doubling the channel dimension. This hierarchical representation enables the model to acquire an overview of multiple scales and enhance the feature representations. In the decoder, the patch-expanding block increases the number of tokens by a factor of 2. The output of each patch-expanding block is then fused with the features from the corresponding encoder layer using a linear layer to recover spatial and fine-grained information. The resulting features are subsequently passed into

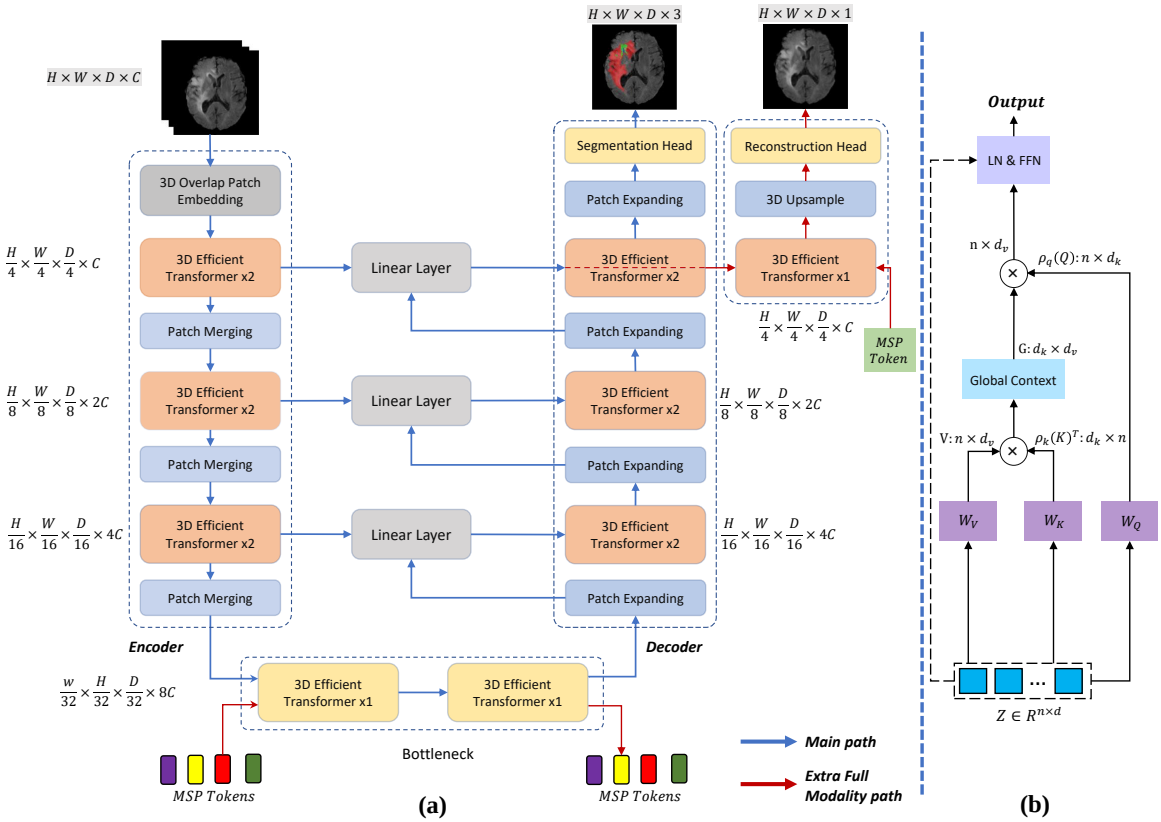


Figure 3: (a) The overview of the proposed network structure. (b) The structure of efficient Transformer.

two 3D efficient Transformer layers. Finally, a linear projection layer generates the final segmentation map.

For the extra full-modality path, we define four modality-specific tokens entered into the bottleneck. We then design a modality reconstruction task to ensure that each token learns specific modality information. One of the four tokens is then randomly selected and fed into the single 3D efficient Transformer layer along with the resultant feature map obtained from the last skip connection in order to reconstruct the specific modality assigned to the token. A 3D upsampling module followed by a linear reconstruction head is finally applied to acquire the modality-specific reconstruction image.

Appendix B. Extreme Missing Modality

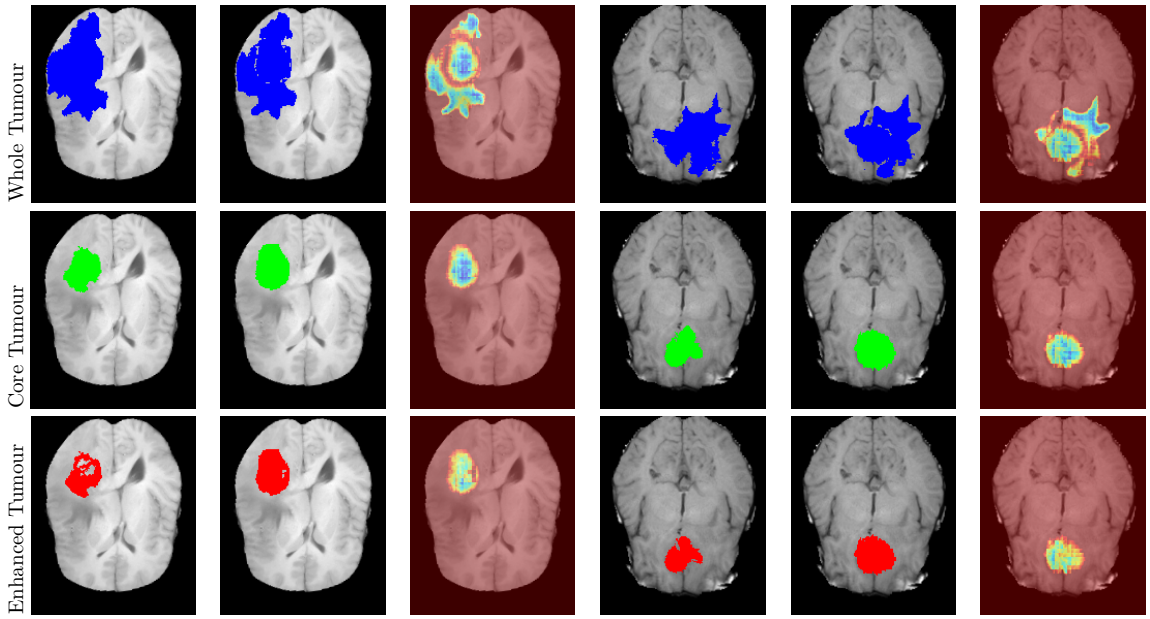
To further provide an insight into the effectiveness of our suggested framework for reconstructing the missing information, we offer quantitative and qualitative results in extremely missing modalities setting as presented in (Azad et al., 2022c). In this respect, we follow (Azad et al., 2022c) and design a scenario where during the training process the missing modality path only uses a single modality to learn the brain tumour segmentation map while benefiting from the full-modality path. During the test time, we only use the trained missing-modality path with a single modality as an input. Table 3 illustrates the quanti-

tative results. For the comparison, we also include our baseline model, which consists of the co-trained Transformer-based U-Net model without any knowledge distillation mechanism. Quantitative results demonstrate that the MMCFormer surpasses the U-Net baseline method significantly. Besides that, our method achieves competitive results on all single modalities compared to the SOTA approaches. More specifically, in the T1, T1ce and T2 modalities, our network surpasses the ACN and SMU-Net models by a large margin. Similarly, for the Flair modality, our method performs better compared to the ACN and HeMIS and HVED methods and is equivalent to the SMU-Net model. The obtained results prove the efficacy of the suggested framework in learning task-specific patterns and recovering the missing information.

Table 3: Quantitative results of the proposed MMCFormer model against the SOTA approaches on BraTS 2018 series with extreme missing modality scenario. We use the average of the whole, enhanced and core tumour segmentation scores to report the dice score for each modality.

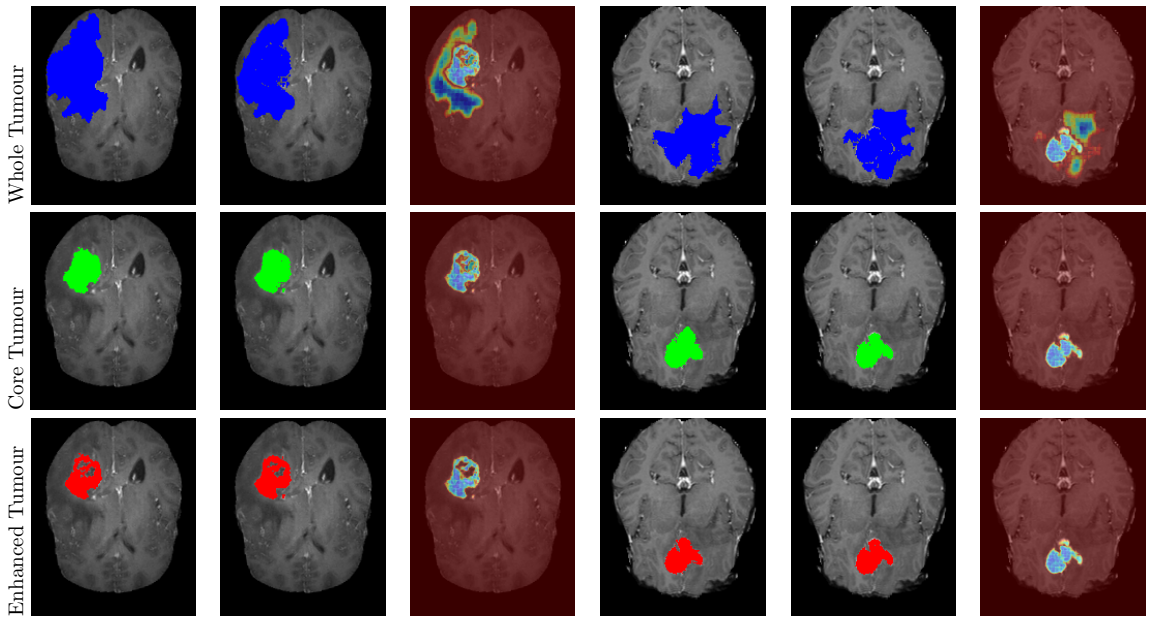
Article	**Dice score**				
	T1	**T1c**	**T2**	**FLAIR**	**AVG**
Our Baseline	61.2	77.3	60.1	58.2	64.2
U-HeMIS (Havaei et al., 2016)	16.7	59.2	36.0	51.5	48.8
HVED (Dorent et al., 2019)	34.4	64.8	55.2	52.4	51.7
ACN (Wang et al., 2021)	63.8	80.3	64.6	65.3	68.5
SMU-net (Azad et al., 2022c)	63.3	80.9	65.3	68.4	69.4
MMCFormer	64.2	81.8	67.8	68.3	**70.5**

To visually analyze the qualitative performance of our suggested framework, we have provided the Grad-CAM (Selvaraju et al., 2017) attention maps in Figure 4-Figure 7 for each modality. In this respect, we trained and evaluated the network with an extremely missing modality setting. It can be seen that the MMCFormer localizes the brain tumour region with high confidence in a single modality case. This might explain the effect of our co-training strategy for recovering the missing information. Additionally, the T1 modality is more effective for characterizing the structural information and less informative for detecting for core tumour region, however, our MMCFormer with a T1 modality can recognize the tumour region with high confidence which indicates the importance of our suggested modules for recovering the missing information. Similarly for other modalities, we can observe that the activation map has a high magnitude around the tumour region and it highly overlaps with the grand truth annotation mask. On top of that, we can observe that the MMCFormer attention has less variance and it is in line with the ground truth map, which shows the effect of reconstructed features for precise boundary prediction.



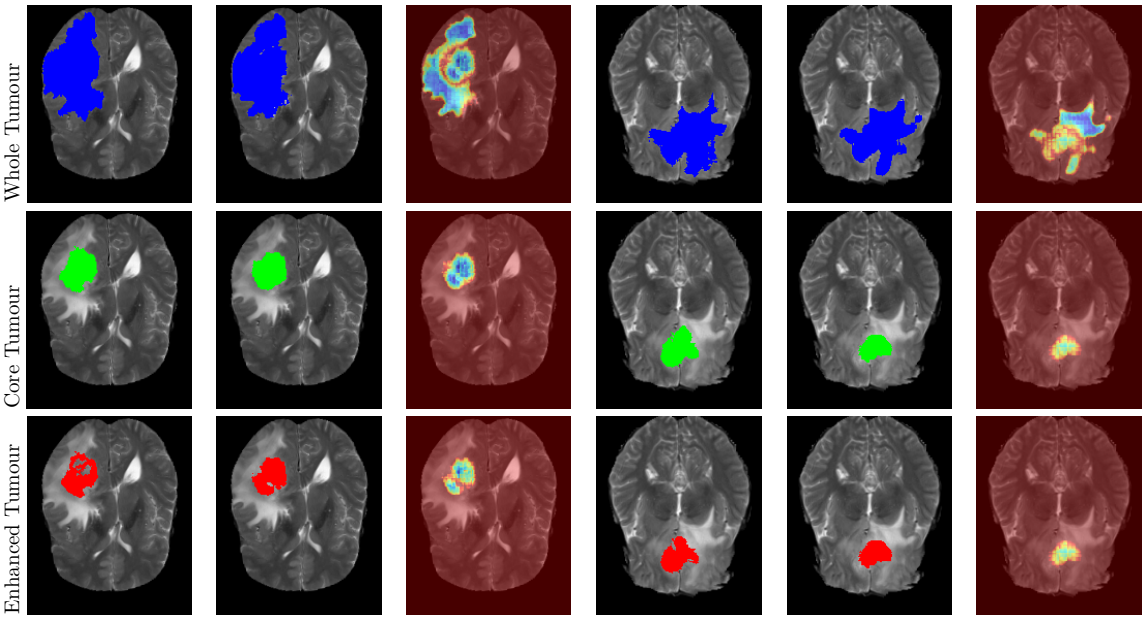
(a) Ground Truth (b) Prediction (c) Heatmap (d) Ground Truth (e) Prediction (f) Heatmap

Figure 4: Visualization of the activation map on T1 modality using our suggested MMCFormer.



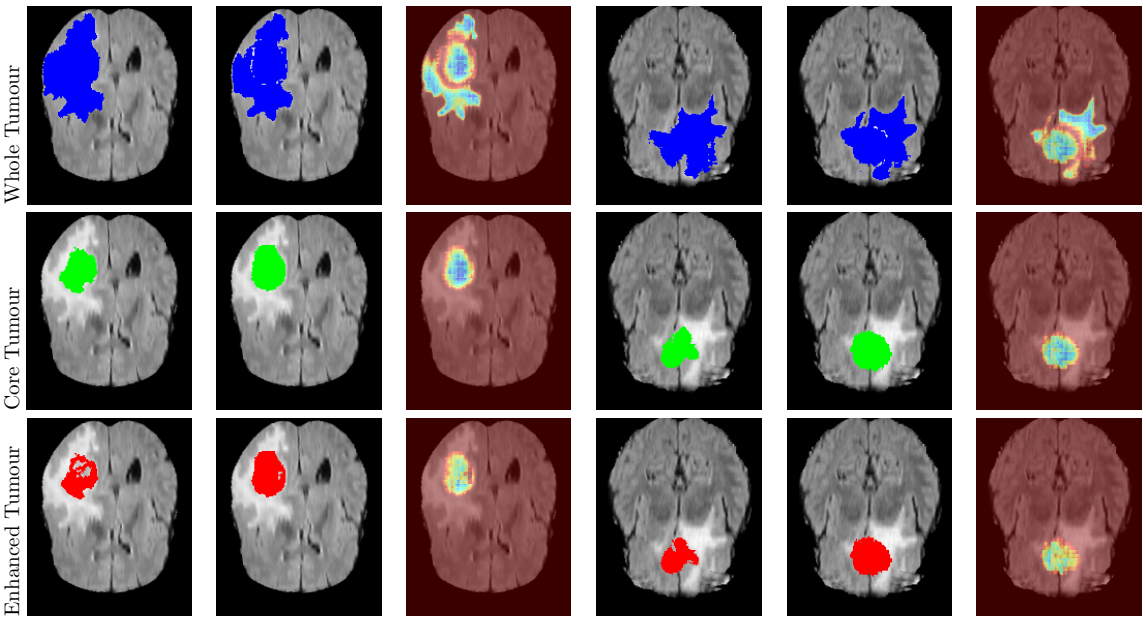
(a) Ground Truth (b) Prediction (c) Heatmap (d) Ground Truth (e) Prediction (f) Heatmap

Figure 5: Visualization of the activation map on T1c modality using our suggested MMCFormer.



(a) Ground Truth (b) Prediction (c) Heatmap (d) Ground Truth (e) Prediction (f) Heatmap

Figure 6: Visualization of the activation map on T2 modality using our suggested MMCFormer.



(a) Ground Truth (b) Prediction (c) Heatmap (d) Ground Truth (e) Prediction (f) Heatmap

Figure 7: Visualization of the activation map on Flair modality using our suggested MMCFormer.