C-MADA: Unsupervised Cross-Modality Adversarial Domain Adaptation framework for Medical Image Segmentation

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ABSTRACT

Deep learning models have obtained state-of-the-art results for medical image analysis. However, CNNs require a massive amount of labelled data to achieve a high performance. Moreover, many supervised learning approaches assume that the training/source dataset and test/target dataset follow the same probability distribution. Nevertheless, this assumption is hardly satisfied in real-world data and when the models are tested on an unseen domain there is a significant performance degradation. In this work, we present an unsupervised Cross-Modality Adversarial Domain Adaptation (C-MADA) framework for medical image segmentation. C-MADA implements an image-level and feature-level adaptation method in a two-step sequential manner. First, images from the source domain are translated to the target domain through an unpaired image-to-image adversarial translation with cycle-consistency loss. Then, a U-Net network is trained with the mapped source domain images and target domain images in an adversarial manner to learn domain-invariant feature representations and produce segmentations for the target domain. Furthermore, to improve the network’s segmentation performance, information about the shape, texture, and contour of the predicted segmentation is included during the adversarial training. C-MADA is tested on the task of brain MRI segmentation from the crossMoDa Grand Challenge and is ranked within the top 15 submissions of the challenge.

Keywords: Domain Adaptation, Image Segmentation, Medical Image Analysis, Generative Adversarial Networks, Unsupervised Learning

1. INTRODUCTION

Medical image segmentation is a critical step in computer-aided diagnosis and therapy. In clinical practice, medical images are usually manually segmented by radiologists, which is a time-consuming and costly process with limited reproducibility\textsuperscript{1}. In the last decade, deep convolutional neural networks (CNNs) have become the state-of-the-art models for automatically segmenting medical images\textsuperscript{2-5}. However, CNNs still require a massive amount of labelled data to achieve a high performance. Moreover, many supervised learning approaches assume that the training dataset (source dataset) and test dataset (target dataset) follow the same probability distribution. Nevertheless, this assumption is hardly satisfied in real-world data. Hence, when neural networks are tested in images that pertain to a different distribution, their performance degrades in proportion to the distribution difference\textsuperscript{6,7}. In medical images, the domain shift between source and target datasets is even more severe given the different imaging modalities, equipment, acquisition protocols, and subject populations\textsuperscript{8}.

Simple solutions for domain shift include sampling images from distinct domains or re-training the model in the target domain. Nonetheless, both strategies require labelling enough data from the target domain, which can be difficult or expensive to acquire. Recently, unsupervised domain adaptation (UDA) techniques have gained attention to reduce the gap between source and target domain distributions in an unsupervised manner.
Most UDA models can be broadly categorized into feature-level adaptation methods, image-level adaptation methods, and combined image- and feature-level adaptation methods. In feature-level adaptation, domain-invariant feature representations between input domains are learned. The aim is to reduce domain-specific information while keeping task-related information. Meanwhile in image-level adaptation, images from one domain are aligned to another in terms of appearance by performing a mapping in raw pixel space. Finally, in the image- and feature-level adaptation the two approaches explained previously are combined in a sequential or synergistic manner to improve the adaptation performance. The latter technique has proven to provide a better segmentation performance as both perspectives are complementary and can further reduce the source-target domain gap. Although good progress has been achieved in UDA, most of the works either focus on the task of classifying medical images or segmenting natural images. The segmentation of medical images is a more complicated task given the complexity and particularities of the images. Little work has been presented in the development of image- and feature-level adaptation methods for medical image segmentation. In\textsuperscript{9} the authors propose a synergistic method where both image- and feature-level architectures are trained simultaneously, which is computationally and memory intensive. Moreover, information about the boundary and texture of the segmentation is not explicitly considered during training, which can decrease the performance when segmenting irregular and ill-shaped structures.

In this work, we present C-MADA, an unsupervised Cross-Modality Adversarial Domain Adaptation framework for medical image segmentation. C-MADA implements an image- and feature-level adaptation in a two-step sequential manner. First is the image-level adaptation step, where images from the source domain are translated to the target domain by implementing an unpaired image-to-image adversarial translation with cycle-consistency loss\textsuperscript{10}. Then, in the feature-level adaptation step, a U-Net network is trained with the transformed source images and target images in an adversarial manner to produce probable segmentations for the target domain. Furthermore, a semantic-aware discriminator is trained with information about the shape, texture, and contour of the produced segmentations to improve the model’s capability of defining the correct shape and delineation of the segmentation. C-MADA is evaluated on the problem of tumor and cochlea brain structure segmentation from the crossMoDa Grand Challenge. Our method has a competitive performance on the challenge, being ranked within the top 15 submissions of the challenge.

The contributions of this work are threefold. First, we propose an image- and feature-level adaptation framework for unsupervised domain adaptation that through its two-step implementation preserves the semantic information and low-level appearance variance. Secondly, we present a semantic-aware discriminator, that receives as input information about the shape, texture, and contour of the predicted segmentations to improve the network’s segmentation capacity in the target domain. Finally, we propose a validation loss function based on what we have denominated the class area ratio metric to monitor the performance of the network on the unlabeled target dataset.

2. METHODS

The C-MADA framework is composed of two sequential steps as presented in Figure 1. In step 1, an image-level adaptation method is implemented to transfer the source domain images to the target domain through a pixel-to-pixel transformation. Afterwards, in step 2 a feature-level adaptation method is proposed to produce probable segmentations for the target domain. These steps are explained next.

2.1 Image-level adaptation

The training dataset is comprised of $N_s$ labeled images $\{(x^*_i, y^*_i)\}_{i=1}^{N_s}$ from the source domain $S$, and $N_T$ unlabeled images $\{x_j\}_{j=1}^{N_T}$ from the target domain $T$. The goal is to learn a mapping function that transfers images from domain $S$ to $T$ in terms of image appearance. Since we assume the morphology of anatomical structures are invariant to domain shifts (i.e., the shape of the region being segmented is not affected by changes in the image domain), the mapped source domain images can approximate the target domain distribution and be used to train a CNN network to segment the target domain images.

The image-level adaptation is performed by implementing the unpaired image-to-image translation adversarial network with cycle-consistency constraint (CycleGAN)\textsuperscript{10}. In this model, one generative adversarial network...
(GAN) learns to transform images from domain $S$ to domain $T$, and another GAN to translate images from domain $T$ to domain $S$. For the first GAN model, a generator network $G_S$ maps the source domain images to the target domain producing fake target domain images $\hat{x}^T$ ($G_S : x^S \rightarrow \hat{x}^T$). Meanwhile, a discriminator network $D_S$ aims to distinguish real target domain images $x^T$ from the fake ones $\hat{x}^T$. Hence, $G_s$ and $D_s$ compete in a two-player minimax game where $G_s$ aims to minimize the objective function displayed in Eq. 1, while $D_s$ tries to maximize it.

$$L_{GAN}(G_S, D_S) = E_{x^T \sim T}[\log D_s(\hat{x}^T)] + E_{x^S \sim S}[\log(1 - D_s(G_s(x^S)))]$$ (1)

In the second GAN model, a similar mapping function from target domain to source domain $G_T : x^T \rightarrow \hat{x}^S$ is implemented. Likewise, a discriminator $D_T$ aims to discriminate between $x^T$ and $\hat{x}^S$. $G_T$ and $D_T$ are trained with a similar loss as in Eq. 1. Moreover, to reduce the space of possible mapping functions and incentivize the translation to be cycle consistent, a cycle consistent loss $L_{cy}c$ as displayed in Eq. 1 is added to the objective function in Eq. 1. The cycle consistent loss encourages $G_s(G_T(x^T)) \approx x^T$ and $G_T(G_s(x^S)) \approx x^S$.

$$L_{cy}c(G_S, D_S) = E_{x^T \sim T}[||G_T(G_S(x^S)) - x^T||] + E_{x^S \sim S}[||G_S(G_T(x^T)) - x^T||]$$ (2)

In Eq. 2 $\|\cdot\|$ refers to L1 loss. Finally, we also apply an identity consistency constraint, that encourages the generators to approximate an identity function when images are mapped to the same domain. This loss regularizes the generator to preserve the color and intensities during the transformation. The identity loss is presented in Eq. 3, where $\|\cdot\|$ refers to L1 loss.

$$L_{identity}(G_S, G_T) = E_{x^T \sim T}[||G_T(x^S) - x^T||] + E_{x^S \sim S}[||G_S(x^T) - x^T||]$$ (3)
The full objective function being optimized during this step is presented in Eq. 4.

\[
L_{adv}(G_S, G_T, D_S, D_T) = L_{GAN}(G_S, D_S) + L_{GAN}(G_T, D_T) + \lambda_1 L_{cyc}(G_S, G_T) + \lambda_2 L_{identity}(G_S, G_T)
\]  

(4)

The generator networks have a ResNet architecture,\textsuperscript{11} while the discriminators have a PatchGAN structure\textsuperscript{12}. Also, we set \( \lambda_1 = 10 \) and \( \lambda_2 = 2.5 \).

### 2.2 Feature-level adaptation

Once the source domain images are translated to the target domain, a U-Net architecture is trained to segment the target domain images in two phases. In the first phase, the residual U-Net is fully trained in a supervised manner using only the translated source dataset \( \{ (\hat{x}^T_i, y^T_i) \}_{i=1}^{N_t} \). The loss function being minimized is a linear combination of the Dice coefficient and cross-entropy loss as presented in Eq. 5:

\[
L_{seg} = \beta \sum_c \alpha_c \left( 1 - \frac{2 \sum \hat{y}_{ic} y_{ic}}{\sum \hat{y}_{ic} + \sum y_{ic}} \right) + (1 - \beta) \sum_i \sum_c (y_{ic} \log(\hat{y}_{ic}) + (1 - y_{ic}) \log(1 - \hat{y}_{ic})) ,
\]  

(5)

where \( y_{ic} \) and \( \hat{y}_{ic} \) are the are the ground-truth label and the predicted probability for pixel \( i \) in class \( c \), respectively. \( \alpha_c \) are weight parameters for the dice loss in class \( c \), and \( \beta \) a weight parameter for the dice loss. We set \( \alpha_0 = 0.1, \alpha_0 = 0.4, \alpha_0 = 0.5 \), and \( \beta = 0.65 \). Moreover, to help the U-Net learn rich hierarchical features, we add a deep supervised layer with an auxiliary segmentation loss\textsuperscript{13} in the second-last up-sampling block. Thus, the final loss function is composed of the loss of the main output and the loss of the deep supervised layer.

In the second phase, a feature-level adaptation method is applied to the fully trained residual U-Net to further reduce the domain shift. This phase is especially necessary when there is a severe domain gap between target and source images. The feature-level adaptation is implemented through an adversarial learning scheme where the U-Net takes the role of the generator \( G \). As shown in Fig. 1, the mapped source domain images \( x^T \) and target domain images \( x_T \) are fed to the generator to produce the predicted segmentations \( G(x^T) = \hat{y}^S \) and \( G(x_T) = \hat{y}^T \), respectively. A discriminator \( D \) receives as input \( \hat{y}^S \) and the ground-truth segmentation from the source domain \( y^S \), in addition to boundary information, and aims to discriminate between the two. Meanwhile, \( G \) is trained to trick the discriminator by learning domain invariant features and producing a probable segmentation for the target domain. The objective function being optimized in this feature-adaptation phase is presented in Eq. 6, where \( G \) looks to minimize it and \( D \) maximize it.

\[
L_{FADP}(G, D) = \mathbb{E}_{x^T \sim T}[\log D_S(\hat{y}^S)] + \mathbb{E}_{x_T \sim S}[\log(1 - D_S(\hat{y}^T))],
\]  

(6)

Inspired by\textsuperscript{14}, the input to \( D \) is the concatenation of the predicted segmentation, the elementwise multiplication of the predicted segmentation and original image, and the boundary of the predicted segmentation by applying a Sobel operator. Therefore, providing \( D \) with enough information about the shape, texture, and contour of the segmented region to force the U-Net to be boundary and semantic-aware.

Moreover, to increase the adaptation in the low-level feature space, we implement an additional auxiliary discriminator network \( D_{aux} \) that takes as input the predicted segmentation for the target domain from the deep supervised layer and \( y^S \), with their corresponding boundary information, and is trained to maximize Eq. 6. Finally, to prevent catastrophic forgetting from the source domain, during each training iteration the U-Net is trained in a supervised manner with the mapped source images applying the loss function in Eq. 5.
2.3 Validation Metric

A challenge that arises when training an UDA model is selecting the weights that will be used for testing. Since there are no labelled images from the target dataset, there is no straight-forward metric that can be used to validate how the network will perform. Therefore, we propose a validation loss function based on an area ratio metric to monitor the performance of the network on the target dataset. Using the ground truth segmentations from the source domain, we compute the average number of pixels that are part of class c per slice (SAvgPixc) as shown in Eq. 7.

\[
SAvgPixc = \frac{\sum_{n_s} \sum_{y^S_{ic}}}{n_s},
\]

where \(n_s\) are the number of slices in the in the source domain, and \(y^S_{ic}\) the pixels in the source domain’s ground truth that correspond to class c. Since the segmented regions should be consistent across the different imaging modalities, we assume \(SAvgPixc\) is a good approximator of the average number of pixels from class c in the target domain segmentation. Therefore, to validate the model during training, we compute the average number of pixels predicted to be part of class c in the target domain segmentation and divide it by \(SAvgPixc\). We have named this metric the class area ratio and prefer weights whose values are close to 1. Moreover, to include information about the segmentation performance of the network in the function we add the dice loss in each class on the source domain. Hence the weight that minimizes the function displayed in Eq. 8 is selected for testing.

\[
Validation Loss = \sum_c \left[ 1 - \frac{\sum_{n_T} \sum_{\hat{y}^T_{ic}}}{SAvgPixc} \right] + \sum_c \left( 1 - \frac{2\sum_{i} \hat{y}^T_{ic}y_{ic}}{\sum_{i} y_{ic} + \sum_{i} \hat{y}^T_{ic}} \right),
\]

where \(n_T\) are the number of slices in the in the target domain, and \(\hat{y}^T_{ic}\) the predicted pixels in the target domain that correspond to class c.

3. RESULTS

C-MADA is evaluated on the task of brain MR image segmentation from the Cross-Modality Domain Adaptation Grand Challenge. The training dataset is composed of 105 contrast-enhanced T-weighted (ce-T1) MRIs with their corresponding ground truth segmentation for the source domain, and 105 unlabeled high-resolution T2-weighted MRIs (hrT2) for the target dataset. The validation set is comprised of 32 unlabeled hrT2 MRIs. The objective is the segmentation of vestibular schwannoma (VS) and cholea. Source and target domain images are resampled to a spatial resolution of 0.468 x 0.4681.5 mm and set to a fixed size of 448x448x120 voxels. Moreover, all pixel intensities are clipped within the 3 standard deviations of the mean and rescales to a range of 0 to 1. The adversarial model in the image-level adaptation is trained for 40 epochs. Meanwhile, the residual U-Net is trained for 500 epochs during phase 1 of the feature-level adaptation, and the adversarial model of phase 2 for 100 epochs. The weights for the U-Net that minimize the validation loss in Eq. 7 are used for evaluation. The model is implemented in Pytorch and trained using a 32 GB V100 GPU.

3.1 Validation Results

The evaluation of the validation cases is carried via online submission to the challenge. The dice similarity coefficient (DSC) and mean average symmetric surface distance (ASSD) are used to assess the segmentation on each validation case. In Table 1 we present the ablation studies of the proposed model using the mean DSC and mean ASSD as evaluation metrics. In Table 1, S1+ Network refers to the implementation of step 1 to produce the image-level adaptation and then fully training the Network with the mapped source domain images to segment the target (i.e. S1+U-Net refers to fully training the U-Net architecture on the mapped source dataset). On the other hand, C-MADA (seg) refers to implementing step 1 and step 2 of the proposed framework but feeding to the discriminator D in phase 2 only the predicted segmentation as input. The results demonstrate that each
step in the framework is necessary for the successful segmentation of the target images. Specifically, applying just an image-level adaptation is not sufficient to provide a good segmentation on the target dataset specially in the cochlea structure. Including the feature-level adaptation by considering only the segmentations produced in phase 2 has a small improvement in the cochlea segmentation. Moreover, providing information about the texture and contour of the segmented images during phase 2 gives the best performance on the segmentation of both substructures. Finally, we also tested training the U-Net directly on the source domain dataset and using it to predict the target dataset, applying only Phase 2 of the framework, and varying the input to the discriminator D in phase 2. Nevertheless, the proposed validation loss function was low in those configurations and decided not to submit the results to the challenge. In Figure 2, the qualitative results of the C-MADA framework on the validation set is presented.

| Method                  | VS Dice  | VS ASSD | Cochlea Dice | Cochlea ASSD |
|-------------------------|----------|---------|--------------|--------------|
| C-MADA                  | 0.647 ± 0.259 | 7.256 ± 12.067 | 0.402 ± 0.161 | 4.064 ± 9.731 |
| C-MADA([seg])           | 0.597 ± 0.281 | 9.679 ± 15.346 | 0.384 ± 0.176 | 1.932 ± 4.055 |
| S1+residualU-Net        | 0.594 ± 0.280 | 7.144 ± 8.286 | 0.361 ± 0.143 | 5.413 ± 6.667 |
| S1+U-Net                | 0.582 ± 0.285 | 9.778 ± 16.831 | 0.265 ± 0.146 | 2.174 ± 4.034 |
| S1+SegAN\textsuperscript{15} | 0.591 ± 0.307 | 5.236 ± 12.543 | 0.117 ± 0.085 | 6.612 ± 7.702 |

Figure 2. Example of the segmentation results of C-MADA on the unlabeled target domain images (hrT2).

3.2 Benchmark Results

To evaluate the performance of C-MADA against the state-of-the-art models, we submitted our model to the crossMoDa challenge to segment the test set cases. Specifically, the test cases are not released to the challenge
participants. Hence, participants were asked to containerize their methods with docker and submit the docker container for evaluation. Similar to the validation set, the mean DSC and mean ASSD metrics are used to evaluate the segmentation. C-MADA is ranked within the top 15 submissions of the challenge, specifically in place 13. In Table 2, the evaluation metrics for C-MADA and competing methods are presented. C-MADA has a competitive performance in the segmentation of the vestibular schwannoma. Given the small and irregular shape of the cochlea, the model has more difficulty segmenting this structure.

Table 2. Comparison of competing methods on the CrossMoDa challenge.

| Team         | VS Dice | VS ASSD | Cochlea Dice | Cochlea ASSD |
|--------------|---------|---------|--------------|--------------|
| Samoyed      | 0.8297  | 0.5232  | 0.8488       | 0.3424       |
| PKU BIALAB   | 0.8707  | 0.366   | 0.7978       | 0.2955       |
| jwc-rad      | 0.8288  | 1.0436  | 0.8217       | 0.2858       |
| MIP          | 0.7995  | 1.2902  | 0.8248       | 0.1822       |
| PremiLab     | 0.7727  | 2.7762  | 0.7967       | 0.2936       |
| Epione-Liryc | 0.7860  | 2.0568  | 0.7658       | 0.3858       |
| MedICL       | 0.7756  | 3.0634  | 0.7445       | 0.5333       |
| DBMI pitt    | 0.4734  | 10.995  | 0.7969       | 0.5086       |
| Hi-Lib       | 0.6686  | 4.3944  | 0.6649       | 1.2663       |
| smrit161096  | 0.7230  | 2.9876  | 0.5131       | 0.9523       |
| IMI          | 0.6004  | 4.4732  | 0.4281       | 9.8191       |
| GapMIND      | 0.6081  | 3.8377  | 0.5176       | 1.6570       |
| C-MADA       | 0.6232  | 7.5786  | 0.3987       | 3.9180       |
| SEU Chen     | 0.1142  | 38.0744 | 0.4945       | 14.0109      |
| skjp         | 0.2104  | 24.483  | 0.2139       | 15.6275      |
| IRA          | 0.1193  | 30.8389 | 0.2142       | 19.5226      |

4. CONCLUSION

In this work, we present C-MADA, an unsupervised cross-modality adversarial domain adaptation framework for medical image segmentation. C-MADA is composed of two steps, the first step is an image-level adaptation where images from the source domain are mapped to the target domain through an unpaired adversarial translation with cycle-consistency loss. In the second step, a feature-level adaptation is applied in an adversarial manner to train a U-Net to produce probable segmentations for the target domain. Furthermore, to encourage a boundary and semantic-aware segmentation, the discriminator is trained with information about the shape, texture, and contour of predicted segmentation. The experiments demonstrate C-MADA has a competitive performance in the difficult task of brain structure segmentation and that each component of the proposed framework is necessary to achieve good results in the unlabeled target dataset.

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