Contrastive andSelectiveHiddenEmbeddings forMedicalImageSegmentation

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Abstract—Medical image segmentation is fundamental and essential for the analysis of medical images. Although prevalent success has been achieved by convolutional neural networks (CNN), challenges are encountered in the domain of medical image analysis by two aspects: 1) lack of discriminative features to handle similar textures of distinct structures and 2) lack of selective features for potential blurred boundaries in medical images. In this paper, we extend the concept of contrastive learning (CL) to the segmentation task to learn more discriminative representation. Specifically, we propose a novel patch-dragsaw contrastive regularization (PDCR) to perform patch-level tugging and repulsing. In addition, a new structure, namely uncertainty-aware feature re-weighting block (UAFR), is designed to address the potential high uncertainty regions in the feature maps and serves as a better feature re-weighting. Our proposed method achieves state-of-the-art results across 8 public datasets from 6 domains. Besides, the method also demonstrates robustness in the limited-data scenario. The code is publicly available at https://github.com/lzh19961031/PDCR_UAFR-MIShttps://github.com/lzh19961031/PDCR_UAFR-MIS.

Index Terms—Medical image segmentation, contrastive learning, uncertainty learning, neural network.

I. INTRODUCTION

MEDICAL image segmentation (MIS) has been widely recognized as a pivot procedure for clinical diagnosis, analysis, and treatment planning. Despite breakthroughs driven by convolutional neural networks (CNN) in recent years, the pace of development for MIS is hindered by two challenges: 1) hard to obtain more discriminative features to tackle the ambiguous boundary and the smooth between-class transition of medical images [1] and 2) difficult to generate more selective features for heterogeneous textures and ambiguous boundaries in medical images [2]. These two challenges prevent CNN from better representation learning and more precise segmentation results.

In the past three years, contrastive learning (CL) has brought impressive breakthroughs and established an overwhelming presence in learning more discriminative representation, which is very suitable for tackling the first challenge. The core concept of CL is the formulation of “pair” [3]–[9]. The formulation includes two aspects: the component of “pair” and the relationship of the components within one “pair”. In previous work, the component is defined as an individual image. The relationship is a rigid bipartition: “positive” or “negative”. For example, different augmentations of one image could be defined as a “positive pair”, whose representation will be pulled together during learning. Distinct images could be defined as a “negative pair”, whose representation will be pushed away. This design is firstly utilized in the unsupervised scenario for backbone pretraining, such as ResNet [10], etc. For supervised classification, [11] extends the definition of “negative pairs” from inter-image to inter-category. Although contrastive learning has been attempted to facilitate MIS [12], [13], they still follow the unsupervised training scheme, and take CL for backbone pretraining. However, the existing formulation of “pair” may not suit MIS due to the following issues:

• The component of “pair”. MIS aims to predict the class label for each pixel within one image, which focuses on intra-image discrimination, instead of inter-image. In this sense, it poses demands for more distinctive local representation learning. Therefore, it would be more helpful to involve two entities within one image (e.g. local patches or regions) as the component of a pair, instead of two images, for modeling the intra-image relationship.
• The relationship within one “pair”. If the component of a pair corresponds to one entity of an image, the
relationship between components becomes the relationship between two entities within one image. Because medical images have the characteristic that the transition between different classes is smooth and the boundary is ambiguous, the representation of components of a pair could be similar. Therefore, the relationship between two entities within one image should be also smooth. So the previous rigid bipartition for relationship is inappropriate which could lead to sub-optimal solutions of MIS.

Thus how to effectively formulate “pair” to improve CL for medical image segmentation task is important.

In this paper, we propose a new formulation of “pair”. Specifically, we argue that local patches, instead of the whole image, are more appropriate for the component of “pair”. Besides, the relationship formulation should also be different. Pairs are not rigidly bipartite as either positive or negative, but should have a more soft relationship. So here the question is: specifically, how to associate patches with its representation for CL? And how could we measure the relationship between different patches?

To this end, we introduce the patch-dragsaw contrastive regularization (PDCR). Two ways are proposed to associate patches with their representations: the receptive-field-based patch-dragsaw (RF-PDCR) and the hierarchical patch-dragsaw (H-PDCR). RF-PDCR, which could be seen as a special case of H-PDCR, is an intuitive and direct way to achieve this. It borrows the concept of the receptive field [14] in MIS framework to link each feature vector from a certain layer with a local patch of a certain location and size. However, RF-PDCR is hard to be conducted among features from deeper levels (e.g. decoder) of the network and across multi-levels, due to the applicability and the characteristic of the receptive field concept. Thus, to extend the applicability and tackle the limitation of RF-PDCR, we further put forward H-PDCR. Specifically, for any layer in CNN, each feature vector is associated with a hierarchical patch series including different sizes of patches, to take advantage of the comprehensiveness of multi-scale information. In this way, both single-level CL and multi-level CL could be achieved.

On the other hand, for the relationship, affinity score is proposed to measure the similarity of two patches, which serves in a soft matter, instead of rigid bipartition. It is calculated based on the foreground ratio for each patch, which is a straightforward and easily-quantifiable metric designed to measure the characteristic of each patch itself. The soft similarity determines the coexisting of tugging and repulsing for the representation of each pair, which could be figuratively described as dragsaw. In this way, PDCR aims to strike a balance that respects the segmentation task as well as exploits the contrastive power.

For the second challenge, due to ambiguous boundaries and heterogeneous textures in medical images [2], high uncertainty would come up upon the classification of pixels in these areas, which generates high gradients during training. Along the training process, these high gradients may distract the learning attention of the network and mislead the optimization. Thus, the minority of features with high uncertainty may harm the network. To solve this problem, we introduce the uncertainty-aware feature re-weighting (UAFR), to ease the influence of pixels with high uncertainty and for a better feature re-weighting. It models the uncertainty for each pixel by generating an uncertainty-aware map, then highlights pixels with low uncertainty while suppressing those with high uncertainty. Notice that UAFR does not need any supervision.

It is worth mentioning that both PDCR and UAFR are designed and implemented in a “lightweight plugin” fashion, meaning that they can be easily integrated into existing segmentation frameworks or training pipelines without extra pre-training. Experiments are conducted across 8 public datasets from 6 domains. The results show that our method consistently outperforms previous work.

Our main contribution can be summarized threefold:

- A new formulation of “pair” is proposed to improve the contrastive learning for supervised MIS, including the component and the relationship of “pair”. On this basis, a novel Patch-dragsaw contrastive regularization (PDCR) is proposed to regularize patch-level relations by contrastive constraints, which is implemented in two ways: Receptive-Field-based PDCR and Hierarchical PDCR.
- Uncertainty-aware feature re-weighting (UAFR) module is designed to avoid the learning-attention shift problem in MIS, which is caused by minority features with high uncertainty due to the characteristics of medical images, and select a better feature.
- State-of-the-art results have been achieved across 8 diverse datasets from 6 domains. Furthermore, we substantiate the potential applicability of proposed methods under a limited data scenario by utilizing only 25% data to outperform the baseline methods with full data.

II. RELATED WORK

A. Architectures for Medical Image Segmentation

A vast of neural networks have been designed and tuned for MIS. Despite the unique design of each architecture, most of the networks employ an encoder-decoder structure with the bypass connection to fuse low-level features with high-level features. Among those designs, FCN [15], UNet [16] and DeepLab [17] function as three milestones. They and their variations provide a stable and consistent baseline for segmentation tasks. Recently, some other methods are proposed [2], [18]–[21]. A structure boundary preserving segmentation framework is proposed in [2] to tackle the ambiguity of boundary. A difficulty-aware deep segmentation network [19] with confidence learning is introduced to obtain more region-wise confidence information.

For 3D MIS, nnUNet [22] shows that network modification may be inferior compared to searching suitable hyper-parameters including augmentations, pre-processing and post-processing techniques, etc. Its pipeline and code-base provide a strong baseline for a broad scope of tasks. [23] proposes global and local contrastive loss for volumetric
medical images in the semi-supervised setting, but it still maintains the rigid bipartition for the relationship between patches.

B. Contrastive Learning

Contrastive learning-based model pre-training has largely bridged the gap between supervised and unsupervised model pretraining [3]–[8], [24] by learning to discriminate positive pairs against negative pairs. SimCLR [5] demonstrates the importance of augmentations and shows it is beneficial to maintain a large number of negative pairs and introduce the projection neck. Besides, contrastive learning is also utilized for supervised scenarios [11], [25]. For supervised classification, [11] extends the definition of “negative pair” from inter-image to inter-category.

Besides backbone pre-training, efforts have also been made to fit CL into segmentation tasks. Most methods target at semi-supervised and unsupervised scenarios. A pixel-wise contrastive loss is proposed in [26] for segmentation pre-training and exploring advantages gained under the semi-supervised scenario. To work with meta-label annotations, [12] adapts CL even when no additional unlabeled data is available.

C. Uncertainty-Guided Segmentation

Several uncertainty-based methodologies are introduced for image segmentation [27]–[32]. According to [27], uncertainty can be divided into two branches in deep learning, aleatoric uncertainty, which is caused by data itself and often occurred in boundaries of objects, and epistemic uncertainty, which is attributed to limited data and insufficient model training. BEP [32] proposes location-adaptive weighting mechanism for semantics-aware feature pooling, which achieves improvements in both image semantic segmentation and classification tasks. For medical image segmentation, [28] quantifies epistemic uncertainty by running a given sample through the model several times with the dropout layers. A novel uncertainty-aware scheme is designed in [30] to enable the model to gradually learn from the meaningful and reliable targets by exploiting the uncertainty information. In [31], common voxel-wise uncertainty which measures with respect to their reliability in medical image is evaluated.

III. PATCH-DRAGSAW CONTRASTIVE REGULARIZATION

In this section, we first give a brief introduction to self-supervised contrastive learning. Then, we introduce the proposed RF-PDCR and H-PDCR.

A. A Review of Self-Supervised Contrastive Learning

The existing self-supervised contrastive learning framework generally uses image as the component of pair and defines their relationship as rigid. It contains three principle components: (i) a transformation collection $\mathcal{T}$ (ii) an encoder network $E(\cdot)$ to encode high-dimensional inputs. (iii) a projection head $P(\cdot)$ to further introduce non-linearity and reduce the dimension of output embeddings. As in [5], a positive pair $(x_i, x_j(i))$ is acquired by applying randomly sampled augmentations $t \sim \mathcal{T}$ of the same image $x$ twice. Since $(\tilde{x}_i, \tilde{x}_j(i))$ and $(\tilde{x}_j(i), \tilde{x}_i)$ are treated as two pairs, a minibatch with size $N_b$ will attribute to $2N_b$ pairs for training. The contrastive loss is:

$$\mathcal{L}_{\text{batch}} = \sum_{i=1}^{2N_b} \mathcal{L}_i$$

(1)

$$\mathcal{L}_i = -\log \frac{\exp(sim(z_i, z_j(i))/\tau)}{\sum_{k=1}^{2N_b} \mathbb{I}[k \neq i] \exp(sim(z_i, z_k))/\tau))$$

(2)

where $z_i = P(E(\tilde{x}_i))$, $\mathbb{I}[k \neq i] \in \{0, 1\}$ returns 1 iff $k \neq i$ and $sim(\cdot)$ denotes the cosine similarity.

B. Receptive-Field-Based Patch-Dragsaw Contrastive Regularization

In this work, we utilize local patches as the component of pair and define a soft relationship between different patches. Two ways are adopted to generate the representation of the patch, RF-PDCR and H-PDCR. RF-PDCR is first introduced, as shown in Fig. 2. We first describe how to generate the representation for each patch, then the relationship between patches is introduced. After that, we illustrate the complete algorithm.

1) Component for Pair and Its Representation: According to [14], each feature vector from a certain layer corresponds to a local patch. Denote the feature vector in layer $l$ as $v_l$, its corresponding patch is denoted as $p_l$. For simplicity, we drop the layer “$l$” in the notation, since RF-PDCR conducts on...
feature vectors from the same layer. Here, to utilize the location information, we encode the position of each patch by concatenating its coordinate (min-x-coordinate, max-x-coordinate, min-y-coordinate, max-y-coordinate) to its feature. Meanwhile, for every layer, we utilize Grid-sampling strategy to select $N$ vectors from its feature.

2) Relationship for Pair: We define the affinity score to measure the soft similarity of every two patches in a pair. Firstly, the foreground ratio vector is obtained to measure the characteristic of each patch, which contains the ratios between the area of each class and the area of the whole patch. Based on the foreground ratio, the affinity score could be calculated.

Specifically, given $(v_i, v_j)$, which contains the location information of its corresponding patch, $(p_i, p_j)$ form the pair. The affinity score $w_{ij} \in [0, 1]$ is a scalar that measures to what extent should this pair be pulling and pushing for the contrastive loss. Denote the receptive field of $v_i$ as $R_i$. $w_{ij}$ is:

$$w_{ij} = \text{aff}(p_i, p_j) = 1 - \frac{1}{M} \sum_{m=1}^{M} |\phi_{im}^m - \phi_{jm}^m|$$

(3)

where $M$ denotes the number of classes and $\phi_{im}^m$ is the foreground ratio of class $m$ for $p_i$. $\phi_{jm}^m$ measures the area ratio between class $m$ and the total area of $p_j$. The more similar the value of $\phi_{im}^m$ and $\phi_{jm}^m$, the greater the value of $w_{ij}$. $\phi_{im}^m$ is:

$$\phi_{im}^m = \frac{\text{Number of pixels in } R_i \text{ which belongs to class } m}{\text{Area of receptive field } R_i}$$

(4)

Specifically, $\phi_{im}^m$ is computed as following. Suppose $v_i$ is sampled from layer $l$. The receptive field $R_i$ is a square, and its side length is denoted as $r_i$. The position of $R_i$ is calculated as follows. Let $o_l$ and $e_l$ denote the start and end location of $v_i$. In our case $o_l = e_l + 1$, meaning sample one vector each time. In each axis (x-axis and y-axis), the start $o$ and end $e$ positions of the receptive field $R_i$ in the original image take the following forms, according to [14], [33]:

$$o = o_l \prod_{t=1}^{z} s_t - \sum_{t=1}^{z-1} p_z \prod_{t=1}^{z} s_t$$

(5)

$$e = e_l \prod_{t=1}^{z} s_t - \sum_{t=1}^{z-1} (1 + p_z - k_z) \prod_{t=1}^{z} s_t$$

(6)

where $k_z$ denotes the kernel size, $s_t$ represents the stride size and $p_z$ is the padding size of a convolutional layer.

On the other hand, the side length of $R_i$ denoted as $r_i$, computed as the following form:

$$r_i = \prod_{t=1}^{z} (k_z - 1) + 1$$

(7)

where $k_z$ and $s_t$ denote the kernel size and the stride size of a convolutional layer, respectively. Meanwhile, $r_i = o_e + 1$. Thus, a feature vector corresponds to a local patch with a specific location and size. Note that the size of the receptive field $r_i$ only depends on layer $l$, not related to specific vectors. The area of $R_i$ equals $r_i^2$, which is the denominator in Eq. (4). Given the locations of vector $v_i$ in the hidden feature, we can calculate the location of $R_i$ in the original image according to Eq. (5) and Eq. (6). With the calculated location of $R_i$, the number of pixels that belong to each class $m$ in $R_i$ can be computed according to the image annotation $G$, which is the numerator in Eq. (4).

3) The Algorithm of RF-PDCR: Algorithm 1 summarizes the Receptive-Field-based Patch-dragsaw. Specifically, it takes the following formation:

$$s_{ij} = \text{sim}(v_i, v_j) = \frac{(v_i)^T v_j}{\|v_i\| \|v_j\|}$$

(8)

$$\mathcal{L} = \sum_{i=1}^{L} \sum_{j=1}^{N} - \log \frac{\exp(s_{ij} \cdot w_{ij}) / \tau)}{\sum_{n=1}^{N} \exp(s_{in} \cdot (1 - w_{in}) / \tau)}$$

(9)

where $s_{ij}$ denotes the cosine similarity of $v_i$ and $v_j$, $l$ denotes the layer and $L$ denotes the number of layers. $(1 - w_{ij})$ measures the dissimilarity.

Algorithm 1 Receptive-Field-Based Patch-drag saw

Input: encoder $E(\cdot)$, constant $N$ and $\tau$

1: for image $I$, annotation $G$ in dataset do
2: for layer $l \in \{1, \ldots, L\}$ in encoder do
3: sampling $\{v_1, \ldots, v_i, \ldots, v_j, \ldots, v_N\}$
4: calculate receptive field according to Eq. (7)
5: encode the location information of each patch
6: for $i \in \{1, \ldots, N\}$ do
7: for $j \in \{1, \ldots, N\}$ do
8: compute the foreground ratio of each class for each patch with Eq. (4)
9: compute $w_{ij}$ with Eq. (3)
10: compute $s_{ij}$ with Eq. (8)
11: end for
12: end for
13: end for
14: compute the loss $\mathcal{L}$ with Eq. (9)
15: update network $E$ to minimize $\mathcal{L}$
16: end for

C. Hierarchical Patch-drag saw Contrastive Regularization

Despite the simplicity of RF-PDCR, it has two limitations: 1) hard to be conducted in architectures of the network other than the encoder, due to the applicability of the receptive field concept; 2) difficult to be conducted among features from multi-level, due to the different size of patches corresponding to different levels of features. Thus, to improve the implementation generalization and for better representation learning, we introduce hierarchical patch-drag saw contrastive regularization (H-PDCR), as illustrated in Fig. 3.
1) Component for Pair and Its Representation: According to [34], each vector from the hidden feature of a certain layer corresponds to a specific location in the original image. Then, a hierarchical patch series with this location as the center and different sizes would be obtained, where the sizes are manually assigned. Denote the $i_{th}$ feature vector from layer $l$ as $v^l_i$, which is associated with a hierarchical patch series $p^l_i$, in which the $k_{th}$ patch is denoted as $p^l_{ik}(k)$. Given $(v^l_i, v^l_j)$, $(p^l_{ik}(k), p^l_{jk}(k))$ form the pair, since their size are similar, which could benefit the contrastive learning. $w^l_{ij}$ is the affinity score of $p^l_{ik}(k)$ and $p^l_{jk}(k)$. Similarly for $v^l_i$ and $v^l_j$ from different layers, $(p^l_{ik}(k), p^l_{jk}(k))$ form the pair. $w^l_{ij}$ is the affinity score of the pair. $pd^l_{ij}$ calculate single layer contrastive loss for a pair. $pd^l_{ij}$ calculate cross layer contrastive loss for a pair.

2) Relationship for Pair: In H-PDCR, CL is conducted among features from single-level and different layers. The computation of affinity score $w$ still follows Eq. (3), but with two kinds of notations:

i. patches from same layer (layer $l$):
Given $(v^l_i, v^l_j)$, $p^l_{ik}(k)$ and $p^l_{jk}(k)$ form the pair, since their size is similar, which could be used to conduct the contrastive learning. $w^l_{ij}(k) = aff(p^l_{ik}(k), p^l_{jk}(k))$ is the affinity score of this pair.

ii. patches from different layers (layer $l$ and layer $l'$):
Given $(v^l_i, v^l_j)$, $p^l_{ik}(k)$ and $p^l_{jk}(k)$ form the pair.

Note that before conducting the contrastive learning across different layers, the channel of the two features will be normalized to 32 by a $1 \times 1$ conv layer, to ensure that $v^l_i$ ($1 \times 32$) and $v^l_j$ ($1 \times 32$) has the same size.$w^l_{ij}(k) = aff(p^l_{ik}(k), p^l_{jk}(k))$ denotes the affinity score.

3) Algorithm of H-PDCR: Algorithm 2 summarizes the contrastive loss. It is:

$$s_{ij}^l = \text{sim}(v^l_i, v^l_j) = \frac{(v^l_i)^T v^l_j}{\|v^l_i\| \|v^l_j\|} \quad (10)$$

$$s_{ij}^{l=+l'} = \text{sim}(v^l_i, v^l_j) = \frac{(v^l_i)^T v^{l'}_j}{\|v^l_i\| \|v^{l'}_j\|} \quad (11)$$

where $l$ and $l'$ denotes the layer, $P$ is the number of patches in the patch series. $v^l_i$ is the $i_{th}$ vector from layer $l$. $(1 - w^l_{ij}(k))$ and $(1 - w^{l=+l'}_{ij}(k))$ measure the dissimilarity.
cross-layers according to the ablation study. UAFR, is added to all encoder and decoder layers (except the neck module in DeeplabV3+). \( \text{N} \) is set to 128, 64, 32, 8, 8, 8, 8, 8 for each layer. \( P \) is set to 3, the size of patches in patch series of H-PDCR is set to \( 5 \times 5, 7 \times 7 \) and \( 9 \times 9 \). Other hyper-parameters like learning rate scheduler, augmentation strategy, etc, are kept the same across all 2D or 3D tasks. For 2D tasks, we utilize the Adam optimizer with the base learning rate of 0.001 and the cosine scheduler. The weight decay is set to 0.00001. Applied augmentation includes scale, flip, rotate, shift, and shear transformation. Specifically, we conduct random scaling between 0.8 and 1.2, random rotation from -90 to 90 degrees, shear from -20 to 20 degrees, shift with 0.1, and random flips for both axes. As for training, the input image is resized to \( 512 \times 512 \) and batch size is set to 64 on 16 NVIDIA GTX 1080Ti GPUs. We train each model for 300 epochs. For 3D tasks, we follow the settings of [57], [58], and the hyper-parameters follow the default settings of nnUNet. Specifically, the input images are first resampled to have an isotropic voxel spacing of \( 0.7\text{mm} \times 0.7\text{mm} \times 0.7\text{mm} \), followed by z-normalization separately applied to each input channel. In the training phase, each image is randomly cropped to the region of nonzero values with the pre-defined resolution. For testing, the final segmentation results are obtained by combining patch-based inference results with a 50 percent overlap. The input size of each patch is modified for each task like nnUNet. We utilize the same data augmentation strategy as [57] in both the training phase and testing phase.

B. Benchmark Studies

Table II shows the results for the proposed model against other state-of-the-art methods for the aforementioned medical image segmentation tasks. It is encouraging to see that our model, with a task-agnostic design, achieves a consistent advantage over other task-tailored counterparts. We believe it is evidence that our proposed method exhibits universal applicability for the medical image segmentation research area.

Besides, we conduct t-tests and calculate the standard deviation on each dataset against methods ranked second and third. Shown in Table III, the results confirm that the improvement against other methods is statistically significant.

C. Ablation Studies

We conduct ablation studies on the ISIC 2016 dataset using DeeplabV3+ with xception encoder as the backbone network. The dataset is chosen for a balance of dataset size and training budget.

1) Effect of the Proposed Two Modules and Computation Complexity Analysis: In this subsection, we investigate whether the proposed two modules are beneficial on top of different architectures on ISIC 2016 dataset. To this end, we add either or both of the two modules to FCN, UNet, in addition to DeeplabV3+, which are arguably the most common segmentation frameworks among others. Table IV shows the results. Two observations are worth noting: Firstly, both PDCR (including RF-PDCR and H-PDCR) and UAFR demonstrate...
consistent improvements on all of the three backbones, indicating the general applicability; Secondly, the two modules are complementary in the sense that they are shown to benefit on top of each other. Besides, we compare the number of parameters and FLOPs in $512 \times 384$ input size for inference on several existing methods, as shown in Table IV. Note that PDCR is only involved in training, and UAFR is a lightweight module.

2) Ablation Study for PDCR: We adopt PDCR and its variations on the backbone to investigate its best configuration.

a) The best configuration: According to Section III, RF-PDCR is only used to encoder layers for the applicability of the receptive field concept, meanwhile H-PDCR could be extended to all the layers in each part of the network.

We investigate where should PDCR be plugged in, by taking the last layer of each block as well as every single layer as candidate sites and ablating PDCR layer-by-layer. Fig. 5 shows the ablation results for RF-PDCR. It can be clearly seen that if RF-PDCR is adopted in a single layer, the performance will be improved no matter adopted in which layer. However, when adopting RF-PDCR in multiple layers simultaneously, we notice that adopting in layer 2, 3, 4 of the encoder performs the best.

TABLE I

| Dataset | Domain | Task | Number of category | Dimension | Modality | Evaluation Protocol |
|---------|--------|------|--------------------|-----------|----------|---------------------|
| ISIC 2016 [36] | PHI [37] | Skin | Lesion seg | 2 | 2D | Dermoscopy 900 train(ISIC2016), 200 test(PHI) (Official split) |
| ISIC 2016 [36] | Skin | Lesion seg | 2 | 2D | Dermoscopy 900 train, 379 test (Official split) |
| ISIC 2017 [38] | Skin | Lesion seg | 2 | 2D | Dermoscopy 2000 train, 600 test (Official split) |
| MC [39] | Lung | Lung seg | 2 | 2D | X-Ray 80 train, 58 test |
| DigestPath [40] | Pathology | Lesion seg | 2 | 2D | Pathology 952 train, 5-fold cross-validation |
| Decathlon [41] | Task01 | Brain | Tumour seg | 4 | 3D | MRI 454 train, 3-fold cross-validation (Official split) |
| Decathlon [41] | Task02 | Heart | Heart seg | 2 | 3D | MRI 20 train, 5-fold cross-validation (Official split) |
| Decathlon [41] | Task03 | Prostate | Prostate seg | 3 | 3D | MRI 32 train, 5-fold cross-validation (Official split) |

TABLE II

RESULTS OF THE PROPOSED MODEL AGAINST STATE-OF-THE-ART METHODS ON A BROAD SCOPE OF MEDICAL IMAGE SEGMENTATION TASKS

| ISIC 2016+PHI2 (Skin) | ISIC 2016 (Skin) | ISIC 2017 (Skin) | MC (Lung) |
|-----------------------|-----------------|-----------------|-----------|
| Methods | DI | JA | AC | Methods | DI | JA | AC | Methods | DI | JA | AC |
| MSRA [42] | 81.57 | 72.33 | | | | | | | | | |
| DFCN [43] | 91.20 | 84.70 | 95.56 | | | | | | | | |
| ECDN [44] | 89.40 | 84.15 | | | | | | | | | |
| Bi et al. [45] | 90.66 | 83.99 | | | | | | | | | |
| SBPS [3] | 91.84 | 84.30 | | | | | | | | | |
| Ours | 93.51 | 86.74 | Ours | 94.51 | 88.94 | 97.71 | Ours | 89.63 | 82.00 | 95.64 | Ours | 95.30 | 99.68 |

TABLE III

STANDARD DEVIATION AND T-TEST AGAINST OTHER METHODS. THE IMPROVEMENT IS STATISTICALLY SIGNIFICANT

| Dataset | Method (Ours vs.) | s-value | p-value | Statistical at p < 0.05 | Standard Deviation |
|---------|-----------------|---------|---------|-----------------|------------------|
| PHI     | S3FR (F1)       | 2.17(56) | 0.0051(DI) | 0.0000(10(DI)) | Yes |
| DFCN    | Bi et al. (F1)  | 5.09(36) | 0.0001(DI) | 0.0000(10(DI)) | Yes |
| ISIC2016| Bi et al. (F1)  | 4.83(56) | 0.0001(DI) | 0.0000(10(DI)) | Yes |
| ISIC2017| Bi et al. (F1)  | 4.93(56) | 0.0001(DI) | 0.0000(10(DI)) | Yes |
| MC      | Bi et al. (F1)  | 5.09(36) | 0.0001(DI) | 0.0000(10(DI)) | Yes |
| DigestPath | Bi et al. (F1) | 5.09(36) | 0.0001(DI) | 0.0000(10(DI)) | Yes |
| Decathlon | Bi et al. (F1) | 5.09(36) | 0.0001(DI) | 0.0000(10(DI)) | Yes |
| SCNNs   | Bi et al. (F1)  | 5.09(36) | 0.0001(DI) | 0.0000(10(DI)) | Yes |
| PROSTATE| Bi et al. (F1)  | 5.09(36) | 0.0001(DI) | 0.0000(10(DI)) | Yes |

TABLE IV

RESULTS OF ABLATION STUDIES FOR DIFFERENT ARCHITECTURES ON ISIC 2016 AND COMPARISON OF COMPUTATION COMPLEXITY. A STRONG AND CONSISTENT IMPROVEMENT IS PROVED.

| Architecture | Parameters | FLOPs | RF-PDCR | H-PDCR | +UAFR | +UAFR | DI | AC |
|--------------|------------|-------|---------|--------|-------|-------|----|----|
| UNet         | 17.3M      | 120.6G| ✓       | 80.92  | 97.47 | 97.32 |
| UNet+       | 17.3M      | 120.6G| ✓       | 80.92  | 97.47 | 97.32 |
| UAFR        | 18.5M      | 120.6G| ✓       | 80.92  | 97.47 | 97.32 |

Notes: PDCR is only involved in training, and UAFR is a lightweight module.
TABLE V
RESULTS OF SIMILAR DESIGNS FOR PDCR ON ISIC 2016. (A) INVESTIGATES SEVERAL VARIATIONS FOR FOREGROUND RATIO $\phi$. (B) INVESTIGATES TWO IMPLEMENTATIONS FOR H-PDCR. (C) INVESTIGATES THE IMPACT OF PATCH POSITION ENCODING. (D) COMPARES OUR METHOD TO A VARIATION OF MEASURING THE AFFINITY SCORE OF PATCHES. (E) COMPARES OUR METHOD TO OTHER SIMILAR-DESIGNED CONTRASTIVE LEARNING METHODS. OUR METHOD OUTPERFORMS OTHER SIMILAR DESIGNS

| Foreground ratio $\phi$ | RF-PDCR | H-PDCR | JA | DI | AC |
|--------------------------|---------|--------|----|----|----|
| 1.1-norm                 | ✔       | ✔      | 87.89 | 93.45 | 96.87 |
| 1.1-norm                 | ✔       | ✔      | 88.43 | 94.18 | 97.25 |
| 2.2-norm                 | ✔       | ✔      | 87.52 | 93.01 | 96.19 |
| Ours                     | ✔       | ✔      | 88.04 | 93.68 | 96.99 |
| Ours                     | ✔       | ✔      | 88.54 | 93.97 | 97.21 |

Method | With or without patch position encoding | JA | DI | AC
---|---|---|---|---|---|
Ours | Without patch position encoding | 88.85 | 94.40 | 97.67 |
Ours | With patch position encoding | 88.94 | 94.51 | 97.71 |

| CL Method | The level of the component for CL | JA | DI | AC |
|-----------|----------------------------------|----|----|----|
BYOL      | Image-level contrastive learning | 86.78 | 92.75 | 95.56 |
SimCLR    | Image-level contrastive learning | 86.88 | 93.01 | 95.75 |
SimSiam   | Image-level contrastive learning | 87.11 | 93.14 | 96.41 |
Ours proposed | Patch-level contrastive learning | 88.94 | 94.51 | 97.71 |

Table VI
RESULTS OF CONTRASTING H-PDCR WITH RF-PDCR.
(A) INVESTIGATES THE IMPACT OF H-PDCR BY ADOPTING IT IN ALL PARTS OF DEEPLABV3+, INCLUDING ENCODER, DECODER AND CROSS-LAYER. (B) COMPARES THE PERFORMANCE OF H-PDCR AND RF-PDCR IN THE ENCODER. H-PDCR PERFORMS BETTER

| ISIC2016 | RF-PDCR (encoder) | H-PDCR (encoder) | H-PDCR (decoder) | H-PDCR (cross-layer) | JA | DI | AC |
|----------|------------------|------------------|------------------|----------------------|----|----|----|
| DeeplabV3+ | ✔                | ✔                | ✔                |                     | 87.20 | 92.66 | 95.38 |
| DeeplabV3+ | ✔                | ✔                | ✔                |                     | 87.72 | 93.11 | 96.53 |
| DeeplabV3+ | ✔                | ✔                | ✔                |                     | 86.70 | 92.31 | 96.32 |
| DeeplabV3+ | ✔                | ✔                | ✔                |                     | 87.00 | 92.65 | 96.30 |
| DeeplabV3+ | ✔                | ✔                | ✔                |                     | 87.50 | 93.16 | 96.81 |
| DeeplabV3+ | ✔                | ✔                | ✔                |                     | 87.38 | 93.23 | 96.82 |
| DeeplabV3+ | ✔                | ✔                | ✔                |                     | 87.03 | 92.84 | 96.54 |
| DeeplabV3+ | ✔                | ✔                | ✔                |                     | 87.99 | 93.45 | 97.01 |

(b) Design variations: We ablate other similar designs for PDCR:
1) Variations for foreground ratio $\phi$ in PDCR: Instead of Eq. (4), we evaluate two other definitions of $\phi$ for each patch: L1-norm and L2-norm. The results are shown in Table V (a), which prove that our definition performs better.
2) Variations for affinity score $w$ in PDCR: Here, we substantiate 3 variations listed as following:
   - **Constant $w$**: downgrades $w$ to a constant temperature coefficient for each two patches ($w = 0.5$).
   - **Rigid bipartite $w$**: setting each two patches as rigid positive or negative pairs like in SimCLR, which indicates that $w = 1$ when a patch with its transformation and $w = 0$ for each two different patches. Note that the transformation here means the data augmentation, which includes scale, flip, rotate, shift, and shear transformation and keeps the same with all the other experiments in Section V A.
   - **Center-location-based $w$**: $w = 1$ when the label of the center location of two vectors are the same, 0 otherwise.
According to the results shown in Fig. 5, our design of $w$ outperforms the other three variations.
3) Variations of two implementations for H-PDCR: There are two different implementations for H-PDCR, the first one is to calculate the contrastive loss for each patch pair in the series first, then average the loss, as mentioned in Eq. (9) of Section III. The second one is to calculate the average of foreground ratios for the patches in a series first, then conduct contrastive learning. We evaluate the impact of these

On this basis, we contrast H-PDCR with RF-PDCR. We conduct experiments in two aspects: investigate the impact of H-PDCR in each part of DeeplabV3+, including encoder, decoder and cross-layer; compare the performance of H-PDCR and RF-PDCR in the encoder (RF-PDCR could only be adopted in the encoder due to its applicability). The results are shown in Table VI. In Table VI (a), the results indicate that adopting manually assigned patches for H-PDCR in all parts of the network could improve the results. Besides, in Table VI (b), while adopting H-PDCR in the decoder and cross-layer, for the encoder, we investigate whether adopting receptive-field patch (RF-PDCR) or manually assigned patches (H-PDCR) performs better. The results show that manually assigned patch (H-PDCR) performs better, proving that H-PDCR could take more advantage of the multi-scale information and facilitate the network.

On the other hand, we investigate the specific configuration of H-PDCR by adopting it on every single layer. The results are shown in Table VII, indicating that adopting H-PDCR on adjacent level of layers could boost the performance more, which is better than adopting on layers with large spans. The best setting for H-PDCR is adopted in single layer (2,3,4 of the encoder) and across features from different layers (layer 2 and 3 of the encoder). In summary: it is suggested to adopt RF-PDCR at central layers of the network, where the receptive field is neither too large nor too small. Similarly with H-PDCR. Besides, H-PDCR could be extended to decoder and cross-layer.
Fig. 5. Ablation study for PDCR on ISIC 2016. We ablate from two aspects: the effect of PDCR in each layer and whether PDCR is better than other similar designs. The red line denotes adding PDCR at each layer in the encoder. The orange, green and purple lines denote adopting three similar designs of affinity score w layer-wisely. The blue dot line denotes using the baseline model and the red dot line denotes the best usage of PDCR. The results show that PDCR is effective for every layer, and performs the best when adding to layer 2, 3 and 4. Besides, PDCR outperforms other similar designs.

Fig. 6. Ablation study for UAFR on ISIC 2016. We ablate from two aspects: the effect of UAFR in each layer and whether UAFR is better than other similar designs. The red line denotes adding UAFR at each layer in the encoder (layer 1-5) and decoder (layer 6-7). The green and purple lines denote layer-wisely adopting two other similar attention mechanisms: SENet and CBAM. The blue dot line denotes using the baseline model and the red dot line denotes the best usage of UAFR. The results show that UAFR is effective for every layer, and performs the best when added at all layers. Besides, UAFR outperforms SENet and CBAM.

TABLE VII
RESULTS OF THE CONFIGURATION FOR H-PDCR ON ISIC 2016,
WHICH INCLUDES THE PERFORMANCE OF SEVERAL LAYERS
AND THE COMBINATION OF THEM. THE BEST SETTING FOR
H-PDCR IS ADOPTED IN SINGLE LAYER (2, 3, 4 OF THE
ENCODER) AND ACROSS FEATURES FROM DIFFERENT
LAYERS (LAYER 2 AND 3 OF THE ENCODER). BESIDES,
ADOPTING H-PDCR ON LAYERS WITH LARGE
SPANS WILL HURT THE PERFORMANCE.

| Encoder Layer | FCRA | HCRA | SDCRA | MDRA | SNRA | DCRA | ACRA |
|---------------|------|------|------|------|------|------|------|
| Layer 1       | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    |
| Layer 2       | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    |
| Layer 3       | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    |
| Layer 4       | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    |
| Layer 5       | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    | ✓    |

Our method outperforms all of them.

3) Ablation Study for UAFR: Similarly to PDCR, we adopt UAFR and its variations on the backbone to investigate its best configuration.

a) The best configuration: We investigate the configuration of UAFR by adopting it in every single layer of DeepLabV3+. As illustrated in Fig. 6, UAFR is more robust against the plugged-in position and performs roughly at both encoder and decoder. We do not add it at aspp neck (“Atrous Spatial Pyramid Pooling”) in DeepLabV3+ framework since it is the concatenation of multiple conv layers. Similarly, the benefits are additive and we finally add them to all layers in the encoder and decoder. To summarize: it is suggested to adopt UAFR at any layer you like in the encoder and decoder.

b) Design variations: We ablate other similar designs for UAFR:

(1) Comparison with other similar-designed methods: We compare UAFR with two uncertainty-based methods, including Active FCN [28], UAMT [30] and two popular attention mechanisms, including SENet [59] and CBAM [60], to see the changes brought to the performance. As seen in Fig. 6 and Table VIII, UAFR outperforms four counterparts by a large margin. It is believed that improvements are gained from regions with ambiguous boundaries region as well as heterogeneous textures. Visualization from Fig. 9 also substantiates our intuition.
TABLE VIII
RESULTS OF OTHER SIMILAR-DESIGNED METHODS FOR UAFR ON ISIC 2016. OUR METHOD PERFORMS THE BEST

| Architecture | Method Type          | JAI  | DI  | AC  |
|--------------|----------------------|------|-----|-----|
| Our proposed | Uncertainty-based learning | 88.94 | 94.51 | 97.71 |
| Active FCN   | Uncertainty-based learning | 83.01 | 91.32 | 95.89 |
| UAMT         | Uncertainty-based learning | 85.47 | 91.53 | 95.70 |
| CBAM         | Attention-based       | 86.48 | 92.66 | 96.45 |
| SENet        | Attention-based       | 86.56 | 92.77 | 96.23 |

TABLE IX
RESULTS OF DESIGN VARIATIONS FOR UAFR ON ISIC 2016.
(A) INVESTIGATE THE IMPACT OF ADOPTING $F(\cdot)$ BEFORE UNCERTAINTY MEASURING. (B) INVESTIGATE THE IMPACT OF DIFFERENT VALUE FOR THE CHANNEL NUMBER $M$ IN $A$. OUR DESIGN PERFORMS THE BEST

| Architecture | Whether adopting $F(\cdot)$ | JAI  | DI  | AC  |
|--------------|-----------------------------|------|-----|-----|
| (a) DeepLabV3+ | No                          | 87.17 | 92.91 | 96.49 |
| DeepLabV3+   | Yes                         | 87.81 | 93.50 | 96.79 |
| Architecture | Channel number $M$ of $A$ | JAI  | DI  | AC  |
| (b) DeepLabV3+ | $M = 1$                     | 87.75 | 93.48 | 96.68 |
| DeepLabV3+   | $M = 2$                     | **87.81** | **93.50** | **96.79** |
| DeepLabV3+   | $M = 5$                     | 87.55 | 93.35 | 96.77 |
| DeepLabV3+   | $M = 10$                    | 87.62 | 93.42 | 96.73 |
| DeepLabV3+   | $M = 50$                    | 87.53 | 93.29 | 96.73 |
| DeepLabV3+   | $M = 100$                   | 87.50 | 93.26 | 96.72 |
| DeepLabV3+   | $M = 500$                   | 86.96 | 92.92 | 96.39 |
| DeepLabV3+   | $M = 1000$                  | 86.86 | 92.90 | 96.28 |

TABLE X
RESULTS OF DIFFERENT CONVOLUTIONAL KERNEL SIZE OF $F(\cdot)$ FOR UAFR ON ISIC 2016. 3 $\times$ 3 KERNEL SIZE PERFORMS THE BEST

| Architecture | Kernel size of $F(\cdot)$ | JAI  | DI  | AC  |
|--------------|---------------------------|------|-----|-----|
| DeepLabV3+   | $1 \times 1$              | 87.14 | 93.13 | 96.77 |
| DeepLabV3+   | $3 \times 3$              | **87.81** | **93.50** | **96.79** |
| DeepLabV3+   | $5 \times 5$              | 87.50 | 93.39 | 96.67 |
| DeepLabV3+   | $7 \times 7$              | 87.27 | 93.23 | 96.73 |

(2) The impact of different variation for $F(\cdot)$: We conduct experiments to evaluate the effect of $F(\cdot)$, including two aspects: whether adopting $F(\cdot)$ before uncertainty measuring; the impact of different output channel size ($M$). In Table IX (a), the results show that $F(\cdot)$ could effectively learn the semantic information of $Q$ and facilitate the following uncertainty measuring. In Table IX (b), the results show that when $M$ equals 2, which is the segmentation class number, the performance is the best. And when $M$ is close to 2, the performance is also close to which of $M = 2$. But, when $M$ is bigger than 100, the performance drops dramatically. These results show that without supervision, the uncertainty measurement does not demand the channel number to be exactly the same as the segmentation class number, it could be calculated with an arbitrary number of channel. But, when the channel number is close to the segmentation class number, the performance would be better, indicating that the network does learn better feature by measuring the uncertainty according to the information of each class.

(3) convolutional kernel size of $F(\cdot)$:
We conduct experiments to evaluate the effect of different convolutional kernel sizes for $F(\cdot)$. The results are shown in Table X, which indicates that $3 \times 3$ is the best setting.

D. On Limited Training Data
Both our PDCR and UAFR are designed for robust and effective performance with limited trainset sizes. In this subsection, we explore the robustness of proposed methods against the data reduction on ISIC 2016 dataset. Specifically, we gradually decrease the amount of training data from 50% of the whole set to 1% with a stride of 5% and see the performance changes along the way. The results are shown in Fig. 7. It is encouraging to see that the performance is less affected by the data size in a broad range from 25% to 100%. Noticeably, the model still performs on par with the whole-set baseline with as little as 20% of overall training data. This property reveals the great potential of proposed methods in handling other especially long-tailed domains where purely big-data-driven methods may not be applicable.
The quantitative and qualitative results verify that it successfully generates more selective features and outperforms other similar variations. This is highly in line with the motivation, which means that the network could generate more discriminative features. Besides, extending PDCR on all architectures (H-PDCR) is better than only adopting on the encoder of the segmentation framework (RF-PDCR). On the other hand, UAFR models the uncertainty of each pixel and poses different weights on features. The quantitative and qualitative results verify that it successfully generates more selective features and outperforms other similar designs. Other than those, promising results have been shown in the limited-data scenario.

VI. CONCLUSION AND FUTURE WORK

In this work, we propose patch-dragsaw contrastive regularization (PDCR) to generate more discriminate features, which is a key challenge of medical image segmentation tasks. In PDCR, we re-formulate the “pair” of contrastive leaning, including the component and the relationship, to regularize patch-level relations by contrastive constraints. Besides, another module named uncertainty-aware feature re-weighting (UAFR) is introduced to perform feature selection according to the uncertainty modeled by the network itself, to generate more selective representations.

The experiment results verify the effectiveness of PDCR and UAFR. Specifically, PDCR proposes a new formulation of the component (local patches) and the relationship (soft instead of rigid) for contrastive learning. The experiment results of PDCR achieve consistent improvement both quantitatively and qualitatively, and outperform other similar variations. This is highly in line with the motivation, which means that the network could generate more discriminative features. Besides, extending PDCR on all architectures (H-PDCR) is better than only adopting on the encoder of the segmentation framework (RF-PDCR). On the other hand, UAFR models the uncertainty of each pixel and poses different weights on features. The quantitative and qualitative results verify that it successfully generates more selective features and outperforms other similar designs. Other than those, promising results have been shown in the limited-data scenario.
In future work, we will improve on two main aspects: (1) Combine more information to measure the affinity score on the basis of foreground ratio information. For instance, spatial distribution or structure information for every two patches in a pair could be considered and measured. (2) Further explore the functionality of the proposed two modules in un-/semi-supervised learning.

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