

Deep Model Generalization in Medical Image Segmentation

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Medical Image Segmentation at a Glance



| 🏛 Educational | Y Structure | | Normal Tissues | Abnormal Tissues | | |
|---|---|-----------------------|--|--|--|--|
| L Modality | Abdomen 10 Colon 1 Kidney 4 | Scenarios | organs (whole/substructure), vessels, cells | tumors, lesions, cancerous cells | | |
| ۲ask type Classification 23 Detection 14 Modeling 4 | Pancreas 1 Spleen 2 Cardiac 2 Heart 9 Head and Neck 33 Brain 20 Cranium 10 Retina 20 | Clinical Relevance | quantification (volume), visualization, intra- operative navigation, radiotherapy (organs at risk), clinical-oriented analysis | tumor quantification, diagnosis, prognosis, biopsy, surgical planning, radiotherapy (GTV/CTV), monitoring, radiomics | | |
| Reconstruction (0) Registration (1) Regression (2) Segmentation (93) | letth 1 Lower Limb 1 Knee 1 Pelvis 7 Cervix 2 Prostate 1 Skin 1 Spine 1 | Challenges | limited contrast, multi-class problems, variances in shape for some large organs, cell overlapping, endoscopy artefacts | small scale, sample imbalance, ambiguous boundaries, various context, irregular shape, limited visibility with specific applications | | |
| Tisplaying 93 of 216 | Comn Breat 2 Upper Linb 0 Upper Linb 0 Upper Linb 0 Upper Linb 0 | | Data perspective: high-dimensional, multi-modal, labor-intensive annotations Value perspective: speed and accuracy, a prerequisite for following-up tasks | | | |
| | Displaying 93 of 216 | | | | | |

Medical Image Segmentation at a Glance



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| Structure Displaying 93 of 216 pttps://grand_challenge.org/ | Spinal Cord 0 Vertebral Column 1 Thorax 3 Breast 2 Lung 3 Upper Limb 0 | Common Issues | Data perspective: high-dimensional, multi-modal, labor-intensive annotations Value perspective: speed and accuracy, a prerequisite for following-up tasks | | | |
| | Displaying 93 of 216 | | | | | |

Spectrum of medical image segmentation methods

- Deformable models, such as snakes, active contours, level-set [T. McInerney and D. Terzopoulos D. MedIA 1996]
- Statistical inference via parametric or nonparametric probability models [D. Pham, C. Xu, and J. Prince Annu Rev Biomed Eng 2000]
- Multi-atlas based segmentation via registration and label fusion [J. Iglesias and M. Sabuncu MedIA 2015]
- Discriminative classifier based methods

$$F_{\theta}(X) \to Z \in \mathbb{R}^{\mathbb{Z}}; \ C_{\phi}(Z) \to Y \in \mathbb{R}^{\mathbb{C}}$$
 $X \to F_{\theta}(\cdot) \circ C_{\phi}(\cdot) \to Y$ Deep Learning

End-to-end 3D Networks for Semantic Segmentation



3D models

Encode richer spatial informationFit to domain knowledge



Skip connection

Short-cut connection facilitate information flow
Mutli-scale feature fusion for pixel-wise prediction





[Chen et al. NeuroImage 2018]

Deep supervision

Enhance gradients with explicit loss propagation
 Speed up training process



[Dou et al. MICCAI 2016; MedIA 2017]



[[]Liu et al. IEEE Access 2020]

Improve Computational Efficiency by Network Design

H-DenseUNet: Hybrid Densely Connected UNet for Liver and Tumor Segmentation



(a)

(b)





| Teem | Lesi | on | Liv | Tumor Burden | |
|---------------|---------------|-------------|---------------|--------------|----------|
| Team | Dice per case | Dice global | Dice per case | Dice global | RMSE |
| our | 72.2 | 82.4 | 96.1 | 96.5 | 0.015 |
| IeHealth | 70.2 | 79.4 | 96.1 | 96.4 | 0.017 |
| hans.meine | 67.6 | 79.6 | 96.0 | 96.5 | 0.020 |
| superAI | 67.4 | 81.4 | 0.0 | 0.0 | 1251.447 |
| Elehanx [40] | 67.0 | - | - | - | - |
| medical | 66.1 | 78.3 | 95.1 | 95.1 | 0.023 |
| deepX [48] | 65.7 | 82.0 | 96.3 | 96.7 | 0.017 |
| Njust768 | 65.5 | 76.8 | 4.10 | 13.5 | 0.920 |
| Medical [41] | 65.0 | - | - | - | - |
| Gchlebus [42] | 65.0 | - | - | - | - |
| predible | 64.0 | 77.0 | 95.0 | 95.0 | 0.020 |
| Lei [49] | 64.0 | - | - | - | - |
| ed10b047 | 63.0 | 77.0 | 94.0 | 94.0 | 0.020 |
| chunliang | 62.5 | 78.8 | 95.8 | 96.2 | 0.016 |
| yaya | 62.4 | 79.2 | 95.9 | 96.3 | 0.016 |

Improve Computational Efficiency by Network Design

3D Rol-aware U-Net for Accurate and Efficient Colorectal Tumor Segmentation



How can AI Segmentations Influence Clinicians?





| Editing Al-based Contour | Traditional Manual Draw |
|--------------------------|-------------------------|
| 18 mins | 30 mins |



- saving 40% time, per case
- process 1 more cancer patient in 1 hour Do more calculations ...

A Gallery of Image Segmentation Scenarios

















Open Problems

Weak label usage, e.g., semi-supervised learning; noisy-label training; unsupervised learning, active learning.

Data scarcity issue, e.g., transfer learning; data augmentation; limited data training.

Interpretability issue, e.g., uncertainty estimation; explainable deep learning; relationship and causality.

Clinical oriented, e.g., large-scale validation; beyond imaging data;

Model generalization.



Model Generalization in Real World Conditions



Data-driven method is sensitive to data mismatch



• Low data quality at inference

- artefacts,
- missing modality,
- unseen severe cases, etc.





• Data heterogeneity

- different vendors,
- imaging protocols,
- patient population



[D. Castro, I. Walker, and B. Glocker. 2019]



Loss for disentangled appearance code:

 $\mathcal{L}_{\mathrm{KL}} = \sum_{i=1}^{M} \mathbb{E}[D_{\mathrm{KL}}(p(a_i)||\mathcal{N}(\mathbf{0}, \boldsymbol{I}))]$

Loss for reconstruction with content code:

 $\mathcal{L}_{\text{rec}} = \sum_{i=1}^{M} ||D_i^r(z, a_i) - x_i||_1, \text{ where } z = \mathcal{F}(\delta_i c_1, ..., \delta_M c_M)$

| Μ | oda | lities | 5 | Dice (| Dice (%) | | | | | | | | |
|--------------|--------------|--------------|--------------|--------|----------|-------|--------------|-------|-------|--------------|-----------|-------|--|
| | | | | Comp | lete | | Core | | | Enhan | Enhancing | | |
| F | T1 | T1c | T2 | Ours | HeMIS | MLP | Ours | HeMIS | MLP | Ours | HeMIS | MLP | |
| - | _ | _ | \checkmark | 85.49 | 58.48 | 61.50 | 58.66 | 40.18 | 37.32 | 37.66 | 20.31 | 18.62 | |
| - | _ | \checkmark | _ | 71.86 | 33.46 | 2.04 | 72.87 | 44.55 | 17.70 | 70.22 | 49.93 | 32.92 | |
| _ | \checkmark | _ | _ | 68.40 | 33.22 | 2.07 | 50.00 | 17.42 | 10.52 | 22.67 | 4.67 | 10.78 | |
| \checkmark | _ | _ | _ | 83.02 | 71.26 | 63.81 | 46.67 | 37.45 | 34.26 | 28.30 | 5.57 | 15.90 | |
| _ | - | \checkmark | \checkmark | 87.53 | 67.59 | 64.97 | 78.46 | 63.39 | 49.38 | 76.82 | 65.38 | 60.30 | |
| _ | \checkmark | \checkmark | _ | 74.59 | 45.93 | 1.99 | 76.40 | 55.06 | 26.55 | 73.95 | 62.40 | 40.93 | |
| \checkmark | \checkmark | - | _ | 87.66 | 80.28 | 78.13 | 60.17 | 49.52 | 48.97 | 35.28 | 22.26 | 25.18 | |
| _ | \checkmark | _ | \checkmark | 87.87 | 69.56 | 66.88 | 64.88 | 47.26 | 43.66 | 41.05 | 23.56 | 26.37 | |
| \checkmark | - | - | \checkmark | 89.08 | 82.10 | 81.35 | 63.51 | 53.42 | 52.41 | 39.72 | 23.19 | 25.01 | |
| \checkmark | - | \checkmark | _ | 88.01 | 79.80 | 81.13 | 78.09 | 66.12 | 65.51 | 76.62 | 67.12 | 66.19 | |
| \checkmark | \checkmark | \checkmark | _ | 87.73 | 80.88 | 82.19 | 80.68 | 69.26 | 69.34 | 78.81 | 71.30 | 70.93 | |
| \checkmark | \checkmark | - | \checkmark | 89.07 | 83.87 | 80.40 | 65.99 | 57.76 | 53.46 | 43.04 | 28.46 | 28.34 | |
| \checkmark | - | \checkmark | \checkmark | 89.06 | 82.78 | 83.37 | 79.47 | 70.62 | 70.45 | 78.07 | 70.52 | 70.56 | |
| _ | \checkmark | \checkmark | \checkmark | 88.26 | 70.98 | 67.85 | 80.84 | 66.60 | 55.40 | 78.56 | 67.84 | 64.81 | |
| \checkmark | \checkmark | \checkmark | \checkmark | 89.07 | 83.15 | 82.43 | 81.19 | 72.50 | 71.46 | 79.13 | 75.37 | 72.08 | |
| A | vera | age | | 84.45 | 68.22 | 60.01 | 69.19 | 54.07 | 47.09 | 57.33 | 43.86 | 41.93 | |

C. Chen, Q. Dou, et al. "Robust Multimodal Brain Tumor Segmentation via Feature Disentanglement and Gated Fusion", MICCAI, 2019.

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Model Generalization in Real World Conditions

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• Data heterogeneity

- different vendors,
- imaging protocols,
- patient population

[D. Castro, I. Walker, and B. Glocker. 2019]

Tackling Data Heterogeneity: does Normalization Help?

An empirical study on the impact of scanner effects with brain imaging

Construct an **age- and sex-matched** dataset with T1-weighted brain MRI from n = 592 individuals, where 296 subjects (146 F) are taken each from the Cam-CAN and UKBB, to simulate a somewhat 'best case scenario' to **remove population bias**.

Very **careful pre-processing** is conducted, including: 1) reorientation, 2) skull stripping, 3) bias field correction, 4) intensitybased linear registration (rigid and affine) to MNI space, 5) whitening for intensity normalization

Site classification with random forest binary classifier

| Stripped | Bias Field | Aligned | Intensities | Accuracy | Avg. Entropy | Avg. Prob. |
|----------|-------------------|------------|-------------|----------|--------------|------------|
| 1 | 1 | rigid | whitening | 96.96% | 0.4039 | 0.8296 |
| ✓ | 1 | affine | whitening | 98.82% | 0.3876 | 0.8397 |
| SPM12 - | Segment | | | Accuracy | Avg. Entropy | Avg. Prob. |
| × | 1 | rigid | graymatter | 80.24% | 0.6363 | 0.6399 |
| × | 1 | non-linear | graymatter | 96.62% | 0.5675 | 0.7234 |
| FSL – FA | ST | | | Accuracy | Avg. Entropy | Avg. Prob. |
| ✓ | 1 | rigid | graymatter | 93.24% | 0.4542 | 0.7968 |
| | | | | | | |

B. Glocker et al. "Machine Learning with Multi-site Imaging Data: An Empirical Study on the Impact of Scanner Effects." Medical Imaging meets NeurIPS Workshop, 2019

Related work: [Shafto et al., 2014; Taylor et al., 2017; Sudlow et al., 2015; Miller et al., 2016; Alfaro-Almagro et al., 2018]

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A case study with prostateT2-weighted MRI image segmentation

| Dataset | Case num | Field strength (T) | Resolution(in- plane/through- plane)(mm) | Coil | Manufactor | |
|---------|-------------|--------------------------|--|------------|------------|--|
| Site A | 30 | 3 | 0.6-0.625/3.6-4 | Surface | Siemens | |
| Site B | 30 | 1.5 | 0.4/3 | Endorectal | Philips | |
| Site C | 19 | 3 | 0.67-0.79/1.25 | No | Siemens | |

| Methods | BFC | NF | Intensities | Site A | Site B | Site C | Overall |
|--------------|-----|----|-------------|--------|--------|--------|---------|
| Separate (A) | × | × | whitening | 90.47 | 76.44 | 56.81 | |
| Separate (B) | × | × | whitening | 70.11 | 90.52 | 50.25 | 90.56 |
| Separate (C) | × | × | whitening | 57.93 | 55.25 | 90.70 | |
| Joint | × | × | × | 86.51 | 88.00 | 86.78 | 87.10 |
| Joint | × | × | histogram | 87.68 | 88.02 | 89.46 | 88.39 |
| Joint | × | × | scaled | 90.43 | 88.06 | 88.26 | 88.92 |
| Joint | × | × | whitening | 90.69 | 89.53 | 90.55 | 90.25 |
| Joint | × | ✓ | whitening | 90.76 | 89.46 | 90.91 | 90.37 |
| Joint | 1 | × | whitening | 90.84 | 89.81 | 90.81 | 90.49 |
| Joint | 1 | ✓ | whitening | 91.14 | 89.75 | 90.83 | 90.58 |

Q. Liu, Q. Dou, et al. "MS-Net: Multi-Site Network for Improving Prostate Segmentation with Heterogeneous MRI Data", IEEE Trans. on Medical Imaging, 2020. Related work: [Karani et al. MICCAI 2018; Gibson et al. MICCAI 2018; John et al. ISBI 2019]

| | Dice Coefficient (mean±std, %) | | | | | | | |
|-------------------------|--------------------------------|--------------------|--------------------|------------------|--|--|--|--|
| Methods | Site A | Site B | Site C | Overall | | | | |
| Tian <i>et al.</i> [26] | 88.23 | 88.23 | — | | | | | |
| Rundo et al. [9] | | — | 88.66 | | | | | |
| Separate | 90.47±3.00 | $90.52{\pm}2.45$ | 90.70 ± 3.34 | 90.56±2.88 | | | | |
| Joint | 90.69 ± 3.05 | $89.53 {\pm} 2.97$ | $90.55 {\pm} 3.18$ | 90.25 ± 3.08 | | | | |
| USE-Net [19] | 90.90±2.41 | 90.17±2.61 | 90.73±2.36 | 90.60±2.50 | | | | |
| Dual-Stream [47] | 90.87±2.85 | $90.57 {\pm} 2.12$ | 90.10 ± 3.28 | 90.51±2.72 | | | | |
| Series-Adapter [48] | 90.80±2.72 | $89.92{\pm}2.80$ | $91.24{\pm}2.21$ | 90.65±2.71 | | | | |
| Parallel-Adapter [23] | 90.61 ± 3.54 | $90.71 {\pm} 2.17$ | $91.30{\pm}2.06$ | 90.88±2.79 | | | | |
| DSBN (ours) | 90.98±2.69 | 90.67±2.22 | $91.07 {\pm} 1.86$ | 90.91±2.36 | | | | |
| MS-Net (ours) | 91.54±2.01 | 91.24±1.97 | $92.18{\pm}1.62$ | 91.66±1.95 | | | | |

Q. Liu, Q. Dou, et al. "MS-Net: Multi-Site Network for Improving Prostate Segmentation with Heterogeneous MRI Data", IEEE Trans. on Medical Imaging, 2020.

Unpaired Multi-modal Learning with Knowledge Distillation

$$\mathbf{z}_{c}^{i} = \frac{1}{\sum_{n} |\mathcal{S}_{c}^{n}|} \sum_{n} \sum_{(w,h) \in S_{c}^{n}} z_{nwhi},$$

$$\mathbf{p}_c^i = \frac{\exp(\mathbf{z}_c^i/T)}{\sum_j \exp(\mathbf{z}_c^j/T)},$$

Minimize probability divergence:

$$egin{split} \mathcal{L}_{ ext{kd}} &= rac{1}{C} \sum_{c} \Bigl(\mathcal{D}_{ ext{KL}}(\mathbf{q}^a_c || \mathbf{q}^b_c) + \mathcal{D}_{ ext{KL}}(\mathbf{q}^b_c || \mathbf{q}^a_c) \Bigr) \,, \ & ext{ where } \mathcal{D}_{ ext{KL}}(\mathbf{q}^a_c || \mathbf{q}^b_c) = \sum_{c} \mathbf{q}^a_c \log rac{\mathbf{q}^a_c}{\mathbf{q}^b_c} \,. \end{split}$$

Q. Dou, Q. Liu et al. "Unpaired Multi-modal Segmentation via Knowledge Distillation", IEEE Trans. on Medical Imaging, 2020.

Q. Dou, Q. Liu et al. "Unpaired Multi-modal Segmentation via Knowledge Distillation", IEEE Trans. on Medical Imaging, 2020.

Unsupervised domain adaptation through pixel-level alignment

C. Chen, Q. Dou, et al. "Semantic-Aware Generative Adversarial Nets for Unsupervised Domain Adaptation in Chest X-ray Segmentation." MICCAI-MLMI'18 (Oral)

Related work: [Y. Huo et al., ISBI 2018; Z. Zhang et al. CVPR 2018; Y. Zhang et al. MICCAI 2018]

Tackling Data Heterogeneity with UDA

Image-to-image transformation with generative adversarial nets

C. Chen, Q. Dou, et al. "Semantic-Aware Generative Adversarial Nets for Unsupervised Domain Adaptation in Chest X-ray Segmentation." MICCAI-MLMI'18 (Oral)

Related work: [Y. Huo et al., ISBI 2018; Z. Zhang et al. CVPR 2018; Y. Zhang et al. MICCAI 2018]

Tackling Data Heterogeneity with UDA

Unsupervised Domain Adaptation: Feature-level Alignment

Train a source domain segmentation model

• joint cross-entropy loss and dice loss

$$\mathcal{L}_{seg} = -\sum_{i=1}^{N^s} \sum_{c \in C} w_c^s \cdot y_{i,c}^s \log(\hat{p}_{i,c}^s) - \lambda \sum_{c \in C} \frac{\sum_{i=1}^{N^s} 2y_{i,c}^s \hat{y}_{i,c}^s}{\sum_{i=1}^{N^s} y_{i,c}^s y_{i,c}^s + \sum_{i=1}^{N^s} \hat{y}_{i,c}^s \hat{y}_{i,c}^s}$$

Q. Dou*, C. Ouyang*, et al. "Unsupervised Cross-Modality Domain Adaptation of ConvNets for Biomedical Image Segmentations with Adversarial Loss.." IJCAI 2018.

Unsupervised Domain Adaptation: Feature-level Alignment

Unsupervised learning with adversarial loss

domain adaptation module (generator):
$$\min_{\mathcal{M}} \mathcal{L}_{\mathcal{M}}(X^{t}, \mathcal{D}) = -\mathbb{E}_{(\mathcal{M}_{A}(x^{t}), F_{H}(x^{t})) \sim \mathbb{P}_{g}}[\mathcal{D}(\mathcal{M}_{A}(x^{t}), F_{H}(x^{t}))]$$

domain critic module (discriminator):
$$\min_{\mathcal{D}} \mathcal{L}_{\mathcal{D}}(X^{s}, X^{t}, \mathcal{M}) = \mathbb{E}_{(\mathcal{M}_{A}(x^{t}), F_{H}(x^{t})) \sim \mathbb{P}_{g}} [\mathcal{D}(\mathcal{M}_{A}(x^{t}), F_{H}(x^{t}))] - \mathbb{E}_{(M^{s}_{A}(x^{s}), F_{H}(x^{s})) \sim \mathbb{P}_{s}} [\mathcal{D}(M^{s}_{A}(x^{s}), F_{H}(x^{s}))], s.t. \|\mathcal{D}\|_{L \leq K}$$

Q. Dou*, C. Ouyang*, et al. "Unsupervised Cross-Modality Domain Adaptation of ConvNets for Biomedical Image Segmentations with Adversarial Loss.." IJCAI 2018. Related work: [K Kamnitsas et al. IPMI 2017]

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Unsupervised learning with adversarial loss

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Q. Dou*, C. Ouyang*, et al. "Unsupervised Cross-Modality Domain Adaptation of ConvNets for Biomedical Image Segmentations with Adversarial Loss.." IJCAI 2018. Related work: [K Kamnitsas et al. IPMI 2017] 22

Related work: [DANN, Ganin et al. JMLR 2016; ADDA, Tzeng et al. CVPR 2017; CycleGAN, Zhu et al. ICCV 2017]

Unsupervised Domain Adaptation: Synergistic Alignment

| Methods | Adap | otation | | | Dic | e | | | | ASI |) | |
|----------------------------------|--------------|--------------|------|------|------|------|---------|------|------|------|------|---------|
| | Image | Feature | AA | LAC | LVC | MYO | Average | AA | LAC | LVC | MYO | Average |
| W/o adaptation | | | 28.4 | 27.7 | 4.0 | 8.7 | 17.2 | 20.6 | 16.2 | N/A | 48.4 | N/A |
| DANN (Ganin et al. 2016) | | \checkmark | 39.0 | 45.1 | 28.3 | 25.7 | 34.5 | 16.2 | 9.2 | 12.1 | 10.1 | 11.9 |
| ADDA (Tzeng et al. 2017) | | \checkmark | 47.6 | 60.9 | 11.2 | 29.2 | 37.2 | 13.8 | 10.2 | N/A | 13.4 | N/A |
| CycleGAN (Zhu et al. 2017) | \checkmark | | 73.8 | 75.7 | 52.3 | 28.7 | 57.6 | 11.5 | 13.6 | 9.2 | 8.8 | 10.8 |
| CyCADA (Hoffman et al. 2018) | \checkmark | \checkmark | 72.9 | 77.0 | 62.4 | 45.3 | 64.4 | 9.6 | 8.0 | 9.6 | 10.5 | 9.4 |
| Dou et al. (Dou et al. 2018) | | \checkmark | 74.8 | 51.1 | 57.2 | 47.8 | 57.7 | 27.5 | 20.1 | 29.5 | 31.2 | 27.1 |
| Joyce et al. (Joyce et al. 2018) | | \checkmark | - | - | 66 | 44 | - | - | - | - | - | - |
| SIFA (Ours) | \checkmark | \checkmark | 81.1 | 76.4 | 75.7 | 58.7 | 73.0 | 10.6 | 7.4 | 6.7 | 7.8 | 8.1 |

C. Chen, Q. Dou et al. "Synergistic Image and Feature Adaptation: Towards Cross-Modality Domain Adaptation for Medical Image Segmentation", AAAI, 2019. (Oral) Related work: [DANN, Ganin et al. JMLR 2016; ADDA, Tzeng et al. CVPR 2017; CycleGAN, Zhu et al. ICCV 2017] 24

A brief overview of existing approaches

Domain Generalization

Problem setting: train on multiple source domains and **directly** generalize to unseen domains

Regularization for generic semantic features

- adversarial feature alignment for domain invariance [Li et al. ECCV 2018]
- decompose networks parameters to domain-specific/invariant [Khosla ECCV 2012]
- data augmentation based methods [Shankar et al. ICLR 2018; Volpi et al. NeurIPS 2018]
- multi-task or self-supervised signals [Ghifary et al. ICCV 2015; Carlucci et al. CVPR 2019]

Tackling Data Heterogeneity for Domain Generalization

Domain Generalization with Gradient-based Meta-learning

Model-agnostic learning: MAML (model-agnostic meta-learning) [Finn et al. ICML 2017]

- MLDG: directly applying episodic training paradigm [Li et al. AAAI 2018]
- MetaReg: meta-learning of weights regularization term [Balaji et al. NeurIPS 2018]
- Episodic training with alternative model updates [Li et al. ICCV 2019]

Episodic training paradigm

Available domains: $D = \{D_1, D_2, ..., D_K,\}$ Neural network is composed of: $F_{\psi} \circ T_{\theta}$

Learning with explicit simulation of domain shift:

At each iteration, split into meta-train D_{tr} and meta-test D_{te} Update the parameters one or more steps with gradient descent:

 $(\psi', \theta') = (\psi, \theta) - \alpha \nabla_{\psi, \theta} \mathcal{L}_{\text{task}}(\mathcal{D}_{\text{tr}}; \psi, \theta)$

Then, apply meta-learning step, to enforce certain properties to be exhibited on held-out domain D_{te} , to regularize semantic features

Global Class Alignment

Inter-class relationships concept is domain-invariant and transferable

• In each domain, compute class-specific mean feature vector:

$$\bar{\mathbf{z}}_{c}^{(k)} = \frac{1}{N_{k}^{(c)}} \sum_{n:y_{n}^{(k)}=c} F_{\psi'}(\mathbf{x}_{n}^{(k)}) \approx \mathbb{E}_{D_{k}}[F_{\psi'}(\mathbf{x}) \mid y=c]$$

- Compute soft label distribution: $\mathbf{s}_{c}^{(k)} = \operatorname{softmax}(T_{\theta'}(\bar{\mathbf{z}}_{c}^{(k)})/\tau)$
- With $(D_i, D_j) \in D_{tr} \times D_{te}$, regularize consistency of inter-class alignment:

$$\ell_{\text{global}}(D_i, D_j; \psi', \theta') = \frac{1}{C} \sum_{c=1}^{C} \frac{1}{2} [D_{\text{KL}}(\mathbf{s}_c^{(i)} \| \mathbf{s}_c^{(j)}) + D_{\text{KL}}(\mathbf{s}_c^{(j)} \| \mathbf{s}_c^{(i)})]$$

(Note: complexity of pairs is controllable via mini-batch sampling in large-scale scenarios.)

D

Local Sample Clustering

feature clusters with domain-independent class-specific cohesion and separation

Use a *metric-learning* approach, with an embedding network and operates in semantic feature space:

• obtain a learnable distance function:

 $d_{\phi}(\mathbf{z}_n, \mathbf{z}_m) = \|\mathbf{e}_n - \mathbf{e}_m\|_2 = \|M_{\phi}(\mathbf{z}_n) - M_{\phi}(\mathbf{z}_m)\|_2$

• metric-learning can rely on contrastive loss [Hadsell et al. CVPR 2006]:

 $\ell_{\rm con}^{n,m} = \begin{cases} d_{\phi}(\mathbf{z}_n, \mathbf{z}_m)^2, & \text{if } y_n = y_m \\ (\max\{0, \, \xi - d_{\phi}(\mathbf{z}_n, \mathbf{z}_m)\})^2, & \text{if } y_n \neq y_m \end{cases}$

• or triplet loss [Schroff et al. CVPR 2015]:

$$\ell_{\rm tri}^{a,p,n} = \max\{0, \ d_{\phi}(\mathbf{z}_a, \mathbf{z}_p)^2 - d_{\phi}(\mathbf{z}_a, \mathbf{z}_n)^2 + \xi\}$$

Medical application of brain tissue segmentation

- data acquisition differences in scanners, imaging protocols, and many other factors
- posing severe limitations for translating learning-based methods in clinical practice
- segmentation of 3 brain tissues: white matter, gray matter and cerebrospinal fluid
- 4 domains corresponding to 4 hospitals

| Train Test | Set-A | Set-B | Set-C | Set-D | DeepAll | MASF |
|---------------|-------|-------|-------|-------|---------|-------|
| Set-A | 90.62 | 88.91 | 88.81 | 85.03 | 89.09 | 89.82 |
| Set-B | 85.03 | 94.22 | 81.38 | 88.31 | 90.41 | 91.71 |
| Set-C | 93.14 | 92.80 | 95.40 | 88.68 | 94.30 | 94.50 |
| Set-D | 76.32 | 88.39 | 73.50 | 94.29 | 88.62 | 89.51 |

MASF: Model-Agnostic Learning of Semantic Features

Datasets

- 1. Multi-Modality Whole Heart Segmentation (MMWHS) Challenge <u>http://www.sdspeople.fudan.edu.cn/zhuangxiahai/0/mmwhs/</u> <u>https://github.com/carrenD/Medical-Cross-Modality-Domain-Adaptation</u>
- 2. MICCAI 2019 MS-CMRSeg Multi-sequence Cardiac MR Segmentation Challenge https://zmiclab.github.io/mscmrseg19/
- 3. MICCAI iSeg 2019 Challenge 6-month Infant Brain MRI segmentation from Multiple Sites <u>http://iseg2019.web.unc.edu</u>
- 4. ISBI 2019 CHAOS Challenge CT-MRI Abdominal Multi-Organ Segmentation https://chaos.grand-challenge.org
- 5. Prostate Segmentation, with several public datasets, i.e., NCI-ISBI 2013 dataset, I2CVB dataset (include multiple sites), PROMISE12 dataset (include multiple sites)
- 6. Chest X-Ray, with several public datasets,
 i.e., ChestX-ray14 NIH, CheXpert, PadChest, Mimic-CXR
 MIDL 2019: <u>https://openreview.net/forum?id=S1gvm2E-t4</u>

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Paper & Code Available at:

Thanks for your attention! Q & A

