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3D Generative Adversarial Network and TransUNet-based approach for Self-supervised region-aware segmentation of COVID-19 CT scans

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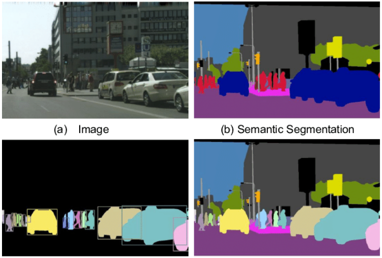
Outline

Introduction

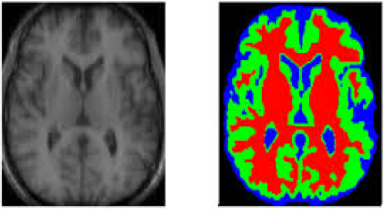
Image segmentation involves dividing an image into several regions or segments, often pixel by pixel, to identify and isolate different structures or objects present.

Image segmentation can :

- Ensure accuracy
- Reduce resource-intensive and time-consuming
- Quantify the detection



(a) Image (b) Semantic Segmentation (c) Instance Segmentation (d) Panoptic Segmentation



(a) coupe axial (b) segmentation des tissus

Figure 1:Image segmentation

Contextualization

Medical image segmentation plays a crucial role in analysis and diagnosis

- Locate and precisely delineate organs, tissues, or lesions.
- Quantification of features: size, shape, or volume

The automatic medical image segmentation models include:

- Fully supervised
- Semi-Supervised
- Weakly-Supervised
- Self-Supervised

We chose to use self-supervised segmentation because it addresses challenges:

- Not enough healthy CT scans ,
- Not Costly : No need to wait for the expert's feedback mainly in labelling data,

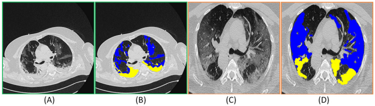


Figure 2:The segmentation of the lungs

Problematic

How can we develop a segmentation model capable of:

- Predicting lesions in COVID-19 CT scans without manual annotation at the pixel level.
- Achieving results that surpass the performance of existing state-of-the-art unsupervised and weakly-supervised segmentation techniques.

Initial approach

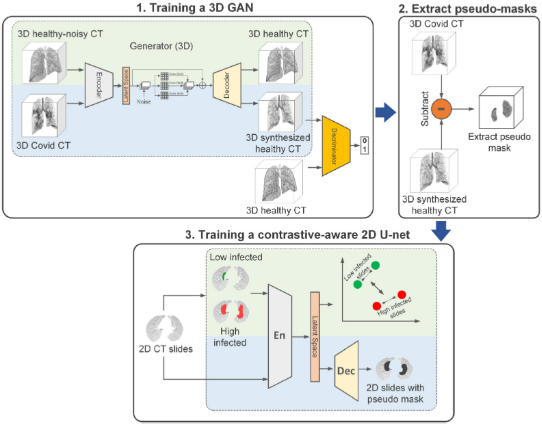
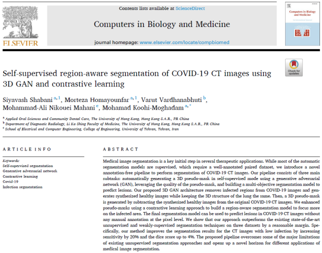


Figure 3 : Original Pipeline



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Self-supervised region-aware segmentation of COVID-19 CT images using 3D GAN and contrastive learning

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ABSTRACT

Medical image segmentation is a key initial step in several therapeutic applications. While most of the automatic segmentation models are supervised, which require a well-annotated paired dataset, we introduce a novel annotation-free pipeline to perform segmentation of COVID-19 CT images. Our pipeline consists of three main subtasks: automatically generating a 3D pseudo-mask in self-supervised mode using a generative adversarial network (GAN), leveraging the quality of the pseudo-mask, and building a multi-objective segmentation model to predict lesions. Our proposed 3D GAN architecture removes infected regions from COVID-19 images and generates synthesized healthy images while keeping the 3D structure of the lung the same. Then, a 3D pseudo-mask is generated by subtracting the synthesized healthy images from the original COVID-19 CT images. We enhanced pseudo-masks using a contrastive learning approach to build a region-aware segmentation model to focus more on the infected area. The final segmentation model can be used to predict lesions in COVID-19 CT images without any manual annotation at the pixel level. We show that our approach outperforms the existing state-of-the-art unsupervised and weakly-supervised segmentation techniques on three datasets by a reasonable margin. Specifically, our method improves the segmentation results for the CT images with low infection by increasing sensitivity by 20% and the dice score up to 4%. The proposed pipeline overcomes some of the major limitations of existing unsupervised segmentation approaches and opens up a novel horizon for different applications of medical image segmentation.

Figure 4: First page of original research article

Proposed approach for self supervised segmentation of Covid 19 CT scans

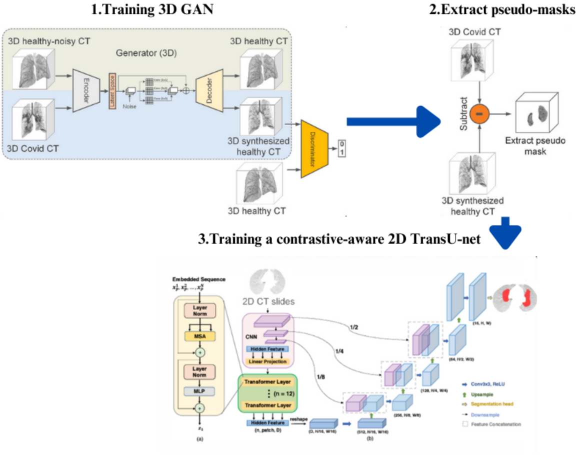

Figure 5 : Our Pipeline: GAN (with Perlin Noise) + contrastive-aware TransUNET Model

Proposed approach for self supervised segmentation of Covid 19 CT scans

- **Phase 1: 3D GAN for Synthesizing Pseudo-Masks**
- **Phase 2: Synthesizing Pseudo Masks**
- **Phase 3: Segmenting the CT scans using TransUNET**

Methods

Phase 1: 3D GAN for Synthesizing Pseudo-Masks

In our study, we used a 3D Generative Adversarial Network (GAN) to transform CT scans of lungs affected by COVID-19 into their healthy counterparts.

- *Train a multi-objective 3D GAN to transform COVID-19 CT sections into healthy CT sections.*
- *Employ two losses simultaneously: one for mapping healthy-to-healthy sections and another for generating semi-healthy sections from infected ones.*
- *Distinguish real healthy CT scans from synthesized healthy scans.*

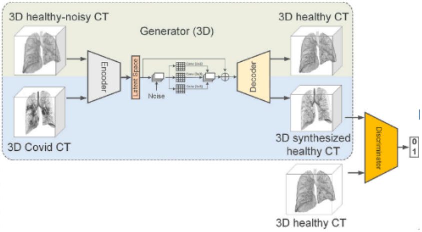

Figure 6 : 3D GAN

Methods

Phase 1: 3D GAN for Synthesizing Pseudo-Masks

To build an effective 3D GAN, two main challenges were adressed:

- **Ensuring the model's generality for various infections:**
  The model's architecture was modified to include a noise adder (Perlin Noise) operator in the encoder-decoder's latent space, which is represented as follows:

$$\hat{I}_H = G(I_C) = De\left(En(I_C) + U_N\right), \tag{1}$$

  where $En : I_C \in \mathbb{R}^{W\times H\times L} \to L_N$ symbolizes the encoder,
  $De : L_N \to \hat{I}_H \in \mathbb{R}^{W\times H\times L}$ is the decoder, and U_N is the noise operator. The noise adder perturbs the latent space to train the generator to remove a wide variety of infections.

Methods

Phase 1: 3D GAN for Synthesizing Pseudo-Masks

- **Maintaining the original lung structure in the generated sections**

we updated the model's weights by incorporating healthy-noisy sections into the training phase. These images were created by adding Perlin noise to healthy 3D CT scans.

The loss function for the proposed 3D GAN is defined as:

$$\begin{aligned}\max_D V(D,G) =& \mathbb{E}_{I_H \sim p_{\textbf{healthy}}}[\log D(I_H)] \\ &+ \mathbb{E}_{I_C \sim p_{\textbf{covid}}}[\log(1 - D(G(I_C)))] \\ &+ \mathbb{E}_{I_H^{Pe} \sim p_{\textbf{noisy\_Healthy}}}[G(I_H^{Pe}) - I_{H_2}],\end{aligned} \tag{2}$$

where I_H denotes the real healthy 3D volume, and I_H^{Pe} is the healthy-noisy image with Perlin noise. By training with both losses, the 3D GAN learns to generate a variety of healthy outputs corresponding to the COVID-19 input images.

Methods

Phase 2: Synthesizing Pseudo Masks

- Synthesize pseudo masks by subtracting the generated healthy CT scans from the original COVID-19 CT scans.
- Pseudo masks emphasize the infected regions within the CT scans.

- To achieve this, we employ the pseudo mask, denoted as $\hat{M}$, which is computed as follows:

$$\hat{M} = I_C - \hat{I}_H \tag{3}$$

Where:
- I_C represents the COVID-positive CT scan, which is an entry of the trained 3D GAN model generator.
- $\hat{I}_H$ represents the output of the 3D GAN, consisting of synthesized pseudo-healthy images.

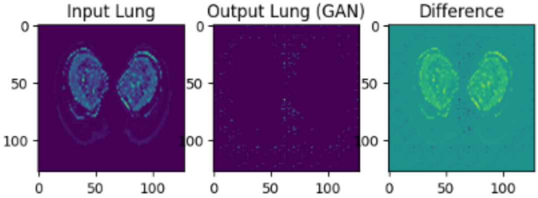

Figure 7 : Example of Mask extraction

Methods

Phase 3: Segmenting the CT scans using TransUNET

- Adapt the segmentation phase by incorporating the TransUNET architecture for precise COVID-19 CT image segmentation.
- Utilize the generated pseudo masks from the previous step as input data for training TransUNET segmentation model.
- Highlight TransUNET's capabilities in effectively segmenting COVID-19-infected regions with exceptional accuracy.

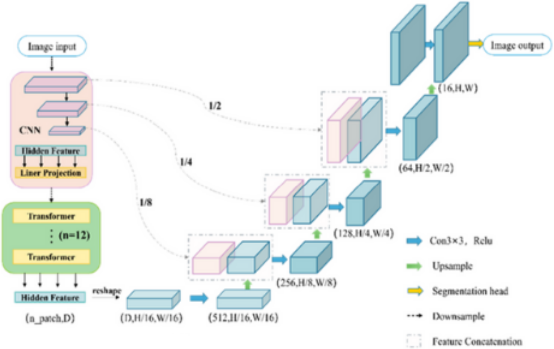

Figure 5: Framework Overview - TransUNet Architecture

Enhanced TransUNET Segmentation Pipeline Incorporating Transformers

Algorithm 1 Enhanced TransUNET Segmentation Pipeline Incorporating Transformers

Inputs: I_c: COVID-19 3D volume, I_h: Healthy 3D volume
Input: I_p: High infected COVID-19 2D slices, I_n: Low infected COVID-19 2D slices
Initialize: G: 3D Generator, D: 3D Discriminator
Initialize: U_{ed}: TransUNET (UNet with Transformer modules), U_e referring to the encoder-part only
Initialize: SEL: Sensitivity Enhanced Loss, ECL: Enhanced Contrastive Loss
for *each epoch in the first training phase (3D GAN G-D Model training)* **do**
Freeze G, Unfreeze D
Calculate generated healthy volumes $\hat{I}_H$ using $G(I_c)$
Update D using I_h and $\hat{I}_H$, by calculating adversarial loss for D as

$$\nabla_{\theta_D} \mathbb{E}[(\log D(I_h) + \log(1 - D(\hat{I}_h)))]$$

Freeze D, Unfreeze G
Update G using I_c, by calculating adversarial loss for G as

$$\nabla_{\theta_G} (\log(1 - D(\hat{I}_h)))$$

Add Perlin Noise to the healthy CT volumes to obtain I_H^{Pe}
Update G using MSE loss of pairs of $\hat{I}_h^{Pe}$ and I_h as input and output, respectively

$$\nabla_{\theta_G} \mathbb{E}[(\|G(\hat{I}_h^{Pe}) - I_h\|_2)]$$

for *each epoch in the second training phase (2D Segmentation Model training)* **do**
Perform a forward pass of the batch through TransUNet
Calculate the contrastive loss
Calculate the mean squared error (MSE) loss
Calculate the sensitivity-enhanced loss
Combine losses and perform backpropagation
Update model weights with the optimizer
Periodically plot loss graphs and sample segmentations
Save model checkpoints

Output: Segmented infection volumes
Output: Updated G and U_{ed} parameters

Methods

Loss functions

Our advanced segmentation model employs two novel loss functions, each meticulously crafted to enhance the model's performance in segmenting COVID-19 infections in lung CT scans. Here, we present the mathematical formulations of these loss functions.

Enhanced Contrastive Loss

$$L_{\text{contrastive}} = -\log \frac{\sum_{i=1}^{N} \exp\left(\frac{\mathbf{f}_i \cdot \mathbf{f}_p}{\tau}\right)}{\sum_{i=1}^{N} \sum_{j=1}^{N} \exp\left(\frac{\mathbf{f}_i \cdot \mathbf{f}_j}{\tau}\right)} \tag{4}$$

where $\mathbf{f}_i$ and $\mathbf{f}_j$ are the flattened and normalized feature vectors of the i^{th} and j^{th} samples, respectively, $\mathbf{f}_p$ represents the feature vector of a positive sample, τ is the temperature parameter, and N is the number of samples.

Methods

Loss functions

When determining the optimal value for τ, stochastic gradient descent can be employed:

1. **Initialize parameters:**
   Initialize the model parameters randomly or with specific values.
2. **Initialize initial learning rate:**
   Choose an initial learning rate (η_0).
3. **Repeat until convergence or maximum iterations reached:**
   3.1 **Randomly choose a pair of examples $(\mathbf{f}_i, \mathbf{f}_p)$:**
   3.2 **Compute the partial gradient:**

$$\nabla L(\tau) = \frac{\mathbf{f}_i \cdot \mathbf{f}_p}{\tau^2} \left(\frac{\exp(\mathbf{f}_i \cdot \mathbf{f}_p / \tau)}{\sum_{k=1}^{N} \exp(\mathbf{f}_k \cdot \mathbf{f}_p / \tau)} - \frac{\sum_{j=1}^{N} \exp(\mathbf{f}_i \cdot \mathbf{f}_j / \tau)}{\left(\sum_{k=1}^{N} \sum_{l=1}^{N} \exp(\mathbf{f}_k \cdot \mathbf{f}_l / \tau)\right)} \right)$$

   3.3 **Update temperature (τ) using a variable learning rate (η_t):**

$$\tau \leftarrow \tau - \eta_t \nabla L(\tau)$$

4. **Stopping condition:** Stop if the maximum number of iterations is reached.

Methods

Sensitivity Enhanced Loss

- **Sensitivity Enhanced Loss**
  - Aims to reduce false negatives in medical diagnostics.
  - Formula:

$$L_{\textsf{sensitivity}} = \frac{1}{N} \sum_{i=1}^{N} [BCE(\mathbf{p}_i, \mathbf{t}_i) \times (1 + \beta \times FN(\mathbf{p}_i, \mathbf{t}_i))]$$

  - $\mathbf{p}_i$: Predicted probability for i^{th} sample.
  - $\mathbf{t}_i$: True label for i^{th} sample.
  - β: Weight amplifying the impact of false negatives.
  - N: Total number of samples.
- **BCE (Binary Cross-Entropy) Loss**
  - Used in the sensitivity enhanced loss.
  - Measures the difference between predicted and true labels.

Results and Discussion

- **Preprocessing of CT Images:** Adjusted size and focus for clarity and consistency. Dataset comprises 50 COVID-positive and 51 COVID-negative CT scans.
- **Cropped Lung Images:** Focused on lung areas to enhance visibility of potential COVID-19 indicators.
- **Data Organization:** Categorized images into two groups: COVID-19 positive and normal scans.
- **Format Conversion:** Transformed images and masks into numpy arrays for efficient computer analysis.
- **Data Storage:** Saved numpy arrays separately, including healthy lung images, infection images, lung masks, and original CT scans. Organization critical for model training and testing with TransUNET-based segmentation.

Results and Discussion

Preprocessing Mosmed CT scans and Hyperparameters Setting

- Resizing followed, where we adjusted each scan to a uniform size while maintaining the aspect ratio to prevent image distortion.
- We performed resampling of CT pixels to standardize the pixel spacing across all scans.
- Ensure that each voxel represented consistent physical dimensions ,a key factor for accurate analysis.

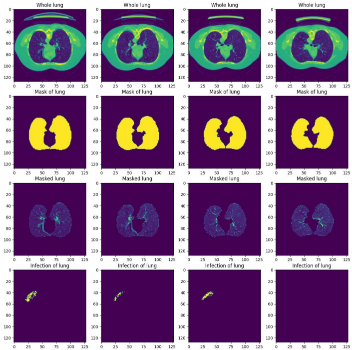

Figure 6:Cropped Lunges by Extracted Masks - Mosmed Data Preprocessing Phase

Results and Discussion

3D GAN Model Training Results

The Figure shows the result of the 3D GAN synthesizing a pseudo-healthy image, to later substract it from the covid-infected image in order to obtain the pseudo-mask highlighting regions of infection for the training of the 2D segmentation model.

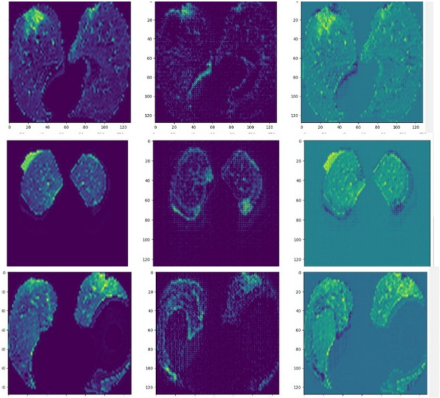

Figure 7:Synthesizing semi-healthy medical images

Results and Discussion

TransUNET Segmentation Encoder-Decoder results

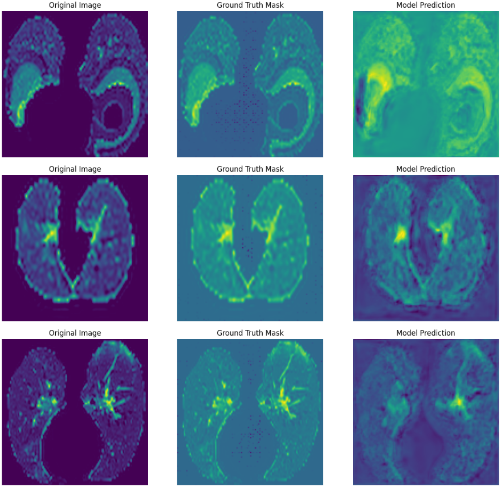

Figure 8:TransUNET Segmentation results

Results and Discussion

Validation Set Overview

In the Mosmed Dataset, our validation set is comprised of 50 COVID-19 CT scans. These scans have ground-truth masking of the infection regions, which is critical for assessing the performance of our image segmentation models.

Metrics

1. Dice Score (DSC): The Dice Score quantifies the spatial overlap between predicted and ground truth segmentation.

2. Sensitivity: Sensitivity measures the model's ability to correctly identify positive instances.

3. Specificity: Specificity gauges the model's capacity to accurately identify negative instances.

Each metric is calculated per slice, and the maximum value across all slices is reported.

Results and Discussion

Metrics Formulation

1. Dice Score (DSC):

$$\text{DSC} = \frac{2 \times \text{TP}}{2 \times \text{TP} + \text{FP} + \text{FN}}$$

where TP is true positives, FN is false negatives.

2. Sensitivity:

$$\text{Sensitivity} = \frac{TP}{TP + FN}$$

where TP is true positives, FN is false negatives.

3. Specificity:

$$\text{Specificity} = \frac{TN}{TN + FP}$$

where TN is true negatives, FP is false positives.
Each metric is calculated per slice, and the reported value represents the maximum across all slices.

Results and Discussion

Evaluation Methodology

Approach:

- Iterate over each CT scan slice in the dataset.
- Calculate Infection Percent: Ratio of infected area to total lung area per slice.
- Apply a thresholding method to segment the infected regions.
- Reshape the masks for metric calculations.
- Compute Dice Score, Sensitivity, and Specificity for each slice.
- Store these scores to analyze overall model performance.

Results and Discussion

Model Performance Comparison

Comparison of Model Performances

Metric	GAN + Perlin Noise + TransUNET		GAN + Perlin Noise + UNET	
	Mean (%)	Std (%)	Mean (%)	Std (%)
Dice Score	50.09	45.44	**72.89**	46.69
Sensitivity	**98.52**	11.29	72.89	46.69
Specificity	**99.99**	1.11e-14	99.63	6.05

Conclusion

Notably, our investigation has outperformed comparable weakly supervised models, demonstrating superior performance on a test dataset, particularly in regions of low infection within CT slices. Despite the utilization of a 3D GAN during training, our final 2D segmentation model offers increased flexibility and faster processing times for clinicians. The model exhibits potential applications in diverse medical imaging scenarios beyond the scope of COVID-19 CT segmentation.

Future Work

- **Enhancement of the GAN Model:** Consider refining our GAN model, possibly exploring advanced architectures such as TransGAN to further improve its performance.
- **Exploration of Alternative Loss Functions:** Investigate the incorporation of alternative loss functions to potentially enhance the model's learning capabilities and segmentation accuracy.
- **Integration of Multi-Modal Information:** Explore the integration of multi-modal information, such as combining CT scans with other imaging modalities, to enhance the overall robustness of the segmentation model.
- **Clinical Validation and Deployment:** Conduct thorough clinical validation studies and explore possibilities for deploying the model in real-world clinical settings, ensuring its efficacy and reliability.
- **Collaboration with Domain Experts:** Collaborate with domain experts and medical professionals to refine the model based on clinical feedback and insights, ensuring alignment with practical medical requirements.

References

- Azad, R., Khodapanah Aghdam, E., Rauland, A., Jia, Y., Haddadi Avval, A., Bozorgpour, A., ... Merhof, D. (2022). *Medical Image Segmentation Review: The Success of U-Net.* `https://arxiv.org/pdf/2211.14830.pdf`
- Moriya, T., Roth, H. R., Nakamura, S., Oda, H., Nagara, K., Oda, M., Mori, K. (2022). *Unsupervised Segmentation of 3D Medical Images Based on Clustering and Deep Representation Learning.* `https://arxiv.org/pdf/1804.03830.pdf`
- Shabani, S., Homayounfar, M., Vardhanabhuti, V., Nikouei Mahani, M.-A., Koohi-Moghadam, M. (2021). *Self-supervised region-aware segmentation of COVID-19 CT images using 3D GAN and contrastive learning. Computers in Biology and Medicine, 149*.
- mkara44. (2023). *transUNET implementation for PyTorch by mkara44 on GitHub.* Available at: `https://github.com/mkara44/transunet_pytorch` (Accessed on 2023-12-13).
- Mosmed AI. (2023). *MosMedData-CT-COVID19-type VII-v 2.* Available at: `https://mosmed.ai/en/datasets/covid191110/` (Accessed on 2023-10-26).