Improved Generative Model for Weakly Supervised Chest Anomaly Localization via Pseudo-paired Registration with Bilaterally Symmetrical Data Augmentation

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Abstract

Image translation based on a generative adversarial network (GAN-IT) is a promising method for precise localization of abnormal regions in chest X-ray images (AL-CXR). However, heterogeneous unpaired datasets undermine existing methods to extract key features and distinguish normal from abnormal cases, resulting in inaccurate and unstable AL-CXR. To address this problem, we propose an improved two-stage GAN-IT involving registration and data augmentation. For the first stage, we introduce an invertible deep-learning-based registration technique that virtually and reasonably converts unpaired data into paired data for learning registration maps. This novel approach achieves high registration performance. For the second stage, we apply data augmentation to diversify anomaly locations by swapping the left and right lung regions on the uniform registered frames, further improving the performance by alleviating imbalance in data distribution showing left and right lung lesions. Our method is intended for application to existing GAN-IT models, allowing existing architecture to benefit from key features for translation. By showing that the AL-CXR performance is uniformly improved when applying the proposed method, we believe that GAN-IT for AL-CXR can be deployed in clinical environments, even if learning data are scarce.

1 Introduction

Chest X-ray (CXR) imaging is used as a first-line test for identifying lung anomalies because it provides fast image generation with a low radiation dose [1]. However, it is difficult to accurately diagnose diseases under fine shading conditions. Existing systems and methods should be further improved as precise anomaly localization in CXR images (AL-CXR) are clinically important. The recent application of deep learning (DL) to CXR diagnosis has substantially improved the detection of anomalies in patients [2, 3, 4]. Nevertheless, apart from simple discrimination, this approach does not guarantee the precise identification of subregions with anomalies. Although class activation maps and their variants have been typically used to achieve AL-CXR, they have limited resolution in blurry maps and show

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clinical limitations regarding interpretation (e.g., it is difficult to obtain normal class activation in a disease-free region).

Generative adversarial network (GAN)-based image translation (GAN-IT) establishes an alternative for detecting abnormal regions in CXR images because it supports high-resolution outputs by applying adversarial learning. It converts real CXR images containing disease regions into normal CXR images, and it has been used to specify abnormal regions in the lung using the differences between the images. Although GAN-IT is promising for AL-CXR, stability and accuracy require further improvement. GAN-IT for AL-CXR has a low performance because learning is performed using unpaired data (i.e., normal/abnormal image pairs taken in different environments from different patients—unpaired, not normal/abnormal image pairs taken under the same conditions of the same patient—paired). For pixel-level CXR-AL, even a small spatial difference between the input and labeled images (e.g., target images before and after translation) notably affects image translation. Therefore, the possible structural mismatch of relative positions in images from unpaired datasets during registration learning may considerably degrade performance.

To improve GAN-IT for AL-CXR, we propose a model-agnostic method called image translation under pseudo-paired registration with bilaterally symmetrical data augmentation (IT-PRBA) and an extension of its registration to DL (IT-DPRBA). Both methods aim to improve the CXR-AL performance through a novel registration technique for pre/postprocessing in conventional GAN-IT models.

The proposed IT-PRBA has a unique and reversible registration without requiring DL network training and generates a coordinate transformation map (i.e., the lung image of a moving patient is fit to a fixed lung region) using only a fixed lung mask. As the proposed registration generates a pseudo-paired (i.e., moving/fixed) dataset with only moving images without applying DL, we call it DL-free pseudo-pair registration (DLF-PR). IT-DPRBA extends IT-PRBA through DL-based registration using a paired dataset obtained by DLF-PR, whereas trained registration instead of DLF-PR is used in IT-PRBA. The DL-based method is called DL-based pseudo-paired registration (DL-PR). Unlike existing DL-based registration techniques that simply learn an unpaired dataset [5, 6], the registration in the proposed IT-DPRBA learns a virtual and reasonable paired dataset. This is because the obtained pseudo-paired dataset is less affected by artifacts owing to variations in an unpaired dataset, thereby facilitating finetuning of detailed deformable positions under a virtual and reasonable paired domain in a registration network. The advanced DLF-PR and DL-PR allow GAN-IT to learn relations between abnormal and normal data in a unified domain. Therefore, regions corresponding to diseases in CXR lung images can be easily learned even with a small training set.

In IT-PRBA and IT-DPRBA, we introduce bilaterally symmetrical data augmentation (BA), which further improves the performance of GAN-IT for CXR-AL by addressing data imbalance in CXR images containing left/right lung lesions. BA converts an image of the left (right) lung into that of the right (left) lung at the pixel level in the standardized/registered domain. It effectively augments disease data by creating a hypothetical patient with a disease on the other side from a patient with a disease in only one of the left and right lungs. BA is easily implemented owing to the reversible nature of the proposed registration techniques.

We evaluated IT-PRBA and IT-DPRBA by integrating them into state-of-the-art GAN-IT models, namely, CycleGAN [7] and contrastive pair translation (CUT) [8]. We observed that the CXR-AL performance (e.g., for tuberculosis or consolidation shadow cases) is considerably improved when applying our proposal. The source code is available at https://github.com/kskim-phd/IT-DPRBA.
2 Related Work

2.1 GAN-Based Anomaly Localization

A GAN is a representative DL architecture to synthesize training sets. It can transform unlearned data into samples within learned data. Schlegl et al. [9] showed that unsupervised learning with GANs using only training data from normal patients allows creating a virtual normal image from the actual image of a patient with anomalies, identifying the abnormal region using the difference between images. Subsequent studies have been conducted to accelerate processing [10], improve performance [11, 12, 13], and apply this method to CXR images [14, 15, 16]. However, unsupervised learning may generate images with high deviations and unstable anomaly localization [17].

Weakly supervised GANs based on training with both normal and abnormal labeled data have recently been adopted to further improve performance. In addition to exploiting abnormal data during learning, such GANs outperform those based on unsupervised learning for accurate anomaly localization and stability [18, 19, 20]. In principle, these methods are based on image translation [21, 22], which synthesizes normal CXR images from CXR images containing disease regions. However, existing GAN- or GAN-IT-based methods for anomaly localization neglect the performance enhancement achievable using registration for learning. In contrast, we explore registration for integration into image translation models as a pre/postprocessing stage aiming to further improve the AL-CXR performance.

2.2 GAN-Based Image Translation

Various GANs for general image translation have been proposed [7, 8, 23, 24, 25, 26, 27]. Zhu et al. [7] first demonstrated that image translation can be performed by bidirectionally connecting two GANs in a CycleGAN. Subsequent studies [8, 23, 27, 26] addressed the structural imbalance between images before and after translation by enhancing the recognition of spatial location information in image feature maps through contrastive learning. A representative model of this approach is CUT [8]). Another follow-up study on CycleGAN was aimed to enhance the conversion performance by separating style information of an image or applying artificial distortion to an image [24, 25]. Unlike our study, these previous developments neglected registration between unpaired images for learning image translation.

Recent GAN-IT models have been developed to improve performance by adopting registration [28, 29, 30, 31]. Arar et al. [28] selectively added a registration network to the input or output of a GAN-IT model, thereby improving the image translation performance by simultaneously learning the translation and registration models. Kong et al. [29] improved the GAN-IT performance by applying data augmentation to introduce random noise for coordinate transformation through registration. Yang et al. [30] demonstrated the contribution of registration to GAN-IT for relating different modalities. Chen et al. [31] used registration and GAN-IT and removed the GAN discriminator to improve performance. However, existing GAN-IT models use an unpaired dataset without preprocessing for training the registration network. In contrast, we use the novel DLF-PR to convert an unpaired dataset into a paired one and propose DL-PR that can be trained with this preprocessed virtually paired dataset to improve the registration performance.
3 Methods

3.1 Image Translation

We consider image translation from input domain $X \subset \mathbb{R}^{h \times w}$ to output domain $Y \subset \mathbb{R}^{h \times w}$. We provide a training dataset for unpaired instances $X = \{x \in X\}$ and $Y = \{y \in Y\}$. Image translation aims to parameterize mapping $K_\theta$ satisfying $K_\theta : X \mapsto Y$. This task can be formulated to determine optimal parameter $\theta^*$ of a translation model as follows:

$$\theta^* = \arg\min_{\theta} |I(X, \hat{Y}_\theta(X)) - I(X,Y)|,$$

where $I$ denotes the mutual information and $\hat{Y}_\theta(X) := \{K_\theta(x) | x \in X\}$ denotes the model translation result for $X$.

3.2 Baseline GAN-IT for AL-CXR

Consider $n$ lung CXR images from patients with anomalies and let the indices and dataset be $\{1 : n\} := \{1, 2, ..., n\}$ and $X = \{x_i\}_{i \in \{1:n\}}$, respectively. In addition, consider $m$ lung CXR images from healthy patients with index and datasets denoted as $\{1 : m\}$ and $Y = \{y_i\}_{i \in \{1:m\}}$, respectively. From the learning data, we train the model using (1) and perform AL-CXR by identifying anomaly map $v_t$ as the difference between test CXR image $x_t$ (normal or abnormal) and its synthesized result $\hat{y}_t = K_{\theta^*}(x_t)$ as follows:

$$v_t = x_t \odot \text{SEG}_{\psi^*}(x_t) - \hat{y}_t \odot \text{SEG}_{\psi^*}(\hat{y}_t),$$

where $\text{SEG}_{\psi^*}$ denotes a pretrained segmentation network that extracts the inner region of the lung as a binary mask. The left- and right-hand terms in (2) refer to the modified CXR images of $x_t$ and $\hat{y}_t$, respectively, in which the outer lung region is set to zero.

3.3 Proposed IT-PRBA

The proposed IT-PRBA comprises three stages: segmentation, registration, and BA. These stages are described in Algorithm 1 and Fig. 1.
We propose a DL-free registration method and its extension using DL. We first describe DLF-PR;

Algorithm 1 IT-PRBA

Input: $x_i$ for $i \in \{1 : n\}$, SEG$_{\theta^*}$ : $\mathbb{R}^{h \times w} \mapsto \mathbb{R}^{h \times w}$

1: for $i = 1$ to $n$ do
2: $s_i \gets$ SEG$_{\theta^*}(x_i)$
3: $(s_i^l, s_i^r) \leftarrow$ split($s_i$)
4: $(s_l(x_i), s_r(x_i)) \leftarrow (s_i^l \odot x_i, s_i^r \odot x_i)$
5: end for

Output: Left and right lung binary masks $(s_i^l, s_i^r)$ and their inner images $(s_l(x_i), s_r(x_i))$ for patient $i$ ($i \in \{1 : n\}$)

2: Registration stage

Input: $x_i$, $s_i^l$, and $s_i^r$ for $i \in \{1 : n\}$

1: for $i = 1$ to $n$ do
2: $(T_{i \rightarrow f}^l, T_{i \rightarrow f}^r) \leftarrow$ REG$(s_i^l, s_i^r)$
3: $(T_{i \rightarrow f}^l, T_{i \rightarrow f}^r) \leftarrow$ REG$(s_i^l, s_i^r)$
4: $(x_{i \rightarrow f}^l, x_{i \rightarrow f}^r) \leftarrow (T_{i \rightarrow f}^l(s_l(x_i)), T_{i \rightarrow f}^r(s_r(x_i)))$
5: end for

Output: Moved left $x_{i \rightarrow f}^l$ and right $x_{i \rightarrow f}^r$ lung images of patient $i$

3: Augmentation stage

Input: $x_i$, $x_{i \rightarrow f}^l$, $x_{i \rightarrow f}^r$, $s_i^l$, and $s_i^r$ for $i \in \{1 : n\}$

1: for $i = 1$ to $n$ do
2: $(\hat{x}_{i \rightarrow f}^l, \hat{x}_{i \rightarrow f}^r) \leftarrow$ (BA$_{r \rightarrow l}$($x_{i \rightarrow f}^l, s_i^l$), BA$_{l \rightarrow r}$($x_{i \rightarrow f}^r, s_i^r$))
3: end for

Output: Augmented (synthesized) left lung $\hat{x}_{i \rightarrow f}^l$ and right lung $\hat{x}_{i \rightarrow f}^r$ images of patient $i$

3.3.1 Segmentation

Segmentation of CXR image $x_i$ extracts the left $(s_i^l)$ and right $(s_i^r)$ lung binary masks and leaves only the region inside the left $(s_l(x_i))$ and right $(s_r(x_i))$ lung images, as shown in Fig. 1. The binary masks are obtained by splitting the entire mask given as the pretrained segmentation model output, SEG$_{\theta^*}(\cdot)$. Then, left $(s_l(x_i))$ and right $(s_r(x_i))$ lung images are obtained by elementwise multiplication $\odot$ of each mask $(s_i^l, s_i^r)$ by $x_i$.

3.3.2 Registration without DL

We propose a DL-free registration method and its extension using DL. We first describe DLF-PR; DL-PR is introduced in Section 3.5. DLF-PR calculates coordinate shift functions $T_{i \rightarrow f}^l$ and $T_{i \rightarrow f}^r$ mapping from left $(s_l)$ and right $(s_r)$ lung masks to those of a fixed lung mask $s_f$, where $i$ and $f$ indicate patient $i$ and fixed, respectively.

To obtain the corresponding maps, we introduce a coordinate domain to convert general coordinate values $(\alpha, \beta) \in \mathbb{R}^2$ of horizontal/vertical axes at a specific position in a CXR image into relative position coordinates in the lung internal region (inside lung mask $s$) as $C_s(\alpha, \beta) \in [0, 1]^2$:

$$C_s(\alpha, \beta) := \left( \frac{-p_1^s}{p_1^s + p_2^s}, \frac{-p_2^s}{p_1^s + p_2^s}, \frac{-q_1^s}{q_1^s + q_2^s}, \frac{-q_2^s}{q_1^s + q_2^s} \right)$$

(3)

Examples using $C_s(\alpha, \beta)$ are shown in Fig. 2. We obtain the longest line starting from the lowest (red) point of each left and right lung, set this line as a new vertical axis and define a perpendicular horizontal
axis, and transform original coordinates \((\alpha, \beta) \in \mathbb{R}^2\) into coordinates \(C_s(\alpha, \beta) \in [0, 1]^2\), which are described by the relative position inside the lung expressed between 0 and 1 along the new horizontal and vertical axes.

Considering relative coordinate domain \(C_s(\alpha, \beta)\), we obtain coordinate shift function \(T_{i \rightarrow f}^l\) such that it maps corresponding relative coordinates \(C_{s_i}(\alpha, \beta)\) of the moving patient’s lung mask, \(s_i\), to be the same as the corresponding relative coordinates, \(C_{s_f}(\alpha, \beta)\), of the still (fixed) patient’s lung mask, \(s_f\). Particularly, the function can be formulated using (5) and (7) for each lung on the left and right sides, respectively:

\[
T_{i \rightarrow f}^l := \{(\alpha, \beta) \mapsto (\alpha^*_l, \beta^*_l) \mid \forall (\alpha, \beta) \in \text{supp}(s_i^l)\},
\]

\[
(\alpha^*_l, \beta^*_l) := \arg\min_{(\alpha', \beta') \in \text{supp}(s_f^l)} \left\| C_{s_i}(\alpha, \beta) - C_{s_f}(\alpha', \beta') \right\|,
\]

\[
T_{i \rightarrow f}^r := \{(\alpha, \beta) \mapsto (\alpha^*_r, \beta^*_r) \mid \forall (\alpha, \beta) \in \text{supp}(s_i^r)\},
\]

\[
(\alpha^*_r, \beta^*_r) := \arg\min_{(\alpha', \beta') \in \text{supp}(s_f^r)} \left\| C_{s_i}(\alpha, \beta) - C_{s_f}(\alpha', \beta') \right\|,
\]

Figure 2: Diagram of proposed DLF-PR process.

Figure 3: Key characteristics of registration and augmentation in IT-PRBA.
and $T_{r\rightarrow f}^l$ as $T_{f\rightarrow f}^l$ and $T_{f\rightarrow s_f}$, respectively. They map transformed coordinates ($\alpha^*, \beta^*$) onto original coordinates ($\alpha, \beta$). The transformation maps $(T_{i\rightarrow f}, T_{f\rightarrow s_i})$ between the lung images of moving and still (fixed) patients can be obtained only from the mask information of the patients, $s_i$ and $s_f$. Hence, the generation of these maps given by (4) and (6) can be compactly expressed as function REG:

$$(T_{l\rightarrow f}^l, T_{l\rightarrow f}^r) \leftarrow \text{REG}(s_i^l, s_f^l), (T_{r\rightarrow f}^l, T_{r\rightarrow f}^r) \leftarrow \text{REG}(s_i^r, s_f^r).$$

The role of these maps is illustrated in Fig. 3. We find the longest vertical line (e.g., yellow vertical lines in Fig. 3) from the lowest point on the outer edge of each lung image and derive a vertical grid that equally divides the vertical line into various intervals. Then, we obtain each horizontal line (e.g., yellow horizontal lines in Fig. 3) that includes each vertical grid perpendicular to the vertical line and derive a horizontal grid that equally divides the horizontal line into various intervals. Then, maps $T_{l\rightarrow f}^l$ and $T_{r\rightarrow f}^l$ are obtained by linearly transforming each point on the grid (e.g., red point for registration in Fig. 3) into a point (e.g., blue point for registration in Fig. 3) obtained by applying the same process to fixed lung mask $s_f$. To fit the registered images to the original images, we obtain inverse coordinate shift maps $T_{f\rightarrow s_i}^l$ and $T_{f\rightarrow s_i}^r$. Additional implementation details for REG are provided in Appendix A (Algorithm 4).

Through registration, the relative position inside the lungs of all patients is fixed at specific coordinates. This facilitates learning of image translation using a GAN, even on a small dataset. We demonstrate the effectiveness of the proposed registration compared with existing technologies in Sections 3.5 and 5.

### 3.3.3 Training Data Augmentation by BA

The proposed BA doubles the number of images by generating opposite (i.e., right and left) lung images from left and right fixed lung images $x_{l\rightarrow f}^l$ and $x_{l\rightarrow f}^r$ as $\hat{x}_{l\rightarrow f}^l$ and $\hat{x}_{l\rightarrow f}^r$, respectively. Because the right lung image has a horizontally narrower lung region owing to the presence of the heart, after flipping the left image to the right, we partially remove the virtual heart region of the flipped image to fit the right lung (i.e., right lung region excluding the heart), as shown in Fig. 3 (blue arrow). Details about the proposed BA are provided in Appendix A (Algorithm 5).
Algorithm 2 Training

Training for baseline
Input: \( X = \{ x_i \}_{i \in \{1:n \}}, Y = \{ y_i \}_{i \in \{1:n \}}, K_\theta \)
1: \( \theta^* \leftarrow \text{argmin}_\theta |I(X, \tilde{Y}_\theta(X)) - I(X, Y)| \)
Output: Trained model \( K_\theta \).

Training for proposed method using IT-PRBA
Input: \( X_r, X_l, Y_r, Y_l \) given by (8), \( K_{\theta_r}, K_{\theta_l} \)
1: \( \theta^*_r \leftarrow \text{argmin}_{\theta_r} |I(X_r, \tilde{Y}_{\theta_r}(X_r)) - I(X_r, Y_r)| \)
2: \( \theta^*_l \leftarrow \text{argmin}_{\theta_l} |I(X_l, \tilde{Y}_{\theta_l}(X_l)) - I(X_l, Y_l)| \)
Output: Trained models \( K_{\theta_r} \) and \( K_{\theta_l} \).

Algorithm 3 Testing

Test of baseline
Input: \( X = \{ x_i \}_{i \in \{1:n \}}, Y = \{ y_i \}_{i \in \{1:n \}}, T_\theta \)
1: \( \tilde{y}_i \leftarrow T_\theta(x_i) \)
Output: Synthesized normal CXR image \( \tilde{y} \) translated from target CXR image \( x_t \).

Testing of proposed method using IT-PRBA
Input: Test CXR image \( x_t \)
1: \( (x_{t\rightarrow f}^l, x_{t\rightarrow f}^r) \leftarrow \text{perform up to step 4 of registration by replacing } x_i \text{ with } x_t \)
2: \( \tilde{y}_t^l \leftarrow T_{f\rightarrow l}^l(s_l(T_{\theta_l}(x_{t\rightarrow f}^l))) \)
3: \( \tilde{y}_t^r \leftarrow T_{f\rightarrow r}^r(s_r(T_{\theta_r}(x_{t\rightarrow f}^r))) \)
4: \( \tilde{y}_t \leftarrow s_t^l \circ \tilde{y}_t^l + s_t^r \circ \tilde{y}_t^r + (1 - s_t^l) \circ x_t \)
Output: Synthesized normal CXR image \( \tilde{y}_t \) translated from target CXR image \( x_t \).

3.4 Application of IT-PRBA to GAN-IT for AL-CXR

3.4.1 Training

Algorithm 2 describes model training using a baseline method and the proposed IT-PRBA. We set the baseline as detailed in Section 3.2. In place of the input and label data used in the baseline, we use input data \( X_l \) and \( X_r \) and label data \( Y_l \) and \( Y_r \) for the left and right lungs, respectively, in the IT-PRBA as follows. From step 2 in the augmentation stage of Algorithm 1, we obtain

\[
X_r = \{ s_r(x_{t\rightarrow f}^r) \}_{i \in \{1:n \}} \cup \{ s_r(x_{t\rightarrow f}^l) \}_{i \in \{1:n \}}, \\
X_l = \{ s_l(x_{t\rightarrow f}^l) \}_{i \in \{1:n \}} \cup \{ s_l(x_{t\rightarrow f}^r) \}_{i \in \{1:n \}}, \\
Y_r = \{ s_r(y_i) \}_{i \in \{1:m \}}, \\
Y_l = \{ s_l(y_i) \}_{i \in \{1:m \}}. \tag{8}
\]

The number of abnormal samples in \( X_r \) or \( X_l \) is twice that in \( X \) after applying the proposed augmentation. Thus, the amount of data can be considerably increased using our method in a clinical environment in which abnormal (e.g., disease) cases are scarce.
3. DL-PR

Registration model

Moving image (e.g., abnormal)

Fixed image obtained by our DLF-PR (e.g., abnormal)

2. Baseline B

Registration model

Moving image (e.g., abnormal)

Fixed image (e.g., normal)

1. Baseline A

Registration model

Moving image (e.g., abnormal)

Fixed image (e.g., normal)

Figure 5: Diagram of proposed DL-PR. Other DL-based baseline techniques (A and B) are unpaired regarding moving and fixed images, impeding proper registration learning (i.e., disease distortion and lung area artifacts as shown in yellow and red boxes respectively). In contrast, DL-PR secures paired (moving/fixed) learning data for the same patient/image source by generating fixed images from moving ones via DLF-PR.

3.4.2 Testing

Algorithm 3 describes model testing using the baseline and proposed IT-PRBA. Typical baseline image translation methods use original CXR image $x_t$ as the input. However, in the method in which the proposed IT-PRBA is applied, registered image $x_{t \rightarrow f}$ of $x_t$ is used as the input. Subsequently, uniform output $K_{\theta^*}(x_{t \rightarrow f})$ is provided and expressed back in the original image coordinates as $\hat{y}_t = T_{f \rightarrow t}(s_l(K_{\theta^*}(x_{t \rightarrow f})))$. Finally, anomaly map $v_t$ is given by (2) from $\hat{y}_t$, where $v_t$ represents the difference in the image information between the original image and virtual normal image generated by the network. In other words, the proposed method allows advanced anomaly localization by performing image translation in the registered domain. This process is performed as a separate network (i.e., $T_{\theta_l}$ and $T_{\theta_r}$) for the left and right lungs (steps 2 and 3), and the results are combined during deregistration (step 4 in Algorithm 3), as illustrated in Fig. 4.

3.5 IT-DPRBA: DL-Based Extension of IT-PRBA

The proposed DLF-PR performs registration using coordinate transformation function $T_{l \rightarrow f}$ given by (4) and (6). The transformation allows the lung region mask of each moving patient to be uniformly mapped onto a reference mask. Hence, a formable instead of deformable coordinate transformation is obtained; however, it cannot achieve perfect lung region coordinate transformation. We address this problem using the proposed DL-PR, which is applicable to any DL-based registration network. Unlike conventional DL-based registration, which uses the learning label as a fixed image, the proposed DL-PR considers a label from a moving image using the DLF-PR output for learning. In other words, existing DL-based registration uses data from different moving and still (fixed) patients, leading to identification
of inexisten diseases in images from healthy moving patients and still (fixed) patients with diseases. Conversely, the proposed DL-PR avoids this problem by learning registration using moving and fixed (i.e., result from DLF-PR) images of the same patient. Fig. 5 shows the differences between DL-PR and existing DL-based registration techniques (baselines A and B) for learning and the different registration performances.

For an accurate comparison, the proposed and existing DL-based registration techniques are formulated in detail as follows. For training of the proposed DL-PR, given a registration network $REG_\phi$ with training parameter $\phi$, the network takes moving image $x_m$ as its input and learns to output pseudo-label $T_{m \rightarrow f}(x_m)$, which is the moved image generated by DLF-PR. The learning objective is given by

$$
\phi_{i \rightarrow f}^{t^*} := \arg\min_{\phi_{i \rightarrow f}} \mathcal{L}_{\phi_{i \rightarrow f}} \left( REG_{\phi_{i \rightarrow f}^{t}}(s_l(x_i)), T_l^{i \rightarrow f}(s_l(x_i)) \right),
$$

(9)

$$
\phi_{i \rightarrow f}^{r^*} := \arg\min_{\phi_{i \rightarrow f}} \mathcal{L}_{\phi_{i \rightarrow f}} \left( REG_{\phi_{i \rightarrow f}^{r}}(s_r(x_i)), T_r^{i \rightarrow f}(s_r(x_i)) \right),
$$

(10)

where $\mathcal{L}_{\phi}(a, b)$ denotes a training loss (e.g., mean squared error) for DL-based registration with network input $a$ (moving image) and label $b$ (fixed image), $s_l(x_i)$ and $s_r(x_i)$ denote the left and right lung images of the moving patient $i$, and $T_l^{i \rightarrow f}(s_l(x_i))$ and $T_r^{i \rightarrow f}(s_r(x_i))$ denote their lung images moved using IT-PRBA.

From learning described in (9) and (10), we can obtain smoother/more deformable coordinate transformation functions $\hat{T}_l^{i \rightarrow f}$ and $\hat{T}_l^{i \rightarrow f}$ (i.e., DL-PR) than those provided by DLF-PR (i.e., $T_l^{i \rightarrow f}$ and $T_r^{i \rightarrow f}$). DL-PR is defined by the following trained registration networks:

$$
\hat{T}_l^{i \rightarrow f} := REG_{\phi_{i \rightarrow f}^{t^*}}, \quad \hat{T}_l^{i \rightarrow f} := REG_{\phi_{i \rightarrow f}^{r^*}}.
$$

Accordingly, we propose an extension of IT-PRBA called IT-DPRBA, which converts coordinate transformation functions $T_l^{i \rightarrow f}$ and $T_r^{i \rightarrow f}$ into $\hat{T}_l^{i \rightarrow f}$ and $\hat{T}_l^{i \rightarrow f}$, respectively (Algorithm 1). This extension provides more stable image registration, and AL-CXR can be performed by applying IT-DPRBA to GAN-IT through the same approach by replacing only the coordinate transformation function, as described in Section 3.4. Detailed performance results are listed in Tables 3 and 4 of Section 4.4.

Unlike the DL-PR objective given by (9) and (10), conventional DL-based registration aims to optimize parameter $\psi$ as $\psi^*$ and obtain coordinate transformation functions $\hat{T}_l^{i \rightarrow f} := REG_{\psi_{i \rightarrow f}^{t^*}}$ and $\hat{T}_l^{i \rightarrow f} := REG_{\psi_{i \rightarrow f}^{r^*}}$:

$$
\psi_{i \rightarrow f}^{t^*} := \arg\min_{\psi_{i \rightarrow f}} \mathcal{L}_{\psi_{i \rightarrow f}} \left( REG_{\psi_{i \rightarrow f}^{t}}(s_l(x_i)), s_l(x_f) \right),
$$

(11)

$$
\psi_{i \rightarrow f}^{r^*} := \arg\min_{\psi_{i \rightarrow f}} \mathcal{L}_{\psi_{i \rightarrow f}} \left( REG_{\psi_{i \rightarrow f}^{r}}(s_r(x_i)), s_r(x_f) \right),
$$

(12)

where $s_l(x_i)$ and $s_r(x_i)$ denote the left and right lung images of the still (fixed) patient, respectively. Training given by (11) and (12) is called DL-based registration baseline A. Baseline A uses image $x_f$ of a patient different from image $x_i$ of a moving patient as a label (i.e., $s_l(x_f)$ and $s_r(x_f)$). This unpaired nature results in unintended disease reduction or distortion artifacts in moved/registered images if the fixed image for training has no disease but the moving image for training has a disease. However, our technique described by (9) and (10) uses the label (fixed) image, whose patient information with image content and structure is the same as that of a moving patient image $x_i$. Hence, in DL-PR, the training
difference between moving and fixed images exists only for coordinate information, thereby ensuring more reliability for registration learning (i.e., Our DL-PR makes a moving patient being registered to a fixed patient paired with the same moving patient, thereby solving disease reduction or distortion artifacts that baseline A may suffer.).

We also consider another learning objective for DL-based registration in registration baseline B. Unlike baseline A given by (11) and (12), baseline B uses only binary mask information (i.e., \( s_i \) and \( s_f \)) depending on whether it belongs to the lung, without exploiting information, \( s(x_i) \) and \( s(x_f) \), of moving and still (fixed) patients, respectively. Baseline B optimizes parameter \( \pi \) as \( \pi^* \) and obtains coordinate transformation functions \( \hat{T}_{i\rightarrow f}^*: \text{REG} \pi^*_i \rightarrow f \) and \( \hat{T}_{r\rightarrow f}^*: \text{REG} \pi^*_{r\rightarrow f} \), as follows:

\[
\pi^*_{i\rightarrow f} := \arg\min_{\pi_{i\rightarrow f}} \mathcal{L}_{\pi_{i\rightarrow f}} \left( \text{REG}_{\pi_{i\rightarrow f}}(s_i), s_f \right),
\]

\[
\pi^*_{r\rightarrow f} := \arg\min_{\pi_{r\rightarrow f}} \mathcal{L}_{\pi_{r\rightarrow f}} \left( \text{REG}_{\pi_{r\rightarrow f}}(s_r), s_f \right).
\]

In this case of baseline B, unlike baseline A, no artifacts such as anomaly reduction or distortion are generated after registration because the pixel values on the inner region of the lung for both moving and fixed images are the same as 1. However, proper registration fails because the relative position between the coordinates after registration is not uniform, resulting in an unrealistic scenario. This is because during training of baseline B, the intersecting coordinate region, in which the binary masks of the moving and still (fixed) patients are 1, shows slight motion compared with other regions.

As shown in Fig. 5 (and Fig. 7), the proposed DL-PR overcomes limitations of baselines A and B (yellow and red boxes in Figs. 5 and 7 respectively). In fact, DL-PR creates a moving/fixed training pair for the same patient to suppress artifacts influencing baseline A and solves the nonuniform registration of baseline B using information of the lung internal structure rather than a simple binary mask.

4 Experiments and Results

4.1 Data Preparation

Table 1: Data splitting (in number of samples) for anomaly detection and localization

| Case            | Normal | Tuberculosis | Consolidation |
|-----------------|--------|--------------|---------------|
| Training set    | 600    | 600          | 600           |
| Test set        | 758    | 150          | 150           |

We used a publicly available dataset [32] with tuberculosis cases representing anomalies. We randomly selected 600 samples from the tuberculosis and normal classes for training \((n, m = 600)\), and the remaining 150 and 758 samples for testing, respectively. In addition to tuberculosis, we collected 750 cases of consolidation patients from publicly available data [33], of which 600 cases were used for training and the remaining 150 cases for testing.

4.2 Lung Segmentation

Table 2: Segmentation performance in terms of IOU and Dice coefficient of method in [34]

| Dataset       | Method in [34] | IOU  | Dice |
|---------------|----------------|------|------|
| JSRT [35]     | 0.939          | 0.969|
| NLM [36]      | 0.942          | 0.970|

We segmented lung regions from each CXR image using a publicly available pretrained lung segmentation network [34] based on a variational autoencoder, which achieves a higher generalization performance than other networks. We used the JSRT [35] and NLM [36] datasets to evaluate the lung segmentation performance of the pretrained network in terms of the intersection over union.
4.3 Evaluation Metrics

We evaluated AL-CXR using difference $v_t$ in pixel values between the reconstructed and original images given by (2).

In addition, we calculated the patient-wise anomaly score to obtain a confidence level for whether the target CXR image contains an anomaly. This score was calculated as the $\ell_2$-norm, $\|H(v_t, \tau)\|_2$, of anomaly map $v_t$, which was obtained by thresholding, via $H(v_t, \tau)$, the absolute value of $v_t$, with a value below $\tau \in (0, 20, 30)$ being set to 0 at the pixel level as follows:

$$H(v_t, \tau) = \begin{cases} v_t(x,y), & \text{if } |v_t(x,y)| > \tau \text{ for } (x,y) \in \text{supp}(v_t), \\ 0, & \text{for all } (x,y) \notin \text{supp}(v_t). \end{cases}$$

(15)

To measure the discrimination ability between normal and abnormal cases, we calculated the region under the receiver operating characteristic curve (AUC) of patient-wise anomaly score $\|H(v_t, \tau)\|_2$.

4.4 AL-CXR Evaluation

By integrating the proposed IT-PRBA or IT-DPRBA, we trained GAN-IT to evaluate anomaly detection and localization. Anomaly localization was performed on the pretrained GAN-IT model described by (1) using training data from normal ($Y$) and abnormal ($X$) cases for tuberculosis or consolidation. The results were compared with those of a baseline using an existing GAN-IT without registration and deregistration, as shown in Fig. 4. For a fair comparison, we applied the GAN-IT CycleGAN [7] or CUT [8] to the proposed and baseline methods. For abnormal data, either tuberculosis or consolidation cases were used. Additional details on the training setup of GAN-IT are provided in Appendix B.

The anomaly detection performance for tuberculosis and consolidation is listed in Tables 3 and 4, respectively. The AUC of the CUT model is higher than that of CycleGAN in all the cases. For CUT, compared with the existing baseline GAN-IT without IT-PRBA or IT-DPRBA (Fig. 4), the proposed IT-PRBA or IT-DPRBA improves the AL-CXR AUCs at various $\tau$ values by more than 4%.

Among the proposed methods, IT-DPRBA outperforms IT-PRBA in most cases (values in boldface). The values showing the highest performance (marked with *) were obtained from IT-DPRBA. These results validate the proposed IT-PRBA and its DL-based extension, IT-DPRBA.

Fig. 6 shows AL-CXR examples using CUT from localization maps $v_t$ given by (2) for tuberculosis or consolidation cases. For simplicity, negative values of $v_t$ are treated as 0. The proposed IT-PRBA
Figure 6: Comparison between AL-CXR maps $v_t$ obtained from proposed method and baseline for (a) tuberculosis and (b) consolidation patients. All were commonly used based on CUT.

and IT-DPRBA detect abnormal regions in the lung images that are not detected by the baselines. Examples using CycleGAN for abnormal cases and CycleGAN/CUT for normal cases are shown in Appendix C (Figs. 13 and 14).
4.5 Ablation Study for Registration and Data Augmentation in IT-PRBA

The proposed IT-PRBA applies DLF-PR and BA to an existing GAN-IT baseline. We conducted an ablation study to confirm whether DLF-PR and BA contribute to AL-CXR, and the results are listed in Tables 5 and 6 for tuberculosis and consolidation cases, respectively. These results show that when registration and data augmentation are sequentially added to the baseline, the AL-CXR performance improves, validating IT-PRBA and its components.

![Figure 7](image-url)
5 Comparison between Proposed and State-of-the-Art Registration Techniques

We compared the proposed registration techniques, namely, DLF-PR and DL-PR, with existing state-of-the-art methods. Coordinate transformation functions \( (T_{l \rightarrow f}, T_{r \rightarrow f}) \) were individually obtained from DLF-PR using (4) and (6), DL-PR \( (\text{REG}_{\phi_{l \rightarrow f}^{*}}, \text{REG}_{\phi_{r \rightarrow f}^{*}}) \), and DL-based registration baselines A \( (\text{REG}_{\psi_{l \rightarrow f}^{*}}, \text{REG}_{\psi_{r \rightarrow f}^{*}}) \) and B \( (\text{REG}_{\pi_{l \rightarrow f}^{*}}, \text{REG}_{\pi_{r \rightarrow f}^{*}}) \).

We used U-Net [37, 38] as the backbone for DL-based registration because it achieves state-of-the-art performance [5]. For training, we used mean squared error \( L_{\phi}(a, b) \) as the loss function and the Adam optimizer [39] with a learning rate of 0.0001. The number of epochs was set to 1000, and the batch size was set to 1.

Fig. 7 shows the registration/moved results from the moving images to the fixed images. Unlike other methods, the proposed DL-PR fully registers images without artifacts (no yellow or red box). Relatively few artifacts are observed in DLF-PR compared with the two existing DL-based baselines. As DLF-PR is not based on DL, it does not require training and provides fast registration. DL-PR does not generate artifacts compared with other methods. Therefore, the proposed DLF-PR and DL-PR are effective and achieve high performance.

6 Conclusion

To improve the AL-CXR performance through GAN-IT, we propose registration and CXR data augmentation techniques for determining lung masks and localizing lung diseases. In existing registration techniques for GAN-IT, the coordinates between the input and output images are inconsistent owing to their unpaired features. The proposed registration and data augmentation techniques perform feature pairing, substantially improving the performance, with IT-DPRBA improving the baseline AUC from 0.82 to 0.93 for tuberculosis cases. Although we only validated our registration-based image translation model on CXR images, its principle can be extended to other applications. We expect that our method will serve as a baseline for anomaly localization even without pixel-level annotations of diseases that can be detected using various medical imaging modalities.

7 Financial Disclosures of All Authors

The authors have no conflicts of interest or financial disclosures to declare.

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A Implementation Details

Algorithm 4 REG

\[ T_{i \rightarrow f}^u, T_{f \rightarrow i}^u \leftarrow \text{REG}(s_i^u, s_f^u) \quad (u \in \{l, r\}) \]

Input: \((s_i, s_f)\) for some \(i \in \{1 : n\}\)

1. \((x_{i}^{\text{low}}, y_{i}^{\text{low}}) \leftarrow \text{find \,(x, y)-coordinate \,s.t. \,y \,is \,given \,as \,the \,smallest \,in \,boundary \,set \,of \,s_i^u\).
2. \((x_{i}^{\text{low}}, y_{i}^{\text{low}}) \leftarrow \text{find \,(x, y)-coordinate \,s.t. \,y \,is \,given \,as \,the \,smallest \,in \,boundary \,set \,of \,s_i^u\).
3. \((x_{f}^{\text{high}}, y_{f}^{\text{high}}) \leftarrow \text{find \,(x, y)-coordinate \,s.t. \,its \,l_2\text{-distance} \,to \,(x_{i}^{\text{low}}, y_{i}^{\text{low}}) \,is \,given \,as \,the \,largest \,in \,boundary \,set \,of \,s_f^u\).
4. \((x_{f}^{\text{high}}, y_{f}^{\text{high}}) \leftarrow \text{find \,(x, y)-coordinate \,s.t. \,its \,l_2\text{-distance} \,to \,(x_{i}^{\text{low}}, y_{i}^{\text{low}}) \,is \,given \,as \,the \,largest \,in \,boundary \,set \,of \,s_i^u\).
5. \(\mathcal{R}_f \leftarrow \text{obtain coordinate rotation function} \mathcal{R}_f \text{ to rotate image } s_f^u \text{ as } \mathcal{R}_f(s_f^u) \text{ s.t. rotated } x_{f}^{\text{low}} \text{ and rotated } x_{f}^{\text{high}} \text{ are equal}
6. \(\mathcal{R}_i \leftarrow \text{obtain coordinate rotation function} \mathcal{R}_i \text{ to rotate image } s_i^u \text{ as } \mathcal{R}_i(s_i^u) \text{ s.t. rotated } x_{f}^{\text{low}} \text{ and rotated } x_{f}^{\text{high}} \text{ are equal}
7. \(\mathcal{V}_i \leftarrow \text{obtain coordinate resizing function} \mathcal{V}_i \text{ s.t. the longest vertical lengths of positive regions in } \mathcal{V}_i(\mathcal{R}_i(s_i^u)) \text{ and } \mathcal{R}_f(s_f^u) \text{ are equal and the corresponding columns are on the same } y\text{-axis coordinates}
8. \(\mathcal{H}_i \leftarrow \text{obtain coordinate resizing function} \mathcal{H}_i \text{ s.t. for each } y\text{-axis coordinate, the horizontal lengths of positive regions in } \mathcal{H}_i(\mathcal{V}_i(\mathcal{R}_i(s_i^u))) \text{ and } \mathcal{R}_f(s_f^u) \text{ are equal}
9. \(T_{i \rightarrow f}^u(-) \leftarrow \text{obtain the final coordinate transform as } \mathcal{R}_f^{-1}(\mathcal{H}_i(\mathcal{V}_i(\mathcal{R}_i(-)))) \text{, where } \mathcal{R}_f^{-1}(-) \text{ denotes the inverse map of } \mathcal{R}_f(-)
10. \(T_{f \rightarrow i}^u(-) \leftarrow \text{obtain an inverse coordinate transform map of } T_{i \rightarrow f}^u(-) \text{ s.t. } T_{f \rightarrow i}^u(T_{i \rightarrow f}^u(-)) = I(-)

Output: \(T_{i \rightarrow f}^u, T_{f \rightarrow i}^u\)

In this section, we detail the implementation of the proposed REG and BA, which are used in Algorithm 1, as Algorithms 4 and 5, respectively.

Registration REG in Algorithm 4 provides coordinate shift functions \(T_{i \rightarrow f}^u\) and \(T_{f \rightarrow i}^u\) mapping from left \(s_i^u\) and right \(s_f^u\) of the lung mask of patient \(i\) to \(s_f^u\) and \(s_f^u\) of a given fixed lung mask \(s_f\), respectively, where \(i\) and \(f\) denote the patient index (for moving images) and fixed image, respectively. Steps 1–4 calculate the longest vertical line (e.g., yellow vertical line in Fig. 3(b)) starting from the lowest point (steps 1 and 2) on the outer edge of each left or right lung mask. Steps 5 and 6 calculate coordinate rotation functions \(\mathcal{R}_i\) and \(\mathcal{R}_f\), which rotate moving mask \(s_i^u\) and fixed mask \(s_f^u\), respectively, thus satisfying their longest lines perpendicular to the horizontal axis and calculated in the previous steps. Step 7 calculates vertical coordinate resizing function \(\mathcal{V}_i\) for the longest vertical line of the lung in moving \(\mathcal{R}_i(s_i^u)\) to match that in fixed \(\mathcal{R}_f(s_f^u)\). Step 8 derives horizontal coordinate resizing function \(\mathcal{H}_i\) for each horizontal length of the lung image while moving \(\mathcal{V}_i(\mathcal{R}_i(s_i^u))\) to match that in fixed \(\mathcal{R}_f(s_f^u)\). Finally, step 9 calculates the coordinate transform map as \(T_{i \rightarrow f}^u(-) = \mathcal{R}_f^{-1}(\mathcal{H}_i(\mathcal{V}_i(\mathcal{R}_i(-))))\). This includes returning the registered image \(\mathcal{H}_i(\mathcal{V}_i(\mathcal{R}_i(s_i^u)))) \text{ to the original axis of rotation.}

The proposed data augmentation algorithms, \(\text{BA}_{r \rightarrow l}\) and \(\text{BA}_{l \rightarrow r}\), in Algorithm 5 generate additional data by transforming the right \((x_{r \rightarrow f}^u, y_{r \rightarrow f}^u)\) and left \((x_{l \rightarrow f}^u, y_{l \rightarrow f}^u)\) lung images into left \((x_{l \rightarrow f}^u, y_{l \rightarrow f}^u)\) and right \((x_{r \rightarrow f}^u, y_{r \rightarrow f}^u)\) lung images, respectively. Because the right lung image has a horizontally narrower lung region owing to the presence of the heart, after flipping the left image to the right (steps 1 and 2 in \(\text{BA}_{r \rightarrow l}\)), we partially remove the inner region of the flipped image considering a synthetic heart region to fit the original right lung, as shown in step 3 of \(\text{BA}_{r \rightarrow l}\).
Algorithm 5 BA

\[
\hat{x}_{l \rightarrow f}^i \leftarrow \text{BA}_{r \rightarrow t}(x_{r \rightarrow f}^i, s_f^j) :
\]

**Input:** \((x_{l \rightarrow f}^i, s_f^j)\) for some \(i \in \{1 : n\}\)

1: \(h_{l \rightarrow f}^i \leftarrow \text{flip} \; R_f(x_{l \rightarrow f}^i)\) horizontally
2: \(h_{l \rightarrow f}^i \leftarrow \text{resize vertically} \; h_{l \rightarrow f}^i\) for its longest vertical line to match that of \(R_f(s_f^j)\)
3: \(h_{l \rightarrow f}^i \leftarrow \text{resize the horizontal length of} \; h_{l \rightarrow f}^i\) to match that of \(R_f(s_f^j)\) at each \(y\)-axis coordinate
4: \(R_f^{-1}() \leftarrow \text{obtain inverse map of} \; R_f()\) s.t. \(R_f^{-1}(R_f(s_f^j)) = s_f^j\)

**Output:** \(\hat{x}_{l \rightarrow f}^i = R_f^{-1}(h_{l \rightarrow f}^i)\)

\[
\hat{x}_{r \rightarrow f}^i \leftarrow \text{BA}_{l \rightarrow r}(x_{l \rightarrow f}^i, s_f^j) :
\]

**Input:** \((x_{l \rightarrow f}^i, s_f^j)\) for some \(i \in \{1 : n\}\)

1: \(h_{r \rightarrow f}^i \leftarrow \text{flip} \; R_f(x_{l \rightarrow f}^i)\) horizontally
2: \(h_{r \rightarrow f}^i \leftarrow \text{resize vertically} \; h_{r \rightarrow f}^i\) for its longest vertical line to match that of \(R_f(s_f^j)\)
3: \(h_{r \rightarrow f}^i \leftarrow \text{remove right-sided/horizontal part of positive regions in} \; h_{r \rightarrow f}^i\) for remaining part to match that of positive regions in \(R_f(s_f^j)\) at each \(y\)-axis coordinate if horizontal length \(l_a\) of positive regions in \(h_{r \rightarrow f}^i\) is larger than \(l_b\) of positive regions in \(R_f(s_f^j)\) (i.e., \(l_a \geq l_b\)). Otherwise, resize it for its length to match \(l_b\)
4: \(R_f^{-1}() \leftarrow \text{obtain inverse map of} \; R_f()\) s.t. \(R_f^{-1}(R_f(s_f^j)) = s_f^r\)

**Output:** \(\hat{x}_{r \rightarrow f}^i = R_f^{-1}(h_{r \rightarrow f}^i)\)

### B Experimental Setup

In all the experiments, we adjusted the image size to \(256 \times 256\) pixels, set the minibatch size to 24 and the number of epochs to 150, and used the Adam optimizer with an initial learning rate of \(4 \cdot 10^{-5}\). To optimize performance, the learning rate was linearly decreased until reaching 0 at the last epoch. We collected CXR unpaired training data corresponding to the input and output of the model to train the GAN-IT model and provided the CXR image of a normal patient by receiving an abnormal CXR image with a specific disease (e.g., tuberculosis [32] and consolidation [33]) as an input. We randomly extracted 600 and 758 CXR images from normal patients for training and testing, respectively, from a publicly available dataset [32]. We randomly selected 600 and 150 CXR images from tuberculosis patients for training and testing, respectively. Furthermore, we randomly selected 600 and 150 CXR images from patients with consolidation for training and testing, respectively, from another publicly available dataset [33]. The dataset in [33] consists of 3578 images of NIH Chest-14 and 13 lung diseases. Of the images, we extracted 750 (600 and 150 for training and testing, respectively) for the diseases with the largest number of data consolidations.
C Visualization Results

Figure 8: Performance comparison between registration techniques for consolidation case. The registered/moved CXR images were obtained from the proposed DL-PR/DLF-PR and baselines A/B. Our registration approach has fewer or no artifacts.
Figure 9: Performance comparison between registration techniques for tuberculosis case. The registered/moved CXR images were obtained from the proposed DL-PR/DLF-PR and baselines A/B. Our registration approach has fewer or no artifacts.
Figure 10: Performance comparison between registration techniques for normal case. The registered/moved CXR images were obtained from the proposed DL-PR/DLF-PR and baselines A/B. Our registration approach has fewer or no artifacts.
Figure 11: Performance comparison of AL-CXR in terms of AUC with varying threshold $\tau = (20, 30, 40)$ (from left to right). Proposed method compared with CUT baseline for (a) tuberculosis and (b) consolidation cases. Proposed method compared with CycleGAN baseline for (c) tuberculosis and (d) consolidation cases.
Figure 12: Examples of lung masks predicted by the segmentation network for (a) normal, (b) tuberculosis, and (c) consolidation cases.
Figure 13: Comparison between anomaly localization maps $v_t$ obtained from proposed method and baseline for (a) tuberculosis and (b) consolidation cases. All were commonly used based on CycleGAN.
Figure 14: Comparison between anomaly localization maps $v_t$ obtained from proposed method and baseline for normal patients. All were commonly used based on (a) CUT or (b) CycleGAN.
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