Unsupervised Domain Adaptation for Low-Dose Computed Tomography Denoising

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ABSTRACT Deep neural networks have shown great improvements in low-dose computed tomography (CT) denoising. Early deep learning-based low-dose CT denoising algorithms were primarily based on supervised learning. However, supervised learning requires a large number of training samples, which is impractical in real-world scenarios. To address this problem, we propose a novel unsupervised domain adaptation approach for low-dose CT denoising. This proposed framework adapts the network pretrained with paired low- and normal-dose phantom images (source domain) to denoise unlabeled low-dose human CT images (target domain). Our framework modifies the action of the domain classifier, enabling the denoising network to be adapted to the target domain. Furthermore, we introduce a new backpropagation method, which we call domain-independent weighted backpropagation. By combining these techniques, we demonstrate that the denoising network can be properly trained without using clinical clean CT images. The experimental results showed that our method exhibited better performance in terms of both objective and perceptual image qualities when compared with current unsupervised denoising algorithms. Our proposed domain adaptation represents a first-use case in the context of CT denoising problems, with the possibility of extension to other image restoration tasks.

INDEX TERMS Low-dose computed tomography (LDCT) denoising, low-dose CT, deep learning, domain adaptation, unsupervised learning.

I. INTRODUCTION X-ray images of the internal organs and other structures of the body, and it is an essential tool for medical diagnosis. However, patient radiation exposure is a major concern when using CT images [1]; thus, low-dose computed tomography (LDCT) is more widely adopted. However, as a counterpart of lowering the dose, it leads to increased noise in the reconstructed CT images, which then hinders an accurate medical diagnosis. This issue specifically motivated LDCT denoising to reduce the noise in LDCT images, and recently, deep learning-based LDCT denoising methods have shown great success in terms of their performance compared to traditional machine learning techniques [2], [3], [4], [5].

Meanwhile, LDCT denoising with convolutional neural networks (CNNs) has shown great performance success, with current methods relying on large amounts of labeled training data to achieve this. However, the costs associated with making huge volumes of labeled data still remain high especially in the medical domain. Thus, many supervised CNN LDCT algorithms have used, for example, a Mayo Clinic dataset [6] or a low-dose CT image and projection...
dataset [7]. In these datasets, quarter-dose CT is obtained via simulation from normal-dose CT using the specific parameters of vendors (i.e., Siemens Healthcare and GE Healthcare). However, because the noise properties of vendors are not normally provided, it is usually not feasible to obtain pairs of normal- and low-dose CT images from various scanners. Moreover, since only a specific dose level (e.g., quarter-dose) is simulated, a network with several dose levels cannot be trained. Even if we solve the financial issue associated with creating more datasets, creating good datasets is not an easy task: First, the specific parameters of the vendors and raw projection data are not always accessible. Second, it takes a substantial amount of time to acquire several dose levels of CT, thus increasing patients’ radiation exposure. Furthermore, even though we obtain CT with pairs of normal- and low-dose CT images from patients, involuntary patient motion can lead to imperfect alignment between the two CT images.

To overcome these dataset limitations, unsupervised learning methods have been proposed. Some studies have used a physics-based CT noise model to simulate additional paired datasets from a noisy CT image [8], [9], while other solutions have included using CycleGAN [10] as a base method to transfer noisy CT to clean CT images using unpaired normal- and low-dose CT images [11], [12], [13]. All these methods have demonstrated excellent performance; however, they still have limitations. If a physics-based CT noise model is inaccurate when applied to make a new simulated paired dataset, the methods in Kim et al. [8] and Yuan et al. [9] cannot train the networks properly. Additionally, Kang et al. [11] specifically applied their method to CT angiography, which is a sequence of CT images; thus, it cannot be used for normal CT images. Tang et al. [12] adopted BM3D [14] to be set as a prior image; thus, the overall performance is determined by the BM3D algorithm. In the study of Gu and Ye [13], AdaIn-CycleGAN was only applied to high-frequency components, with noise in the low-frequency components ignored.

Another way to overcome the challenge of obtaining a paired normal- and low-dose dataset is unsupervised domain adaptation: Models are trained with labeled data in one source domain and facilitate the adaptation of the acquired knowledge/model to another similar—yet different—target domain. Domain adaptation overcomes the problem of domain shift, which is defined as a difference in the distribution of the source and target samples. The most typically studied form of dataset shift is covariate shift [15]. If \( p_s(x), p_t(x) \) denote the source and target domain distribution, and \( x_s, x_t \), \( y \) denote the input in source, target domain and the output, respectively, the covariate shift case is \( p_t(y|X_t) \neq p_s(y|X_s) \), but \( p_t(x_t) = p_s(x_s) \). Many applications in computer vision, such as classification, detection, and segmentation, encounter this covariate shift problem. In this case, the goal of the domain adaptation is then often expressed as finding a transformation, \( T \), such that \( p_t(T(x_t)) = p_s(T(x_s)) \) or \( p_t(T(x_t)) = p_t(x_t) \). These scenarios are depicted in Fig. 1.

However, these strategies, which share the same output space as a discrete number of classes, cannot be directly applied to an image enhancement problem like denoising. This is because the distributions of clean CT images in the source and target domain also differ depending on the domain, which means \( p_t(y|X_t) \neq p_s(y|X_s) \). The domain shift still exists in clean CT images in both domains, thus, the same transformation as observed in the above scenarios cannot cover some paths to be trained to recover clean CT images in target domain. Thus, domain adaptation for LDCT should be developed differently from that in the covariate shift case. We show this scenario in Fig. 2.

In this paper, we propose a novel unsupervised domain adaptation for LDCT denoising. First, we trained a denoiser with noisy and clean phantom CT images from the source domain and also trained a domain classifier with noisy phantom CT (source domain) and real CT images (target domain). A well-trained domain classifier can provide two benefits when it trains a denoiser for the target domain: 1) it can guide the pretrained denoiser for CT images in the source domain so that it adapts to produce clean CT images with the distribution of the target domain, and 2) it can provide weights based on domain-irrelevant pixel-wise loss that improves the denoising performance of the target domain regardless of its original distribution.

The action of the domain classifier has the same goal as the discriminator in the adversarial networks [16] in terms of optimizing the denoiser or generator in the target domain. However, the domain classifier acts as a smarter guide than a discriminator. The domain classifier not only adapts the denoiser output to the target domain, but also enables domain-independently leveraging the pixel-wise loss of the source domain to improve the denoising performance. We could get information about which pixels do not belong strongly to the source domain by obtaining the saliency map of the domain classifier with respect to each input. The pixel-wise loss in the source domain can be re-weighted pixel-by-pixel using the saliency map, allowing the use of rich source domain information to learn the denoising task.
regardless of the source distribution mapping. We call this domain-independent weighted backpropagation.

The main contributions of this paper are as follows:

- We propose an unsupervised domain adaptation suitable for LDCT denoising for the first time, which differs from conventional domain adaptation where the output space is shared. We demonstrate the possibility of using a domain adaption method for LDCT denoising, and the proposed domain adaptation method can extend to full image restoration research in which domain adaptation methods are rarely used.
- We propose a novel strategy for solving domain adaptation in a denoising problem. We specifically suggest domain-independent weighted backpropagation, guided by a domain classifier, which allows the denoiser to leverage rich source domain information without learning the source distribution mapping.
- We conduct rigorous and extensive experiments on real datasets (in-vivo and phantom data) to demonstrate the proposed network performance. The extensive experimental results reveal that the proposed methods successfully solve the domain shift in the case of a denoising problem. Moreover, we prove that our method improves the denoising performance when compared to existing state-of-the-art self-learning algorithms.

A. RELATED WORK

1) LOW-DOSE CT DENOISING

With the emergence of deep learning technologies, convolutional neural networks (CNNs) have demonstrated a great advancement in computer vision research [17] and are specifically applied in medical imaging fields. This trend continued in CT imaging and research on LDCT denoising with CNNs was also developed. In the early stages, [2], [3], [4], [5], which optimized the pixel-level loss, have demonstrated excellent performance compared to the above-mentioned traditional machine learning algorithms. However, the output images from these algorithms have been blurred, with the edges or detailed textures lost. To solve these problems, perceptual loss [18] and the generative adversarial network (GAN) [16] were adopted to elevate the perceptual quality [19], [20], [21], [22], [23], [24], [25], [26].

Recently, unsupervised learning methods became a main topic in LDCT denoising, and it requires only noisy CT images, not a pair of normal- and low-dose CT images. There are several methods for natural image denoising, including Noise2Void [27], Neighbor2Neighbor [28], Noisier2Noise [29], NoisyAsClean [30], Noise2Self [31], are developed, but these methods cannot be applied directly to LDCT denoising due to the inherent noise texture of CT, which is very different from that of the natural image. Specifically, these methods have been unable to recover anatomical details and have led to blurred effects in edges. Thus, in LDCT denoising, unsupervised learning has been researched on its own way. For instance, Kim et al. [8] and Yuan et al. [9] combined physics-based CT noise model with Noisier2Noise [29] and Noise2Noise [32], respectively.

CycleGAN [10] with additional adjustments was applied to LDCT denoising [11], [12], [13], [33].

2) UNSUPERVISED DOMAIN ADAPTATION

Domain adaptation was proposed to handle the lack of training data issue in supervised learning. A common assumption behind machine learning or deep learning algorithms is that the training set and test set have identical data distributions. However, in real-world applications, this assumption does not always hold, with a domain shift existing between the labeled source domain and unlabeled target domain [34], [35]. Domain adaptation is a way to reduce this domain shift problem.

A type of traditional domain adaptation is metric learning [36], [37], [38]. They formulate metric distances and optimized them to minimize the effect of domain-induced changes in the feature distribution. In unsupervised learning, subspace-based methods [39], [40], [41] learn a common subspace that is shared by the two domains. Another popular unsupervised domain adaptation approach consists of aligning the distributions. The maximum mean discrepancy (MMD) [42] and sample reweighting [43] are examples of the distribution match. When the original distributions are very different from target domain distributions, transformation learning can be a more successful method for distribution matching. Transfer component analysis [44], domain invariant projection [45], correlation alignment [46], and statistically invariant embedding [47] are types of transformation learning.

With the success of deep learning, the concepts of machine learning algorithms have been translated to deep neural networks [46], [48], [49]. Recently, domain adversarial networks [50], [51], [52] have been introduced. In adversarial domain adaptation, a domain discriminator is trained to distinguish whether a feature is from the source domain or target domain. The goal of the training is to make the feature be considered domain-invariant so that the learned feature can confuse the domain discriminator. Our proposed method is similar to adversarial domain adaptation, as we use a domain discriminator; however, it is also different because the trained domain discriminator acts as a smart guide inducing the denoiser to produce only clean outputs, which have distribution in the target domain, in comparison to the goal of adversarial networks being to fool the discriminator so that it cannot discriminate the learned feature.

II. METHOD

A. OVERALL ARCHITECTURE

In this paper, we propose a new domain adaptation strategy that adapts the denoiser trained with the paired CT images in the source domain to the target domain, where the CT images have a different distribution than the source domain and clean CT images do not exist. There are two steps involved in training the denoiser to generate clean CT images with the distribution of the target domain: pretraining and domain adaptation.
FIGURE 3. Overall architecture of the proposed method. The denoiser and the domain classifier are pretrained in step 1. In step 2, the domain classifier conveys $L_{da}$ to the denoiser, which adapts the denoiser output with the distribution of the source domain to the target domain. $L_{sidp}$ is calculated with the denoised output from the denoiser ($\hat{y}_s$), a clean image in the source domain ($y_s$), and two source-independent masks of $\hat{y}_s$ and $y_s$. This is used for domain-independent weighted backpropagation. An augmented noisier image ($x_t + n_p$) and noisy image ($x_t$) from the target domain are used to calculate $L_{aug}$.

In the pretraining step, we trained the denoiser with noisy and clean CT images from the source domain and trained the domain classifier with noisy CT images from the source and target domain. Then, in the domain adaptation step, we adapted the denoiser with the help of the domain classifier. Domain adaptation loss and domain-independent weighted backpropagation are introduced with the well-trained domain classifier.

The domain adaptation loss is defined as the mean squared error (MSE) loss of the domain classifier between the predicted domain of the outputs of the denoiser and the label of the target domain (set to 1). This adapts the denoiser to generate clean CT images based on the distribution of the target domain.

The problem here is that training the denoiser to optimize the pixel-wise loss of the source domain dataset counteracts the role of the domain classifier in adapting the denoiser to generate clean CT images in the target domain. As the denoiser output moves into the target domain, the pixel-wise loss in the source domain increases because the clean ground truth CT images remain in the source domain. Thus, we need a strategy to facilitate the denoiser to weaken the learning of domain-specific characteristics while preserving the denoising performance of domain-independent characteristics.

This was achieved by introducing domain-independent weighted backpropagation. Because the saliency map [53] from the domain classifier indicates that the importance of each pixel when the domain classifier distinguishes the source domain or target domain, it can show which pixels are strongly affected by the source domain or not. Thus, before applying pixel-wise loss between predicted clean output CT image and clean ground truth CT image from source domain, we re-weighted value of pixels in both images with the modified saliency map to reduce source domain specific characteristics. Then, we backpropagate the model and update the denoiser. We call this process as a domain-independent weighted backpropagation.

Finally, following an accurate physics-based noise generation pipeline [54], we numerically generated noisier CT images in the target domain by inserting the realistically simulated noise to the original low-dose CT images. In this way, we generated pairs of the synthesized noisier input and the original low-dose output for training based on the self-supervised denoising framework, Noisier2Noise [29]. By introducing the synthetic noisier CT images in the target domain, we can further enhance the performance of the denoiser. Furthermore, the phantom CT images in the source domain lack detail and texture. In contrast, because the noisy images of Mayo clinic in the target domain have more complicated patterns than the phantom CT images, the augmented noisier CT images inherently have richer textures. Thus, a pair of augmented noisier and noisy CT images can supplement the weakness when we train the denoiser network only with CT images from the source domain.

Commonly used notations in the paper are summarized in Table 1 for ease of reading.

B. PRETRAINING THE DENOISER AND DOMAIN CLASSIFIER

1) DENOISER
The denoiser is denoted as $D(\cdot)$. With a pair of noisy and clean CT images from the source domain, we trained the denoiser with the following loss function:

$$L = \frac{1}{N_s} \sum_{i=1}^{N_s} ||D(x_s^{(i)}) - y_s^{(i)}||$$  (1)

where $x_s^{(i)}$ and $y_s^{(i)}$ are the pair of the noisy and clean CT images with the distribution $p_s$ in the source domain, and $N_s$ is the total number of paired samples of the source domain.
TABLE 1. Summary of the notation.

| Notation | Meaning |
|----------|---------|
| \(p_s(x)\) | Distribution over \(x\) in the source domain |
| \(p_t(x)\) | Distribution over \(x\) in the target domain |
| \(D(\cdot)\) | Denoiser |
| \(DC(\cdot)\) | Domain classifier |
| \(M\) | Domain-independent mask |
| \(n_p\) | Poisson noise |
| \(x_s\) | Noisy CT images in the source domain |
| \(x_t\) | Noisy CT images in the target domain |
| \(x_s^+\) | Noiser CT images, \(x_s + \text{Poisson noise}\) |
| \(y_s\) | Clean CT images in the source domain |
| \(y_t\) | Clean CT images in the target domain |
| \(d_s\) | Source domain label, 0 |
| \(d_t\) | Target domain label, 1 |
| \(d_i\) | Output of the denoiser with \(x_s, D(x_s)\) |
| \(d_i^+\) | Output of the denoiser with \(x_s^+, D(x_s^+)\) |
| \(\hat{d}_i\) | Output of the denoiser with \(x_t, D(x_t)\) |

2) DOMAIN CLASSIFIER

We trained a domain classifier to distinguish CT images in the source domain from CT images in the target domain. To accurately train the domain classifier, noisy and clean CT images from both the source and target domains are required. However, in unsupervised domain adaptation, clean CT images in the target domain are not available. Thus, we trained only with noisy CT images from the source and target domains, and this setup was well-suited for the domain classifier training. When we analyze the histogram distribution from both domains, even if the clean and noisy CT images from one domain differ in terms of noise level, they show a similar distribution pattern when compared to those from another domain. An example of this distribution pattern is depicted in Fig. 4. From the experiences, we can infer that the domain classifier accuracy was sufficiently high to discriminate between the domains with both noisy and clean CT images. The detailed performance results are further explained in section III-C.

At the training time, a large set of training data, which consists of randomly selected noisy images, \(x_1, x_2, \ldots, x_N\) from both the source and target domains with the marginal distributions \(p_s(x)\) and \(p_t(x)\) are provided. The MSE loss is used for training the domain classifier [55]. \(d\) denotes the binary variable indicating the domain label for the \(i\)-th example. \(d_i = d_s\) when \(x_i\) comes from the source distribution, \(x_i \sim p_s(x)\), and \(d_i = d_t\) when \(x_i\) comes from the target distribution, \(x_i \sim p_t(x)\). \(d_s\) and \(d_t\) denote 0 and 1, respectively. We trained the domain classifier with the following loss function:

\[
L_{DC} = \frac{1}{N} \sum_{i=1}^{N} (d_i - DC(x_i))^2
\]  

(2)

C. TRAINING THE DENOISER BY DOMAIN ADAPTATION

Once we trained the domain classifier, we used it for the pretrained denoiser to produce clean CT images with the distribution, \(p_t\), in the target domain. The well-trained domain classifier has two capabilities: 1) it predicts from which domain the CT images came, and 2) it can identify which pixels strongly affect the domain-specific characteristics by constructing a saliency map. These two capabilities are deployed for the domain adaptation loss and domain-independent weighted backpropagation.

1) DOMAIN ADAPTATION LOSS

The goal of the domain adaptation loss is to adapt the denoiser to predict only the clean CT images in the target domain. The problem with training the denoiser with noisy and clean CT images from the source domain is that the denoiser cannot generate the clean CT images of the target domain. Fig. 5 shows that the denoiser, which is trained with a source
domain dataset, failing to generate clean CT images of the target domain. The output image loses the characteristics of the target domain, such as a detailed texture, gaining instead a simple texture characteristic of source domain images. It signifies that the denoised output image of the target domain is shifted to the source domain.

To adapt the denoiser to the target domain, all output from the denoiser would be in the target domain even though the denoiser is trained on a pair of source domain. We accomplished it by introducing domain adaptation loss ($L_{da}$) so that the outputs of the source and target domain could be generated as those of the target domain by the domain classifier.

To learn the denoiser’s output distribution to be in the target domain over data $x$ from both the source and target domain, $L_{da}$ is formulated as follows:

$$L_{da} = \mathbb{E}_{x \sim p(x)}(d_t - DC(D(x))^2 + \mathbb{E}_{x \sim p(x)}(d_t - DC(D(x))^2)$$

our goal is to minimize $L_{da}$ and Equation (3) can be reformulated as follows:

$$L_{da} = \int_p \rho_t(x)(d_t - DC(D(x))^2 dx$$

$$+ \int_p \rho_t(x)(d_t - DC(D(x))^2 dx$$

$$= \int_p \rho_t(x) + \rho_t(x)][d_t - DC(D(x))^2 dx$$

By finding the solution to the derivative of $L_{da}$ with respect to $x$ and setting it as 0, the optimal value of $L_{da}$ in Equation (4) can be obtained:

$$DC(D(x)) = d_t$$

Since $DC(\cdot)$ is fixed, $D(x)$ will be optimized to give the output the distribution of the target domain. Equation (3) can be formulated with data samples as follows:

$$L_{da} = \frac{1}{N_s} \sum_{i=1}^{N_s} (d_t - DC(D(x_i))^2 + \frac{1}{N_t} \sum_{i=1}^{N_t} (d_t - DC(D(x_i))^2$$

Equation (6) was used when training the denoiser.

2) DOMAINE-INDEPENDENT WEIGHTED BACKPROPAGATION

The denoising task can be learned by the denoiser via supervised learning with a pair of noisy and clean CT images in the source domain. However, supervised learning in the source domain heavily influences the denoiser to produce output distributed only in the source domain. It disrupts the role of the domain adaptation loss, which guides the denoiser to learn to map the distributions of both the source and target domain to the target domain. Thus, when we train the denoiser with the pair of noisy and clean samples in the source domain, we need to exclude the effect of the distribution mapping from the source to the source domain.

The source domain mapping can be excluded by leveraging the saliency map of the pretrained domain classifier. The saliency map shows the weights of each pixel that is strongly involved in the domain. We obtained the saliency visualization using a method of Simonyan et al. [53]. An image-specific class saliency map of the domain classifier with respect to the denoised clean image, $\hat{y}_s$, can be obtained in the direction of maximizing the loss of the domain classifier ($L_{max}$). $L_{max}$ can be maximized by specifying the domain label as the opposite domain label, such as 1 for the source domain.

$$L_{max} = \frac{1}{N_s} \sum_{i=1}^{N_s} (DC(d_t - \hat{y}_s(i))^2$$

The saliency map of image I ($S_I$) can be formulated as the derivative of $L_{max}$ with respect to image I, with each given image $I_0$ as follows:

$$S_{I_0} = \frac{\partial L_{max}}{\partial I} \bigg|_{I_0}$$

By transforming the saliency map ($S_{I_0}$) with a negative exponential term, we can reverse the weight of each pixel.

$$M_{I_0} = e^{-|S_{I_0}|}$$

Because high values in this transformed map indicate that it is highly uncorrelated with the domain-specific characteristics, each pixel implies the extent of the source domain independency. Thus, this mask can be called a source domain-independent mask. An example of a saliency map and its corresponding domain-independent mask of the source domain image are shown in Fig. 6.

Multiplying the source domain-independent mask to the pair of clean and denoised image from the denoiser in the source domain, we can define a new loss function: source domain-independent loss.

$$L_{sidp} = \frac{1}{N_s} \sum_{i=1}^{N_s} ||M_{x_s(i)}\hat{y}_s(i) - M_{y_s(i)}y_s(i)||$$

Then, the domain-independent weighted backpropagation was performed by updating gradient with the source domain-independent loss. With domain-independent weighted backpropagation, we can train the denoiser to learn denoising tasks with the noisy and clean data in the source domain without mapping distributions from the source to the source domain.
3) AUGMENTED NOISIER CT IMAGES IN TARGET DOMAIN
To train the denoiser more precisely without clean images in the target domain, we generated synthetic noisier CT images in the target domain. Given the standard deviation, $\sigma_n$, of the noisy target domain images, $x^t$, the augmented noisier CT images, $x^t_i$, were synthesized by adding additional Poisson noise, $n_p$. The $n_p$ value was determined to be $1.5 \times \sigma_n$, corresponding to 20% dose of clinical routine protocol through denoising performance analysis according to the combination of various noise models and noise levels (see Table 3). With the augmented noisier and noisy pair, $(x^+_t, x^t_i)$, we defined the augmented loss ($L_{aug}$) as follows:

$$L_{aug} = \frac{1}{N_t} \sum_{i=1}^{N_t} ||D(x^+_t) - x^t_i||$$  \hspace{1cm} (11)

4) OVERALL LOSS FUNCTIONS FOR THE DENOISER
The overall loss function is combination of the three losses: domain adaptation loss ($L_{da}$), source domain-independent loss ($L_{sidp}$), and augmented loss ($L_{aug}$). $L_{da}$ aims to direct both the denoised source image and the denoised target image to the target domain. In $L_{sidp}$, a domain-independent mask, $M_f$, is generated for each source domain image by reducing the domain dependency through the saliency map of DC. $L_{aug}$ is the $L1$ loss between the denoiser output of the augmented noisier target created by adding the Poisson noise and the noisy target.

$$L = \alpha_{da}L_{da} + \alpha_{sidp}L_{sidp} + L_{aug}$$  \hspace{1cm} (12)

$\alpha_{da}$ and $\alpha_{sidp}$ are the weight of $L_{da}$ and $L_{sidp}$, respectively. $\alpha_{da}$ was set as 0.1, and $\alpha_{sidp}$ was decreased from 1 by a ratio of 0.1 for every 10,000th iteration.

The overall training procedure is presented in Algorithm 1.

### III. EXPERIMENTAL RESULTS
#### A. IMPLEMENTATION DETAILS
We used EDSR [56] as the backbone of the denoiser, which consists of 16 residual blocks and one convolution layer each on top and bottom with a global skip connection. The residual blocks contained Conv2d-BN-ReLU-Conv2d-BN layers with skip connections. We eliminated the up-sample layer that enables the super-resolution task and set 96 as the feature dimension. The size of kernel, stride and padding of residual block are set to 3, 1, and 1, respectively. We used discriminator [10] as the backbone of the domain classifier. It contained four convolution blocks consisting of Conv2d-BN-LeakyReLU layers with a negative slope of 0.2 and one convolution layer each on top and bottom. The size of kernel, stride and padding of convolution block are set to 4, 2, and 1, respectively. Each feature dimension of the convolution block was set to 64, 128, 256, and 256. The domain classifier was trained in Step 1 and frozen in Step 2.

In each training batch, a random patch with a size of $80 \times 80$ was extracted as the input for the domain classifier and denoiser. We used the Adam solver [57]. The dataset has been preprocessed to clip between $[-1000, 400]$ Hounsfield Unit (HU) and normalized to $[0, 1]$. The values of PSNR and SSIM in the experimental results were measured with CT images in the display window $[-160,240]$ HU, which has 400 as WW and 40 as WL.

#### B. IN-VIVO AND PHANTOM DATA ACQUISITION
For the source domain data, an anthropomorphic phantom of the chest and pelvis was acquired with a CT scanner, the GE Discovery RT. The exposure levels of the high-dose dataset were 70.72 mAs and 88.4 mAs for the chest and pelvis, respectively. The low-dose dataset exposure levels were 13.26 mAs and 17.68 mAs for the chest and pelvis, respectively.

For the target domain data, we used the publicly available dataset of 2016 NIH-AAPM-Mayo Clinic Low Dose CT Grand Challenge [6]. The fully anonymized dataset was obtained after approval by the institutional review board of the Mayo Clinic. The Mayo dataset contains de-identified CT images of ten patients, and we used only 1 mm-thicknesses in the dataset. The full-dose exposure level was 200 mAs. The low-dose dataset was acquired by inserting Poisson noise into the projection data, which corresponds to 25% of the full dose. We randomly divided the training and validation

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**Algorithm 1** An Algorithm of Overall Training Process.

**Step 1** for Pretraining Denoiser ($D$) and Domain Classifier ($DC$). **Step 2** for Domain Adaptation of $D$ to the Target Domain

**[Step 1]**

Initialize: $D$, $DC$.

**for number of training iteration do**
- Sample minibatch of $K$ sample $(x_s^{(1)}, y_s^{(1)}), \ldots, (x_s^{(K)}, y_s^{(K)})$ from the source domain.
- Sample minibatch of $K$ sample $(x_t^{(1)}, \ldots, (x_t^{(K)})$ from the target domain.
- $L_D = 1/K \sum_{i=1}^{K} ||D(x_s^{(i)}) - y_s^{(i)}||$.
- Minimize $L_D$ w.r.t $D$.
- $L_{DC} = 1/K \sum_{i=1}^{K} DC(x_t^{(i)}) - d_s^2 + 1/K \sum_{i=1}^{K} DC(x_t^{(i)}) - d_t^2$.
- Minimize $L_{DC}$ w.r.t $DC$.

end for

**[Step 2]**

Initialize: $\alpha_{da} = 0.1$, $\alpha_{sidp} = 1$.

, set $D$, $DC$ with pretrained weight from Step 1 and freeze $DC$.

**for number of training iteration do**
- Sample minibatch of $K$ sample $(x_s^{(1)}, y_s^{(1)}), \ldots, (x_s^{(K)}, y_s^{(K)})$ from the source domain.
- Sample minibatch of $K$ sample $(x_t^{(1)}, \ldots, (x_t^{(K)})$ from the target domain.
- Generate Poisson noise $n_p$.
- $\alpha_{sidp} = (0.1)^{floor(iteration/10,000)}$.
- $\alpha_{sidp} = D(x_s^{(i)}), \hat{y}_t^{(i)} = D(x_t^{(i)}), L_{da} = 1/K \sum_{i=1}^{K} ||\hat{y}_t^{(i)} - y_s^{(i)}||$.
- $L_{sidp} = 1/K \sum_{i=1}^{K} ||\hat{y}_t^{(i)} - y_s^{(i)}||$.
- Calculate overall loss: $L = \alpha_{da}L_{da} + \alpha_{sidp}L_{sidp} + L_{aug}$.
- Minimize $L$ w.r.t $D$.

end for
of the CT slices of seven patients with a ratio of 0.95:0.05 (training:validation). The CT slices of the other three patients were used for testing.

C. PERFORMANCE OF DOMAIN CLASSIFIER WITHOUT CLEAN LABELS
We evaluated whether the domain classifier could properly identify which CT images belong to the source versus the target domain. Not only we tested if the domain classifier can distinguish noisy CT images in the source and the target domain, we also investigated if the domain classifier could discriminate clean CT images in the source and target domain. To evaluate the domain classifier, we averaged its outputs for each input: noisy \( (x_s) \) and clean \( (y_s) \) CT images in the source domain, and noisy and clean CT images in the target domain \( (x_t \text{ and } y_t) \). The results of the domain classifier’s performance evaluation are summarized in Table 2. As expected, the average predicted value of the domain classifier was close to \( d_s, 0 \), with the noisy \( (x_s) \) and clean \( (y_s) \) CT images in the source domain and close to \( d_t, 1 \), with
these images in the target domain \((x_t, y_t)\). Thus, we could confidently use the domain classifier, which was pretrained with only noisy CT images in the source and target domain, because it can discriminate CT images without using clean labels in terms of whether they are from the source or the target.

D. DOMAIN GAP ANALYSIS

We conducted an experiment to determine how the output of the denoiser is shifted from the source to the target domain when our proposed method is applied. We tested the domain shift in the output of three denoisers: \(D_s\), \(D_t\), and \(D_{tnoadp}\). \(D_s\) is the denoiser trained with only noisy and clean CT images in the source domain via supervised learning. \(D_t\) is the denoiser of our proposed method that is adapted from the source domain to the target domain. \(D_t\) is trained with the domain adaptation loss, domain-independent weighted backpropagation (source domain-independent loss), and augmented loss. Among these losses, the domain adaptation loss plays a major role in shifting the domain of the denoiser output to the target domain. So, we additionally trained a target domain adapted denoiser, \(D_{tnoadp}\), without domain adaptation loss to compare the extent of the domain shift.

In experiment (1) in Fig. 8, the domain gap between the denoised source images \(\hat{y}_s\) and the target domain images \((x_t, y_t)\) was examined quantitatively. Since \(D_s\) was trained to generate clean denoised images in the source domain, the denoised image of \(D_s\) was far from the target domain image. On the other hand, the output image's domain of \(D_{tnoadp}\) and \(D_t\) moved to the target domain; the distance between the denoised source image and the target domain decreased.

In experiment (2) of Fig. 8, we show the domain gap between the denoised target images \(\hat{y}_t\) and source domain images \((x_s, y_s)\). As \(\hat{y}_t\) of \(D_{tnoadp}\) and \(D_t\) shifted farther away from the source domain compared to the \(\hat{y}_t\) of \(D_s\), the distance between \(\hat{y}_t\) and the source domain gradually increased. Since the \(L_{dis}\) was added in \(D_t\), the domain adaptation to the target domain appeared to be more effective in \(D_t\) than \(D_{tnoadp}\).

According to [58], the style of an image can be expressed as the mean and standard deviation of the features. In order to measure the domain distance \(d_{domain}\), the distance between two different domain images, \(x \sim p_x, y \sim p_y\), can be measured as follows:

\[
d_{domain} = \sqrt{\left( \frac{E}{x \sim p_x} (\mu_x) - \frac{E}{y \sim p_y} (\mu_y) \right)^2 + \left( \frac{E}{x \sim p_x} (\sigma_x) - \frac{E}{y \sim p_y} (\sigma_y) \right)^2} \quad (13)
\]

For each of the three denoisers, the transition of the domain distance between \(\hat{y}_s\) and the target domain images and between \(\hat{y}_t\) and the source domain images can be measured by Equation (13). Fig. 8 shows that from \(D_s\) to \(D_{tnoadp}\) and \(D_t\), \(\hat{y}_t\) is gradually getting closer to the target domain as the domain adaptation continues. Also, it can be confirmed that \(\hat{y}_s\) gradually moves away from the source domain.

E. OPTIMAL VALUE OF AUGMENTED NOISER LEVEL

We found the optimal noise level of the augmented noisier CT images in the target domain by comparing the performance of the denoiser with various noise levels. The performance was measured with PSNR and SSIM without considering the perceptual quality with the predicted clean CT images from the denoiser and the ground truth clean CT images in the target domain. The noise level of the Poisson noise was adjusted based on the ratio of the standard deviation of the Poisson noise \(\sigma_n\) to the standard deviation of the estimated noise in the target domain \(\sigma_{n_t}\). The ratio \(\sigma_n / \sigma_{n_t}\) was changed from 0.5 to 2.5 by a factor of 0.5 and the results are summarized in Table 3. When \(\sigma_{n_t} = 1.5 \times \sigma_n\), the denoiser exhibited the best performance in terms of PSNR and SSIM.

F. DENOISING RESULTS

We present the experimental results of our network and comparisons against various self-supervised and unsupervised networks. Noise2Void [27], Neighbor2Neighbor [28], Noiser2Noise [29], NoisyAsClean [30], BM3D [59], NLM [60] were used for a benchmark study. We optimized current benchmarking models to show the best performance and used U-Net [61] as the network architecture. When we optimized all the comparative algorithms in the benchmark study, we only used the low-dose images of the Mayo.
Clinic dataset with approximately one quarter dose, which was used to represent noisy target domain images ($x_t$). The quantitative performance was measured in terms of PSNR and SSIM, and a visual qualitative comparison was also made using representative images of each algorithm. As shown in Table 4, Noise2Void, Neighbor2Neighbor, Noisier2Noise, and NoisyAsClean exhibited poor results, but NoisyAsClean recorded a relatively good SSIM score. BM3D, NLM, and our network recorded high PSNR, but BM3D and NLM recorded poor SSIM results. In Fig. 7, the output images of Noise2Void, Neighbor2Neighbor, Noisier2Noise, and NoisyAsClean are noisy compared with the normal-dose reference images. The results of BM3D and NLM are clean but oversmoothed. Especially in NLM, most of the microstructure is not visible. NoisyAsClean has better perceptuality compared to the other algorithms, but the noise is not sufficiently removed. Our algorithm reconstructed fine structural details of the images more effectively with a good perceptuality compared with the others and also recorded the highest PSNR and SSIM.

### G. ABLATION STUDY

In this section, we describe an ablation study we performed to show whether the augmented loss ($L_{aug}$), domain adaptation loss ($L_{da}$), and domain-independent weighted backpropagation ($L_{sidp}$) help improve the denoising performance. We first examine the effect of the augmented noisy target dataset in Table 5 (1)~(3). In (1)~(3), the network is trained in one step. In (1), the network is trained in the source domain by minimizing the source domain loss ($L_s$) between the denoised source image ($\hat{y}_s$) and clean source image ($y_s$). Due to the domain shift, the recorded PSNR and SSIM in the target were very low and the contrast of the output image was extremely distorted (Fig. 9 (b)). In (2)~(3), the networks are trained by minimizing $L_{aug}$ or $L_s + L_{aug}$, and the results show that simply adding the target domain’s pixel-wise loss can help the domain adaptation to the target domain compared to (1). However, the noise was not sufficiently removed (Fig. 9 (c)) or the output image was oversmoothed (Fig. 9 (d)).

In (4)~(6), we trained the network on Step 2 using a pretrained model of (1). In (4)~(5), each experiment shows the effects of $L_{da}$, $L_{sidp}$ compared with (3), respectively. If we adopted the domain-independent weighted backpropagation in source dataset, we moved $\checkmark$ from $L_s$ to $L_{sidp}$. In (4), when $L_{da}$ is used to train the model without $L_{sidp}$, the denoised source image ($\hat{y}_s$) gradually moves to the target domain, but the clean source image ($y_s$) remains in the

### Table 4. Quantitative denoising results of representative self-supervised denoising methods using only the same quarter low-dose CT images.

| Models                  | PSNR | SSIM |
|-------------------------|------|------|
| Baseline                | 22.690 | 0.780 |
| Noise2Void [27]         | 23.258 | 0.787 |
| Neighbor2Neighbor [28]  | 24.651 | 0.809 |
| Noisier2Noise [29]      | 25.416 | 0.815 |
| NoisyAsClean [30]       | 25.495 | 0.822 |
| BM3D [59]               | 26.616 | 0.795 |
| NLM [60]                | 26.545 | 0.815 |
| Ours                    | 26.728 | 0.823 |
source domain. It leads improvement limitations regarding the denoising performance due to the increased $L_1$ loss of the source domain. In (5), when we use $L_{sidp}$ to train the model without $L_{da}$, the denoising performance is still not very high in the target domain due to a lack of domain shift toward the target domain. Therefore, the noise still remains in the output images (Fig. 9(e)−(f)). When $L_{da}$ and $L_{sidp}$ are used together to train the model, in (6), even if the distribution of $\tilde{y}_s$ moves away from $y_s$, the loss between the two can be reduced by domain-independent weighted backpropagation; thus, domain adaptation to the target becomes possible. As a result, model trained in the two steps by minimizing $L_{aug} + L_{da} + L_{sidp}$ recorded the best performance in the target domain. Example image of (6) is presented in Fig. 9(g) and shows great denoising performance and perceptuality.

### IV. DISCUSSION AND CONCLUSION

This study has introduced a novel LDCT denoising approach based on unsupervised domain adaptation. This approach effectively transferred knowledge from a labeled source domain (i.e., phantom CT images) to an unlabeled target domain (i.e., real human CT images) with different data distributions. As a result, superior noise reduction performance was derived compared to various existing self-supervised or unsupervised models. This results was achieved due to the newly proposed features, including the domain classifier for image denoising, the domain adaptation loss, and the domain-independent weighted backpropagation.

Although domain adaptation approaches have been developed in the computer vision field in the context of a covariate shift [15] (e.g., classification, detection, and segmentation) by taking full advantage of domain-invariant characteristics, they are not directly applicable to image denoising problems. This is because the distributions of clean images in the source and target domain also differ, and thus, the covariate shift is not a valid assumption in this image restoration problem. Given the results of this study, it was demonstrated that our proposed domain adaptation technique can be successfully applied to LDCT image denoising. The applications of this proposed domain adaptation-based approach are not limited to image denoising, but can be easily extended to other various image restoration/enhancement tasks [62], in which a domain adaptation method has not been commonly used.

For the unsupervised domain adaptation featured in this study, phantom data is used as the source domain data, and real human data obtained at a low dose is utilized as the target data. These experimental settings are ideal for performing LDCT denoising, since it is relatively easy to build abundant labeled source phantom data compared to acquiring labeled target data (i.e., paired low- and full-dose patient images). Moreover, because our setup utilizes phantom data, there is no need for the common concern of unsupervised domain adaptation that accessing the source data makes that data risky for decentralized private data [63]. Recently, unsupervised domain adaptation studies [63], [64] that do not even depend on source label data are being attempted. If these approaches are adopted in the future, more convenient LDCT denoising will be possible.

In conclusion, we have made the first attempt to improve the LDCT image quality through an unsupervised domain adaptation framework. Extensive experimental results show that the proposed methods convincingly solve the domain shift in the LDCT denoising problem. It is also observed that the proposed method qualitatively and quantitatively outperform the existing state-of-the-art self-learning algorithms in noise removal. Moreover, our unsupervised domain adaptation framework is universally applicable to various types of image distortions and many different restoration models, and has great potential for clinical use as there is no need for clean labels.

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(Jaay-Yeon Lee and Wonjin Kim contributed equally to this work.)

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I. Introduction

Domain adaptation is a critical task in medical imaging, particularly in low-dose computed tomography (LDCT) denoising, where the goal is to improve image quality while reducing radiation exposure. This involves transferring knowledge from a high-dose, high-quality domain to a low-dose, low-quality domain, often without paired training data. Various techniques have been proposed to address this challenge, including unsupervised methods that rely on domain-invariant features and supervised methods leveraging paired training data. In this paper, we focus on unsupervised domain adaptation approaches for LDCT denoising.

II. Related Work

A. Deep Learning for CT Denoising

Recent advances in deep learning have enabled the development of powerful models for CT denoising. These models, however, have primarily been trained on high-dose datasets, which may not generalize well to low-dose scenarios.

B. Domain Adaptation in Medical Imaging

Domain adaptation has been explored in medical imaging to reduce the need for expensive, high-dose training data. Techniques include adversarial training, feature synthesis, and joint optimization.

C. Unsupervised Domain Adaptation

Unsupervised domain adaptation methods, such as CycleGAN, have been applied to medical imaging for tasks like multi-modal image registration and segmentation.

III. Unsupervised Domain Adaptation for LDCT Denoising

In this work, we propose an unsupervised domain adaptation approach using the AdalN-based tunable CycleGAN. This method aims to learn domain-invariant representations that can be used to denoise low-dose CT images.

IV. Methodology

A. AdalN-based CycleGAN

The AdalN-based CycleGAN is designed to adapt to different domains without paired data, leveraging perceptual losses and adversarial training.

B. LDCT Denoising Task

The denoising task is formulated as a minimization problem, where the goal is to minimize the discrepancy between high-dose and low-dose images.

V. Experimental Results

The proposed method is evaluated on a public dataset, demonstrating its effectiveness in improving image quality while maintaining diagnostic confidence.

VI. Conclusion

Unsupervised domain adaptation offers a promising approach for LDCT denoising, enabling the use of existing high-quality datasets to enhance image quality in low-dose scenarios. Further research is needed to explore the robustness and generalization of these methods in clinical settings.
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