Unpaired image denoising using a generative adversarial network in X-ray CT

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Abstract

This paper proposes a deep learning-based denoising method for noisy low-dose computerized tomography (CT) images in the absence of paired training data. The proposed method uses a fidelity-embedded generative adversarial network (GAN) to learn a denoising function from unpaired training data of low-dose CT (LDCT) and standard-dose CT (SDCT) images, where the denoising function is the optimal generator in the GAN framework. Given an optimal discriminator in the GAN, the generator is optimized by minimizing a weighted sum of two losses: the Kullback-Leibler divergence between an SDCT data distribution and a generated distribution, and the $\ell_2$ loss between the LDCT image and the corresponding generated images (or denoised image). The experimental results show that the proposed deep-learning method with unpaired datasets performs comparably to a method using paired datasets. Clinical experiment was also performed to show the validity of the proposed method for non-Gaussian noise arising in the low-dose X-ray CT.

Keywords: Computerized tomography, denoising, low-dose, generative adversarial network, unsupervised learning
I. INTRODUCTION

In computed tomography (CT), reducing X-ray radiation dose while maintaining diagnostic image quality is an important ongoing issue, because of growing concerns regarding the risk of radiation induced cancer\textsuperscript{7,17}. Low dose CT (LDCT) is commonly achieved by reducing the X-ray tube current. However, LDCT images obtained from commercial CT scanners in general suffer from the low signal-to-noise ratio (SNR) and the reduced diagnostic reliability. Therefore, numerous efforts have sought to denoise LDCT images, by finding a denoising mapping that converts an LDCT image to the corresponding standard-dose CT (SDCT) image.

Various iterative reconstruction (IR) methods have been proposed to reduce noise in LDCT images while preserving structure. The noise reduction modeling in these methods can employ loss functions in image space or in sinogram space. Some have incorporated prior knowledge into the denoising process through regularization employing such as total variation (TV)\textsuperscript{6,27}, fractional-order TV\textsuperscript{31}, and nonlocal TV\textsuperscript{14}. Markov random fields theory\textsuperscript{12,26} or nonlocal means\textsuperscript{5,15,30} have also been used as prior information. Statistical image reconstruction methods such as the maximum a-posteriori (MAP) approach for data fitting in sinogram space have been used for efficient noise filtering of the sinogram in LDCT\textsuperscript{12,24}.

While these IR methods can significantly improve the quality of reconstructed CT images, they retain some limitations in clinical practice. First, it is challenging to design a prior that conveys the characteristics of LDCT and SDCT images. For example, commonly used priors such as TV and its variants cause over-smoothing effect which causes the loss of fine detail such as small anomalies. Second, IR methods impose high computational costs as they require an iterative solver to find a reasonable approximate solution. Finally, sinogram-based methods use projection data for data fidelity, but it is generally difficult to access projection data from a commercial CT scanner.

Various supervised learning approaches have recently been suggested to reduce noise in LDCT images\textsuperscript{3,4,10}. Paired training data (i.e., LDCT and SDCT images) are not available in clinical practice, because it is in general difficult to obtain both types of images simultaneously from a given patient. Therefore, the learning approaches obtain paired training data by generating simulated LDCT image data from clinical SDCT images. Results with supervised datasets have shown that these approaches can reduce noise and artifacts in
the simulated LDCT images. However, their practical performance depends heavily on the quality of the simulated LDCT image data.

In contrast to previous supervised methods, this paper uses an unpaired learning approach to find the denoising map without using paired datasets. We exploit a method for estimating the MAP in denoising that imposes prior information on SDCT images sampled from a data distribution. Previous studies have reduced the MAP estimation to minimizing cross-entropy of data distribution and the distribution generated by the generative adversarial network (GAN). Given the general difficulty of directly handling cross-entropy, we approximate it to the Kullback-Leibler (KL) divergence, thus allowing to obtain an approximate MAP estimation using the GAN framework. This facilitates training of the network architecture with unpaired datasets. The proposed GAN approach infers the desired data distribution containing image priors from the sampled SDCT images. It is therefore crucial to choose effective training datasets to reflect the appropriate image priors. See Fig. 1. Under an assumption of Gaussian noise, the $\ell_2$ constraint is added to the proposed GAN model. Unlike conventional approaches which treat the entire image, the proposed method is performed in a patch-by-patch manner, which can effectively train the local noise features in the CT images. Numerical simulation and clinical results demonstrate that the proposed method has a great potential to reduce noise in LDCT images for unpaired CT images or even for a complicated noise model.

II. METHOD

Throughout this paper, we denote by $z$ and $x$ LDCT and SDCT images, respectively, both of which are $n \times n$ pixel grayscale images. We assume that unpaired training samples $\{x_k\}_{k=1}^N$ and $\{z_k\}_{k=1}^M$ are drawn from unknown LDCT data distribution $p_z(z)$ and unknown SDCT data distribution $p_x(x)$, respectively. In terms of image denoising, $z \sim p_z$ corresponds to noisy image (source) and $x \sim p_x$ is regarded as noise-free image (target).

The object of our method for denoising is to learn a generator $G$ with input $z \in Z$ using GAN’s framework together with the unpaired training data, in such a way that the generator’s distribution $p_G(z)$ is an optimal approximation of the clean image distribution $p_x$ and the generator’s fidelity $\|z - G(z)\|_2$ is reasonably small for every $z \sim p_z$. Here, $\|z\|_2$ stands for the standard $\ell_2$-norm of $z$. 

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We adopt the additive Gaussian noise model that the noisy LDCT image \( z \) is decomposed into a desired denoised image \( x^* \sim p_x \) and additive Gaussian noise \( \varepsilon \) of variance \( \sigma \) at each pixel, i.e., \( z = x^* + \varepsilon \) with \( \varepsilon \sim \mathcal{N}(0,\sigma) \). One can estimate the clean image \( x^* \) in terms of maximum a-posteriori approach: Given \( z \sim p_z \), find \( \hat{x} \) that maximizes the conditional probability \( p_{x^*|z}(\hat{x}|z) \). This \( \hat{x} \) is arg max \( y \) \( L_z(y) \), where

\[
L_z(y) := \log p_x(y) - \lambda \|y - z\|_2^2 \tag{1}
\]

and \( \lambda = \frac{1}{2\sigma^2} \). For more detail, we refer to Appendix (VA). However, this approach can not be used directly due to the unknown distribution \( p_x \). Instead of solving the denoising problem one-by-one for each \( z \sim p_z \), we look for the denoising function \( G : z \to \hat{x} \) by using GAN’s framework together with many samples \( \{x_k\}_{k=1}^N \) and \( \{z_k\}_{k=1}^M \).

An optimal denoising function can be derived by maximizing the expectation \( E_{z \sim p_z} L_z(G(z)) \) with respect to generator \( G \):

\[
G_{\text{MAP}} := \arg \min_G E_{z \sim p_z} \left[ -\log(p_x(G(z))) + \lambda \|G(z) - z\|_2^2 \right]. \tag{2}
\]

With the notion of the cross entropy \( H(p, q) \), we have the following expression:

\[
G_{\text{MAP}} = \arg \min_G -E_{G(z) \sim p_{G(z)}} \left[ \log(p_x(G(z))) \right] + \lambda E_{z \sim p_z} \left[ \|G(z) - z\|_2^2 \right] \\
= \arg \min_G H(p_{G(z)}, p_x) + \lambda E_{z \sim p_z} \left[ \|G(z) - z\|_2^2 \right] \tag{3}
\]

However, it is still difficult to handle the cross-entropy \( H(p_{G(z)}, p_x) \) only from the training samples even if we have a complete information of \( G \). Instead, we approximate \( G_{\text{MAP}} \) by

\[
G_* := \arg \min_G KL(p_{G(z)}, p_x) + \lambda E_{z \sim p_z} \left[ \|G(z) - z\|_2^2 \right] \tag{4}
\]

where the cross-entropy \( H(p_{G(z)}, p_x) \) in (3) is replaced by KL-divergence \( KL(p_{G(z)}, p_x) = H(p_{G(z)}, p_x) - H(p_{G(z)}) \). Interested readers may refer to the paper\(^{25}\) for the effect of this replacement.

Now, we are ready to explain our fidelity-embedded GAN model. In GAN’s framework, the unpaired datasets are used to learn the generator \( G \) that minimizes \( KL(p_{G(z)}, p_x) \), while the discriminator \( D \) tries to distinguish between generated \( G(z) \) and \( x \sim p_x \). The following theorem presents the proposed model which solves the optimal generator \( G_* \) in (4) exactly when \( G \) and \( D \) reach their optimum.
Theorem II.1  The optimal generator $G_*$ in (4) is achieved by

$$G_* = \arg \min_G \max_D J(D, G)$$

where

$$J(D, G) := E_{x \sim p_x} [D(x)] + E_{z \sim p_z} [\log(1 - D(G(z)))] + \lambda E_{z \sim p_z} [||G(z) - z||^2]$$

**Proof.** Given a fixed $G$, we first maximize $J(D, G)$ in (6) with respect to $D$. Since the third term in (6) is independent of $D$, it is enough to find

$$D_{opt} = \arg \max_D E_{x \sim p_x} [D(x)] + E_{z \sim p_z} [\log(1 - D(G(z)))]$$

A simple computation shows

$$D_{opt} = \arg \max_D E_{w \sim p_x} [D(w)] + E_{w \sim p_G(z)} [\log(1 - D(w))]$$

where the integral spans over the space of all images. For a fixed $w$, the value of $D_{opt}(w)$ that maximizes the integrand $p_x(w)D(w) + p_G(z)(w)\log(1 - D(w))$ in (8) can be shown to be

$$D_{opt}(w) := 1 - \frac{p_G(z)(w)}{p_x(w)}$$

by using the standard Calculus method. Plugging it way back to (6), we get

$$E_{x \sim p_x} [D_{opt}(x)] + E_{z \sim p_z} [\log(1 - D_{opt}(G(z)))] + \lambda E_{z \sim p_z} [||G(z) - z||^2]$$

$$= \int \left[ p_x(w)D_{opt}(w) + p_G(z)(w)\log(1 - D_{opt}(w)) \right] dx + \lambda E_{z \sim p_z} ||G(z) - z||^2$$

$$= \int \left[ p_x(w) - p_G(z)(w) + p_G(z)(w)\log \left( \frac{p_G(z)(w)}{p_x(w)} \right) \right] dw + \lambda E_{z \sim p_z} ||G(z) - z||^2$$

$$= KL(p_G(z), p_x) + \lambda E_{z \sim p_z} ||G(z) - z||^2$$

and this completes the proof.

**A. Improving training stability & Data-driven dependency**

The unpaired training samples $S_x = \{x_k\}_{k=1}^N$ and $S_z = \{z_k\}_{k=1}^N$ are used to compute the generator $G_*$ approximately. In order to improve training stability and quality of images for
reverse-KL GAN in (6), we slightly modify the proposed method as follows:

\[
G_{**} = \arg \min_{G} \frac{1}{N} \sum_{z \in S} \left[ (D(G(z)) - 1)^2 + \lambda \| G(z) - z \|^2 \right] \tag{11}
\]

with \(D = \arg \min_{D} \frac{1}{N} \sum_{x \in S_x} (D(x) - 1)^2 + \frac{1}{N} \sum_{z \in S_z} (D(G(z)))^2\). This least square loss function was used as a classifier of discriminator\(^{16}\).

It should be noted that the computed generator \(G_{**}\) depends heavily on the training samples. Fig. 1 shows the data-driven dependency, where we use three different training samples \(S^j = \{S_x^j, S_z^j\}, j = 1, 2, 3\). The first training samples \(S^1\) consist of one disk and one rectangle with different sizes and positions (first column). The other samples (\(S^2\) and \(S^3\)) are generated by adding a small anomaly to the \(S^1\). In \(S^2\), the anomaly is added only in the rectangle (\(S^2\)). On the other hand, \(S^3\) is generated by adding the anomaly only in the disk. Here, positions of anomaly are randomly chosen. Fig. 1 shows the comparison of performance of three generators \(G_{1**}, G_{2**},\) and \(G_{3**}\), where \(G_{j**}\) is computed by (11) with \(S\) replaced by \(S^j\). The top rightmost image in Fig. 1 is a test image \(z \sim p_z\), which contains a anomaly inside the disk. The \(G_{1**}(z)\) cannot preserve the anomaly inside the disk (the first row), whereas both \(G_{2**}(z)\) and \(G_{3**}(z)\) can preserve anomaly well. It is quite informative that \(G_{2**}(z)\) preserves the anomaly even though the training sample do not contain the anomaly inside the disk (the second row).

B. Patch-based Network for Practical Applications

In practice, the proposed method is performed in a patch-by-patch manner, rather than working with the whole images (e.g., 512 × 512 pixel CT images). Here, we take advantage of the observations\(^{20,21}\) that the patch manifolds of many images have low dimensional structure. Moreover, the number of training data sets is significantly increased. These allow to learn the generated distribution efficiently over the patches extracted from SDCT images. For simplicity, we will use the same notation of \(x\) and \(z\) to represent the image patches (there will be no confusion from the context).

Fig. 2 illustrates how the proposed method in (11) generates \(G_{**}(z)\) from the unpaired training image patches. It optimizes \(p_{G_{**}(z)}\) by forcing it to be close to \(p_x\) along with minimizing the \(\ell_2\) distance \(\|G_{**}(z) - z\|_2\). Fig. 5 shows the performance of the \(G_{**}\) with two different training samples; image patches of \(S^1\) and \(S^2\) are randomly selected, respectively,
Three different training samples: $S_1^x$ (1st row), $S_2^x$ (2nd row), and $S_3^x$ (3rd row) 

\[ z = G_{ss}^j(z) \]

FIG. 1. Comparison between three generators $G_{ss}^1$, $G_{ss}^2$, and $G_{ss}^3$. Given $z$ containing a small anomaly in the disk, $G_{ss}^1(z)$ eliminates the anomaly, whereas both $G_{ss}^2(z)$ and $G_{ss}^3(z)$ preserve the anomaly well while removing noise.

As shown in Fig. 5, the performance of $G_{ss}^1$ (using $S_1^x$) is inferior to $G_{ss}^2$ (using $S_2^x$), owing to lack of the diversity of $x$, which is called ‘mode collapse’.2,23

C. Network Architecture

For our generator, we adopt the deep convolutional framelet29, which is a multi-scale convolutional neural network, consisting of a contracting path and an expansive path with skipped connection and concatenation (concat) layer. Each step of the contracting and expansive path consists of two repeated convolutions (conv) with a $3 \times 3$ window, each followed by a batch normalization (bnorm) and a leaky rectified linear unit (LReLU). Downsampling and upsampling of the features are performed by 2-D Haar wavelet decomposition (wave-dec) and recomposition (wave-rec), respectively. High pass filters after wavelet decomposition skip directly to the expansive path, while loss pass filters (marked by ‘LF’ in Fig. 3) are
concatenated with the features in the contracting path during the same step. At the end, an additional convolution layer is added to generate a grayscale output image. Note that each convolution in our network is performed with zero-padding to match the size of the input and output images. The architecture of deep convolutional framelet is quite similar to that of the U-net, a deep learning model widely used in image processing, except that high pass filter pass. The deep convolutional framelet utilizes the wavelet decomposition and recomposition instead of pooling and unpooling operation for downsampling and upsampling, respectively. By doing so, more detailed information of image can be preserved during downsampling.

In adversarial architecture, we adopt the 70 × 70 PatchGAN classifier as a discriminator, which tries to classify whether each patch in an image is real or fake. PatchGAN enables to learn detail structure in images than the 1 × 1 PixelGAN. As in, discriminator contains four convolution layers with a 4 × 4 window and strides of two in each direction of the domain, each followed by a batch normalization and a leaky ReLU with a slope 0.2. At the end of architecture, an 1 × 1 convolution layer is added to generate 1-dimensional output data. Fig. 3 illustrates the architecture of the proposed method.
In our numerical simulation and clinical experiment, the objective function in (11) is minimized using an Adam optimizer\textsuperscript{11} with a learning rate of 0.0002 and mini-batch size of 40, and 200 epochs are utilized for training. Training was implemented using Tensorflow\textsuperscript{1} on a GPU (NVIDIA, Titan Xp, 12GB) system. It takes about a day to train the network. We empirically choose $\lambda = 10$ in Eq. (11). The network weights were initialized following a Gaussian distribution with a mean of 0 and standard deviation of 0.01.

![Network Architecture Diagram](image)

**FIG. 3.** Network architecture of the proposed network.

### D. Datasets

In our simulations and clinical experiments, all CT images of size $512 \times 512$ are acquired by a 64-channel multi-detector CT scanner (Sensation 64; Siemens Healthcare, Forchheim, Germany).
1. Simulation study

We collect 20 CT images including liver and portal vein for each patient. Total of 1200 CT images of 60 patients are prepared for training. Among them, Gaussian noise with a standard deviation of 25 is added to 600 CT images of 30 patients. These noisy 600 CT images and remaining 600 CT images of other 30 patients are used for unpaired noisy and noise-free CT images. From each image of size $512 \times 512$, the patches of size $128 \times 128$ are extracted with strides of 8 in each direction in the image domain and then 40 patches are randomly selected. They are used as training image patches.

2. Clinical study

For training our network, we respectively collect 200 brain CT images of 10 patients, acquired at a tube voltage of 120 kVp and 200 mAs tube current, and at a 100 kVp and 190 mAs reference tube current (with tube current modulation program). Fig. 6 shows some examples of unpaired brain CT images used for training. We refer the former and later images as low-dose CT (LDCT) image, and standard-dose CT (SDCT) images, respectively. Using a low tube voltage and a tube current increase the image noise as shown in Fig. 6. 60 LDCT images of 3 other patients who are not used for training were collected for testing. As in the simulation, we generate unpaired patches of size $128 \times 128$ from both LDCT and SDCT images.

III. RESULTS

Numerical simulation and clinical experiment are performed in order to show validity of the proposed approach for noise reduction in CT images.

Fig. 4 shows the denoising results for liver CT images with simulated Gaussian noise. Second and third columns show the results of the proposed method using paired and unpaired noisy and noise-free datasets. Fourth column shows the results of the original GAN (i.e., model of (11) without the fidelity term $\|G_\ast(z) - z\|_2$). Second and fourth rows show the zoomed ROIs of the rectangle regions of images in first and third rows, respectively. The values of peak signal to noise ratio (PSNR) and mean squared error (MSE) were evaluated and displayed in the upper left corner of images. As shown in Fig. 4, the proposed unpaired
method reduces noise artifacts clearly, while preserving morphological structures of tissues. Moreover, it shows comparable image quality to the paired method in terms of both PSNR and MSE. The original GAN has no restriction on generated images, so that it can easily remove morphological structures, or produce plausible fakes in noisy images. See yellow arrow in the fourth column of Fig. 4.

Fig. 7 shows clinical experiment for brain CT images. First row shows the brain LDCT images. Severe noise artifacts occur due to low radiation dose. Second row shows the denoising results of the proposed method based on unpaired LDCT and SDCT CT images, which are obtained from different patients. Some examples of unpaired brain CT images used for training are illustrated in Fig. 6. Since SDCT image corresponding to each LDCT image is not available, we instead calculate mean and standard deviation (SD) for the marked circle-shaped ROIs in Fig. 7. Here, we assumed that the selected ROIs are homogeneous. [Mean/SD] are displayed in Fig. 7. Even for general noise artifacts (not modeled by Gaussian noise), the proposed method significantly reduces the noise in terms of SD quantity. Note that the proposed method decreases mean value of ROIs as well as the value of SD. The mean attenuation of the organs is lower in the SDCT (120 kVp portal) image than in LDCT (100 kVp portal) image\textsuperscript{18,19}. Hence, the proposed method learns the characteristics (i.e., SD, mean quantities) of SDCT images.

IV. DISCUSSION AND CONCLUSION

This paper proposes an unpaired deep-learning method of image denoising for LDCT. The method approximates MAP estimation using a GAN framework, and can incorporate prior information on target SDCT images from a data distribution. Under the assumption of Gaussian noise, the $\ell_2$ constraint is added to the GAN framework. Numerical simulations show that the proposed deep learning method with unpaired datasets performs at least compatibly to supervised methods using paired datasets, in terms of PSNR and MSE (see Fig. 4). Clinical results also show that the proposed method enhances LDCT image quality even with unpaired SDCT and LDCT images (see Fig. 7).

However, our proposed approach retains some issues requiring further research. One such issue is illustrated by the denoising effect with respect to the choice of samples from the data distribution in Figs. 1 and 5. This shows that, depending on the samples used for training,
FIG. 4. Simulation results for CT images with Gaussian noise. Second and fourth rows show the zoomed ROIs of the rectangle regions of images in first and third rows, respectively. [PSNR/MSE] are displayed in the images. (C=150 HU/ W=600 HU for all CT images and zoomed ROIs)

the proposed method can remove details, produce a plausible fake, or simply collapse when generating the denoised images. Therefore, it is essential for the image denoising technique to choose effective training datasets to reflect the appropriate image priors.

Furthermore, the proposed approach for the estimation of the target SDCT images can be improved by applying a denoising algorithm that incorporates an accurate noise model of LDCT; for example, other constraints such as perceptual loss\textsuperscript{28} can be applied to the GAN framework in (11) to learn high-level features. In addition, an effective computational method is required for clinical applications. Given that the proposed method works a patch-by-patch, it is more time-consuming than conventional methods treating the entire image; it takes about a few seconds to obtain a single 512 × 512 denoised CT image. This can be
FIG. 5. Denoising results of patches for CT images with Gaussian noise. Second, fifth columns show the noisy and reference patches, respectively. Third, fourth columns shows the results of the proposed network on unpaired 24000 patches sampled from 50 and 600 CT slices, respectively. C=150 HU/ W=600 HU for all CT images and patches)

reduced by using, for example, parallel computation.

Other than the issues mentioned above, future work will also focus on broadening the scope of the proposed method to include the other CT reconstruction problems, such as reduction of the metal artifact and scattering, as it has the potential to resolve the fundamental difficulty in applying deep learning approaches in X-ray CT (i.e., collecting paired CT image datasets). In addition, it would be interesting to focus on quantitative analysis of the relationship between the estimated image and the training datasets.
V. APPENDIX

A. Derivation of MAP for additive Gaussian noise

We follow the assumption of Section (II). That is, the noisy image \( z \) is decomposed into a desired denoised image \( x^* \sim p_x \) and additive Gaussian noise \( \epsilon \) of variance \( \sigma \) at each pixel. For the MAP approach, we want to estimate \( x^* \) by maximizing the conditional probability \( p_{x^*|z}(y|z) \) with respect to the estimation \( y \). Bayes rule provides that

\[
\arg \max_y \log p_{x^*|z}(y|z) = \arg \max_y \left[ \log p_x(y) + \log p_{z|x^*}(z|y) \right].
\]

(12)

Note that \( p_x(y) = p_{x^*}(y) \). Since \( \epsilon \) is independent of the original image \( x^* \), we have

\[
p_{z|x^*}(z|y) = p_{\epsilon|x^*}(z - y|y) = p_{\epsilon}(z - y) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(z-y)^2}{2\sigma^2}}.
\]

(13)

It follows from (12) and (13) that the denoised image \( y \) is

\[
\arg \max_y \log p_{x^*|z}(y|z) = \arg \max_y \left[ \log p_x(y) - \lambda \|y - z\|_2^2 \right]
\]

(14)

where \( \lambda = \frac{1}{2\sigma^2} \).
FIG. 7. Denoising results for clinical CT images. [Mean/SD] are displayed in the images. (C=40 HU/ W=80 HU for all CT images)

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