



Pre-trained Diffusion Models for Plug-and-Play Medical Image Enhancement

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Abstract. Deep learning-based medical image enhancement methods (e.g., denoising and super-resolution) mainly rely on paired data and correspondingly the well-trained models can only handle one type of task. In this paper, we address the limitation with a diffusion model-based framework that mitigates the requirement of paired data and can simultaneously handle multiple enhancement tasks by one pre-trained diffusion model without fine-tuning. Experiments on low-dose CT and heart MR datasets demonstrate that the proposed method is versatile and robust for image denoising and super-resolution. We believe our work constitutes a practical and versatile solution to scalable and generalizable image enhancement.

1 Introduction

Computed Tomography (CT) and Magnetic Resonance (MR) are two widely used imaging techniques in clinical practice. CT imaging uses X-rays to produce detailed, cross-sectional images of the body, which is particularly useful for imaging bones and detecting certain types of cancers with fast imaging speed. However, CT imaging has relatively high radiation doses that can pose a risk of radiation exposure to patients. Low-dose CT techniques have been developed to address this concern by using lower doses of radiation, but the image quality is degraded with increased noise, which may compromise diagnostic accuracy [9].

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MR imaging, on the other hand, uses a strong magnetic field and radio waves to create detailed images of the body’s internal structures, which can produce high-contrast images for soft tissues and does not involve ionizing radiation. This makes MR imaging safer for patients, particularly for those who require frequent or repeated scans. However, MR imaging typically has a lower resolution than CT [18], which limits its ability to visualize small structures or abnormalities.

Motivated by the aforementioned, there is a pressing need to improve the quality of low-dose CT images and low-resolution MR images to ensure that they provide the necessary diagnostic information. Numerous algorithms have been developed for CT and MR image enhancement, with deep learning-based methods emerging as a prominent trend [5, 14], such as using the conditional generative adversarial network for CT image denoising [32] and convolutional neural network for MR image Super-Resolution (SR) [4].

These algorithms are capable of improving image quality, but they have two significant limitations. First, **paired images are required for training**, e.g., low-dose and full-dose CT images; low-resolution and high-resolution MR images). However, acquiring such paired data is challenging in real clinical scenarios. Although it is possible to simulate low-quality images from high-quality images, the models derived from such data may have limited generalization ability when applied to real data [9, 14]. Second, **customized models are required for each task**. For example, for MR super-resolution tasks with different degradation levels (i.e., 4x and 8x downsampling), one may need to train a customized model for each degradation level and the trained model cannot generalize to other degradation levels. Addressing these limitations is crucial for widespread adoption in clinical practice.

Recently, pre-trained diffusion models [8, 11, 21] have shown great promise in the context of unsupervised natural image reconstruction [6, 7, 12, 28]. However, their applicability to medical images has not been fully explored due to the absence of publicly available pre-trained diffusion models tailored for the medical imaging community. The training of diffusion models requires a significant amount of computational resources and training images. For example, openai’s improved diffusion models [21] took 1600–16000 A100 hours to be trained on the ImageNet dataset with one million images, which is prohibitively expensive. Several studies have used diffusion models for low-dose CT denoising [30] and MR image reconstruction [22, 31], but they still rely on paired images.

In this paper, we aim at addressing the limitations of existing image enhancement methods and the scarcity of pre-trained diffusion models for medical images. Specifically, we provide two well-trained diffusion models on full-dose CT images and high-resolution heart MR images, suitable for a range of applications including image generation, denoising, and super-resolution. Motivated by the existing plug-and-play image restoration methods [26, 34, 35] and denoising diffusion restoration and null-space models (DDNM) [12, 28], we further introduce a paradigm for plug-and-play CT and MR image denoising and super-resolution as shown in Fig. 1. Notably, it **eliminates the need for paired data**, enabling greater scalability and wider applicability than existing paired-image dependent

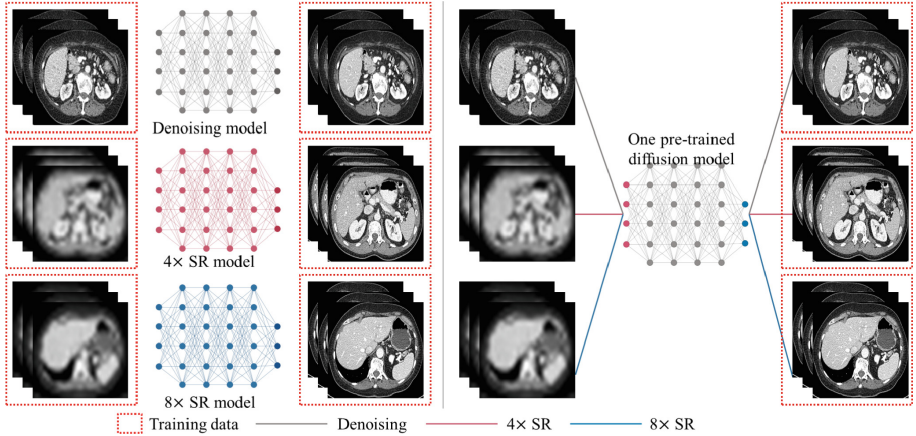


Fig. 1. Comparison of (a) the common paired-image dependent paradigm and (b) the plug-and-play paradigm for medical image enhancement. The former needs to build customized models for different tasks based on paired low/high-quality images, while the latter can share one pre-trained diffusion model for all tasks and only high-quality images are required as training data. The pre-trained model can handle unseen images as demonstrated in experiments.

methods. Moreover, it **eliminates the need to train a customized model for each task**. Our method does not need additional training on specific tasks and can directly use the single pre-trained diffusion model on multiple medical image enhancement tasks. The pre-trained diffusion models and PyTorch code of the present method are publicly available at <https://github.com/bowang-lab/DPM-MedImgEnhance>.

2 Method

This section begins with a brief overview of diffusion models for image generation and the mathematical model and algorithm for general image enhancement. We then introduce a plug-and-play framework that harnesses the strengths of both approaches to enable unsupervised medical image enhancement.

2.1 Denoising Diffusion Probabilistic Models (DDPM) for Unconditional Image Generation

Image generation models aim to capture the intrinsic data distribution from a set of training images and generate new images from the model itself. We use DDPM [11] for unconditional medical image generation, which contains a diffusion (or forward) process and a sampling (or reverse) process. The diffusion process gradually adds random Gaussian noise to the input image x_0 , following a Markov Chain with transition kernel $q(x_t|x_{t-1}) = \mathcal{N}(x_t; \sqrt{1 - \beta_t}x_{t-1}, \beta_t\mathbf{I})$,

where $t \in \{1, \dots, T\}$ represents the current timestep, x_t and x_{t-1} are adjacent image status, and $\beta_t \in \{\beta_1, \dots, \beta_T\}$ is a predefined noise schedule. Furthermore, we can directly obtain x_t based on x_0 at any timestep t by:

$$q(x_t|x_0) = \mathcal{N}(x_t; \sqrt{\alpha_t}x_0, (1 - \bar{\alpha}_t)\mathbf{I}), \quad \text{e.g., } x_t = \sqrt{\alpha_t}x_0 + \sqrt{(1 - \bar{\alpha}_t)}\epsilon, \quad (1)$$

where $\alpha_t := 1 - \beta_t$, $\bar{\alpha}_t := \prod_{s=1}^t \alpha_s$, and $\epsilon \sim \mathcal{N}(\mathbf{0}, \mathbf{I})$. This property enables simple model training where the input is the noisy image x_t and the timestep t and the output is the predicted noise ϵ_θ (θ denotes model parameters). Intuitively, a denoising network is trained with the mean square loss $\mathbb{E}_{t,x} \|\epsilon - \epsilon_\theta(x_t, t)\|^2$. The sampling process aims to generate a clean image from Gaussian noise $x_T \sim \mathcal{N}(\mathbf{0}, \mathbf{I})$, and each reverse step is defined by:

$$x_{t-1} = \frac{1}{\sqrt{\alpha_t}} \left(x_t - \frac{1 - \alpha_t}{\sqrt{1 - \bar{\alpha}_t}} \epsilon_\theta(x_t, t) \right) + \beta_t z; \quad z \sim \mathcal{N}(\mathbf{0}, \mathbf{I}). \quad (2)$$

2.2 Image Enhancement with Denoising Algorithm

In general, image enhancement tasks can be formulated by:

$$y = Hx + n, \quad (3)$$

where y is the degraded image, H is a degradation matrix, x is the unknown original image, and n is the independent random noise. This model can represent various image restoration tasks. For instance, in the image denoising task, H is the identity matrix, and in the image super-resolution task, H is the downsampling operator. The main objective is to recover x by solving the minimization problem:

$$x^* = \arg \min_x \|y - Hx\|^2 + R(x), \quad (4)$$

where the first data-fidelity term keeps the data consistency and the second data-regularization term $R(x)$ imposes prior knowledge constraints on the solution. This problem can be solved by the Iterative Denoising and Backward Projections (IDBP) algorithm [26], which optimizes the revised equivalent problem:

$$x^*, \hat{y}^* = \arg \min_{x, \hat{y}} \|\hat{y} - x\|_{H^T H} + R(x) \quad \text{s.t. } \hat{y} = H^\dagger y, \quad (5)$$

where $H^\dagger := H^T(HH^T)^{-1}$ is the pseudo inverse of the degradation matrix H and $\|f\|_{H^T H} := f^T H^T H f$. Specifically, x^* and \hat{y}^* can be alternatively estimated by solving $\min_x \|\hat{y} - x\|_2^2 + R(x)$ and $\min_{\hat{y}} \|\hat{y} - x\|_2^2$ s.t. $H\hat{y} = y$. Estimating x^* is essentially a denoising problem that can be solved by a denoising operator and \hat{y}^* has a closed-form solution:

$$x^* = \text{Denoiser}(\hat{y}); \quad \hat{y}^* = H^\dagger y + (I - H^\dagger H)\hat{x}. \quad (6)$$

Intuitively, IDBP iteratively estimates the original image from the current degraded image and makes a projection by constraining it with prior knowledge. Although IDBP offers a flexible way to solve image enhancement problems, it still requires paired images to train the denoising operator [26].

2.3 Pre-Trained Diffusion Models for Plug-and-play Medical Image Enhancement

We introduce a plug-and-play framework by leveraging the benefits of the diffusion model and IDBP algorithm. Here we highlight two benefits: (1) it removes the need for paired images; and (2) it can simply apply the single pre-trained diffusion model across multiple medical image enhancement tasks.

First, we reformulate the DDPM sampling process [11] $x_{t-1} \sim p_\theta(x_{t-1}|x_t) = \mathcal{N}(x_{t-1}; \mu_\theta(x_t, t), \beta_t \mathbf{I})$ into:

$$x_{0|t} = \frac{1}{\sqrt{\bar{\alpha}_t}} (x_t - \sqrt{1 - \bar{\alpha}_t} \epsilon_\theta(x_t, t)), \quad (7)$$

and

$$x_{t-1} = \frac{\sqrt{\bar{\alpha}_{t-1}}\beta_t}{1 - \bar{\alpha}_t} x_{0|t} + \frac{\sqrt{\bar{\alpha}_t}(1 - \bar{\alpha}_{t-1})}{1 - \alpha_t} x_t + \beta_t z. \quad (8)$$

Intuitively, each sampling iteration has two steps. The first step estimates the denoised image $x_{0|t}$ based on the current noisy image x_t and the trained denoising network $\epsilon_\theta(x_t, t)$. The second step generates a rectified image x_{t-1} by taking a weighted sum of $x_{0|t}$ and x_t and adding a Gaussian noise perturbation.

As mentioned in Eq. (3), our goal is to restore an unknown original image x_0 from a degraded image y . Thus, the degraded image y needs to be involved in the sampling process. Inspired by the iteration loop in IDBP, we project the estimated $x_{0|t}$ on the hyperplane $y = Hx$:

$$\hat{x}_{0|t} = H^\dagger y + (I - H^\dagger H) x_{0|t}. \quad (9)$$

It can be easily proved that $H\hat{x}_{0|t} = HH^\dagger y + Hx_{0|t} - HH^\dagger Hx_{0|t} = y$. By replacing $x_{0|t}$ with $\hat{x}_{0|t}$ in Eq. (8), we have:

$$x_{t-1} = \frac{\sqrt{\bar{\alpha}_{t-1}}\beta_t}{1 - \bar{\alpha}_t} \hat{x}_{0|t} + \frac{\sqrt{\bar{\alpha}_t}(1 - \bar{\alpha}_{t-1})}{1 - \alpha_t} x_t + \beta_t z. \quad (10)$$

Algorithm 1 shows the complete steps for image enhancement, which inherit the denoising operator from DDPM and the projection operator from IDBP. The former employs the strong denoising capability in the diffusion model and the latter can make sure that the generated results match the input image. Notably, the final algorithm is equivalent to DDNM [28], but it is derived from different perspectives.

Algorithm 1. Pre-trained DDPM for plug-and-play medical image enhancement**Require:** Pre-trained DDPM ϵ_θ , low-quality image y , degradation operator H

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- 1: Initialize $x_T \sim \mathcal{N}(\mathbf{0}, \mathbf{I})$.
 - 2: **for** $t = T$ **to** 1 **do**
 - 3: $x_{0|t} = \frac{1}{\sqrt{\alpha_t}} (x_t - \sqrt{1 - \alpha_t} \epsilon_\theta(x_t, t))$ // Denoise x_t with pre-trained DDPM
 - 4: $\hat{x}_{0|t} = x_{0|t} - \Sigma_t H^\dagger (H x_{0|t} - y)$ // Project $x_{0|t}$ on the hyperplane $y = Hx$
 - 5: $x_{t-1} = \frac{\sqrt{\alpha_{t-1}} \beta_t}{1 - \alpha_t} \hat{x}_{0|t} + \frac{\sqrt{\alpha_t(1 - \alpha_{t-1})}}{1 - \alpha_t} x_t + \beta_t z, z \sim \mathcal{N}(\mathbf{0}, \mathbf{I})$ // Sampling
 - 6: **end for**
 - 7: **return** Enhanced image x_0
-

3 Experiments

Dataset. We conducted experiments on two common image enhancement tasks: denoising and SR. To mimic the real-world setting, the diffusion models were trained on a diverse dataset, including images from different centers and scanners. The testing set (e.g., MR images) is from a new medical center that has not appeared in the training set. Experiments show that our model can generalize to these unseen images. Specifically, the denoising task is based on the AAPM Low Dose CT Grand Challenge abdominal dataset [19], which can be also used for SR [33]. The heart MR SR task is based on three datasets: ACDC [1], M&Ms1-2 [3], and CMRxMotion [27]. Notably, the presented framework eliminates the requirement of paired data. For the CT image enhancement task, we trained a diffusion model [21] based on the full-dose dataset that contains 5351 images, and the hold-out quarter-dose images were used for testing. For the MR enhancement task, we used the whole ACDC [1] and M&Ms1-2 [3] for training the diffusion model and the CMRxMotion [27] dataset for testing. The testing images were downsampled by operator H with factors of $4\times$ and $8\times$ to produce low-resolution images, and the original images served as the ground truth.

Evaluation Metrics. The image quality was quantitatively evaluated by the Peak Signal-to-Noise Ratio (PSNR), Structural SIMilarity index (SSIM) [29], and Visual Information Fidelity (VIF) [24], which are widely used measures in medical image enhancement tasks [9, 17].

Implementation Details. We followed the standard configuration in [21] to train the diffusion model from scratch. Specifically, the diffusion step used a linear noise schedule $\beta \in [1e-4, 0.02]$ and the number of diffusion timesteps was $T = 1000$. The input image size was normalized to 256×256 and the 2D U-Net [23] was optimized by Adam [13] with a batch size of 16 and a learning rate of 10^{-4} , and an Exponential Moving Average (EMA) over model parameters with a rate of 0.9999. All the models were trained on A100 GPU and the total training time was 16 d. The implementation was based on DDNM [28]. For an efficient sampling, we used DDIM [25] with 100 diffusion steps. We followed the degradation operator settings in DDNM. Specifically, we used the identity matrix I as the degradation operator for the denoising task and scaled

the projection difference $H^\dagger(Hx_{0|t} - y)$ with coefficient Σ to balance the information from measurement y and denoising output $x_{0|t}$. The downsampling operator implemented with *torch.nn.AdaptiveAvgPool2d* for the super-resolution task. The pseudo-inverse operator H^\dagger is I for the denoising task and upsampling operator for the SR task.

Comparison with Other Methods. The pseudo-inverse operator H^\dagger was used as the baseline method, namely, $x^* = H^\dagger y$. We also compared the present method with one commonly used image enhancement method DIP [10] and two recent diffusion model-based methods: IVLR [6], which adopted low-frequency information from measurement y to guide the generation process towards a narrow data manifold, and DPS [7], which addressed the intractability of posterior sampling through Laplacian approximation. Notably, DPS used 1000 sampling steps while we only used 100 sampling steps.

Table 1. Performance (mean \pm standard deviation) on CT denoising task. The arrows indicate directions of better performance.

Methods	PSNR \uparrow	SSIM \uparrow	VIF \uparrow
Baseline	24.9 \pm 2.4	0.778 \pm 0.07	0.451 \pm 0.07
DIP [10]	25.9 \pm 2.4	0.783 \pm 0.06	0.444 \pm 0.07
IVLR [6]	25.8 \pm 2.3	0.695 \pm 0.11	0.432 \pm 0.09
DPS [7]	26.5 \pm 2.3	0.791 \pm 0.08	0.475 \pm 0.09
Ours	28.3 \pm 2.8	0.803 \pm 0.11	0.510 \pm 0.10

4 Results and Discussion

Low-Dose CT Image Enhancement. The presented method outperformed all other methods on the denoising task in all metrics, as shown in Table 1, with average PSNR, SSIM, and VIF of 28.3, 0.803, and 0.510, respectively. Supplementary Fig. 1 (a) visually compares the denoising results, showing that the presented method effectively removes the noise and preserves the anatomical details, while other methods either fail to suppress the noise or result in loss of tissue information.

We also used the same pre-trained diffusion model for simultaneously denoising and SR by setting H as the downsampling operator. Our method still achieves better performance across all metrics as shown in Table 2. By visually comparing the enhancement results in Fig. 1 (b) and (c), our results can reconstruct more anatomical details even in the challenging noisy $8\times$ SR task. In contrast, DIP tends to smooth tissues and ILVR and DPS fail to recover the tiny structures such as liver vessels in the zoom-in regions.

Table 2. Evaluation results of joint denoising and super-resolution for CT images.

Methods	Noisy 4× SR			Noisy 8× SR		
	PSNR ↑	SSIM ↑	VIF ↑	PSNR ↑	SSIM ↑	VIF ↑
Baseline	20.4±0.6	0.583±0.06	0.191±0.01	18.4±0.6	0.484±0.06	0.087±0.01
DIP [10]	21.8±0.7	0.642±0.06	0.243±0.02	19.6±0.7	0.560±0.07	0.146±0.02
IVLR [6]	25.1±2.5	0.715±0.10	0.417±0.09	24.6±2.8	0.702±0.12	0.395±0.11
DPS [7]	25.1±2.8	0.172±0.13	0.416±0.12	24.7±3.1	0.705±0.14	0.398±0.12
Ours	26.2±2.6	0.743±0.10	0.446±0.10	25.9±3.1	0.731±0.13	0.431±0.12

Table 3. Evaluation results of heart MR image super-resolution tasks.

Methods	4× SR			8× SR		
	PSNR ↑	SSIM ↑	VIF ↑	PSNR ↑	SSIM ↑	VIF ↑
Baseline	23.5±0.6	0.734±0.03	0.288±0.01	19.9±0.7	0.646±0.04	0.123±0.01
DIP [10]	27.0±0.8	0.784±0.02	0.392±0.02	22.6±0.8	0.712±0.03	0.224±0.02
IVLR [6]	25.4±0.7	0.731±0.03	0.355±0.02	21.2±0.8	0.622±0.04	0.180±0.02
DPS [7]	25.6±0.8	0.741±0.03	0.335±0.03	21.2±0.8	0.635±0.04	0.177±0.02
Ours	26.9±0.8	0.805±0.025	0.416±0.03	22.4±0.8	0.700±0.03	0.226±0.02

MR Image Enhancement. To demonstrate the generality of the presented method, we also applied it for the heart MR image 4× and 8× SR tasks, and the quantitative results are presented in Table 3. Our results still outperformed IVLR and DPS in all metrics. DIP obtains slightly better scores in PSNR for the 4× SR task and PSNR and SSIM for the 8× SR tasks, but visualized image quality is significantly worse than our results as shown in Supplementary Fig. 2, e.g., many anatomical structures are smoothed. This is because perceptual and distortion qualities are in opposition to each other as theoretically proven in [2]. DIP mainly prioritizes the distortion measures for the noise-free SR tasks while our results achieve a better trade-off between the perceptual and distortion quality.

5 Conclusion

In summary, we have provided two well-trained diffusion models for abdomen CT and heart MR, and introduced a plug-and-play framework for image enhancement. Our experiments have demonstrated that a single pre-trained diffusion model could address different degradation levels without customized models. However, there are still some limitations to be solved. The degradation operator and its pseudo-inverse should be explicitly given, which limits its application in tasks such as heart MR motion deblurring. Although the present method is in general applicable for 3D images, training the 3D diffusion model still remains prohibitively expensive. Moreover, the sampling process currently requires multiple network inferences, but it could be solved with recent advances in one-step

generation models [15] and faster algorithms [16]. Despite these limitations, the versatile and scalable nature of the presented paradigm has great potential to revolutionize medical image enhancement tasks. Future work could focus on developing more efficient algorithms for 3D diffusion models and expanding this paradigm to more clinical applications such as low-dose PET denoising.

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