Title: Unsupervised Low-Dose CT Image Denoising Using Diffusion Model

Low-dose CT image denoising is a critical task in medical image computing, with supervised deep learning methods showing significant progress in recent years. However, these methods often require training on both low-dose and regular-dose CT images, which can be challenging to obtain in clinical settings. Existing unsupervised deep learning methods either rely on a large number of low-dose CT images for training or depend on specially designed data acquisition processes to obtain training data. To address these limitations, we propose a novel unsupervised method that only utilizes regular-dose CT images during training, enabling zero-shot denoising of low-dose CT images. Our method leverages the diffusion model, a powerful generative model. We first train a cascade of unconditional diffusion models capable of generating high-quality regular-dose CT images from low resolution to high resolution. The cascading structure facilitates the training of high-resolution diffusion models. Subsequently, we introduce low-dose CT images as likelihoods into the reverse process of the diffusion model, combining with the prior provided by the diffusion model to iteratively solve multiple maximum a posteriori (MAP) problems for denoising. Additionally, we propose a method to adaptively adjust the balance between likelihood and prior coefficients in MAP estimation, allowing for the adaptation to different noise levels in low-dose CT images. We evaluate our method on low-dose CT datasets from different regions and dose levels. Results demonstrate that our method outperforms the current state-of-the-art unsupervised methods and surpasses several supervised deep learning methods.

Low-dose computed tomography (CT) imaging has garnered increasing attention due to its significant reduction in radiation dose. While low-dose CT reduces the risk of patient exposure to X-rays, it often results in poor quality reconstruction images and noticeable noise, potentially hindering accurate diagnosis. To improve the image quality of low-dose CT, various algorithms have been developed, including sinogram filtration, iterative reconstruction, and image denoising. Among these methods, low-dose CT image denoising is widely used as it does not involve the reconstruction process and can be applied to different CT imaging systems.

In the past decade, driven by rapid advancements in deep learning technology, deep neural networks have become powerful tools for low-dose CT image denoising, achieving significant success. Typically, deep learning-based methods learn end-to-end mappings from low-dose to regular-dose CT images in a supervised manner. Initially, convolutional neural networks (CNNs) were the most commonly used method for low-dose CT image denoising. To enhance the visual quality of denoised images, generative adversarial networks (GANs) have also been employed for low-dose CT image denoising. Furthermore, Transformer-based networks further enhance the performance of low-dose CT image denoising.

However, the success of supervised deep learning algorithms largely relies on a large number of paired training data. Unfortunately, obtaining such data in clinical settings is challenging due to adherence to the "as low as reasonably achievable" principle. Therefore, it is crucial to develop high-performance methods leveraging deep neural networks without requiring a large amount of labeled data.

Some existing methods attempt to address this issue using different strategies. One class of methods relies on training data obtained through special acquisition schemes. Yuan et al. proposed Half2Half, which utilizes paired half-dose CT images to train a neural denoiser. Wu et al. developed a method for training low-dose CT image denoising networks using odd-even projection reconstruction. Another class of methods relaxes the conditions of training data but still requires a large number of low-dose CT images for training. For example, Du et al. proposed learning invariant representations from noisy images and reconstructing clean observations. Liu et al. employed reversible neural networks to simulate paired regular-dose and low-dose CT images for unpaired training. Niu et al. proposed a similarity-based unsupervised deep denoising method to handle correlated noise in CT images.

Unlike the aforementioned unsupervised methods, our proposed method does not require paired regular-dose and low-dose CT images or any low-dose CT images for training. We only utilize regular-dose CT images to train a denoising diffusion probability model and then leverage the pre-trained diffusion model's embedded prior information to achieve zero-shot denoising of low-dose CT images. The diffusion model defines a constant forward process and realizes image generation through iterative solving of the reverse process. The diffusion model not only achieves state-of-the-art generative results but also provides analytical representations of the data distribution during generation, which cannot be achieved by models such as GANs. Given the diffusion model's powerful generative and representation capabilities, some studies have explored its prior application in downstream tasks such as image reconstruction and restoration. However, most of these methods either ignore the presence of noise or only consider simple noise scenarios. In our method, we first propose to incorporate the diffusion prior into the maximum a posteriori (MAP) framework to address the low-dose CT image denoising problem. Additionally, we introduce two adaptive strategies to improve the coefficients in MAP estimation, balancing likelihood and prior in the presence of complex noise levels in low-dose CT images.

we train the diffusion model using regular-dose CT images. Previous studies have emphasized the challenge of directly generating high-resolution images of size 512×512. We adopt a cascaded generation approach to address this issue. Specifically, we generate low-resolution images from random noise and then adjust the resolution to generate high-resolution images of size 512×512. Subsequently, we propose an algorithm that incorporates the pre-trained diffusion model into the MAP denoising framework. In each iteration of the diffusion model's generation process, we introduce low-dose CT images and solve multiple MAP estimation problems to ensure high likelihood between the generated images and the input low-dose CT images while maintaining good image quality. Additionally, considering the different noise levels exhibited in different low-dose CT slices, we design two adaptive strategies to improve coefficients in MAP estimation, balancing likelihood and prior. The algorithm utilizes the improved coefficients to recover denoising processes at intermediate time steps, adapting to different noise levels in low-dose CT images.

In conclusion, the Dn-Dp algorithm is a completely unsupervised method for denoising low-dose CT images using diffusion prior. It only requires training the network with regular-dose CT images. The algorithm includes training a cascade diffusion model to generate regular-dose CT images and iteratively solving multiple MAP estimation problems in the reverse process of the diffusion model. This ensures high likelihood between the generated images and the input low-dose CT images while maintaining good image quality. To address different noise levels in low-dose CT images, two adaptive strategies are employed to adjust coefficients in MAP estimation, balancing likelihood and prior. We also introduce a method to recover denoising at intermediate stages with more accurate coefficients. The method demonstrates excellent performance in quantitative metrics and visual effects, especially in denoising quarter-dose abdominal CT images, even outperforming supervised methods. Furthermore, our aim is to extend the diffusion prior-based method to CT reconstruction algorithms starting from the sinogram domain.