Denoising stimulated Raman histology using weak supervision to improve label-free optical microscopy of human brain tumors

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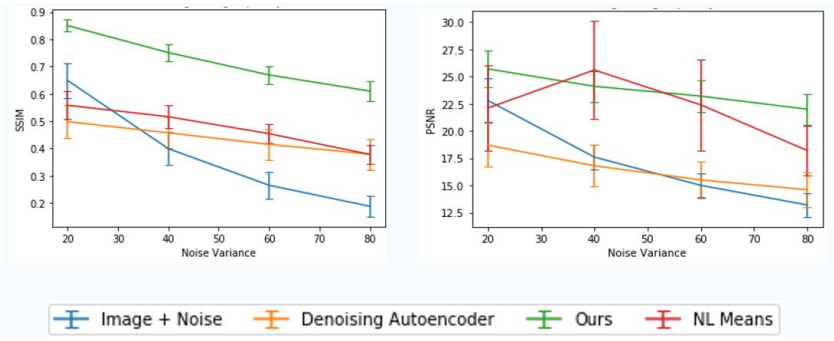
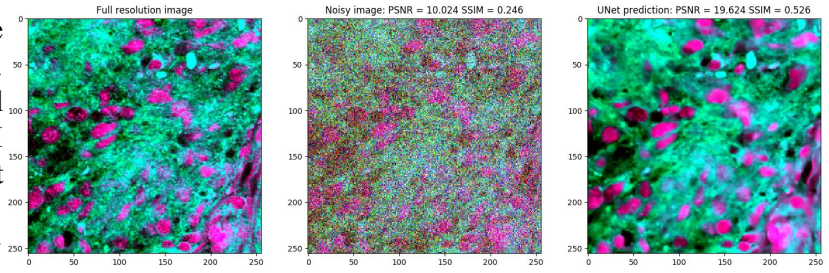
Background. The quality of biomedical imaging is an essential determinant of its diagnostic power. Unfortunately, even under optimal conditions, there are intrinsic and extrinsic factors that can lead to low-quality or nondiagnostic biomedical images. Stimulated Raman scattering microscopy is a label-free, optical imaging method that produces high-resolution histologic images of fresh, unprocessed biomedical specimens in the operating room. We have previously demonstrated that stimulated Raman histology (SRH) is equivalent to standard-of-care H&E histology for providing intraoperative brain tumor diagnosis. However, using Raman scattering as a label-free contrast mechanism is subject to image degradation both from microscope laser aberrations and the biochemical properties of imaged specimens (e.g. dense collagen, hemorrhagic tissue, etc). Here, we aim to address the inverse problem of denoising SRH images using a training algorithm that leverages weak supervision based on perceptual whole slide-level image quality ratings. Our method is able to restore low-quality and nondiagnostic SRH images without the need for paired training data.

Methods. Our SRH database consists of 572 specimens from patients who underwent brain tumor or epilepsy surgery. The images were split into three groups based on their perceptual quality as rated by a trained neuropathology specialist: low-quality, average-quality, and high-quality. Training and validation datasets were generated from the high-quality group by using additive Gaussian noise with variances sampled randomly from a uniform distribution (σ^2 range 20-80). Paired noisy and target images were then used to train a deep denoising neural network with a U-Net architecture. Reference image quality metrics, including peak signal-to-noise ratio (PSNR) and structural similarity index (SSIM), and a non-reference image quality metric, named BRISQUE, were used to compare the performance of our model versus a deep denoising autoencoder and a non-learning denoising method called non-local means. Finally, we used the BRISQUE metric to compare the SRH image quality improvement of unmodified images versus the denoised images from the low-quality and average-quality groups.

Results. Using 1,000 patches from the high-quality group test set with varying levels of Gaussian noise, our model achieved a higher PSNR and SSIM, and lower BRISQUE scores compared to the denoising autoencoder (See Graph with SRH example) and a higher SSIM, comparable PSNR, and lower BRISQUE scores compared to the non-local means algorithm. Furthermore, using unmodified images from the low-quality group, our model achieved a lower BRISQUE score compared to the denoising autoencoder and non-local means algorithm (image + noise 41.3 +/- 6.4 vs. our model 36.3 +/- 8.5 vs. denoising autoencoder 63.7 +/- 2.6 vs. non-local means 40.4 +/- 5.5). Denoised low-quality SRH images showed significant qualitative improvement and restoration of diagnostic histologic features.





Conclusion. Here, we demonstrate how our weakly supervised denoising method can be used to improve the quality of SRH using a large, unpaired clinical dataset. Our model performed better than denoising autoencoders as measured by both reference and non-references quality metrics. Importantly, our model outperformed autoencoders by an increasing degree as the quality of the image decreased (σ^2 = 20, 40, 80). Our method provides a means of improving histopathological diagnostic accuracy by decreasing the level of low-quality or nondiagnostic data that can result from using Raman scattering as a contrast mechanism for optical imaging. While our method was validated in the context of neuro-oncology, many of the diagnostic features in brain tumors are found in other malignancies. We describe a general method that can be applied to any clinical SRH dataset to improve the diagnostic power of intraoperative label-free optical microscopy.