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

Esteban Urias, MHS[1], Christopher Freudiger, PhD[2], Daniel Orringer, MD[3] Honglak Lee, PhD[4], Todd Hollon MD[1]

[1] Department of Neurosurgery, University of Michigan [2]Invenio Imaging, Inc., [3]Department of Neurosurgery, New York University, [4]Computer Science and Engineering, University of Michigan

*Correspondence: uesteban@med.umich.edu

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.

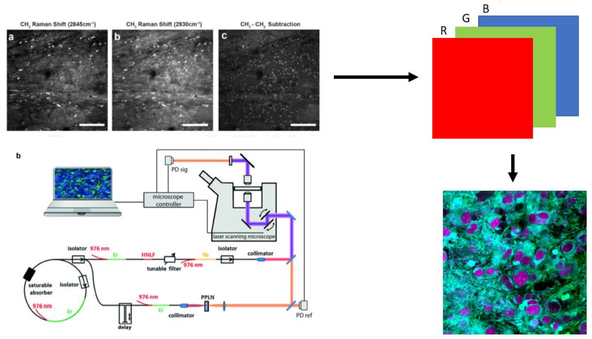


***Figure 1**: SRH signal capture and image generation.* By measuring different wavelengths of the Raman shifts, this modality is able to capture a CH2 signal corresponding to lipids, CH3 signal corresponding to protein, and the CH3 minus CH2 signal corresponding to nuclei. We combine these three signals into a three channel RGB image to produce an image like the one shown.

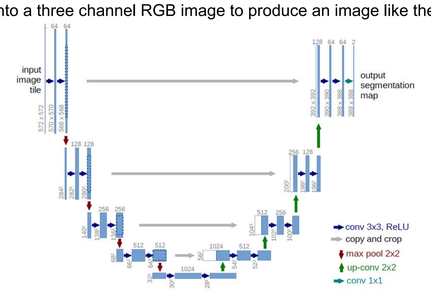


***Figure 2**:* U-net architecture. In general, it consists of downsampling encoder and upsampling decoder regions joined by skip connections at each level. Input and output have dimensions 256x256x3 pixels.

Objectives

- We propose a solution to the problem of denoising SRH images using a training algorithm that leverages weak supervision based on perceptual image quality ratings.
- Our goal is to restore low-quality and nondiagnostic SRH images without the need for paired training data.

Dataset

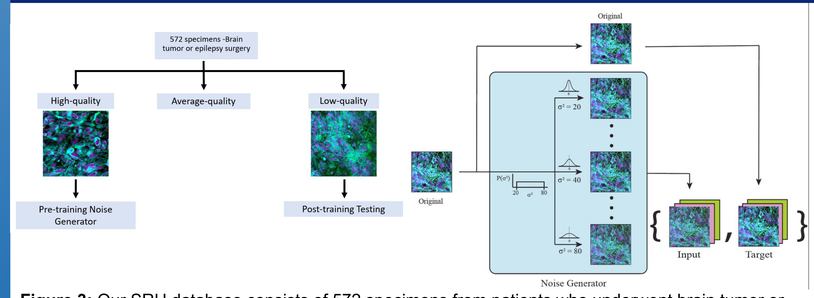


Figure 3: Our SRH database consists of 572 specimens from patients who underwent brain tumor or epilepsy surgery. The images were split into three groups based on their perceptual quality as rated by a trained neuropathology specialist: low-quality, average-quality, and high-quality. Training and validation 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.

Results

Trained network results on High Quality Images

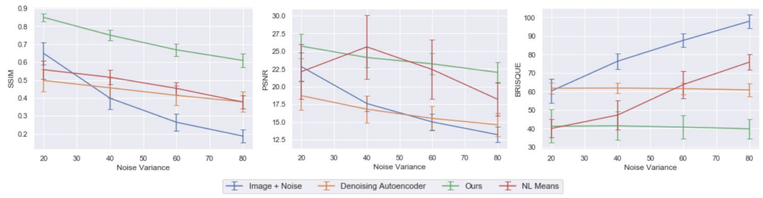


Figure 4: Paired noisy and target images were then used to train a deep denoising neural network with a U-Net architecture. Reference image quality metrics, including peak signal-to-noise ratio (PSNR) and structural similarity index (SSIM), and a non-reference image quality metric, named BRISQUE, were used to compare the performance of our model versus a deep denoising autoencoder. Using 1,000 patches from the high-quality group test set with varying levels of Gaussian noise, our model achieved a higher SSIM, mostly higher PSNR, and mostly lower BRISQUE scores compared to the denoising autoencoder and non-local means algorithm. Higher SSIM, higher PSNR, and lower BRISQUE scores are associated with higher image quality.

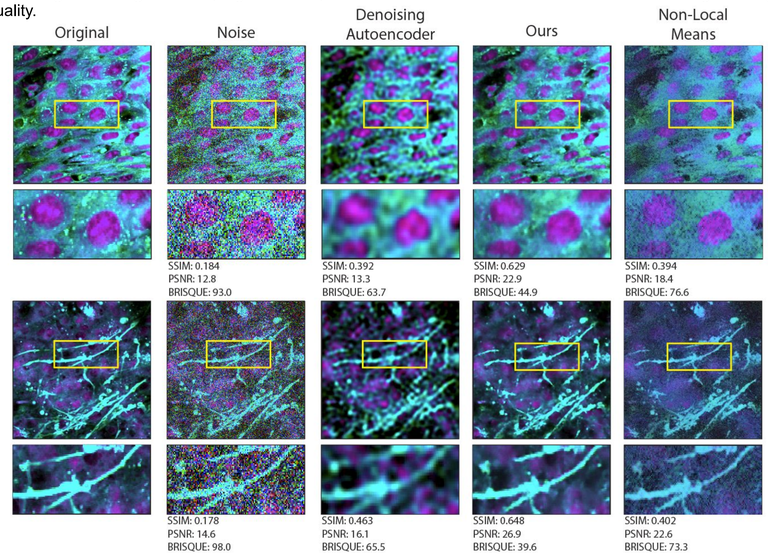
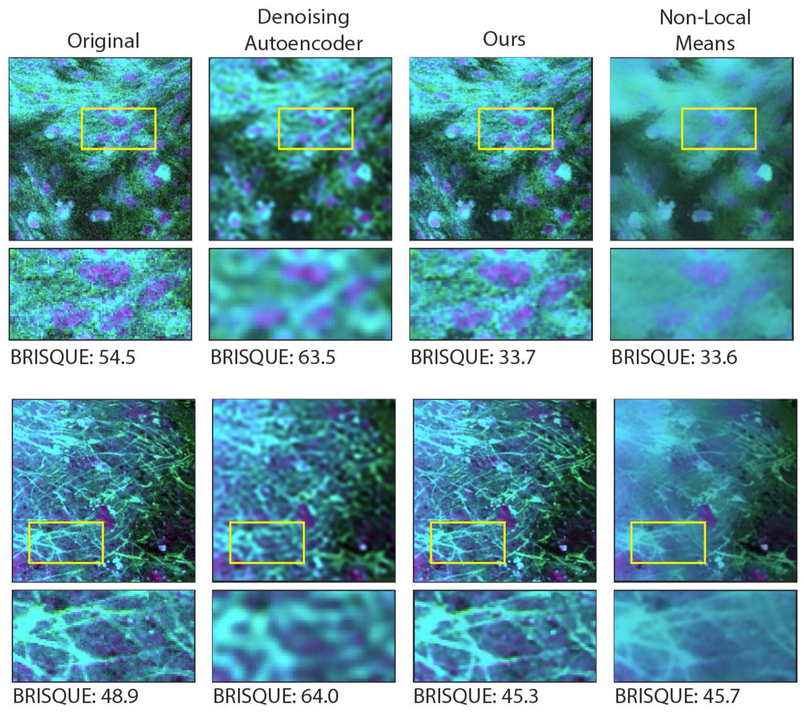


Figure 5: Denoised high-quality SRH images with artificially generated noise showed significant qualitative improvement and restoration of diagnostic histologic features, including nuclear chromatin patterns and axon-like structures.

Trained network results on Low Quality Images

Figure 6: Using unmodified images from the low-quality group, our model achieved a lower BRISQUE score compared to the original low-quality image, the denoising autoencoder, and non-local means algorithm. Denoised low-quality SRH images showed significant qualitative improvement and restoration of diagnostic histologic features.

	BRISQUE Score
Image + Noise	41.3 +/- 6.4
Denoising Autoencoder	63.7 +/- 2.6
Ours	36.3 +/- 8.5
Fast Non-Local Means	40.4 +/- 5.5



Conclusion

- Our network outperformed other learning and non-learning denoising methods in restoring SRH images.
- We generated our own paired dataset by leveraging weak supervision based on perceptual image quality ratings.
- This has been validated for neuroncology but could be expanded to include other malignancies that share similar diagnostic features.

References

- Ronneberger, Olaf, Philipp Fischer, and Thomas Brox. "U-net: Convolutional networks for biomedical image segmentation." *International Conference on Medical image computing and computer-assisted intervention*. Springer, Cham, 2015.
- Hollon, Todd C., et al. "Near real-time intraoperative brain tumor diagnosis using stimulated Raman histology and deep neural networks." *Nature medicine* 26.1 (2020): 52-58.
- Hollon, Todd C., et al. "Rapid, label-free detection of diffuse glioma recurrence using intraoperative stimulated Raman histology and deep neural networks." *Neuro-Oncology* (2020).
- Khalsa, Siri Sahib S., et al. "Automated histologic diagnosis of CNS tumors with machine learning." *CNS oncology* 0 (2020): CNS56.