

Quantifying microvascular alterations due to a pharmacological agent.

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Abstract — A study of the effects of pharmacological agents such as carbon monoxide releasing molecules (CORM2) on skeletal muscle microvasculature may uncover novel treatments. This study used intravital microscopy imaging data obtained from rat skeletal muscle. The imaging data was processed to extract microvascular networks before and after application of CORM2. It was found that CORM2 augments capillary radius, as well as leads to capillary recruitment, factors that improve tissue oxygenation. However, our preliminary data also shows that it may additionally augment undesirable network heterogeneity.

Clinical Relevance — Biophysical quantification of micro-vascular alterations due to biochemical stimulation will permit development of novel pharmacological therapies and highlight associated risks.

I. INTRODUCTION

Diseases such as sepsis and diabetes affect microvasculature throughout the body deleteriously. Novel pharmacological treatments are required to effectively treat the conditions. However, pharmacological agents themselves may present additional risks that must be assessed prior to drug development. This study processes microvasculature data emerging from an intravital microscopy imaging study.

II. METHODS

In previous experiments, intravital microscopy generated 23 videos of rat muscle vasculature, spanning 1000 x 1000 microns over 30 minutes. CORM2 was administered to each animal approximately 10 minutes into the observation.

The videos were processed using FiJi-ImageJ semi-automatically. Using a combination of multi-thresholding and available segmentation methods, vessel networks were skeletonized. The skeletons were overlaid with the images to permit manual measurement of representative radii. The networks were refined to retain vessels that has red blood cells.

III. RESULTS

Figure 1, A shows representative network from the same animal before and after administration of CORM2. The effects of CORM2 were to dilate capillaries, recruit additional

capillaries. The data indicates an increased capillary flow heterogeneity as some functional vessels did not have flow in them post CORM2 treatment.

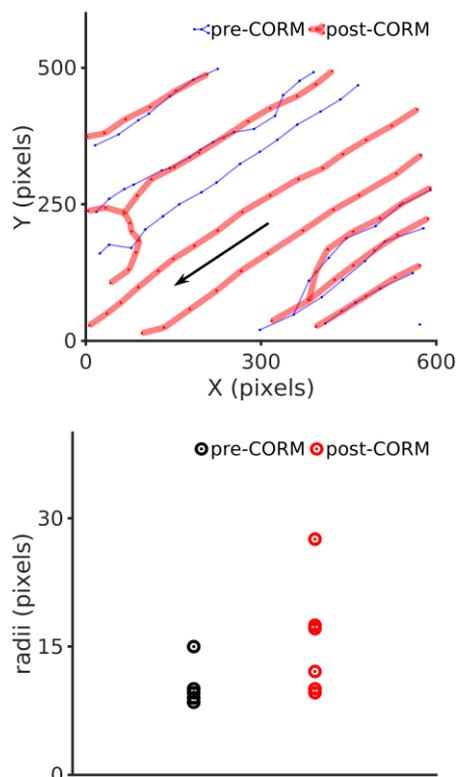


Figure 1. Semi-automatically segmented microvasculature networks in a small region of interest. A: Networks from the same rat prior to CORM2 treatment (blue) and after CORM2 treatment (red). The black arrow shows the direction of red blood cell movement. B: Representative radii from the two networks before (black) and after (red) CORM2 treatment.

IV. DISCUSSION & CONCLUSION

Quantification of the network will reveal structural properties, and permit assessment of tissue oxygenation.

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