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Publication Date

2015

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Characterizing Fibrosis in Mouse Kidney Using Fluorescence Lifetime and Second Harmonic Generation Imaging Microscopy in Unilateral Ureteral Obstruction Model

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Abstract

Renal tubulointerstitial fibrosis is considered to be the final common pathway for most forms of chronic kidney disease (CKD). Fibrosis has been traditionally characterized by histological studies such as Picro–Sirius Red (PSR) staining, Masson Trichrome staining or collagen immunohistochemistry. Such methods are limited due to variability in staining and pathologist scoring. The goal of this study is to compare histologic measures of renal fibrosis to Fluorescence Lifetime Imaging (FLIM) and Second Harmonic Generation (SHG) techniques in our deep tissue imaging microscope called DIVER. Male C57Bl6 mice were subjected to unilateral ureteral obstruction (UUO), a well–characterized model of fibrosis. At 21 days, both kidneys were collected. Serial sections of both kidneys were analyzed by PSR staining or FLIM with SHG. Quantification of a whole kidney section from the PSR staining showed $34.32\pm0.99\%$ area of fibrosis in the injured kidney compared to $5.55\pm1.07\%$ in the control kidney. Using the Phasor approach to FLIM, comparisons between the two kidneys show that the auto fluorescence lifetime signature give rise to two well separate phasor clusters. Quantification of ten different fields of view for each kidney from SHG suggests the presence of more collagen I in the diseased kidneys ($17.44\pm4.21\%$ compared to $2.59\pm1.98\%$ control kidney). In conclusion, the combined FLIM and SHG images let us establish a criterion for quantitative determination of fibrosis directly from the microscope images.