Serial 2-photon imaging of the kidney reveals the dynamics of kidney fibrosis after acute injury

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Intravital Multiphoton Microscopy (MPM) is a powerful imaging modality for the investigation of renal pathophysiology in mice [1]. It uniquely allows to assess renal function and morphology at the same time and in the living animal. Following the implementation of an Abdominal Imaging Window (AIW) [2], it is possible to assess the same kidney regions by MPM serially for up to several weeks and to obtain longitudinal information regarding cellular behavior and changes in tissue structure.

Fibrosis is believed to play a key role in chronic kidney disease (CKD) onset and progression [3]. To halt CKD, inhibition of fibrosis has been explored both experimentally and in clinical trials. However, evidence for direct harmful effects of fibrosis is limited, as its close association with tissue injury hampers distinguishing between correlation and causation.
To investigate if fibrosis accelerates kidney injury through deterioration of injury-adjacent uninjured nephrons, we applied serial in vivo microscopy of transgenic mouse kidneys in two models of focal injury and used genetic lineage tracing to track renal fibroblasts at the interphase of injured and uninjured tissue over time. We demonstrate that fibroblast recruitment occurs reversibly, locally restricted, and injury-dependent.

Here, we use serial in vivo MPM to decipher tubular and interstitial remodeling processes after AKI over time and demonstrate important insights into the mechanisms of AKI-CKD transition.

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