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DETECTION OF DIFFUSE AND FOCAL CARDIAC FIBROSIS IN MOUSE PRESSURE-OVERLOAD HYPERTROPHY USING MRI T1 MAPPING

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Introduction Diffuse interstitial fibrosis is present in diverse cardiomyopathies and is associated with poor prognosis. Current fibrosis quantitation is through invasive biopsy sampling which is not representative of the whole heart. Here we investigated the accuracy and sensitivity of MRI based T1 mapping for detection of diffuse cardiac fibrosis in a pressure overload mouse model generated by transverse aortic constriction (TAC).

Methods and Results Mice (12 week old male C57Bl6) were subjected to TAC (n=14) or sham (n=8) surgery. The angiotensin II receptor blocker Losartan was given to half the mice in the drinking water (1g/L) for the duration of the study. MRI was performed using a 9.4 T MRI system (Agilent) at 7 and 28 days and showed elevated left ventricular mass, increased end diastolic and systolic volume, and decreased ejection fraction in TAC groups. Late gadolinium enhanced MRI detected signal enhancement at the point of right ventricular insertion into the left ventricle in the majority of TAC mice, representative of focal areas of fibrosis as confirmed by Sirius Red staining of tissue sections. The extracellular volume fraction (ECV), calculated from pre and post gadolinium contrast T1 measurements, was elevated after TAC and directly correlated with histological measurement of collagen volume fraction from Sirius Red stained heart sections. Losartan treatment reduced dysfunction in TAC mice and lessened the increase in ECV and collagen volume fraction.

Conclusion We show for the first time that cardiac MRI can detect reduced cardiac function and focal, as well as diffuse cardiac fibrosis in mice 28 days after TAC. These changes were reduced by standard pharmacological therapy and supported by histological analysis. T1 mapping offers an accurate and sensitive measurement of diffuse fibrosis in a clinically relevant animal model and can be used to monitor novel therapeutic strategies. animal model and can be used to monitor novel therapeutic strategies.