Introduction: Crohn’s disease causes chronic transmural bowel wall inflammation, which often leads to luminal narrowing. Chronic inflammation leads to deposition of collagen in the bowel wall. Magnetization transfer (MT) MRI is sensitive to water interacting with large macromolecules such as collagen. Our previous work demonstrates that MT helps detect the presence of collagen in the bowel wall in an animal model of Crohn’s disease (1). Anti-TNF-α has been shown to reduce inflammation in murine (2) and human (3) Crohn’s disease. In this work, we study rats treated with rat-specific anti-TNFα to determine if MT can detect differences in the development of fibrosis with and without treatment.

Methods: Adult female pathogen free Lewis strain rats underwent laparotomy. Purified peptidoglycan-polysaccharide (PG-PS) was injected intramurally (12.5 μg rhamnose/gm body weight; 0.05 ml/injection site) into standardized locations in the cecum, distal ileum and Peyer’s patches. PG-PS injected rats develop early-phase inflammation at the injection sites in the first 24 hours, followed by a late-phase typified by late-phase inflammation and intense fibrosis beginning at approximately 14 days post-laparotomy. By 21 days post-laparotomy, rats develop bowel wall thickening, intra-abdominal adhesions, and granulomas studded throughout the bowel, liver and spleen. Human Serum Albumin (HSA) injected control animals developed less late-phase inflammation than untreated rats (17.79±6.24 vs. 7.06±0.73; p=7.7E-07). There was a trend toward decreased pro-inflammatory cytokines in anti-TNFα treated rats including IL-1 (5.63±1.54 vs. 10.27 ± 1.74; p=0.028), IL6 (23.60 ± 9.42 vs. 9.19±1.09; p=0.0000). Pro-fibrotic factors were less in anti-TNFα treated rats including procollagen I (2.93±0.67 vs. 9.19±1.09; p=0.000019), and procollagen III (2.19±0.34 vs. 7.06±0.73; p=7.7E-07). There was a trend toward decreased pro-inflammatory cytokines in anti-TNFα treated rats including IL-1 (5.63±1.54 vs. 10.27 ± 1.74; p=0.028), IL6 (23.60 ± 9.42 vs. 9.19±1.09; p=0.000019), and TNFα (2.40 ± 0.41 vs. 3.09 ± 0.44; p = 0.13). MTR correlates with concentration of type III collagen (R² = 0.39 p < 0.0001 n = 38).

Results: PG-PS rats treated with anti-TNFα (n=15) developed lower gross gut scores than untreated (n=11) PG-PS rats (3.87±3.02 vs. 12.53±3.70, p=6.1E-08) (Fig.1). MTR of anti-TNFα treated rats were significantly lower than untreated rats (17.79±6.24 vs. 27.95±5.80; p=0.0001) (Fig 2.). Gross gut scores correlate with MTR (rho=0.91) (Fig.3).

Discussion: We have demonstrated that MT is sensitive to changes in fibrosis that occurs with anti-TNFα treatment. These findings support MT as a non-invasive method for detecting and quantifying intestinal fibrosis.