

Supporting Information (SI)

Title: Simultaneous molecular MRI of extracellular matrix collagen and inflammatory activity to predict abdominal aortic aneurysm rupture

Author list: Lisa C. Adams, Julia Brangsch, Carolin Reimann, Jan O. Kaufmann, Rebecca Buchholz, Uwe Karst, Rene M. Botnar, Bernd Hamm, Marcus R. Makowski

Figures

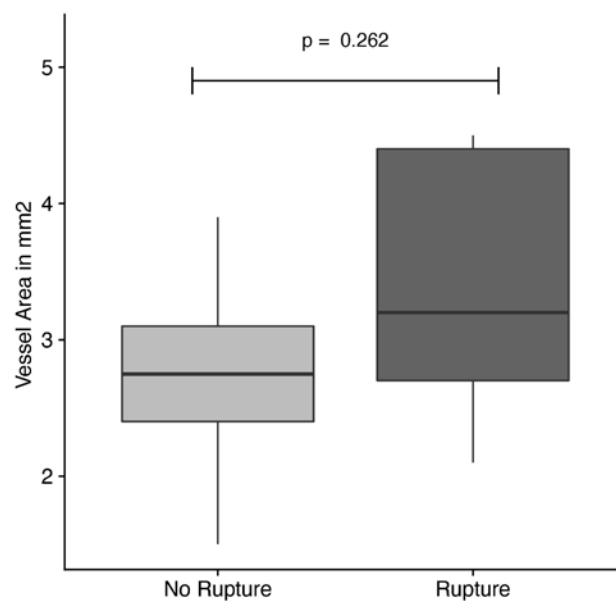


Figure S1. Differences in vessel area (mm²) between stable and rupturing AAAs. There was no significant difference (p=0.262).

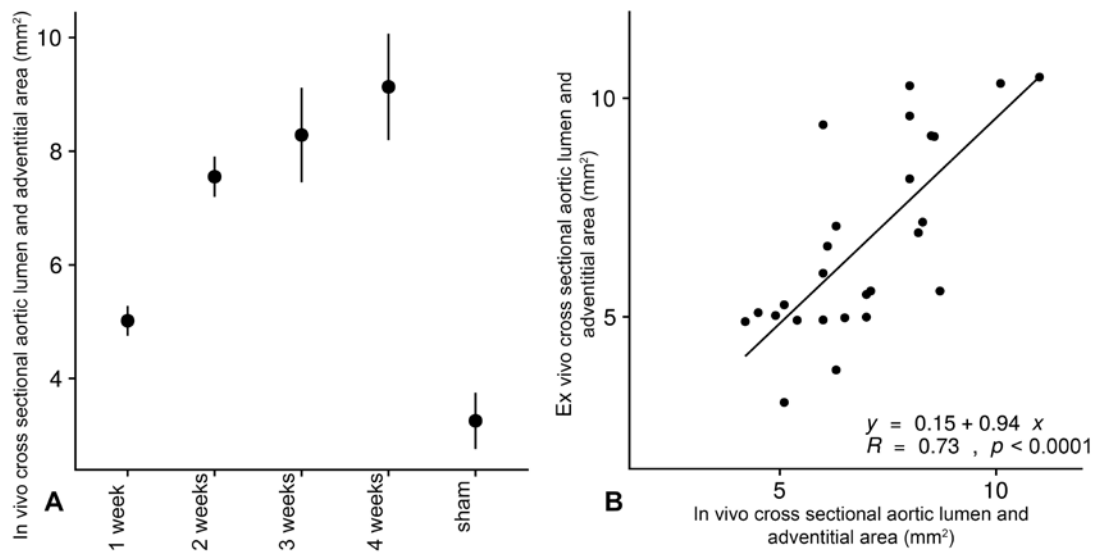


Figure S2. In vivo and ex vivo measurements of the aneurysmal adventitial area. A) In vivo MR measurements revealed an increase in the aneurysmal adventitial areas (mm²) over the course of four weeks with continuous Angiotensin II release, which can be seen as an indicator for aneurysm development. B) In vivo MR measurements furthermore showed a close correlation with ex vivo measurements on cryosections with a correlation coefficient of R=0.73.

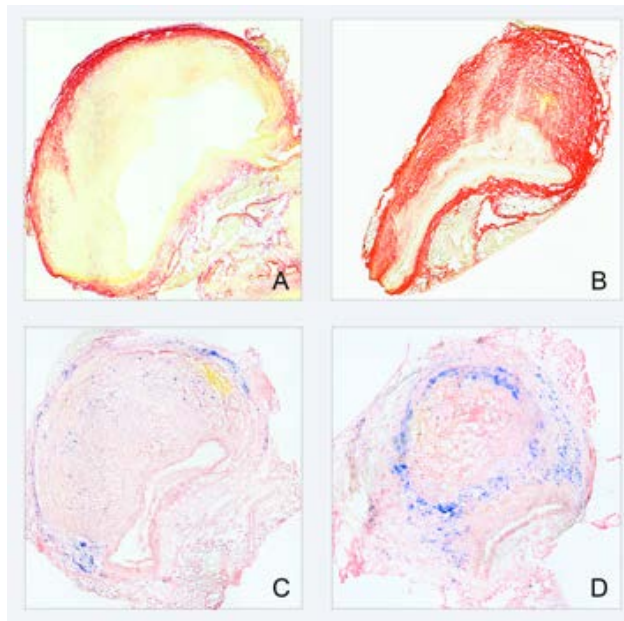


Figure S3. Different collagen and iron content observed by histology. A, representative image of a collagen-poor four-week old aneurysm. B, representative image of a collagen-rich two-week old aneurysm. This correlated with the different enhancement patterns observed by MRI, also with regard to the longitudinal study. C and D, representative images of a two-week-old aneurysm with comparatively low (C) and a four-week-old aneurysm with high (D) iron content, indicative of macrophage activity and inflammatory processes.

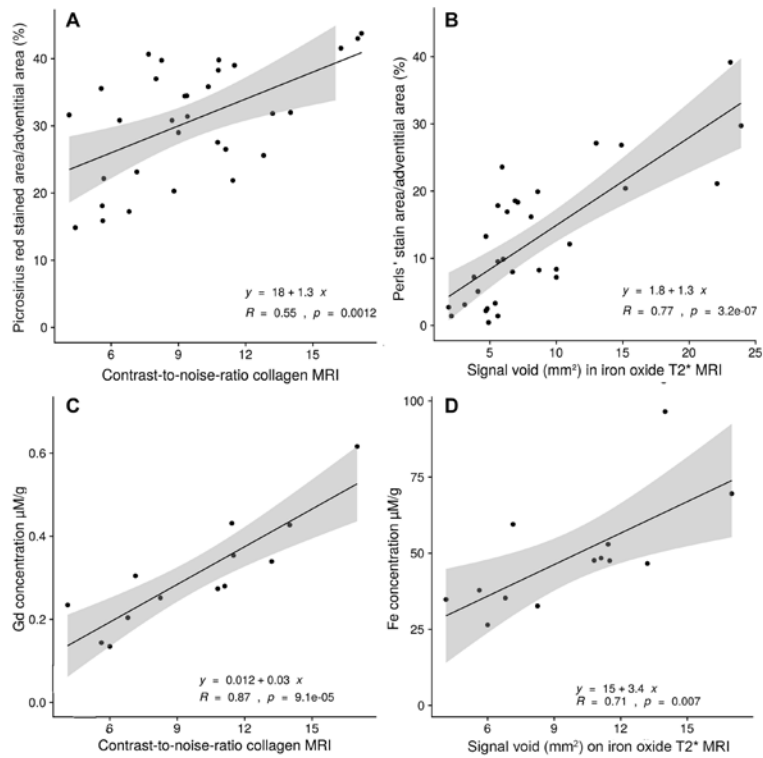


Figure S4. Correlation of *in vivo* and *ex vivo* measurements. *A*) *In vivo* CNR measurements after injection of the collagen-specific probe showed a moderated correlation with *ex vivo* histological Picrosirius Red-stained sections. *B*) *In vivo* measured areas of T2* signal voids (mm²) strongly correlated with histological measurements on Perls' Prussian-Blue-stained sections. *C*) ICP-MS revealed a strong correlation between gadolinium concentration and *in vivo* CNR measurements after the injection of the collagen-targeted probe. *D*) A strong correlation was also observed between the iron concentration as determined by ICP-MS and the size of the T2* signal voids following the administration of the iron-oxide particles. In summary, these measurements indicate a moderate to strong agreement between *in vivo* and *ex vivo* measurements of the collagen specific probe and the iron oxide particles. *Abbreviations:* CNR: Contrast to noise ratio; ICP-MS: Inductively coupled mass spectroscopy.

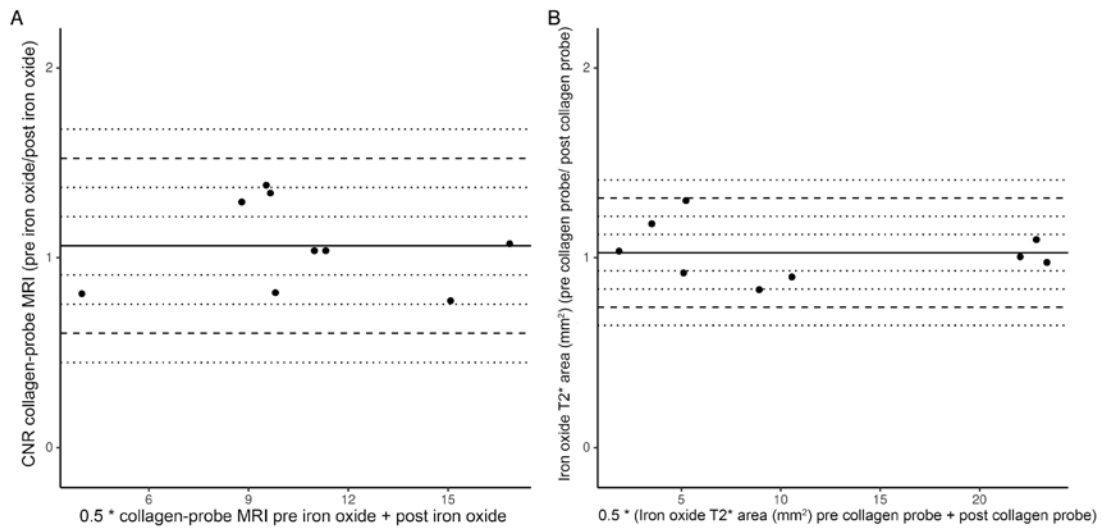


Figure S5. Effect of both imaging probes on the visualization of each other. *A)* To evaluate the potential influence of iron-oxide particles on the assessment of the collagen-targeted probe, T1-weighted MRI was performed prior and 24 hours after the injection of iron-oxide particles. An excellent correlation of CNR measurements prior to and after the injection of iron-oxide particles could be demonstrated (ICC= 0.99 (95% confidence interval: 0.97-0.99)). *B)* T2*-weighted MRI was also performed prior to and after the injection of the collagen-targeted probe in order to investigate a potential effect of the collagen-targeted probe on the evaluation of the iron-oxide particles. These measurements showed a good correlation with an ICC of 0.82 (95% confidence interval: 0.40-0.96). *Abbreviation:* CNR: contrast-to-noise-ratio.

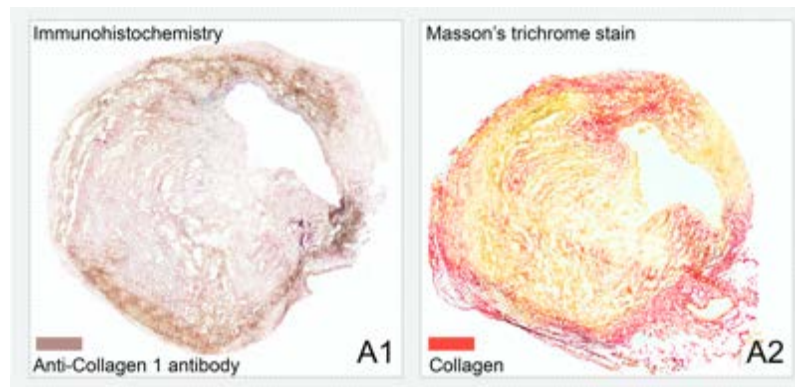


Figure S6. Ex vivo immunohistochemistry and picrosirius red staining. A1, anti-collagen-1-antibody staining and B1, picrosirius red staining for visualization of collagen fibers, confirming the co-localization of collagen-1-specific immunohistochemistry with picrosirius red staining. Areas positive for collagen 1 in immunohistochemistry correspond well to the red areas highlighted by Picrosirius red staining.