MRI of colon wall thickness - a biomarker in experimental mouse inflammatory disease?

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MRI is emerging as an alternative technology to monitor patients with ulcerative colitis or Crohn's disease (Ajaj VM et al; Maccioni F et al., 2005). Inflammatory biomarkers in inflammatory bowel disease (IBD) are needed that can be used in man as well as in experimental animals in *e.g.* evaluation of putative drugs. Previous studies have observed increased colon wall thickness *in vivo* in IBD patients by using computed tomography and MRI. The aim of the present study was to investigate if colon wall thickness, measured *in vivo* by using MRI, can reflect inflammation in an experimental mouse colitis model.

Materials and Methods: Acute and chronic colonic inflammation were chemically induced by exposing animals to 3% dextran sulphate sodium (DSS) in the drinking water during five days (Melgar et al., 2005). Imaging was performed 5 (reflecting acute inflammation) or 21 days (reflecting chronic inflammation) after DSS exposure. MR scanning was performed on a 4.7 T BioSpec (Bruker, Germany). Respiration was tracked by a small pressure sensitive pad on the abdomen connected to a computer controlled monitoring system (SA Instruments, USA). The colon anatomy was outlined with a 3D fat saturated T2w RARE with 0.13x0.13x0.2 mm^3 resolution (TR=2500 ms, TE=58 ms). The data was acquired at end expiration. Buscopan® (5 mg/kg, i.p.) was administered to minimize peristalsis prior acquisition of data. After imaging, colonic inflammation was subjectively assessed using the following scores: stiffness (0-2), oedema (0-3), visible ulcerations (0-1) and thickness (0-4). Based on these scores, an overall score was obtained, with the maximal score being 10. The colon wall thickness, measured with MRI, was defined as an average of three slices located approximately 10, 20 and 30 mm from the rectum, at three equally spaced positions per slice. Moreover, colon wall thickness was measured in corresponding histological sections. Serum haptoglobin levels served as a systemic inflammatory marker.

Results: A significant increase of colon wall thickness was observed *in vivo* in acutely ($P<0.01$, ANOVA, Tukey´s test) and chronically inflamed animals ($P<0.01$, ANOVA, Tukey´s test) compared to healthy mice, a finding also observed histologically (figure 1). Colon wall thickness in acutely and chronically inflamed animals were also significantly correlated with the inflammation colonic scores assessed *ex vivo* after the imaging session ($r=0.79$, $P<0.001$, figure 2). Furthermore, haptoglobin levels in healthy and inflamed mice were significantly correlated with colon wall thickeness ($r= 0.81$, $P<0.001$, Spearman rank correlation).

Discussion: Our results show that MRI can be used to depict healthy mouse colon as well as experimental colitis, and that colon wall thickness may be used to reflect inflammation in experimental colitis. Colon wall thickness may be a useful biomarker in validation of candidate drugs in longitudinal studies from mice to man. However, future studies are needed to reveal if colon wall thickness may be a biomarker that can respond to pharmacological treatment.

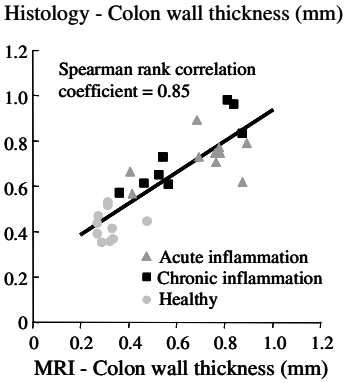

Figure 1. Mouse colon wall thickness measured with MRI *in vivo*, and correlation with colon wall thickness in corresponding histological sections.

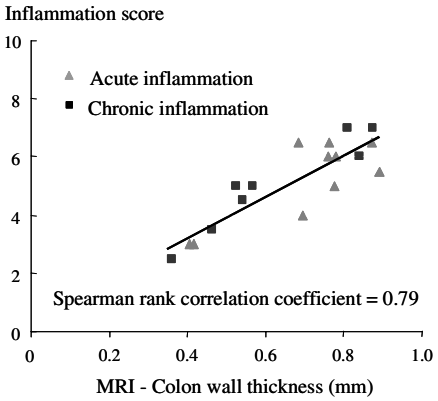

Figure 2. Colonic inflammation score assessed subjectively *ex vivo* correlated to colon wall thickness measured *in vivo* by using MRI.

References

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