19F MRI of Colitis-Associated Colon Cancer (CACC) in a Murine Model of Inflammatory Bowel Disease

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Target Audience: This study is for MRI researchers interested in tracking inflammatory processes that precede the development of cancer.

Purpose: Inflammatory bowel diseases (IBD) significantly increases the risk of colitis-associated colon cancer (CACC), and previous studies have shown that longevity and severity of inflammation are directly correlated with the risk of CACC1,2. However, these studies were based on colonoscopy and mucosal biopsy, invasive diagnostic methods that cause patient discomfort and sampling errors. The aim of this study is to non-invasively image inflammatory sites and the subsequent formation of premalignant lesions. To this end, perfluorocarbon (PFC) emulsions and 19F MRI were used to longitudinally follow the inflammatory sites and visualize the onset of CACC development in the colon of an IBD mouse model.

Methods: IBD-driven CACC model: The protocol developed by Neufert et al. was followed3. Five female AJ mice (8 wk, 18-20g) were treated with an intraperitoneal injection of azoxymethane (AOM, 10mg/kg) on day 0 and fed with 2.5% (w/v) dextran sodium sulfate (DSS) solution every 3 weeks until week 7 (Fig. 1). PFC injection: 200μl of perfluoro-15-crown-5-ether emulsion (Celsense Inc., VS-580H) was injected through the tail vein 48 hours before the first MRI.

In vivo & ex vivo imaging: In vivo MR imaging was performed periodically from day 50 to day 120 using a 11.7T Bruker Scanner and a double tuned 20 mm 19F/1H transceiver coil (Bruker Biospin). 1H images were acquired using a fast spin echo sequence (RARE, TR/TE=1200/30 ms, Matrix size=256x256, FOV=3.2cm x 2cm, Rare Factor=8, Slice Thickness=2mm). 19F MR images were acquired using the same FOV and slice thickness using a fast spin echo sequence (RARE, TR/TE=1000/14ms, Matrix size=64x32, rare factor=8). After in vivo imaging, the colons were excised and fixed in 4% paraformaldehyde. Ex vivo images were acquired with a 750 MHz microimaging system and a 25mm 19F-1H/17O double channel volume coil (Bruker Biospin). Colon tissues were cut longitudinally after MR imaging for histological evaluation of CACC development.

Results and Discussion: 19F signals could be detected in the colon wall after the onset of IBD (Fig.2). Since PFC emulsions label macrophages with high specificity4,5, these signals are derived from macrophages that have infiltrated the colon wall as a result of inflammation driven by DSS. The 19F signal in the colon wall steadily decreased over time. CACC tumor outgrowths were observed from d80 on at the inflammatory sites. In vivo data were validated by ex vivo imaging of excised colon tissues that enabled us to exactly co-localize the inflammatory sites and tumor mass (Fig.3). As the colon tissues were examined longitudinally, several tumors could be observed, specifically arising from the regions with 19F signals.

Conclusion: We demonstrated the feasibility of 19F MR imaging to non-invasively visualize inflammatory lesions leading to the formation of CACC tumor growths. Both in vivo and ex vivo images show the inflammatory sites on the colon wall, and the CACCs were detected growing from within those inflammatory sites. Future studies will tell if the 19F signal intensity can be used as a surrogate marker for premalignant lesion formation.

References