Development of Nanoparticle-Based Magnetic Resonance Colonography

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Objectives: The aim of this study was to develop a novel nanoparticle-based magnetic resonance (MR) colonography technique, which enabled us to generate contrast-enhanced MRI of the colonic walls via transrectal administration of MR-visible nanoparticles.

Methods: We produced two types of colonic-absorbable solid lipid nanoparticles (SLNs) by loading the SLNs with (a) gadolinium diethylenetriaminepenta acetic acid (Gd-DTPA for MRI) to construct Gd-SLNs; and (b) otcadecylamine-fluorescein isothiocyanate (ODA-FITC for histologic confirmation) to construct Gd-FITC-SLNs. Via a series of in vitro experiments, we first evaluated the size distribution and Gd-DTPA entrapment efficiency of these SLNs. For in vivo validation, thirty mice were randomly divided into different study groups based on transrectal enema with various SLNs and control agents, including (i) Gd-SLNs (40 mg/ml, n=6); (ii) Gd-FITC-SLNs (40 mg/ml, n=6); (iii) blank SLNs (40 mg/ml, n=6); (iv) Gd-DTPA (10 mg/ml, n=6); and (v) water (n=6). MR colonographies using T1-weighted fluid-attenuated inversion-recovery (FLAIR) sequence (TR/TE/TI, 3000/20/800) were then performed to detect various SLNs, compared to different control agents, in the colonic walls. MRI findings were correlated with subsequent histological confirmation.

Results: In vitro studies showed that the size distribution of SLNs ranged at 50-300 nm with their Gd-entrapment efficiency at approximately 56%. Of in vivo studies, MRI demonstrated bright enhancement of colonic walls with decreased T1 relaxation times in all mice treated by transrectal infusions of Gd-SLNs or Gd-FITC-SLNs. Fluorescent microscopy localized the delivered Gd-FITC-SLNs in both extracelluar spaces and cytoplasms, appearing as highly-concentrated green fluorescent spots distributed through all layers of the colonic walls (Figure 1).

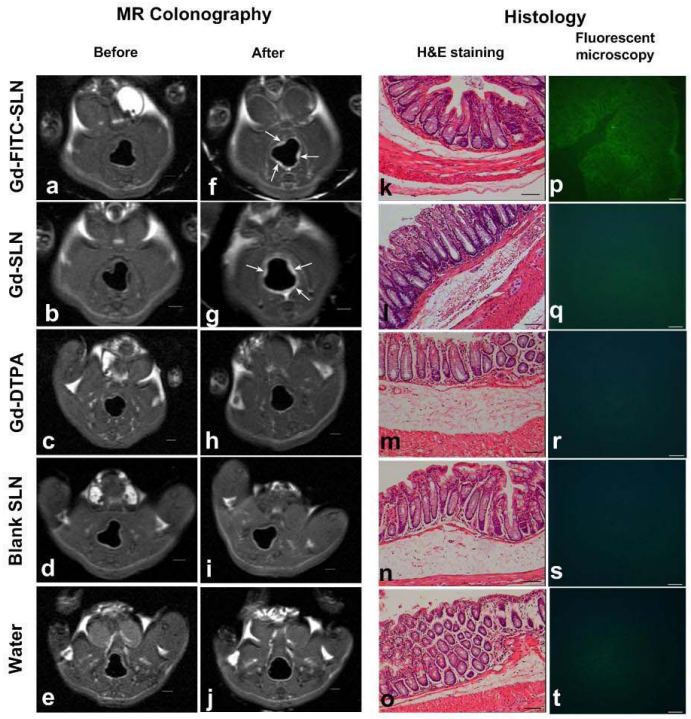

Figure 1. (a-j) Axial MR colonographies of the mouse rectums with T1-weighted FLAIR sequence (TR/TE/TI, 3000/20/800) before (a-e) and 20 minutes after (f-j) intracolonic administration of Gd-FITC-SLNs (a&f), Gd-SLNs (b&g), Gd-DTPA-only (c&h), blank SLNs (d&i), and water (e&j). MR colonographies show contrast enhancement (arrows on f&g) of the rectal walls after intracolonic administration of Gd-FITC-SLNs and Gd-SLNs. This finding is not seen in the three control groups with Gd-DTPA-only (h), blank SLNs (i), and water (j). (k-t) Corresponding histological confirmation with H&E staining (k-o) and fluorescent microscopy (p-t) among different animal groups with various treatments of Gd-FITC-SLNs (k&p), Gd-SLNs (l&q), Gd-DTPA (m&r), blank SLNs (n&s), and water (o&t). Fluorescent microcopy reveals green fluorescent signals only in Gd-FITC-SLNs-treated tissues (due to FITC emission, image p), which is not visualized in other four control groups. This finding indicates the successful infiltration of SLNs to the colonic wall via the intracolonic enema approach.

Conclusion: This study establishes the "proofs-of-principle" of a new imaging technique — nanoparticle-based MR colonography by combining the advantages of both MR technology and nanotechnology. Nanoparticle -based MR colonography may open new avenues for efficient management of colorectal diseases.

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