A Novel Gd-Sucrose Scaffold for Oral Administration in MR-Colonography at 7 T

Published date: May 27, 2014

Technology description

Approximately 50,000 people died of colon cancer annually, making it the second leading cause of cancer morbidity in the United States. This has led the American Cancer Society to recommend regular colonoscopy for people over 50, as a means of early detection. However compliance has been underwhelming due to the invasive and unpleasant nature of the screening and prepatory phases. A less invasive method of early cancer detection has been developed using a Gadolinium-DOTA-sucrose-derived agent taken orally. The molecule is trapped in the small bowel in healthy subjects (until rectally passed) but in subjects with colonic polyps or cancerous lesions, it disperses out of the colon possibly due to destruction of the mucosal layer and is secreted in the urine. Urine analysis can then be used to identify subjects with possible neoplasms in a non-invasive manner. The scaffold might also be linked to tumor targeted ligands to enhance MR colonography.

COMMERCIAL OPPORTUNITY

One in twenty people will develop Colorectal Cancer (CRC) in their lifetime. Early detection has been shown to greatly improve prognosis (5yr survival Stage I:87% vs. Stage IV:12%), and the American Cancer Society recommends that everyone have a colonoscopy every ten years starting at age 50. Even with these guidelines, only 40% of CRCs are detected early, as colonoscopy is expensive, invasive, and requires sedation and a cathartic bowel preparation, resulting in patient non-compliance.

The market is attractive as evidenced by the market capitalization of Exact Sciences of approximately $2B with what analysts are calling an addressable market of almost $1B. Exact Sciences' product Cologuard was just approved in August 2014, and looks at the methylation of NDRG4 and BMP3, KRAS point mutations and does an ELISA assay to determine the concentration of hemoglobin in a patient stool sample. However, there may be room for multiple products in this market particularly for products where the patients do not need to collect their own stools.

A patient can drink the Gadolinium-DOTA-sucrose-derived agent, and the presence of colonic lesions or cancer could be detected with a simple urine analysis, and substituting another lanthanide metal Europium for Gadolimium may result in an even more sensitive assay.

Methods such as CT and MR-colonography are emerging as non-invasive options, but also require a bowel cleanse, are insensitive to small polyps and (in CT) expose healthy subjects to undue radiation. However, better oral MRI contrast agents might also be developed by linking our Gadolinium-DOTA-

sucrose-derived agent to tumor targeted ligands. These molecules might build up at the tumor site, allowing for enhanced non-invasive imaging of previously undetectable small or flat polyps

TECHNOLOGY

A Gadolinium-DOTA sucrose-derived agent was synthesized with eight Gadolinium-DOTA chelates per sucrose and a molecular structure to induce stiffness and increase the rotational correlation time. For in vivo assessment, SCID mice were intra-rectally injected with human CRC cells. Then, the mice received the Gadolinium-DOTA sucrose-derived agent by oral gavage, which increased tumor visualization by 40% above MRI with no contrast agent. Only mice with tumors (n=4) showed traces of the Gd-DOTA sucrose molecule in the bladder, compared to control mice (n=3) with no signal.

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