An Ultrasound-Activated MRI Contrast Agent and Drug Delivery System

Published date: Jan. 15, 2010

Technology description

Tech Summary:We propose a new class of nanoparticles that can mask (via encapsulation) an MRI contrast agent or a therapeutic cargo, aggregate in a targeted tissue and then selectively release the cargo and/or activate MRI contrast upon treatment with ultrasound.
Technology Description:This nanoparticle technology is a platform technology with multiple applications such as the diagnosis and monitoring of vesicoureteral reflux disease (VUR) in children and targeted drug delivery to tissue.
Our nanoparticle is unique in the following ways:
• It contains a core that is radio-opaque, allowing for the imaging of tissue, including tumors, by X-ray or computed tomography.
• It has a protective shell that sequesters any cargo, such as a contrast agent or cytotoxin, from its environment. This shell can be selectively cracked open by applying an external source of energy such as ultrasound, to release its contents.
• The synthetic process of manufacturing these nanoparticles is such that the particles can be created to any given size with precision.
These properties enable simultaneous and targeted diagnosis and treatment of disease.VURis the improper flow of urine from the bladder up to the kidneys, which leads to kidney infection, scarring, renal failure and the need for dialysis and renal transplant. There are 50,000 new cases of VUR each year in the U.S.
The gold standard for diagnosis and surveillance of VUR is the voiding cystourethrogram (VCUG). This procedure uses X-rays with an iodinated contrast medium to image the retrograde flow of urine. Its use results in undesired radiation exposure to the gonads, which can have longterm negative effects. VCUG also requires a catheter to be placed through the urethra and into the bladder. This is extremely traumatic to children and their parents.
Some pediatric urologists advocate the use of nuclear voiding cystograms, which decrease patient radiation exposure by 10-fold, for follow-up studies. But most will use a VCUG as the initial study because it provides superior anatomic definition. According to the National Institutes of Health (NIH) 2006 Strategic Plan for Pediatric Urology, finding a catheter-free VCUG procedure is a national health research priority.

In this application, our gadolinium-containing nanoparticle has been designed to be sufficiently small to filter through the kidneys into the bladder in its masked and inactive state. Application of ultrasound to the bladder unmasks the gadolinium core, allowing the physician to monitor the flow of urine using MRI.

Our nanoparticle technology is used here to create a new contrast agent for VCUGs, leading to a novel system of detection that eliminates traumatic catheterizations and minimizes radiation exposure.

Cancer Therapy

Application in targeted drug delivery includes, but is not limited to, the delivery of chemotherapy. In this application, the nanoparticles are designed to take advantage of the enhanced permeability and retention (EPR) effect associated with cancer. Due to their rapid growth, tumors require the formation of large amounts of new blood vessels. However, these blood vessels are poorly constructed and porous. Similarly, the lymphatics, or waste system, are not well developed and do a poor job at removing the materials that have leaked out of the blood vessels and into the tumor beds. Leveraging the EPR effect is a proven viable approach allowing the nanoparticles to preferentially accumulate in the tumors over other parts of the body. The ability to deliver cytotoxins to the tumor bed will dramatically reduce systemic exposure to the cytotoxin, thereby decreasing the debilitating side effects. Cytotoxin efficacy can potentially increase by allowing for higher drug doses to be administered due to improved dose-related side effects.

Research Tool

Our nanoparticle can also be designed as a useful research tool to perform real time in vivo imaging of the biodistribution of a studied cargo.

Application area

VUR

Advantages

• Modular size of particles (5nm<200 nm): under 10nm the nanoparticles can pass through the kidneys and be safely voided
• Nanoparticles between 50 – 200 nm can optimize the EPR effect to selectively deliver drug to tumor beds
• Eliminates traumatic catheterizations
• Minimizes radiation exposure
• Mitigates systemic side effects
• Increases amount of drug being delivered to tumors

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