Glucose-conjugated magnetonanoparticles for visualization and treatment of neoplasms and neurological disorders by MRI

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SUMMARY

Researchers at the UCLA Semel Institute for Neuroscience and Human Behavior have developed magnetic nanoparticles (MNPs) functionalized with deoxyglucose that can be used as tissue-specific contrast agents for MRI. These novel MNPs can help physicians and researchers to differentiate neoplastic, epileptic, parkinsonian, or Alzheimer tissues from normal tissue based on the metabolic activity of the tissue.

BACKGROUND

A number of imaging techniques are currently used to diagnose, stage, and monitor neurological disorders and tumors, but each available technique has major drawbacks and limitations. For example, electroencephalograms (electric) and magnetoencephalogram (magnetic) are only sensitive to sources that are up to a few centimeters below the scalp surface and cannot detect epileptic sources of activity that are deeper in the brain parenchyma. Also, these methods rely on the presence of ictal or interictal activity, which may not be present at the time of recording. Electrocorticogram and depth-implanted electrodes, which are two additional electric-based detection techniques are invasive surgical techniques of considerable cost and cause discomfort in patients. For tumor detection and grading, radioactive techniques, such as positron emission tomography (PET), PET-CT, and single photon emission computed tomography, are often used. These techniques require radioactive substances that have short half-life times, are not widely available, and are limited in their usefulness as diagnostic techniques. Thus, a non-invasive method that allows for the accurate, high-contrast differentiation between disease tissue from (either cancer or neurological disorders) normal tissue would be greatly beneficial to patients and healthcare professionals.

INNOVATION

Researchers at UCLA Semel Institute for Neuroscience and Human Behavior have developed magnetic nanoparticles (MNPs) that have been functionalized and can be injected into the blood stream of a patient to differentiate anatomically and functionally, neoplastic, epileptic, parkinsonian, or Alzheimer tissues from normal tissue on MRI scans. This technology acts as a tissue-specific contrast agent for MRI that allows physicians and researchers to image normal and disease tissue based on their levels of metabolic and functional activity in order to supplement their diagnosis, prognosis, and treatment plan for the patient. The MNPs are designed to pass the blood brain barrier, which allows for imaging of the central nervous system, and have a long half-life, which makes it feasible to monitor development and progression of tissue changes over time without the need for renewed administration of the imaging agent. Further, disease-specific MNP derivatives have been produced by attaching additional functional groups, such as other single molecules, antibodies, carbohydrates, and polypeptides. The additional attachments could provide more specific tissue targeting or aid in treating the patient's condition. For example, MNPs equipped with levodopa, or L-DOPA, could be used to diagnose and aid in treatment of patients with Parkinson's disease.

APPLICATIONS

- Differentiating normal tissue from diseased tissue by MRI
- Grading the stage of cancer or other disease
- Guiding physician decisions about treatment
- Tracking efficiency of treatment (e.g. monitoring tumor progression and size)
- Predicting the likelihood that a given individual will develop or is at risk for a disease
- Targeted drug therapy
- Attaching additional moieties for targeted therapeutics

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INVENTORS

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OTHER INFORMATION

KEYWORDS

Medical Imaging, Epilepsy, Central Nervous System, Cancer, Oncology, magnetic resonance imaging, MRI, computed tomography, CT, positron emission tomography, PET, magnetic nanoparticles, functionalized nanoparticles, targeted therapeutics, blood-brain barrier

CATEGORIZED AS

- **Imaging**
  - Medical
- **Medical**
  - Diagnostics
  - Disease: Cancer
  - Disease: Central Nervous System
  - Imaging
  - Research Tools
- **Nanotechnology**
  - Tools and Devices

RELATED CASES

2008-030-0

- Particles could be modified to be compatible with computed tomography (CT) or PET scans
- Research applications (e.g. monitoring brain tissue while testing the effect of various external and internal stimuli)

ADVANTAGES

- Direct method to detect and image metabolically active (or inactive) tissues
- Can cross the blood brain barrier
- Long half-life (hours to days)
- Long shelf-life (6-12 months)
- Non-invasive and safe
- No surgery required
- No radioactive tracers required
- MRI equipment is already widely available in hospitals and clinics
- Could provide validated, targeted treatment (has the ability to monitor that the drug is delivered)

STATE OF DEVELOPMENT

The inventors have generated glucose-conjugated as well as over a a dozen other distinct -conjugated MNPs, and have used them to detect glioma, medulloblastoma, lung and colon cancers, Parkinson and Alzheimer diseases, and localize epilepsy in animal models.

RELATED MATERIALS

- Akhtari M, Bragin A, Cohen M, et al. Functionalized magnetonanoparticles for MRI diagnosis and localization in epilepsy. Epilepsia. 2008;49(8):1419-30.
- Akhtari M, Bragin A, Moats R, Frew A, Mandelkern M. Imaging brain neuronal activity using functionalized magnetonanoparticles and MRI. Brain Topogr. 2012;25(4):374-88.
- Akhtari M, Pope W, Mathern G, Moats R, Frew A, Mandelkern M. Functionalized magnetonanoparticles in visualization of intracranial tumors on MRI. Mol Imaging Biol. 2013;15(3):299-306.

PATENT STATUS

Country	Type	Number	Dated	Case
Belgium	Issued Patent	2265174	06/18/2018	2008-030
Switzerland	Issued Patent	2265174	06/18/2018	2008-030
Germany	Issued Patent	60 2009 052 661.8	06/18/2018	2008-030
Spain	Issued Patent	2265174	06/18/2018	2008-030
France	Issued Patent	2265174	06/18/2018	2008-030
United Kingdom	Issued Patent	2265174	06/18/2018	2008-030
Italy	Issued Patent	502018000025934	06/18/2018	2008-030
Netherlands (Holland)	Issued Patent	2265174	06/18/2018	2008-030
United States Of America	Issued Patent	9,011,913	04/21/2015	2008-030
United States Of America	Issued Patent	8,445,021	05/21/2013	2008-030

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Non-Invasive Method For Determination Of Tissue Electrical Conductivity
- Visualization of Alzheimer's Disease on MRI

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