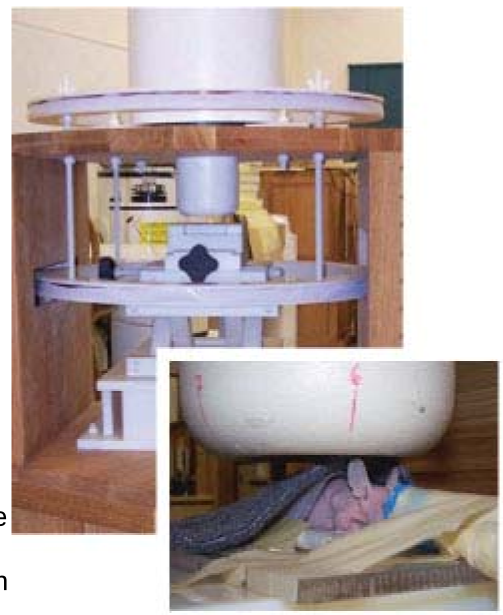
FULL STORY

Detecting, Treating Cancer

12/8/2010 Magnetic nanoparticles – targeted towards specific types of disease – can now be used to detect and locate disease sites.



One of several SQUID sensors used to detect nanoparticles in the test subjects.

Magnetism has special properties that can be utilized to detect disease by combining nanotechnology and ultra-sensitive magnetic sensors. Senior Scientific LLC, Albuquerque, NM, has been developing instrumentation and methods for taking advantage of these properties in the detection – and treatment – of various forms of cancer. Edward Flynn, PhD, president of Senior Scientific has been leading a team of scientists dedicated to research in order to bring this new technology to market.

Flynn has based his works on his experience in the use of magnetic spectrometers in nuclear physics, and in measurement of magnetic fields from the brain, known as magnetoencephalography (MEG). These applications reflect the large range of magnetic fields that may be encountered in medical applications as emitted by the very small objects. Detection of these smallest fields is made possible by advances in sensor developments including Superconducting Quantum Interference Devices (SQUIDs) and more recently by Atomic Magnetometers.

The rapid advancement of nanotechnology in conjunction with magnetology has opened up a new area of nanomedicine referred to as magnetic relaxometry – medical applications using materials at the nanoscale – one billionth of a meter in size. In this case, small molecular packets or nanoparticles (small polymers, gold or iron-oxide particles) are used as imaging agents for devices such as MRI or PET, or as therapeutical agents, delivering drugs to diseased sites. Magnetic nanomedicine takes advantage of the magnetic properties of iron-oxide nanoparticles that can enhance imaging possibilities as contrast agents in MRI or in drugs – but without radiation. Magnetic relaxometry goes one step farther by using an additional unique feature of magnetic nanoparticles referred to as superparamagnetic. Simply put, superparamagnetic nanoparticles may be manipulated to increase, dramatically, the imaging contrast between targeted disease sites and particles that are loose in the blood stream, reducing or eliminating false positives.

Simplistically, superparamagnetic particles act like particles without magnetic properties until exposed to a magnetic field and then they behave like small magnets. The implication is that a collection of particles does not exhibit an external magnetic field and do not attract each other because of the effects of thermal noise. However, in the presence of a magnetic field, these particles all align and produce a large magnetic moment, making them very amenable to detection by sophisticated magnetic sensors. Moreover, by using the proper particle size, it is possible to discriminate between particles that have bound to cancer cells and particles that remain free in the blood. This eliminates a major problem in other forms of imaging cancer such as MRI or PET, where unbound particles used for detection may show signals at sites other than the tumor.

In the magnetic relaxometry method, magnetic nanoparticles are targeted toward specific types of cancers where, based on experience, large numbers of these particles will attach themselves to pre-identified cancer cells. When introduced to a magnetic field, this targeted group of cancer cells aligns and produces a magnetic moment, which can then be used to directly determine the number of cells in the sample. It is straightforward to extend this method to detection of tumors in animals – and eventually, humans.

Senior Scientific, in collaboration with the University of New Mexico Health Sciences Center, has carried out a large number of animal experiments where xenograft human tumors have been grown on immune-deficient mice. The mice were injected with specific antibody- targeted magnetic nanoparticles and then placed under an array of SQUID sensors. In these preliminary animal experiments, a SQUID sensor array was used and the mouse placed on a movable stage allowing measurements at several stage positions relative to the array. After the magnetization pulse occurred, the resulting magnetic fields were analyzed using a multiple magnetic dipole model to deduce how many tumors the mouse had, what their locations were, and how many cancer cells were contained in each tumor.

Another strategy that has been used preceding FDA approvals for human studies is phantoms that mimic actual human organs such as the breast, ovaries, or kidneys. In this method, magnetic nanoparticles attach to cells of interest, then live cultures of these cells are placed within the phantoms and introduced to a magnetic field, producing a magnetic moment. After measuring the results of these magnetic moments, it is possible to deduce the sensitivity, specificity, and imaging capability of this method as it would apply directly to human use.

One major advantage of using magnetic relaxometry is that the low frequency magnetic fields, when measured, go transparently through tissue and bone as well as non-metallic phantoms. Thus, like MRI – and unlike X-rays – there are no losses due to intervening tissue and measured fields can be traced back to their sources without perturbation. These results have indicated that tumors can be located to within a few millimeters, and typical cancer cells can be detected down to a level of less than one-hundred thousand millimeters – in contrast to detection by a standard X-ray mammogram, which requires one-hundred million millimeters to indicate a tumor. Because of this transparency of magnetic fields, the magnetic relaxometry method appears to be an ideal solution for those cases where standard imaging methods do not work well.
For example, in mammography cases where there is substantial radiation scarring from previous treatment or other defects in the breast configuration, magnetic relaxometry will be quite effective. Since the nanoparticles are targeted through specific antibodies, there are no false positives and no unnecessary surgery. The sensitivity of this technique would permit earlier detection of cancer in many cases and could be applied where there is suspicion of cancer, such

as through the presence of markers in the blood, or where there is a genetic history of concern. However, this sensitivity could have maximum value in looking for metastasis following surgery if markers or metastatic cells in the blood are observed indicating the cancer has spread.

Therapeutic Benefits

The use of magnetic nanoparticles via this methodology can also lead to several therapeutic benefits as well. In identifying cancer through targeting, the nanoparticles are attached only to cancer cells and their location is identified through the sensor arrays. Thus localized hyperthermia therapy is an extremely significant option for treatment. Application of a very localized RF field will make the cancer cells, and only the cancer cells, oscillate in this field, thereby heating up, and destructing – as opposed to a more general hyperthermia method where application of RF fields to a tumor location heats up all of the cells with the hope that the cancer cells will die first.

An additional option is to use a multi-functional nanoparticle that contains both the targeting antibody and an anti-cancer drug. Upon identification of the site by the sensor array using magnetic relaxometry or other methods, the drug-delivery particles could be further enhanced by external magnetic concentration. The anti-cancer drugs can then be released by a variety of methods such as application of a small RF field to permit a coating polymer to open up and release the drug. This method of therapy will markedly reduce side effects of anti-cancer drugs that are introduced into the entire body.

As these therapy methods are introduced following detection and localization, the magnetic relaxometry sensor system can be used to monitor their effectiveness because it can determine the number of cells present and can also determine cell loss as the therapy is introduced.

Today, using magnetic relaxometry, we are able to do in vitro testing of bone marrow samples donated by human patients who have been treated for leukemia in order to determine whether or not leukemia cells are still present. The nature and specificity of this testing method improves detection about 50X over currently used technologies. Finally, by repeating the vitro testing cycle, magnetic relaxometry can determine the end point of the therapy and thus minimize the need for unnecessary therapy, reducing further damage to the patient.

The magnetic relaxometry method of nanomedicine appears to hold great promise in the clinical world for both detection and treatment of cancer and other diseases. It is relatively inexpensive, involves no radiation or exposure to high magnetic fields, and can be repeatedly applied to detection of cancer in a patient with no accumulating side effects.

Senior Scientific is funded by Small Business Innovative Research Grants from the National Institutes of Health. In addition, Senior Scientific collaborates with the University of New Mexico and the Center for Integrative Nanotechnology, a DOE laboratory at Sandia National laboratory.

Dr. Flynn and Senior Scientific (www.seniorscientific.com) are also making progress to move the technology "from bench to bedside" by working closely with Manhattan Scientifics (www.mhtx.com) to commercialize bio-magnetic diagnostic technology for breast, ovarian, leukemia, prostate, melanoma, and other cancers. Senior Scientific is funded by Small Business Innovative Research Grants from the National Institutes of Health, and also collaborates with the University of New Mexico and the Center for Integrative Nanotechnology at Sandia National Laboratory.

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