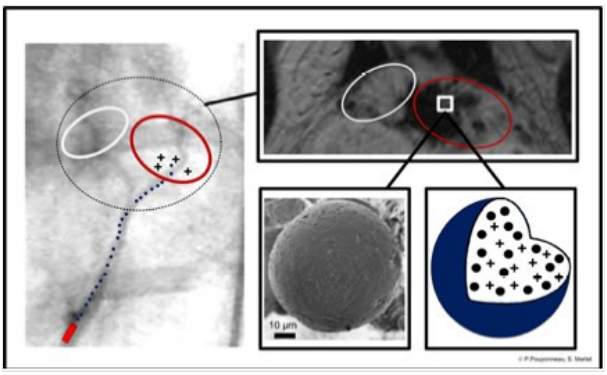
Nanoparticles Make First Successful MRI-guided Drug Delivery

FRIDAY, 25 MARCH 2011 13:35

Researchers in Montreal say they have accomplished the first delivery of a therapeutic agent to a liver tumor using nanoparticles and Magnetic Resonance Imaging (MRI) technology.

In a proof-of-concept study, researchers led by Pierre Pouponneau, a doctoral candidate in the Nanorobotics Laboratory of Dr. Sylvan Martel, at the Polytechnique Montréal,
demonstrated the ability to use a MRI technology to precisely guide a special nanoparticle to deliver a dose of doxorubicin to a liver tumor in a living rabbit. The study was published online ahead of the May issue of Biomaterials.



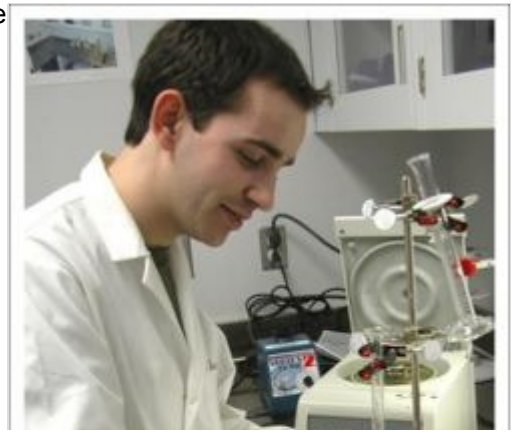
Left: Using a magnetic field generated with an upgraded MRI, researchers guide the nanoparticles through the hepatic artery. Red oval marks part of the liver; Red bar is the catheter. Right: Image of liver using magnetic resonance shows drug released near tumor. Key: Blue dots are the therapeutic magnetic microcarriers (TMMC); + represents anticancer agent; (Credit: Image courtesy of Polytechnique Montréal)

“The nanoparticles are made of polymer that dissolves in the body,” Martel told The Hub by phone. “They can be designed to dissolve at different rates, so that sustained doses can be delivered over a period of time. Each nanoparticle contains the cancer-killing drug, but about 30 percent of the contents is a magnetic agent that acts like a contrast agent.”

Martel said that using a 1.5 Tesla MRI they are able to fully saturate the body with a magnetic field, and in the presence of that magnetic field the magnetic agent inside the microcarrier allows them to guide the nanoparticles very precisely to the tumor. When the polymer nanoparticles reach the destination they biodegrade and release the therapeutic agent. In this case of liver cancer, the chemotherapy agent doxorubicin was delivered, but Martel says any number of therapeutic agents, including radioactive isotopes could be used depending on the target tumor.

Asked if this technology was more specific to tumors than the monoclonal antibody therapies that are currently used to specifically target cancerous tissues, Martel said that this nanoparticle approach won’t replace monoclonal antibody therapies, rather it is complementary to it and can only be used for certain kinds of tumors.

Therapeutic magnetic microcarriers (TMMCs) are particularly attractive for treating brain tumors as theoretically the TMMCs can cross the blood-brain barrier. In the liver with many bifurcated blood vessels the approach can be used to deliver a higher percentage of a therapeutic agent to the tumor.



In the study, Pouponneau’s team used nanoparticles made of a biodegradable polymer measuring 50 microns in diameter. This is slightly under the diameter of a human hair. Each microcarrier contained a tiny dose of doxorubicin along with the agent that in effect turns the microcarrier into a tiny magnet.

The particles are then inserted via a catheter into the hepatic artery. Using an upgraded 1.5 Tesla clinical MRI scanner, they manipulate the magnetic field to guide the particles to the tumor.

Martel explained that where blood vessels branch in a “Y” roughly 50 percent of a conventional therapeutic agent will go one way continuing on to the tumor vasculature, and 50 percent will go to other areas of the liver causing adverse side effects.

Pierre Pouponneau helped develop medical magnetic microcarrier for targeting tumor cells. (Credit: Image courtesy of Polytechnique Montréal)

The magnetic guidance helps to steer a much higher percentage of the drug-carrying nanoparticles through all the bifurcations in blood vessels in the liver leading to the tumor.

Martel says that depending on the size of the tumor being targeted, a few hundred to a few thousand nanoparticles can be used to deliver an effective dose of medicine. He noted that an advantage of this approach is that it doesn’t damage blood vessels. Current catheter delivery of chemotherapy involves threading the catheter deep into liver vessels as close as they can get to the tumor, which damages blood vessels. As a result patients must wait some days or weeks for the vessels to repair themselves before undergoing another dose.

Using the therapeutic magnetic microcarriers, they don’t need to thread the catheter so far into the vessels. As a result there is no damage to the blood vessels, allowing administration of multiple doses on consecutive days if needed.

Martel said any 1.5 Tesla MRI scanner can be used for nanoparticles down to the size of 800 microns but smaller than that requires hardware and software upgrades to the MRI scanner but that it is not anything that cannot be done to existing machines, should this technique reach clinical use.

Clinical trials in humans, however, are four to seven years away Martel says because they have several obstacles to overcome before they are ready for human trials.

“We need to demonstrate that this offers a large enough improvement in drug delivery to be worth funding,” Martel said. “We need to quantify the value, and we need to prove that is safe and effective. That all takes time and money, and we need funding to continue.”

By Michael O’Leary, contributing writer, Health Imaging Hub

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