

50 years after the release of the film 'Fantastic Voyage,' science upstages fiction

August 24 2016



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Fifty years to the day after the film *Fantastic Voyage* was first shown in theatres, the Polytechnique Montréal Nanorobotics Laboratory is unveiling a unique medical interventional infrastructure devoted to the fight against cancer. The outcome of 15 years of research conducted by Professor Sylvain Martel and his team, it enables microscopic nanorobotic agents to be guided through the vascular systems of living bodies, delivering drugs to targeted areas.

An action-packed 100,000-kilometre journey in the human body

Fantastic Voyage recounted the adventure of a team of researchers shrunk to microscopic size who, aboard a miniature submarine, travelled into a patient's body to conduct a medical operation in a surgically inoperable area. This science fiction classic has now been eclipsed by procedures and protocols developed by Professor Martel's multidisciplinary team comprising engineers, scientists and experts from several medical specialties working together on these projects that herald the future of medicine.

"Our work represents a new vision of cancer treatments, with our goal being to develop the most effective transportation systems for the delivery of therapeutic agents right to tumour cells, to areas unreachable by conventional treatments," says Professor Martel, holder of the Canada Research Chair in Medical Nanorobotics and Director of the Polytechnique Montréal Nanorobotics Laboratory.

Conveying nanorobotic agents into the bloodstream to reach the targeted area right up to the tiniest capillaries without getting lost in this network stretching about 100,000 kilometres—two-and-a-half times the Earth's circumference—is a scenario that has been turned into reality. This is an adventure-filled journey for these microscopic vehicles that must

confront the powerful onslaught of arterial blood flow, the mazes of the vascular network and the narrowness of the capillaries—just like the film's heroes!

"Doctors" invisible to the naked eye

To conduct this [fantastic voyage](#), Professor Martel's team is developing various procedures, often playing a pioneering role. These include navigating carriers just a fraction of the thickness of a hair through the arteries using a clinical magnetic resonance imaging (MRI) platform, the first in the world to achieve this in a living organism, in 2006. This exploit was followed in 2011 by the guidance of drug-loaded micro-transporters into the liver of a rabbit.

Limits to the miniaturization of artificial nanorobots prevent them from penetrating the smallest blood vessels, however. For this, Professor Martel plans to have them play the role of Trojan horses, enclosing an "army" of special bacteria loaded with drugs that they will release at the edges of these small vessels.

Able to follow paths smaller than a red blood cell, these self-propelled bacteria move at high speed (200 microns per second, or 200 times their size per second). Once they are inside a tumour, they are able to naturally detect hypoxic (oxygen-starved) zones, which are the most active zones and the hardest to treat by conventional means, including radiotherapy, and then deliver the drug.

Professor Martel's team has succeeded in using this procedure to administer therapeutic agents in colorectal tumours in mice, guiding them through a magnetic field. This has just been the subject of an article in the renowned journal *Nature Nanotechnology*, titled Magneto-gerotactic Bacteria Deliver Drug-containing Nanoliposomes to Tumour Hypoxic Regions. "This advanced procedure, which provides optimal

targeting of a tumour while preserving surrounding healthy organs and tissue, unlike current chemotherapy or radiotherapy, heralds a new era in cancer treatment," says Dr. Gerald Batist, Director of the McGill Centre for Translational Research in Cancer, based at the Jewish General Hospital, which is collaborating on the project.

Professor Martel's projects also focus on the inaccessibility of certain parts of the body, such as the brain, to transporting agents. In 2015, his team also stood out by successfully opening a rat's blood-brain barrier, temporarily and without damage, providing access to targeted areas of the brain. This feat was achieved through a slight rise in temperature caused by exposing nanoparticles to a radiofrequency field.

"At present, 98% of drug molecules cross the blood-brain barrier only with great difficulty," notes Dr. Anne-Sophie Carret, a specialist in hematology-oncology at Montréal's Centre hospitalier universitaire Sainte-Justine and one of the doctors collaborating on the project. "This means surgery is often the only way to treat some patients who have serious brain diseases. But certain tumours are inoperable because of their location. Radiation therapy, for its part, is not without medium- and long-term risk for the brain. This work therefore offers real hope to patients suffering from a brain tumour."

\$4.6 million in equipment for a one-of-a-kind future medical laboratory

This new investment in the Nanorobotics Laboratory represents \$4.6 million in infrastructure, with contributions of \$1.85 million each from the Canada Foundation for Innovation (CFI), and the Government of Québec. Companies including Siemens Canada and Mécanik have also made strategic contributions to the project. This laboratory now combines platforms to help develop medical protocols for transferring

the procedures developed by Professor Martel to a clinical setting.

The laboratory contains the following equipment:

- a clinical MRI platform to navigate microscopic carriers directly into specific areas in the vascular system and for 3D visualization of these carriers in the body;
- a specially-developed platform that generates the required magnetic field sequences to guide special bacteria loaded with therapeutic agents into tumours;
- a robotic station (consisting of a robotized bed) for moving a patient from one platform to another;
- a hyperthermia platform for temporary opening of the blood-brain barrier;
- a mobile X-ray system;
- a facility to increase the production of these cancer-fighting bacteria.

"We are pleased to contribute to the development of state-of-the-art infrastructure in Montréal that will help create medical procedures that promise to revolutionize cancer treatments," says Gilles Patry, CEO, Canada Foundation for Innovation.

For her part, Dominique Anglade, Québec Minister of the Economy, Science and Innovation and Minister Responsible for the Digital Strategy, states: "The Government of Québec is proud to support Professor Martel's work, which reflects the excellence and avant-gardist nature of Québec research in the life sciences sector. Moreover, the numerous partnerships established in the Nanorobotics Laboratory are bolstering the industry's expertise and capacity to innovate."

Dr. Gilles Soulez, whose team at the imaging research platform of the research centre of the Centre hospitalier de Université de Montréal has

been the first collaborator with Professor Martel's team in the development of these protocols, states: "The nanomedicine heralded by Professor Martel's projects will enable us to improve the targeting of tumours during liver-tumour chemoembolization procedures and thereby to treat tumours more effectively while lowering systemic toxicity and reducing side effects."

Christophe Guy, CEO of Polytechnique Montréal, says: "The projects being conducted by Professor Martel and his team are representative of our institution's leadership in biomedical engineering teaching and research. They also embody our vision of an area of research that has a positive impact on society and our fellow citizens."

Provided by Polytechnique Montréal

Citation: 50 years after the release of the film 'Fantastic Voyage,' science upstages fiction (2016, August 24) retrieved 10 April 2024 from <https://medicalxpress.com/news/2016-08-years-fantastic-voyage-science-upstages.html>

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