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**Medical robots**

# Swallow the surgeon

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Ronald Grant Archive

**Biomedicine: Tiny medical robots are being developed that could perform surgery inside patients with greater precision than existing methods**

IN THE 1966 film “Fantastic Voyage”, a submarine carrying a team of scientists is shrunk to the size of a microbe and injected into a dying man. The crew’s mission is to save the man’s life by dissolving a blood clot deep inside his brain. After a harrowing journey through the patient’s body, the scientists succeed: the clot is destroyed and the patient cured.

For decades, scientists and fiction writers alike have been fascinated by the possibility of tiny machines that can enter a patient, travel to otherwise inaccessible regions, and then diagnose or repair problems with far less pain and with far greater precision than existing medical procedures. In his famous speech from 1959, “There’s Plenty of Room at the Bottom”, Richard Feynman, an American physicist, called this concept “swallow the surgeon”. More recently proponents of nanotechnology have imagined swarms of “nanobots”—tiny machines just billionths of a metre, or nanometres, across—that might fix mutations in a person’s DNA or kill off cancer cells before they have a chance to develop into a tumour.

Such nanobots still exist only in the realm of science fiction, of course, and it may take decades before they become practical. But there is progress in developing small medical robots for sensing, drug delivery or surgery inside the human body. The most clinically advanced devices focus on the human gastrointestinal (GI) tract, since it is easily accessible and can accommodate objects several centimetres in size. In addition, researchers are developing micro-robots, with dimensions measured in millimetres or micrometres (a human hair is around 100 micrometres in diameter), which should be able to reach more delicate areas, such as the inside of the eyes or the bloodstream.

Among the pioneers of gastrointestinal devices is Given Imaging, an Israeli company that developed the “Pillcam”—a camera-equipped capsule that measures 1.1cm in diameter and 2.6cm in length, and can be swallowed. On its journey through the GI tract the device takes pictures which are transmitted to a computer. Because it causes less discomfort and is more effective than other diagnostic methods for examining the small bowel, it has become widely used since its introduction in 2001.


Although the Pillcam is technically not a robot—it is a passive device that relies on the body's regular peristaltic contractions to propel it through the intestine—its success opened up the field, says Paolo Dario, a professor of biomedical robotics at Scuola Superiore Sant'Anna in Pisa, Italy. Research groups around the world are now taking the next steps. At Dr Dario's laboratory, the Centre for Research in Microengineering, scientists have been designing prototypes of capsule robots that have legs for active locomotion. The legs, which are slightly curved, resemble those of insects, with tiny hooks on the tips of their feet to provide enough friction to enable movement in a slippery environment. This should allow the robots to crawl around the GI tract and obtain detailed images, dispense therapeutics or, with the right surgical tools, perform biopsies.

## Some assembly required

Dr Dario's group is also collaborating with other European researchers on an ambitious project called ARES (short for Assembling Reconfigurable Endoluminal Surgical system). Its objective is to design a modular gastrointestinal robot made up of individual pieces that are small enough to be swallowed, one at a time. Once inside the stomach, the idea is that these pieces will assemble themselves into a larger robotic device. The aim is to build an "operating room" inside a patient that can be controlled from the outside by a doctor, says Dr Dario, who is co-ordinating the project.

He and others in the field acknowledge that there are many obstacles to overcome. A big problem, for example, is how to provide power to tiny medical robots. Batteries can provide enough energy for passive capsules like the Pillcam, but robots with active locomotion pose more of a challenge, and micro-robots are likely to need more energy than batteries can store at such small scales. Instead of adding a power source to the device, which increases its weight and bulk, one approach is to apply external magnetic fields to a small robotic device that contains magnetic material, allowing it to be steered simply by controlling the magnetic fields around it.

Scientists from the Institute of Robotics and Intelligent Systems at the Swiss Federal Institute of Technology (ETH) in Zurich plan to use this technique to steer tiny robots inside the eye for sensing, drug delivery and surgery. Current retinal procedures to repair detachments or rips, for example, may involve several incisions in the eye and stitches to tie off the perforated areas.

Using a micro-robot, by contrast, might involve only one incision and smaller surgical instruments. It might thus require only a mild topical anaesthetic and no stitches, since eye incisions at very small scales can self-seal, says Jake Abbott, a researcher at the institute who is working on the project. In addition, micro-robots could deliver drugs directly to veins inside the retina that have become obstructed by clots, a condition that can cause blindness and for which there is at present no reliable cure. Researchers at the ETH have designed a special ophthalmoscope with which they plan to track the robots inside the eye.

Sylvain Martel and his colleagues at the NanoRobotics Laboratory at Ecole Polytechnique de Montréal in Canada are also using magnetic fields, but in a different way. They are using fields generated by a magnetic-resonance imaging (MRI) machine to ferry small beads through the bloodstream with the goal of delivering therapeutics close to tumours. This has several advantages, says Dr Martel. For one thing, most hospitals already have an MRI machine, so there is no need to construct or buy additional equipment. Furthermore, as well as propelling a magnetic device through the body, an MRI machine can also locate it.

All of this is possible because an MRI machine contains both a large magnet that creates a strong magnetic field, and also a set of gradient coils that superimpose weaker but adjustable fields upon it. These coils are normally used to select slices for creating three-dimensional images, but the magnetic fields they create can also be used to exert a force on a small magnetic object inside a scanner. Dr Martel and his colleagues have developed software to do just that. Last year his team achieved a milestone when it manoeuvred a 1.5-millimetre bead through a 5-millimetre artery in a living pig. Since then the researchers have reduced the bead's size to about 250 micrometres.

But magnetic propulsion has some drawbacks. The fields must be carefully controlled, or they could cause a micro-robot to go off course, with potentially harmful or even fatal consequences inside a human body. And the fields produced by gradient coils in a conventional MRI machine are not strong enough to pull on particles below about 250 micrometres in size, says Dr Martel, though an upgraded MRI system with more powerful coils could propel beads as small as 50 micrometres, he adds. Still, that means smaller blood vessels and other delicate areas inside the body remain out of reach.

## Borrowing from nature

To circumvent these problems, some researchers are looking to nature for inspiration. Microbes, for example, have developed successful methods to manoeuvre within bodily fluids. Whereas large animals swim by pushing against water with their fins or limbs, this approach is ineffective at very small scales. To microbes, fluids appear thick and still, and viscosity is the main force small organisms must reckon with. As a result, bacteria have developed a unique way of swimming: using tiny rotary motors called flagella, which resemble corkscrews.

James Friend, co-director of the Micro/Nanophysics Research Laboratory at Monash University near Melbourne, Australia, is building a flagella-inspired micro-motor he hopes will one day propel a micro-robot through an artery or vein. At the core of the motor are piezoelectric materials—special crystals or ceramics that change shape very slightly in the presence of an electric field. When such a material is placed in a rapidly alternating electric field, it starts to vibrate. That vibration can then be coupled to another structure to turn a rotor, which in turn operates a flagellum-like tail. In recent years Dr Friend has built successively smaller versions of his motor—the current version is 250 micrometres in diameter. Providing an on-board power supply is difficult, however, so he is investigating the use of external magnetic fields to power the device.

An alternative approach is not to imitate nature, but to harness it—by hitching a ride with a bacterium. To get beyond the size limitations of magnetic beads inside an MRI scanner, Dr Martel and his colleagues are also working with "magnetotactic" bacteria, which orient themselves with magnetic fields. Because they are so tiny (only about two micrometres across), they are not strong enough to swim against the blood flow of larger vessels, though they are able to swim through vessels as little as four micrometres in diameter. Dr Martel's idea is to use the larger magnetic beads to transport the bacteria close to a tumour, and then release them and coax them, using applied magnetic fields, to swim to the tumour and deliver a therapeutic payload. Preliminary experiments in rats suggest that the bacteria can be steered toward tumours using specially designed magnetic coils.

Metin Sitti, director of Carnegie Mellon University's NanoRobotics Lab in Pittsburgh, Pennsylvania, is using bacteria as biological motors to propel small spheres through fluids. Instead of relying on an external system for controlling their movements, Dr Sitti and a colleague use chemical signals to tell the bacteria what to do. In recent experiments they proved that they could stop and start the bacteria's flagella simply by exposing them to two different kinds of substances. Successful steering of the bacteria will be the subject of further tests, says Dr Sitti, but could be done via chemotaxis—a process by which small organisms follow gradients in the concentration of a particular chemical in order to find food or escape from toxic substances.

Medical robots have much potential, but many of the proposed devices, especially those that incorporate biological organisms, may not be practical for many years. Dr Sitti, for one, acknowledges that his project may take a decade or longer to commercialise. But other efforts, such as adding active locomotion to gastrointestinal capsules, may be only a few years away. Dr Dario says medicine is "at the beginning of a new era" as open-wound surgery gives way first to minimally invasive techniques, and then to procedures that will be completely concealed and leave no visible scars. Evidently the ideas depicted in "Fantastic Voyage" continue to resonate: a remake of the film is due to be released in 2010.