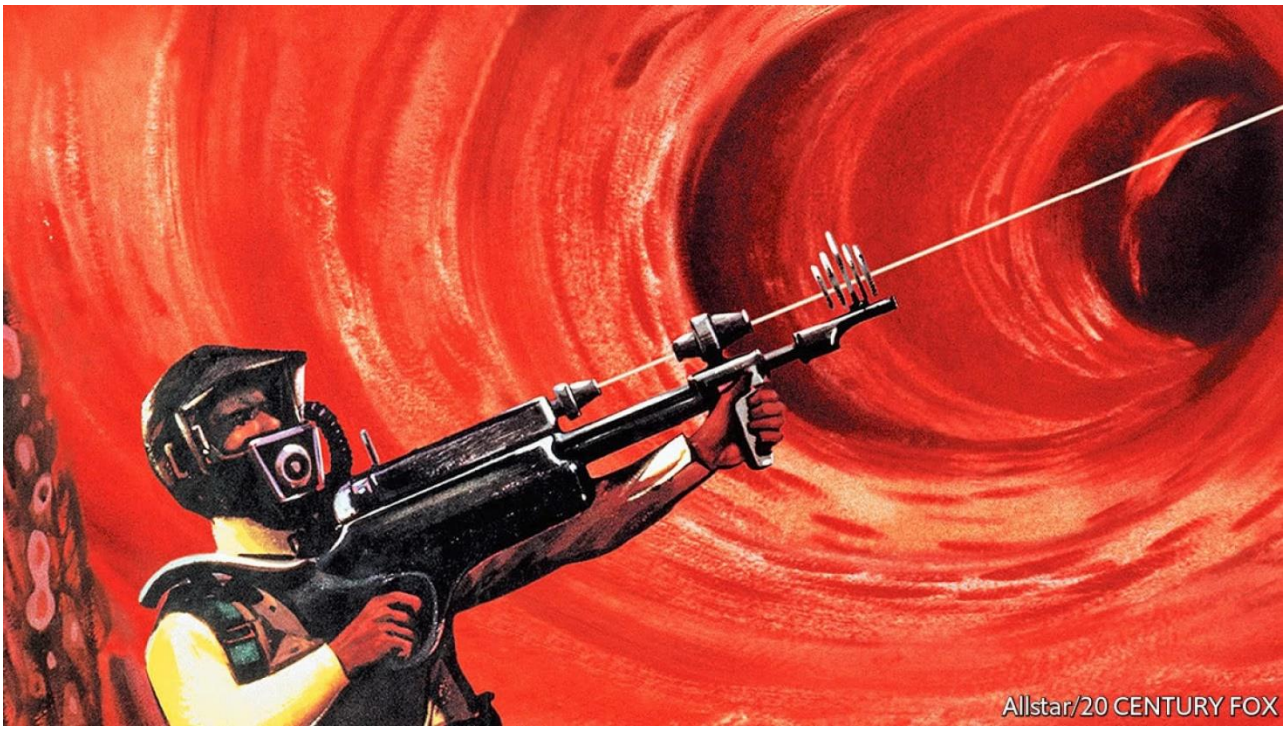
The Economist

Combating cancer

Microscopic lasers may stop tumours spreading around the body

How to blow cancer cells up from the inside



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IT IS more than 50 years since “Fantastic Voyage” hit the silver screen. The film’s premise, shrinking a submarine and her crew of doctors to the point where they can travel through a patient’s bloodstream to repair damage *in situ*, though entertaining, remains as absurd as it was in 1966. Not so the idea that therapeutic machines small enough to circulate in this way might be built. Indeed, perhaps inspired by the film, several such efforts have been made. Some are drug-delivery devices. Some are ways of concentrating externally applied energy into tissue that needs to be killed. And they are starting to be approved for clinical use.

The latest attempt, by Vladimir Zharov of the University of Arkansas and Mark Stockman of Georgia State University, in Atlanta, involves injecting cancer patients with hordes of tiny lasers that will seek out and destroy so-called circulating tumour cells (CTCs). These are cells that have broken off a primary tumour and which, if left unchecked, might lodge in various parts of the body and turn into secondary cancers, a process called metastasis.

The minuscule lasers which the pair use, of a type developed a few years ago by Dr Stockman, are called “spasers”. This is short for surface-plasmon amplification by stimulated emission of radiation. Surface plasmons are clouds of electrons that oscillate over a conductive surface. Spasers generate them in response to stimulation by an external light source.

A red blood corpuscle has, for reference, a diameter of about 7,000nm (nanometres, or billionths of a metre). The spasers created by the two researchers, by contrast, are a mere 22nm across. They consist of a gold core with a diameter of 10nm surrounded by a silica shell doped with fluorescent dyes. The outer surface of this shell is coated with folic acid.

A conventional laser consists of a resonator (usually a chamber with mirrors at either end, between which the light being amplified bounces), and a gain medium, which sits between the mirrors and takes external energy (also often in the form of light) and employs it to amplify the bouncing light. In the spasers Dr Zharov and Dr Stockman are using, the gold acts as the resonator and the doped silica as the gain medium. Instead of amplifying light, the system amplifies plasmons oscillating across the surface of the gold sphere.

The device’s other ingredient, the folic acid, is its guidance system. Unlike most healthy cells, cancer cells are usually covered with folate-receptor molecules. If a spaser comes into contact with such a cell, it therefore tends to stick. So, if a horde of spasers is injected into someone with metastasising cancer, those spasers should quickly track down CTCs in the bloodstream or lymphatic system and bond to them. Laboratory studies show that, often, dozens of spasers will attach themselves to a single cell. Once attached, they are quickly absorbed into that cell.

Spasers so absorbed can be employed for two purposes: diagnosis and destruction. Shining low-level laser light into a patient, either through his skin or (to reach deeper inside) through a fibre-optic probe, causes cancerous cells containing spasers to shine brightly. That reveals their locations. Applying more powerful laser pulses (though still at a level harmless to humans) transforms the spasers into killers. The

idea behind this was Dr Zharov's. In a piece of past research he turned a laser onto some cells from a melanoma, an aggressive form of skin cancer. One characteristic of melanomas is the presence in them of particles of melanin, a dark pigment. These particles absorbed the laser light, heated up, and, he discovered, thus created bubbles of steam around themselves that could kill the cells they were in.

The researchers' plan was to use their spasers to do something similar to CTCs, with the spasers substituting for melanin particles. And it worked. The external laser pulses stimulated the spasers to produce plasmons that heated the water surrounding them in a cell to well over 100°C. That created steam bubbles, the sudden formation of which generated shock waves which blew the affected cells to bits.

To exploit this effect therapeutically, Dr Zharov and Dr Stockman plan to fit patients with special wrist sensors. Such a sensor will use low-level laser light to detect spaser-carrying CTCs passing through blood vessels beneath. It will then swiftly activate a high-powered laser to destroy those cells. With luck, this arrangement will keep secondary cancers at bay while a patient's primary tumour is dealt with. Spaser treatment would then continue for a while longer, to deal with leftover CTCs.

Animal trials having been promising; the two researchers are now planning to test the system in people. They are also trying to tweak their spasers to respond to infra-red, rather than visible light. Infra-red penetrates tissue more deeply than visible light can manage, so an infra-red-sensitive spaser should be more effective.

Exactly how good an executioner of human CTCs the spaser system will be remains to be seen. But even a partial slaughter would inhibit metastasis. And that would have a potent effect on treatments for all sorts of cancers.