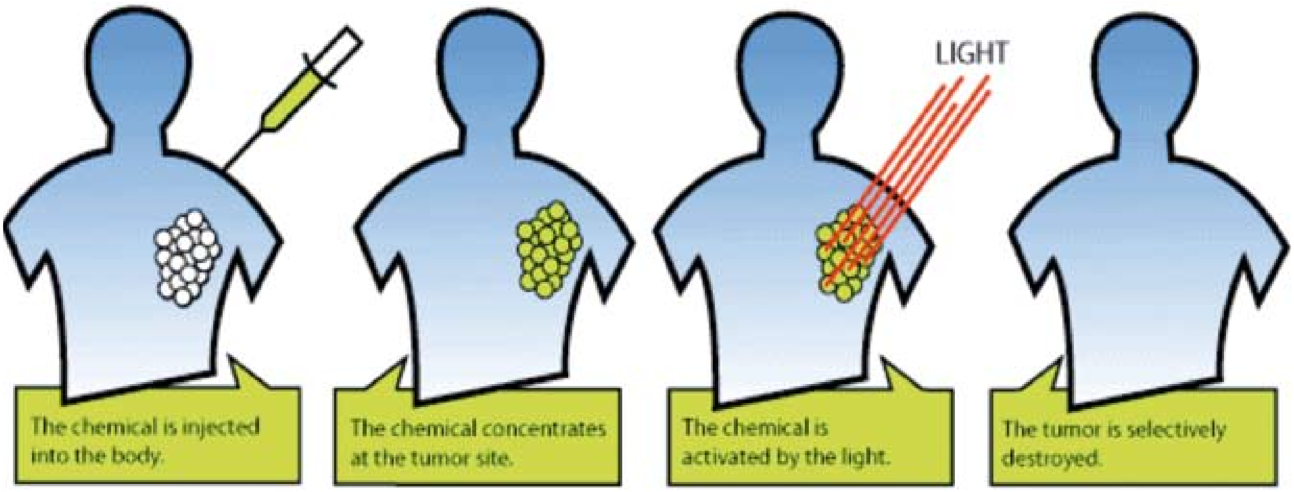


Principle of photodynamic therapy.

Project number: IPD100020
Project name: Image-guided and/or targeted photodynamic therapy using a combination of a new photosensitizer with upconverting nanoparticles (IMPACT)
Goal: to increase the clinical value of photodynamic therapy by ultimately developing a dedicated multispectral-camera platform for detection and treatmentnanophotonics

Selective and sensitive detection and treatment of tumours with light

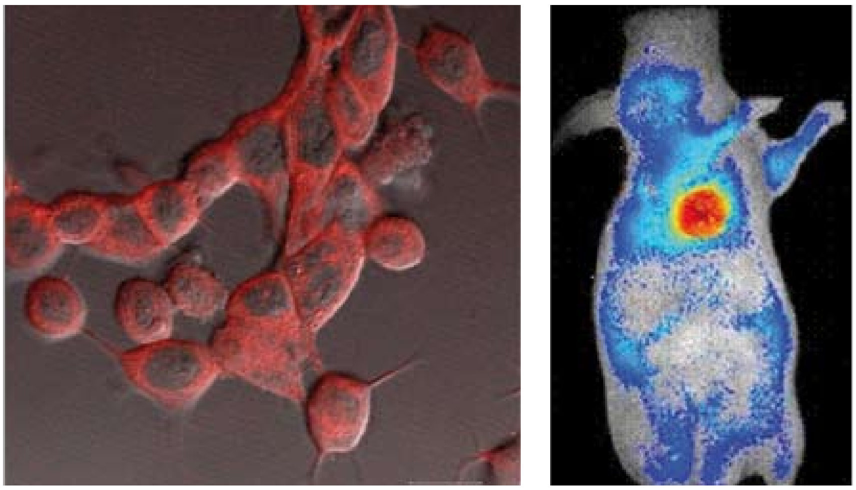
In the fast-developing field of cancer research, a recent and promising technique is photodynamic therapy: killing tumour cells with the aid of laser light. Although already used in clinical settings, photodynamic therapy is not without its side effects and limitations. The IOP project 'IMPACT' is developing techniques to make photodynamic therapy suitable for a wider range of tumours and to reduce its side effects. A major deliverable will be a combined detection and treatment device.

Being able to accurately differentiate between healthy tissue and cancer tissue is key in surgical oncology. The slightest differences in colour and structure can be indicative of diseased tissue. In making that distinction, surgeons depend heavily on their experience, their vision and their tactile sense. Estimations show that approximately 25% of patients have to return for a second operation to remove cancer tissue that was left behind. In the future, surgical procedures can be drastically improved by selectively staining the tumour using a tumour-specific fluorescent dye. That will make the tumour's boundaries clearly visible to the surgeon. "Image-guided surgical treatment will be a big step forward," says Clemens Löwik, Professor of Molecular Endocrinology and Molecular Imaging at the Leiden University Medical Center. "But even better results could be accomplished by killing the cancer cells using light, instead of surgery."

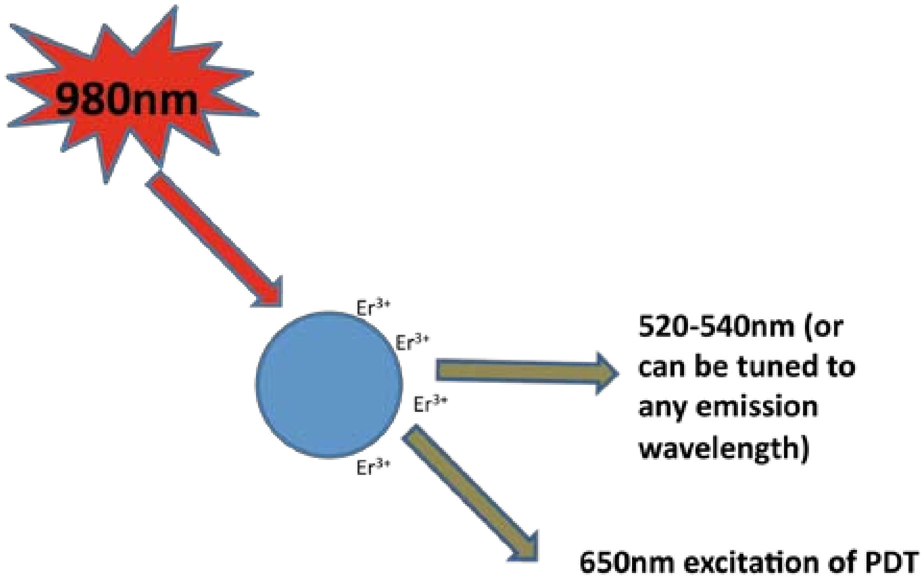
Injected nanoparticles "travel" through the body to the tumour

New photosensitizer

The treatment of cancer with light – known as photodynamic therapy – involves injecting the patient with a photosensitizer. The chemical is harmless on its own, but once illuminated it becomes extremely toxic. Tissues containing the photosensitizer will be killed almost instantaneously upon illumination. "In other words, simply shining light on a tumour will destroy it," Löwik says. There are three major issues with the photosensitizers currently being used, such as Foscan. First, the photosensitizer remains in the body for six weeks. "During that period, exposure to light causes severe skin burns," Löwik explains. "It can even result in blindness. To prevent that from happening, patients have to stay inside throughout the entire period." Secondly, the photosensitizer is present in both healthy and cancer tissue. As a result, illumination kills not only the tumour but also the healthy tissue surrounding it. Finally, the visible light that is used to activate the photosensitizer does not penetrate very deeply, since it is effectively absorbed by human tissue. This limits the treatment to small and very superficial tumours.



The photosensitizer Bremachlorin, which is also fluorescent, specifically targets tumour cells (left). On the right, a tumour in a mouse that has accumulated Bremachlorin and is imaged with a near-infrared camera system.



A nanoparticle filled with Bremachlorin is activated with 980nm laser light. This causes the nanoparticle to locally generate a tuneable internal light source. Bremachlorin is activated with a wavelength of 650nm.

Seaweed

The IMPACT project addresses those three issues. Within the project, a new photosensitizer is currently under development that will leave the body within days, if not hours. That photosensitizer accumulates selectively in tumours, thus reducing any collateral damage to healthy tissue during treatment. Moreover, it will use near-infrared light instead of visible light or far-red light. Near-infrared light can travel deeper into tissue, enabling the treatment of larger tumours. As Löwik explains: “The new photosensitizer, Bremachlorin, is derived from the seaweed spirulina and has been shown to target tumour cells specifically.
We don’t know why it is so highly selective, but that makes it far easier to detect a tumour’s boundaries with exactness. Moreover, it leaves the skin cells within three to four hours and the whole body is clean after 24 hours.”
Bremachlorin is put into nanoparticles, which - once injected - “travel” through the body to the tumour. Subsequently, laser light with a wavelength of 980nm, which penetrates deeper into tissue than visible light can, causes the nanoparticles to locally generate an internal light source of a different wavelength. This internally emitted light can be tuned to match the wavelength needed to activate the Bremachlorin, causing the tumour cells to die. The efficient use of this procedure, known as upconversion, will be one of the project’s deliverables.

Commercially interesting

The project will result in a platform that contains all the necessary instrumentation for this kind of photodynamic therapy. The platform will consist of a multispectral camera, software that will automatically determine the exact region that needs to be treated, and an image-guided laser system that will effectively kill the tumour cells. Löwik expects the total package and the underlying intellectual property to be commercially very interesting. The companies O2view and Percuros are engineering and delivering the technology necessary for imaging and laser treatment, while the academic partners of the consortium will focus on optimising the nanoparticles as well as testing the therapy in mice.

Participants:
- Leiden University Medical Center
- Van ’t Hoff Institute for Molecular Sciences (University of Amsterdam)
- Academic Medical Center, Amsterdam
- Percuros
- O2View

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