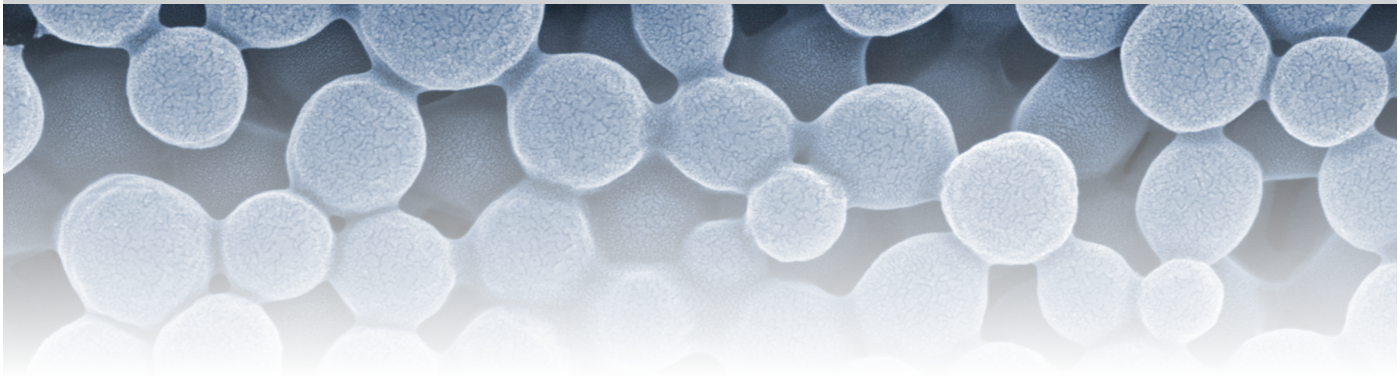
FACTS

SINTEF Materials and Chemistry

Biotechnology and Nanomedicine

June 2015



Multifunctional polymeric nanoparticles for drug delivery and imaging

Background

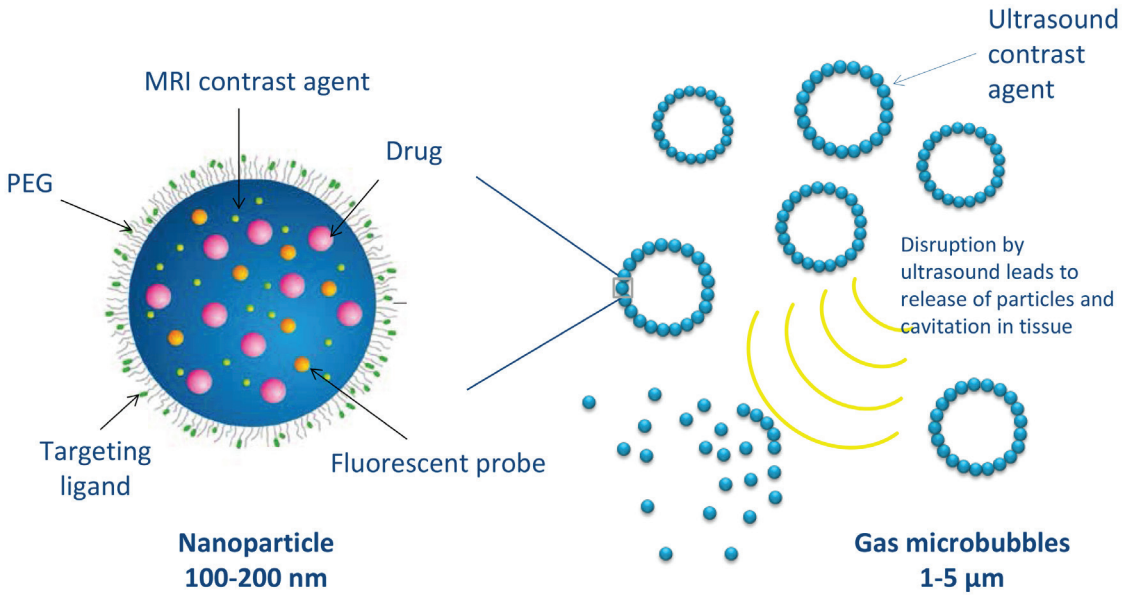
Nanoparticles represent promising carriers for efficient drug delivery for various diseases. Nanoparticles with multiple functionalities, such as imaging and therapy as well as cell targeting, open new possibilities in the combination of diagnosis and therapy into so called *theranostic* nanoparticles.

Combining multifunctional nanoparticles with ultrasound exposure may further enable therapeutic molecules to reach their targets while limiting the exposure to normal tissue. SINTEF has developed a unique multimodal, multifunctional drug delivery system consisting of *gas microbubbles stabilized by polymeric nanoparticles* to be used in ultrasound-mediated drug delivery and imaging.

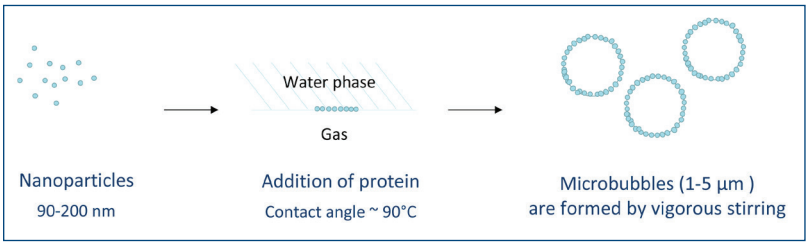
Theranostic nanoparticles and gas microbubbles

Polymeric nanoparticles (100-200 nm) loaded with drugs and imaging agents are produced in a single step. The particles are composed of a biocompatible and biodegradable polymer, poly(alkyl cyanoacrylate) (PACA), and coated with a hydrophilic layer of poly(ethylene glycol) (PEG) to increase blood circulation time. The nanoparticles can also be targeted for specific biomarkers and thus guided to the disease site. The nanoparticles are prepared by a one-step miniemulsion process, which is simple, cost-efficient and scalable. High drug loads, up to 50%, are possible.

Ultrasound-mediated diagnosis and treatment with multifunctional nanoparticles and gas microbubbles



In a second step, gas-filled microbubbles (1-5 µm) stabilized by a shell of the multifunctional nanoparticles are prepared. Gas microbubbles injected into the blood stream can be used both for ultrasound imaging of the tissue vasculature and to facilitate transport and uptake of nanoparticles and drugs.

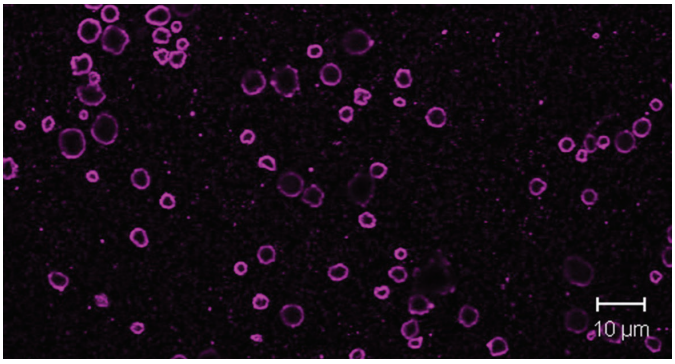


Stabilization of gas microbubbles using polymeric nanoparticles

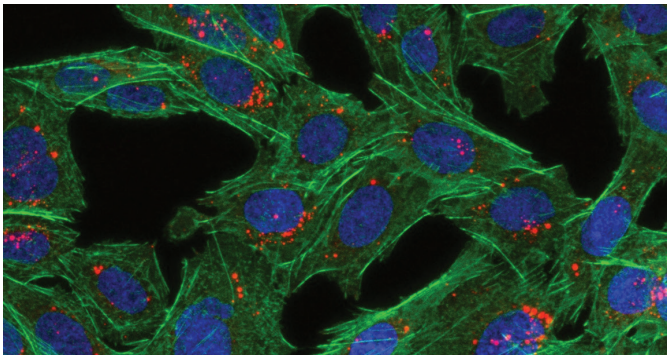
Innovative, novel drug delivery system

The nanoparticle-coated gas microbubbles are injected into the blood stream. Due to the targeting moieties on the nanoparticle surface, the gas microbubbles travel to the disease site, e.g. a tumor, where they accumulate. The gas microbubbles can be monitored using ultrasound imaging. Focused ultrasound waves are then used for destroying the bubbles, thereby releasing the drug-carrying nanoparticles; in addition the nanoparticles are forced into the diseased tissue by sonoporation caused by the focused ultrasound.

The nanoparticles degrade in the body and release the drug locally. In this way, the majority of the drug is delivered to the disease site and not to healthy tissue, thereby limiting severe side effects of the drug. In addition, the nanoparticles may be loaded with contrast agents for e.g. MRI thus allowing additional monitoring of the nanoparticle uptake in tissue.

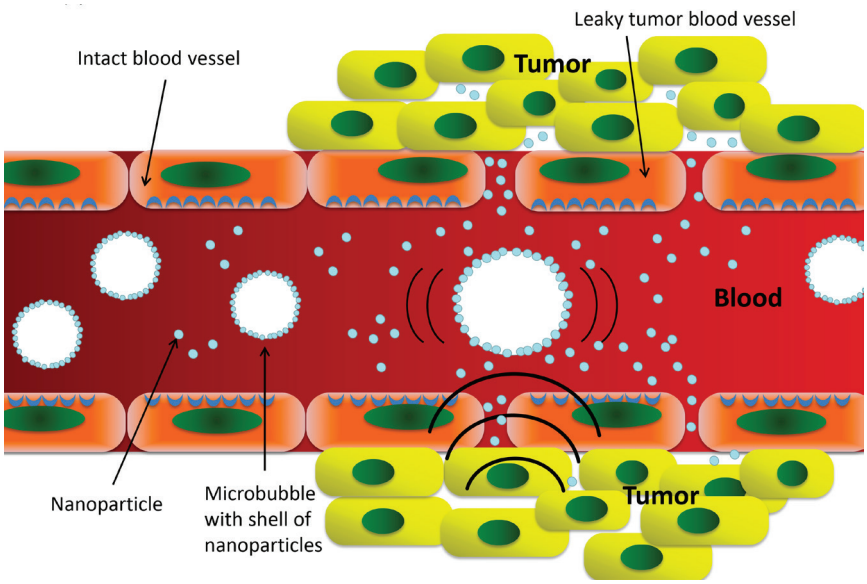


Confocal Laser Scanning Microscopy image of gas microbubbles stabilized by PACA nanoparticles



Rat brain endothelial cells that have taken up nanoparticles. Cell bodies are green, nuclei are blue and nanoparticles are red (Image: Habib Baghirov)

Microbubbles stabilized by nanoparticles circulate in the blood. Microbubbles and nanoparticles are too large to penetrate normal blood vessels. Focused ultrasound applied at the tumor site leads to oscillation and destruction of the microbubbles, releasing the nanoparticles from the microbubble surface. Due to leaky tumor blood vessels and ultrasound the nanoparticles can diffuse into the tumor and release their payload.



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