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FRAUNHOFER-INSTITUT FÜR BIOMEDIZINISCHE TECHNIK IBMT

1 - 3 *3-D reconstruction of optoacoustic signals of blood vessels and gold nano-rods (blue) in the knee of an arthritic mouse.*

OPTOACOUSTIC MOLECULAR IMAGING

Situation

Molecular imaging allows to visualize the presence of biological marker molecules in vivo. Most imaging methods are limited either by a low penetration depth (optics) or by the application of ionizing radiation (PET, SPECT).

Ultrasound is also basically suitable for molecular imaging. However, the contrast agents (micro bubbles) are limited to the vascular system due to their size. Optoacoustic imaging is a new hybrid modality that combines the advantages of acoustics and optics.

Ultrasound signals are generated by the absorption of light. These signals can be utilized for imaging that combines the high contrast of optics with the high resolution of acoustics. When combined with biologically functionalized contrast agents, optoacoustic techniques can be used for molecular imaging.

The achievements of Fraunhofer IBMT in the field of molecular imaging range from synthesis and functionalization of contrast agents to design and assembly of complete imaging systems and their application in proof-of-concept experiments.

Solution

Fraunhofer IBMT built several hardware platforms, which are suited for microscopic and macroscopic molecular imaging based on optoacoustic techniques. For preclinical molecular imaging in a small animal model, single-element ultrasound transducers are operated in a confocal optoacoustic imaging setup.

With respect to contrast agents, different particle types have been developed. Due to their high plasmon resonance, gold nano-rods are the most efficient contrast agent. However, their usage is currently limited to preclinical studies because of unresolved biocompatibility issues.

Fraunhofer Institute for Biomedical Engineering IBMT
Prof. Dr. Heiko Zimmermann
Prof. Dr. Günter R. Fuhr
Joseph-von-Fraunhofer-Weg 1
66280 Sulzbach
Germany

Contact

Ultrasound
Dr. Marc Fournelle
Medical Ultrasound
Telephone +49 6894 980-220
Fax +49 6894 980-234
marc.fournelle@ibmt.fraunhofer.de

www.ibmt.fraunhofer.de

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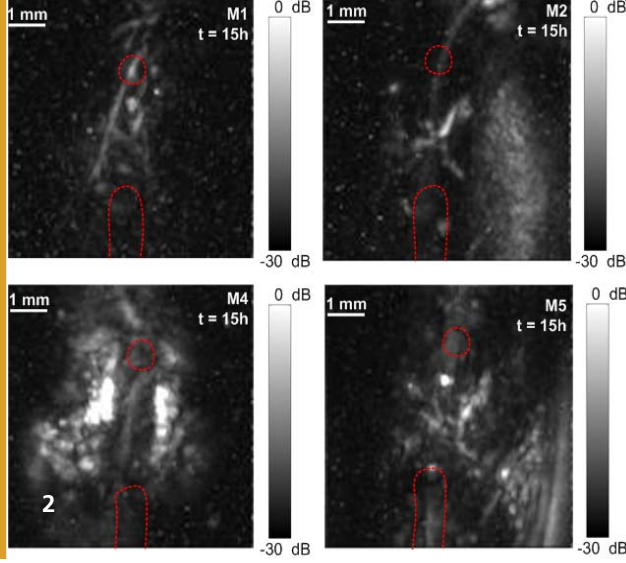

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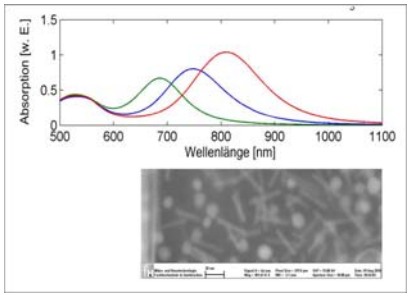
Technical data

Preclinical optoacoustic molecular imaging:

- 30 MHz focused single-element transducers in used in confocal optoacoustic setup
- resolution of about 90 µm (lateral), depending on the transducer type
- combined imaging US/OA
- intrinsic 3-D imaging

Contrast agents:

- gold nanorods with tuneable absorption in VIS/NIR (500 nm to 1200 nm)
- dye-loaded polymer particles
- magnetite particles
- PEGylation
- antibody coupling



Impact of the aspect ratio on the absorption maximum.

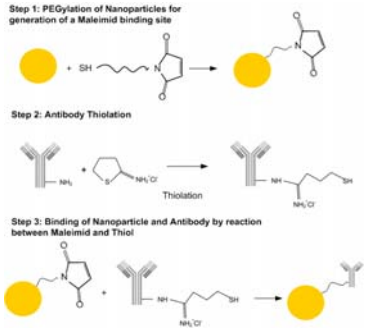
Contrast agents

In optoacoustic imaging, several types of nanoparticles can be used as contrast agents. The relevant parameter of such a contrast agent is its absorption coefficient.

Fraunhofer IBMT has developed and characterized several types of contrast agent particles based on gold, polymers and magnetite.

Gold nanoparticles have the highest absorption cross-section and are chemically inert. Furthermore, there was no evidence of cytotoxic effects in several in-vitro testing systems. However, there use remains limited to the preclinical field.

For enhancement of the contrast agents' specificity, polyethylene glycol (PEG) allowing to link such nanoparticles to biological ligands (antibodies, peptides) are used.



Functionalization of nanoscaled contrast agents for selective contrast enhancement.

Applications

Optoacoustic techniques allow to acquire signals with molecular specificity with relatively little technical effort and without any ionizing radiation. The detectability of low concentrations of nanoparticles (ranging from nMol down to pMol) has already been shown with Fraunhofer IBMT systems. The used of molecular optoacoustic imaging remains limited to the preclinical field since no clinically certified contrast agents are available nowadays. However, proof-of-concept experiments showing the potential of optoacoustic techniques for imaging with molecular specificity have already been performed in a small animal model. Therefore, applications are primarily in preclinical research in the fields of dermatology, oncology and rheumatoid diseases. However, the range of applications of the technology can be expanded to other fields as soon as adequate contrast agents are available.

1 *IBMT nanorods with varying aspect ratio.*

2 *Optoacoustic imaging using gold nanorods, which have agglomerated specifically in the knee joint of an arthritic mouse due to functionalizing by the antibody Infliximab (top row: control measurement, low signal amplitude; bottom row: specific signal enhancement due to functionalized nanorods).*