Project:

LUS BUBBLE

Technological key words:

photoacoustic imaging, photoacoustic microsurgery, plasmonic nanoparticles, digital holography

Industrial sectors addressed:

Biomedical imaging, noninvasive microsurgery,drug delivery

Total project costs: 999.708,00 Euros

Partners' descriptions:

- **Institute of Applied Physics** (IFAC, www.ifac.cnr.it) belongs to the National Research Council, the main public organization for research and innovation in Italy. IFAC enjoys solid background in nanomedicine and biomedical optics. IFAC will be in charge of the assembly, physio- and bio-chemical investigation of the particles and the optical excitation and detection of the bubbles. IFAC will be responsible for the scientific coordination and exploitation of the project developments.

- **Giotto Biotech S.r.l.** (www.giottobiotech.com) is a spin-off of Florence University (Italy) and is specialized in the production of proteins, synthetic inhibitors and metallorganic products of interest to the biotech and biopharma industries. Giotto will provide for the organic interface of the particles, in order to impart biocompatibility and specificity for the malignant cells of interest and take care of the scalability of the overall particle preparation.

- **Asclepion Laser Technology** (ALT, www.asclepion.com) originated as a spin- off from Carl Zeiss Meditech in Jena (Germany) and grew over the years to become a global player in the markets of medical lasers for applications in esthetical medicine, dermatology, dentistry and surgery. ALT will customize a portable Q-switched laser to ignite the bubbles and cooperate with MOS technologies and Muenster University to image the cells by a new digital holographic microscope equipped with a flow chamber.

Co-funded by the 7th Framework Programme of the European Union

- **Actis Active Sensors S.r.l**. is a Tuscan SME for system engineering in the interdisciplinary fields of electronics and photonics and a solid background for biomedical applications. In this proposal Actis will provide advice on the design of the instrumental platform and develop the synchronization of optical and acoustical components in a single platform, which will be tested at IFAC. In addition Actis will undertake the management of the Tuscan part of the project.

- **Esaote S.p.a.** (www.esaote.com) is one of the world leading manufacturers of ultrasound systems and dedicated MRI systems. Together with Florence University as its subcontractor, Esaote will undertake the design and preparation of equipment for the acoustical excitation and detection of bubbles by suitable transducers and electronics, which will be adapted from equipment in medical use.

Project abstract:

The scope of this project is the demonstration of a platform to image and treat cancer by the use of microbubbles triggered by the combination of optical and acoustical excitation of plasmonic particles delivered to malignant cells. The introduction of plasmonic particles for cancer imaging and treatment is becoming a clinical option. Innovative gold nano-shells, cages and rods are being engineered to target and sensitize tumors to near infrared (NIR) light for photoacoustic imaging, which combines optical contrast and acoustical detection, and therapy by optical hyperthermia. The main drawbacks of optical hyperthermia are its need for high contrast and its invasive profile, which dissipates the potential of plasmonic particles to accumulate into cancer cells with good specificity. One alternative may be the use of short and intense light pulses to trigger bubbles and impart damage to individual subcellular targets. While this approach has been demonstrated with gold nano-spheres resonating at green frequencies that are problematic for biomedical scopes, the use of NIR resonant particles conflicts with their optical instability. We propose to develop multishell particles of high damage threshold and synchronize an optical and acoustical activation to mitigate the optical requirements to generate bubbles and enable their manipulation. Mini invasive and destructive bubbles for imaging and therapy will be investigated in phantoms and cellular cultures. This project fits in the expanding market for efficient, mini invasive and cost effective solutions for cancer imaging and treatment. Pioneering innovation at the crossroads of nanomedicine, biomedical optics and acoustics will be pursued by customized modification of plasmonic particles in ongoing clinical trials and the adaptation of laser and ultrasound devices in common clinical use.

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The endpoint of this project will be the proof of concept of a novel technology to detect and destroy malignant cells in benchtop tests with cellular cultures and the design of protocols for in vivo tests with rodents.

Expected results and exploitation plan:

- The principal results of LUS BUBBLE will be the proof of concept in vitro of a novel technology to image and treat cancer by the use of vapor microbubbles that will be excited and probed by the combination of light and ultrasound. Specificity will be pursued by the use of smart contrast agents that will feature high optical absorbance and stability and the ability to recognize malignant cells. Along with this general result, innovation will be generated in strategic technologies, including a versatile photoacoustic platform, multifunctional nanoparticles and a new microscope.

- During the course of the project, the exploitation plan will consist of specific actions to protect the intellectual property and to generate awareness amongst potential stakeholders by the scientific literature and technical events. After the end of the project, additional financial resources will be searched for in order to start preclinical trials in vivo and to pursue commercial developments.