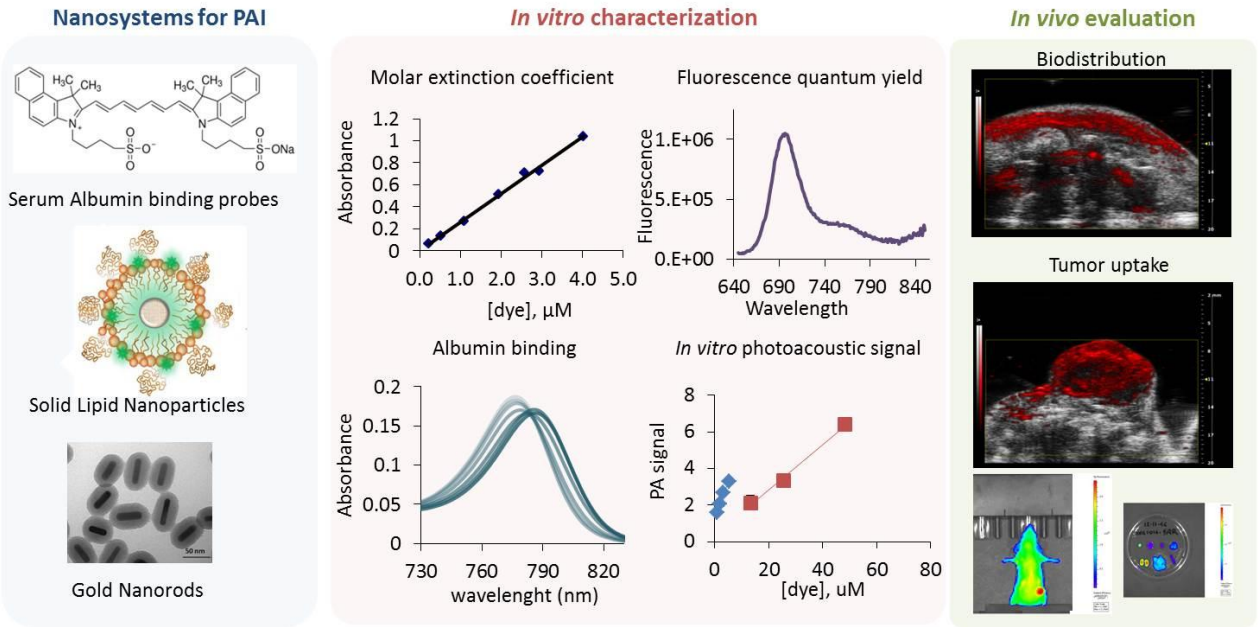
Nano-sized systems for imaging, a focus on photoacoustic imaging

Martina Capozza
Centro Ricerche Bracco, Bracco Imaging S.p.A., Colleretto Giacosa (To), Italy
martina.capozza@bracco.com
Tutors: Enzo Terreno, Alessandro Maiocchi

Photoacoustic imaging (PAI) is a new biomedical imaging modality based on laser-generated ultrasounds that allows the detection of endogenous and exogenous chromophores absorbing within the near-infrared wavelength range (NIR, ~600-1000 nm). Recently, PAI is applied to several biomedical areas including oncology, cardiovascular, neuroscience, gastroenterology, chronic inflammation, dermatology, to detect physiopathological processes in animal models and in human subjects during exploratory trials[1]. In order to explore the potentiality of new contrast agents for photoacoustic imaging, the *in vitro* characterization and *in vivo* application of some nano-sized probes is investigated. Nano-sized agents with long circulation times accumulate preferentially into tumor tissue due to the enhanced permeability and retention (EPR) effect[2]. However, it is known that this effect is heterogeneous among tumor types and within individual tumors. Therefore, the availability of an imaging tool that can report on the extent of the EPR effect could in principle improve the effectiveness of the administered therapy, particularly in the case of nanomedicines, providing additional insights on the response monitoring. We focus on different nano-sized systems with different dimensions for a detailed evaluation of their extravasation properties in tumor tissues. The nano-sized systems tested are: (i) a fluorescent small molecule with albumin binding properties, characterized by and average diameter of 5 nm; (ii) dye-loaded Solid Lipid Nanoparticles (SLNs, with a mean diameter of 45 nm); (iii) Gold Nanorods, non-spherical nanosystems with average dimensions: 40 nm x 10 nm. The main properties that influence the generation of photoacoustic signal, such as molar extinction coefficient, fluorescent quantum yield and albumin binding are investigated *in vitro*. Moreover, the photoacoustic signal is also measured by means of an agar phantom in different media such as phosphate buffer and serum. Based on the above parameters, a subset of nano-sized probes having enhanced photoacoustic signal is identified and their investigation is extended to healthy animals to confirm their *in vivo* efficiency. Near Infrared optical imaging is employed to characterize the biodistribution in the main organs and tumors of a subset of fluorescent probes.



1. Valluru, K. S.; Wilson, K. E.; Willmann, J. K., Photoacoustic Imaging in Oncology: Translational Preclinical and Early Clinical Experience. *Radiology* **2016,** *280* (2), 332-49.
2. Matsumura, Y.; Maeda, H., A new concept for macromolecular therapeutics in cancer chemotherapy: mechanism of tumoritropic accumulation of proteins and the antitumor agent smancs. *Cancer Res* **1986,** *46* (12 Pt 1), 6387-92.