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Surface chemistry-mediated metal nanoclusters for in vivo shortwave infrared imaging

In vivo optical imaging is nowadays widely used for cancer diagnosis and image-guided therapy with various devices that have already entered into the clinic. However, current fluorescence imaging is worth improving in spatial and temporal resolution in deep tissues. A novel approach relies on collecting optical signal from the second near-infrared window between 900 to 1700 nm called Shortwave InfraRed (SWIR). The use of this wavelength range should considerably reduce light scattering and absorption by blood and tissues in vivo improving sensitivity and spatial resolution in depth [1-3].

There is a high need to develop bright and safe contrast agents in this spectral window especially with emission at longer wavelength (>1250nm). In this context we develop gold nanoclusters (Au NCs) with different surface chemistry to enhance and red-shift their photoluminescence to the SWIR windows [3-4].

We evaluated then the impact of light scattering effects on spatial resolution in different shortwave infrared (SWIR) sub-regions by analyzing two SWIR emissive phantoms made i) polydimethylsiloxane (PDMS)-Au NCs composite covered with mice skin, and ii) capillary tubes filled with Au NCs at different depth in intralipids. We demonstrated the significant improvement of spatial resolution and reduced scattering collecting photons in the second SWIR windows between 1500 and 1700 nm and confirmed these results in mice with the observation of the blood network few mm deeper in mice [5].

New imaging processing methods are also necessary to enable sharp and detail reconstruction deeper in tissues. To address a clinical need for non-invasive high-resolution imaging of vascular and lymphatic networks at cellular level, we propose the use of a new bright SWIR emitting contrast agent based on ultra-small gold nanoclusters in pathological animal models presenting vascular disorders. We report also new imaging methods based on a series of Monte Carlo restoration (MCR) and on segmental analyses to provide a highly detailed mapping on the vasculature of mice. Imaging processing based on MCR enables more than one order improvement of spatial resolution with reduced scattering to distinguish non-invasively blood vessels deeper than 4mm. Segmentation analyses showed an increase of vessels complexity in transgenic mice KO BMP9 which confirmed previous ex vivo studies performed at the cellular level [6].

In conclusion, we presented new a method of high resolution, non-invasive, in vivo vascular imaging obtained using water-soluble and bright SWIR-emitting gold nanoclusters presenting an anisotropic surface charge combined with SWIR detection and Monte Carlo processing of the images. We applied this approach to quantify vessel complexity in mice presenting vascular disorders.

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