Harmonic nanoparticles for tissue imaging in the NIR II spectral window

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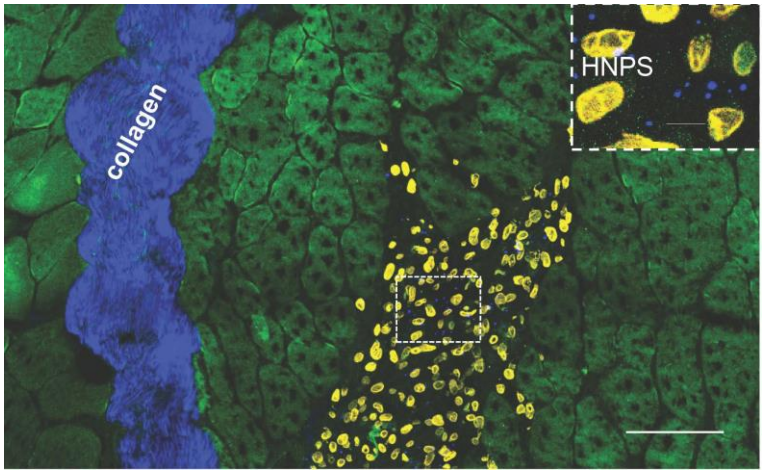
The term Harmonic Nanoparticles (HNPs) designates a family of metal oxide nanocrystals possessing appealing optical properties aside from classical luminescence. In fact, because of the lack of inversion symmetry in their crystal structure, these materials display high nonlinear optical response. In particular, the lowest nonlinear term of their nonlinear susceptibility, $\chi^{(2)}$, is non vanishing differently from the case of isotropic materials. For this reason, they are primarily employed in imaging applications based on second harmonic generation. [1] We have recently shown that third and even fourth harmonic generation are also very efficient for some of these materials, hence the name. [2] The distinctive features of HNPs as opposed to luminescent ones include their fully coherent emission, the absence of bleaching/blinking, and spectral flexibility (spanning from the ultraviolet to the infrared). This last asset is particularly appealing for bio-imaging applications, as HNPs allows imaging beyond the "classical" tissue transparency window (NIR I: 650-950 nm), in the newly investigated NIR II (1100-1350 nm) and NIR III (1600-1870 nm) windows. Working in these spectral regions enables sensibly deeper imaging penetration because of reduced scattering at longer wavelengths. After introducing the nonlinear optical properties of HNPs we will discuss their *in vivo* use for tracking labelled cells by simultaneous second and third harmonic acquisition, demonstrating highly specific retrieval of cancer metastases in lungs and stem cells in muscle tissue at > 1 mm depth.



Mutiphoton microscopy image of HNPs-labelled stem cells in murine muscle. Second harmonic emission in blue.

[1] *ACS Nano*, **6** (3), 2542–2549 (2012); *Mol. Pharmaceutics*, **10**, (3) 783-792 (2013)
[2] *ACS Photonics*, **2** (10), 1416–1422 (2015); *Sci. Rep.* **6**, 25415 (2016)