From whole body to subcellular imaging by applying single bimodal nanofluorinated probes compatible with both MRI and Raman imaging

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In the current clinical practice and biomedical research fields, several successful imaging tools allow to localize specific probes at different imaging scales (from subcellular to whole body size), using distinct imaging techniques (e.g., fluorescence, MRI or PET imaging) and corresponding specific probes. Besides, what it is not obvious today is the visualization of a single probe with different imaging approaches, focused on different imaging scales. As an example, common strategies used to detect specific MRI probes from whole body to cellular or tissue level include the combination of both MRI contrast agents and fluorescence molecules, with limitations related to stability, durability, accuracy, and technical complexity.

Here we reveal the capability to detect fluorinated (^{19}F) nanoprobes *in vivo* by ^{19}F-MRI, across the whole body, and microscopically, at tissue and cellular level, by confocal Raman imaging. This is possible thanks to unique features of perfluorinated molecules clearly showing both MRI and Raman signals.

We firstly demonstrated the possibility to detect these bimodal nanoprobes at sub-cellular level and in multiplexing modalities using Raman imaging. Thereafter, a mice model with multifocal neural inflammation in the spinal cord (resembling human multiple sclerosis) was employed to follow the inflammation sites on whole body by *in vivo* MRI, after treatment with fluorinated nanoprobes. Next, fresh frozen sections of spinal cord were collected and directly analysed by Raman microscopy without further labelling or staining. The Raman analysis not only allowed the direct localization of the fluorinated nanoprobes in the tissue at high resolution but also revealed the biomolecular composition of the surrounding tissue portions, thanks to intrinsic label-free features.

These data may open the possibility to use such type of probes for research or clinical purposes. The chemical versatility of these fluorinated nanoprobes may permit further chemical functionalization and subsequent targeting. For instance, the detection of tumours by MRI, followed by its intraoperative or *ex-vivo* localization by non-invasive Raman imaging is a possible application.