Spectroscopic and photoacoustic characterization of encapsulated iron oxide super-paramagnetic nanoparticles as a new multiplatform contrast agent

Paolo Armanetti, Alessandra Flori, Cinzia Avigo, Luca Conti, Barbara Valtancoli, Debora Petroni, Saer Doumett, Laura Cappiello, Costanza Ravagli, Giovanni Baldi, Andrea Bencini, Luca Menichetti

PII:	S1386-1425(18)30220-8
DOI:	doi:10.1016/j.saa.2018.03.025
Reference:	SAA 15897
To appear in:	*Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*
Received date:	22 September 2017
Revised date:	9 March 2018
Accepted date:	10 March 2018

Please cite this article as: Paolo Armanetti, Alessandra Flori, Cinzia Avigo, Luca Conti, Barbara Valtancoli, Debora Petroni, Saer Doumett, Laura Cappiello, Costanza Ravagli, Giovanni Baldi, Andrea Bencini, Luca Menichetti , Spectroscopic and photoacoustic characterization of encapsulated iron oxide super-paramagnetic nanoparticles as a new multiplatform contrast agent. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Saa(2017), doi:10.1016/j.saa.2018.03.025

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

journal homepage: www.elsevier.com/locate/saa

Spectroscopic and photoacoustic characterization of encapsulated iron oxide super-paramagnetic nanoparticles as a new multiplatform contrast agent

Paolo Armanetti[a], Alessandra Flori[b], Cinzia Avigo[a], Luca Conti[c], Barbara Valtancoli[c], Debora Petroni[a], Saer Doumett[d], Laura Cappiello[d], Costanza Ravagli[d], Giovanni Baldi[d], Andrea Bencini[c], Luca Menichetti[a*]

[a]Istituto di Fisiologia Clinica, CNR, Via Giuseppe Moruzzi 1, Pisa 56124, Italy; [b]Fondazione Regione Toscana G. Monasterio, Via Giuseppe Moruzzi 1, Pisa 56124, Italy; [c]Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, Via della Lastruccia 3, 50019 Sesto Fiorentino, Firenze, Italy; [d]Colorobbia Consulting Srl, via Pietramarina 123, 50053 Sovigliana – Vinci, Italy.

Abstract: Recently, a number of photoacoustic (PA) agents with increased tissue penetration and fine spatial resolution have been developed for molecular imaging and mapping of pathophysiological features at the molecular level. Here, we present bio-conjugated near-infrared light-absorbing magnetic nanoparticles as a new agent for PA imaging. These nanoparticles exhibit suitable absorption in the near-infrared region, with good photoacoustic signal generation efficiency and high photo-stability. Furthermore, these encapsulated iron oxide nanoparticles exhibit strong super-paramagnetic behavior and nuclear relaxivities that make them useful as magnetic resonance imaging (MRI) contrast media as well. Their simple bio-conjugation strategy, optical and chemical stability, and straightforward manipulation could enable the development of a PA probe with magnetic and spectroscopic properties suitable for *in vitro* and *in vivo* real-time imaging of relevant biological targets.

Keywords: photoacoustic imaging, optoacoustic imaging, magnetic resonance imaging, contrast media, biomedical imaging, contrast agent

1. Introduction

The laser-induced photoacoustic (PA) effect has recently been implemented in biomedical imaging. This effect occurs when a tissue, irradiated with a nanosecond laser pulse, is stimulated by light absorption and produces acoustic waves due to thermo-elastic processes. The laser-induced acoustic waves generated in the tissue provide molecular information based on the optical absorption, and this information can be correlated with standard echographic images. PA imaging (PAI) is a non-ionizing imaging technique that can reveal *in vivo* features [1] at high contrast and high resolution, thereby providing different functional information (i.e. blood oxygen saturation, oxygenated-deoxygenated hemoglobin ratio, early angiogenic states, or hypermetabolism) [1–3]. The performance of a PA system can be enhanced by using contrast agents [4–7], such as near-infrared (NIR) dyes and/or nanoparticles, that improve the sensitivity and spectroscopic specificity of a PA signal. This extends the range of applications of PAI, including the detection of specific molecular targets [8].

Magnetic resonance imaging (MRI) and PAI are currently being investigated for *in vivo* applications through a multimodal approach [9]. In this report, we describe the simple synthesis and characterization of a biocompatible hybrid nanosystem (also referred to as a fluorescent "nanobioreactor" or "NBRfluo"). Carboxy-terminated poly (D,L-lactide-co-glycolide)-block-poly(ethylene glycol) (PLGA-b-PEG-COOH) nanoparticles with an average hydrodynamic diameter of 40 nm, containing iron oxide clusters, were used as probes after loading a *de novo*-synthesized NIR fluorescent dye. Compared

*Corresponding author: tel.: +39 0503152137; fax: +39 0503152971
E-mail addresses: luca.m@ifc.cnr.it