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Oxygen vacancy-regulated superparamagnetic iron oxide nanoparticles for magnetic particle imaging

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Abstract

Magnetic particle imaging (MPI) is an emerging medical imaging technique with the advantages of high sensitivity, linear quantitation, and no ionizing radiation. In MPI, superparamagnetic iron oxide nanoparticles (SPIOs) serve as the sole signal source, making their properties critical for imaging performance. This study investigates the influence of oxygen vacancies in SPIOs on MPI performance. We synthesized SPIOs with varying degrees of oxygen vacancies and systematically evaluated their MPI performance. The results demonstrate a non-monotonic relationship: MPI signal initially increases and then decreases with increasing oxygen vacancy number. SPIOs with two oxygen vacancies exhibited optimal MPI imaging performance, providing effective evidence for designing high-performance MPI tracers.

I. Introduction

Magnetic particle imaging (MPI) is an emerging molecular imaging technology that visualizes the *in vivo* distribution of superparamagnetic iron oxide nanoparticles (SPIOs). It offers significant advantages, including high sensitivity, linear quantitation, no inherent tissue background signal, and zero ionizing radiation exposure [1]. These features make MPI a powerful tool for longitudinally monitoring disease progression and tracking cells or therapeutic agents. Since the MPI signal originates exclusively from SPIOs, optimizing their magnetic properties is essential for enhancing MPI performance. These properties are highly dependent on nanoparticle composition, size, and morphology, among other factors [2].

Oxygen vacancy is a common lattice defect in metal oxides. Previous studies have established that oxygen vacancies can modulate the T1-weighted magnetic resonance imaging contrast of SPIOs, primarily by altering water molecule coordination or changing the valence states of iron ions [3]. However, MPI operates on a fundamentally different principle as a tracer imaging technique. The impact of oxygen vacancies in SPIOs on MPI performance remains unexplored. Therefore, this study

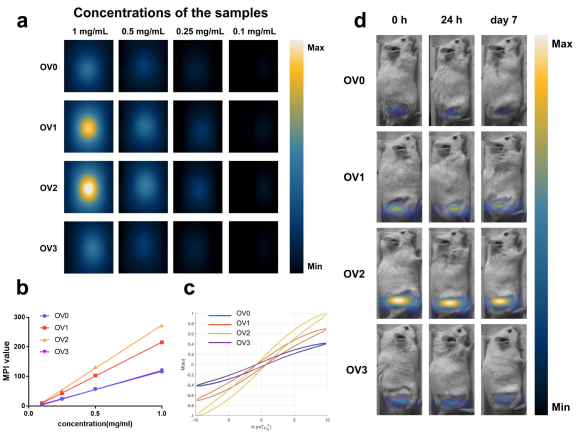

Figure 1: **a.** MPI images of the SPIOs with OV0, OV1, OV2, and OV3 at concentrations of 1, 0.5, 0.25, and 0.1 mg/mL (100 µL). **b.** Linear regression analysis of MPI signal intensity versus concentration. **c.** Normalized M-H curves for the four SPIO types. **d.** *In vivo* MPI images of CT26 tumor-bearing mice injected with OV0, OV1, OV2, and OV3 SPIOs at 0 h, 24 h, and day 7 post-injection (n = 3).

aims to systematically investigate the effects of oxygen vacancy in SPIOs on their MPI imaging efficacy.

II. Methods and materials

SPIOs with controlled the number of oxygen vacancy were synthesized: no oxygen vacancy (OV0), one vacancy (OV1), two vacancies (OV2), and three vacancies (OV3), with the oxygen vacancy number increasing sequentially. The MPI signal intensity of each sample was measured using an MPI scanner (MOMENTUM™ Imager, Magnetic Insight Inc.) at iron concentrations of 1, 0.5, 0.25, and 0.1 mg/mL (100 µL sample volume). Normalized magnetization (M-H) curves were acquired via magnetic particle spectroscopy.

For *in vivo* MPI, a CT26 subcutaneous colorectal tumor model was established in male BALB/c mice. Seven days post-inoculation, mice were randomly divided into four groups (n = 3 per group) and received intratumoral injections (50 µL, 1 mg/mL) of OV0, OV1, OV2, or OV3 SPIOs. MPI scans were performed at 0 h, 24 h, and day 7 post-injection. Following *in vivo* imaging, major organs (heart, liver, spleen, lung, kidney) were harvested for hematoxylin and eosin (H&E) staining to evaluate biosafety.

III. Results

Figure 1a and b present representative MPI images and the corresponding quantitative signal intensities, respectively. The normalized M-H curves are shown in Figure 1c.

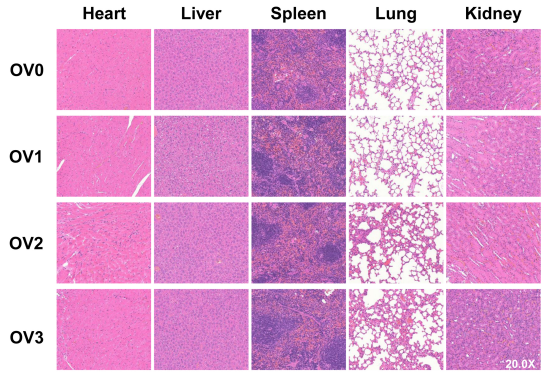

Figure 2: H&E staining of the heart, liver, spleen, lung, and kidney from mice treated with OV0, OV1, OV2, or OV3 SPIOs.

The MPI signal exhibited a non-monotonic dependence on the number of oxygen vacancy, initially increasing and then decreasing. SPIOs with two oxygen vacancies (OV2) demonstrated superior MPI performance. As shown in Figure 1b, the MPI signal intensity for all SPIO types showed a linear concentration dependence. The OV2 group generated an MPI signal 2.3-fold higher than the OV0 group. Notably, the signal from the OV3 group was comparable to that of the OV0 group and lower than both OV1 and OV2, indicating that MPI performance does not simply improve with higher vacancy counts. An optimal intermediate oxygen vacancy number (OV2) exists for maximizing MPI signal.

The *in vivo* MPI images of the CT26 tumor-bearing mice showed the consistent trend with *in vitro* MPI samples in the groups of OV0, OV1, OV2, and OV3. OV2 group consistently showed the highest tumor signal intensity among them until day 7 post-injection.

H&E staining of major organs (Figure 2) revealed no significant histological abnormalities in any treatment group, confirming the good biocompatibility of all synthesized SPIOs (OV0, OV1, OV2, and OV3).

IV. Conclusions

This study demonstrates that the number of oxygen vacancy in SPIOs is a critical parameter influencing MPI performance. The relationship follows a bell-shaped curve: the MPI signal first increases and then decreases with increasing the number of oxygen vacancies, with an optimum observed for SPIOs containing two oxygen vacancies (OV2). This finding provides a crucial design principle for developing high-performance SPIO tracers at MPI applications.

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Author's statement

The authors declare that there are no conflicts of interest.

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