MagnetoTheranostics RTD 2013

# From superparamagnetic nanoparticles to cancer detection and treatment

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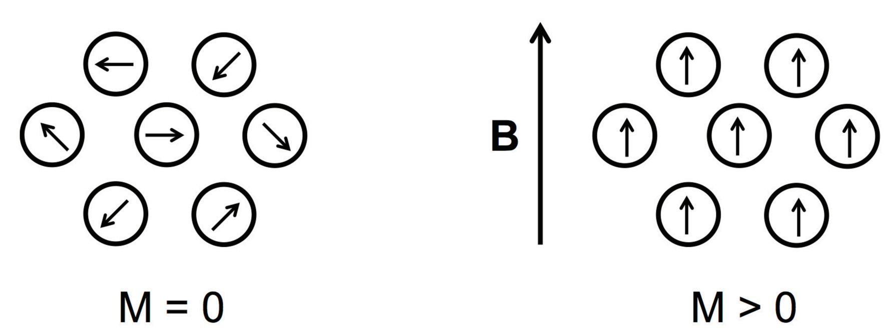
## Introduction

Patients with **advanced-stage prostate tumors** frequently undergo radical prostatectomy and lymph node dissection. Precise identification of the metastases location would allow distinction between healthy and cancerous tissue, and their subsequent treatment would be highly beneficial to the patient. **Superparamagnetic iron oxide nanoparticles (SPIONs)** are of great potential to achieve this goal, serving as contrast agent for **magnetic resonance imaging (MRI)** of tumors and inducing mild **hyperthermia** when subjected to an alternating magnetic field for tumor treatment.

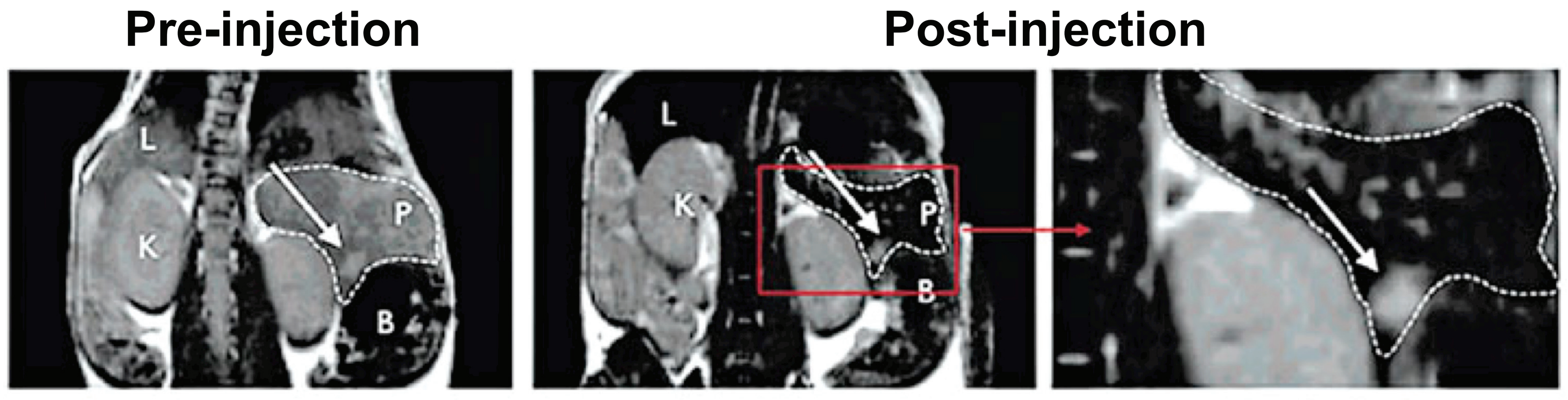
## SPIONs for cancer detection by MRI

SPIONs consist of single crystal domains with magnetization that can randomly change direction ($M_{average} = 0$). When placed in a constant magnetic field, the particle's spins align and are magnetized.




The magnetized spins shorten the spin relaxation process of adjacent hydrogen atoms from $H_2O$. When subjected to radiofrequencies, the magnetized spins shortly change their orientation before coming back to their initial magnetization, giving rise to T1 and T2 relaxation times and MR images.

**Pre-injection** **Post-injection**




MRI on T2-weighted sequences of pancreatic ductal adenocarcinoma

(Hofmann-Amtenbrink et al, Superparamagnetic nanoparticles – a tool for early diagnostics, Swiss Medical Weekly, 2010)

## SPIONs for cancer treatment by hyperthermia

The energy transmitted to a tissue under the form of heat per Fe mass ($W/g_{Fe}$) is given by the **specific loss power (SLP)**:

$$SLP\,(r) = \frac{\mu_0^2 M_S^2 (\frac{4}{3}\pi r^3) H_0^2}{3 k_B T \rho_{Fe_2O_3} \tau} \, \frac{(2\pi f \tau)^2}{1+(2\pi f \tau)^2} \longrightarrow \tau = \frac{\tau_B * \tau_N}{\tau_B + \tau_N}$$

where the relaxation time τ can be of two origins:

**Brownian relaxation time $\tau_B$** arising from the particle's rotation in the fluid due to Brownian motion

$$\tau_B = \frac{3\eta(\frac{4}{3}\pi r_h^3)}{k_B T}$$

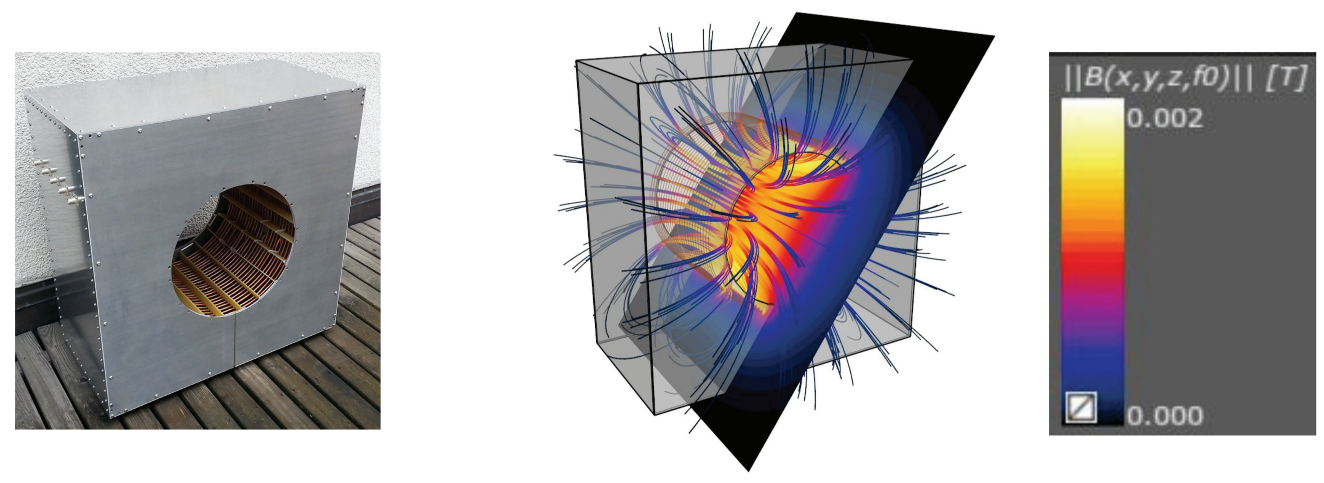
**Néel relaxation time $\tau_N$** coming from the oscillation of the particle's magnetization

$$\tau_N = \tau_0 e^{\frac{K(\frac{4}{3}\pi r^3)}{k_B T}}$$

Both relaxation times generate energy losses, mostly transmitted to the surrounding tissue under the form of heat. **Optimizing the particle's size allows us to reach optimal heating efficiencies for cancer treatment.**

$\mu_o$ magnetic permeability, $M_s$ saturation magnetization, $r_h$ hydrodynamic radius, r crystalline radius and K anisotropy constant of particles; $H_o$ amplitude and f frequency of the alternating magnetic field; η viscosity of the fluid

Heating of the SPIONs with an **alternating magnetic field at 300 kHz** gives the best compromise between relaxation losses and unwanted heating of healthy tissues. The applicator design provides a homegeneous field such that placement of the patient in the applicator is not critical.




## Optimization of SPION's size for hyperthermia

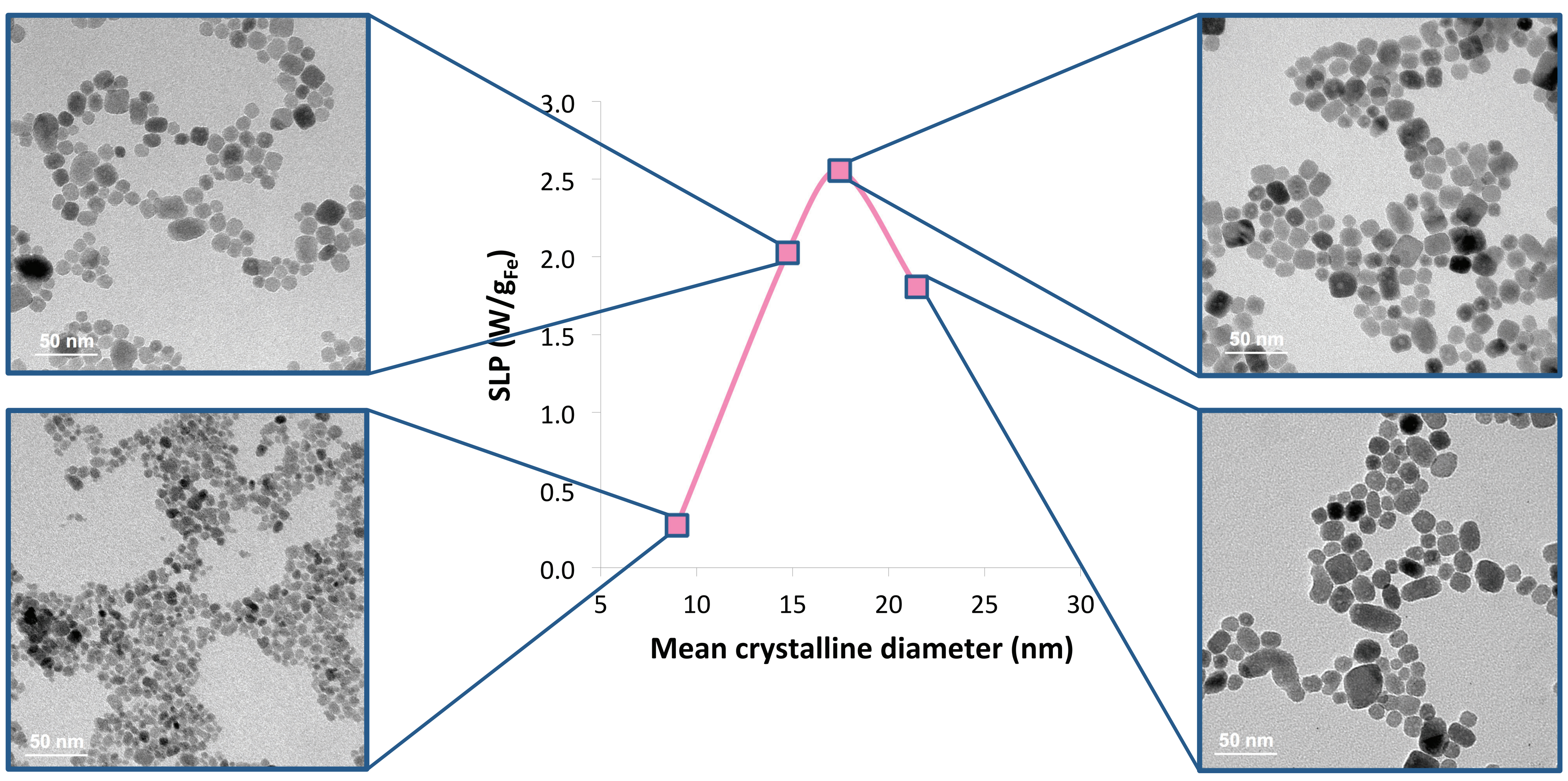
Crystalline mean diameter and representative images of SPIONs obtained from transmission electron microscopy, as well as the SLP values calculated theoretically for each particle size distribution:

**Mean crystalline diameter:** **14.7 ± 5.0 nm**

**SLP = 1.68 $W/g_{Fe}$**

**Mean crystalline diameter:** **9.0 ± 2.5 nm**

**SLP = 0.28 $W/g_{Fe}$**




**Mean crystalline diameter:** **17.4 ± 4.7 nm**

**SLP = 2.34 $W/g_{Fe}$**

**Mean crystalline diameter:** **21.5 ± 6.3 nm**

**SLP = 1.38 $W/g_{Fe}$**