

# MicroCT Imaging Based Theoretical Simulation and Protocol Design in Magnetic Nanoparticle Hyperthermia of Research (NSF CBET-1335958)

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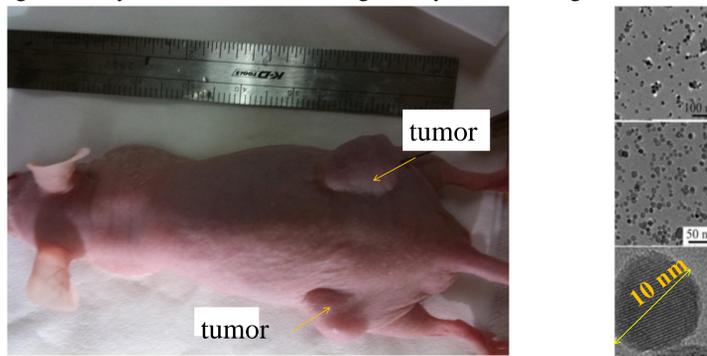
## Project Summary

Magnetic nanoparticles can generate heat when subject to an alternating magnetic field. It holds a high cell-killing potential in cancer treatment because it can deliver confined thermal energy to tumors. Nanoparticle distribution in tumors is a major factor in determining treatment efficacy. Unfortunately, particle spreading is difficult to model due to tumor heterogeneous structures and complex processes such as particle deposition, agglomeration, and intake. The goal of the research projects is to develop an imaging based simulation method to improve simulation accuracy in hyperthermia, therefore, achieving individualized treatment designs for cancer patients using magnetic nanoparticle hyperthermia. The specific aims of the research are:

1. To utilize a microCT system to obtain tumor geometry and nanoparticle distribution in prostate tumors implanted in mice. Controllable nanoparticle deposition patterns unique to individual tumor groups will be visualized and quantified.
2. To develop computational algorithms to identify optimized heating protocols for groups representing various infusion rates. The tumor geometry and particle distribution obtained from the microCT scan will be generated and exported for heat transfer simulation. Thermal damage region will be simulated to determine optimal treatment protocols.
3. To implement the optimal heating protocols to human prostatic tumors implanted in mice during *in vivo* magnetic nanoparticle hyperthermia. The success of the designed protocols will be verified via measured tumor temperatures, histological analyses of thermal damage, and tumor shrinkage monitoring.

## Methods

1. Prostatic Tumors (PC3) Implanted in Mice
2. Iron Based Nanoparticle Solution
3. MicroCT Image System
4. Matlab, SAS, and COMSOL software
5. Magnetic Nanoparticle Heating Induced by an Alternating Magnetic Field
6. Temperature Measurements during Heating
7. Histological Analyses and Tumor Shrinkage Study after Heating



## Summary

*In vivo* animal experiments are performed on nude mice bearing PC3 tumors to investigate how infusion rate affects the distribution of nanoparticles, using high-resolution microCT imaging technique. This study has identified infusion strategies to achieve repeatable and controllable nanoparticle deposition patterns. A tumor model and nanoparticle distribution model are generated based on microCT images and imported to COMSOL finite element software to simulate temperature elevations and thermal damage in PC3 tumors implanted in mice to determine an optimal heating protocol. Later heating experiments are performed followed the designed protocol. The efficacy of the designed heating protocol is tested by performing a tumor shrinkage study and histological analyses. Compared to the control tumor group without heating when the tumors continues to grow, it is seen that the tumor group with heating shows complete disappearance of tumors with no regrowth observed over an eight week period, implying complete damage to the cancer cells. Histological analyses demonstrate irreversible damage in terms of necrosis occurring in the entire tumor region, including the tumor periphery. One observes serious cellular morphological changes suggesting that the tumor cells will not grow back, consistent with the results in the tumor shrinkage study.

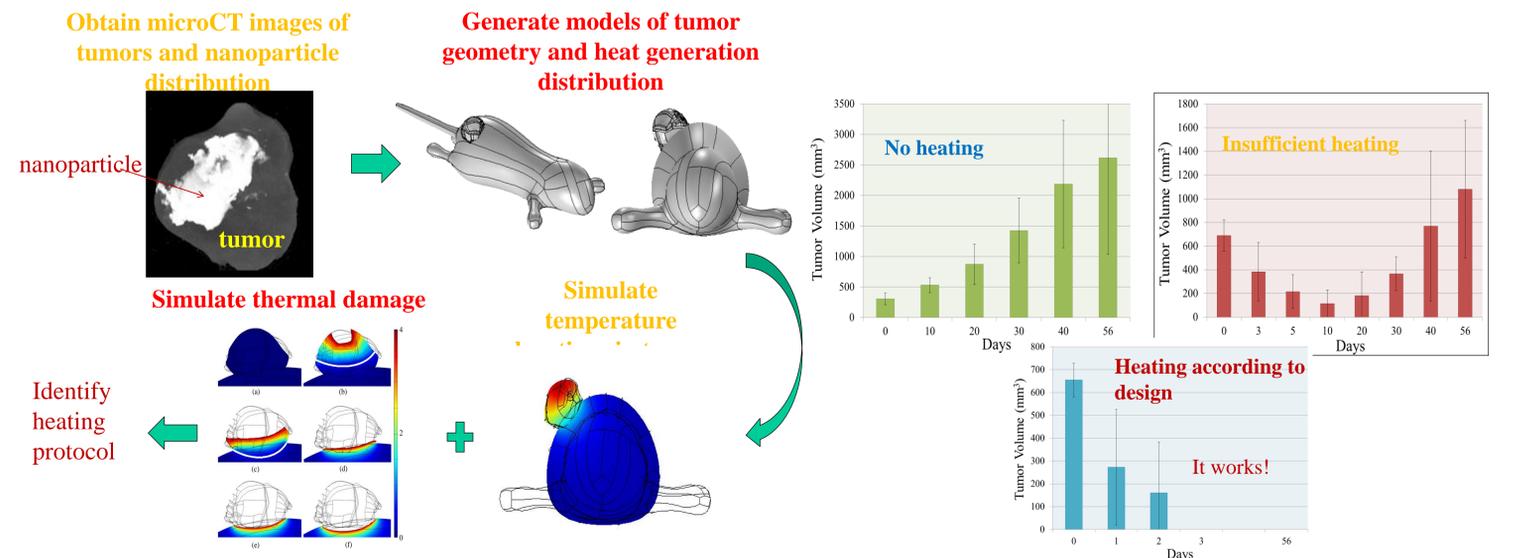
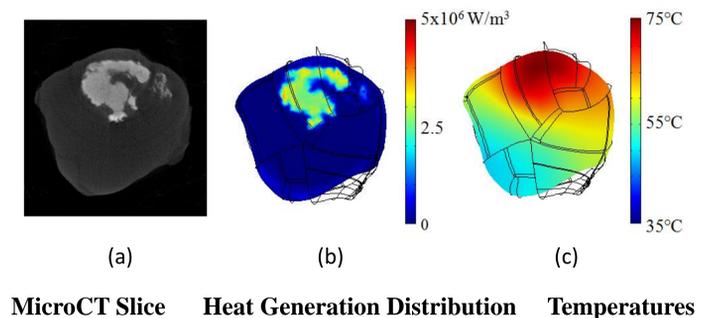
## Radio Frequency Generator



An alternating magnetic field generated by a two-turn coil



## MicroCT Imaging System



## References:

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2. LeBrun, A., Joglekar, T., Bieberich, C., Ma, R. and Zhu, L.. Identification of Infusion Strategy for Achieving Repeatable Nanoparticle Distribution and Quantifiable Thermal Dosage in Magnetic Nanoparticle Hyperthermia. *International Journal of Hyperthermia*, 32(2):132-143, 2016.
3. LeBrun, A., Ma, R. and Zhu, L.. MicroCT image based simulation to design heating protocols in magnetic nanoparticle hyperthermia for cancer treatment. *Journal of Thermal Biology*, in press, eprinting, available online, July 2016.
4. LeBrun, A., Joglekar, T., Bieberich, C., Ma, R. and Zhu, L.. Treatment efficacy for validating microCT based theoretical simulation approach in magnetic nanoparticle hyperthermia for cancer treatment. *ASME Journal of Heat Transfer*, in press, 2016.

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