Theranostic Nanoparticle-Mediated Tumor Ablation in a Rat Model of Metastatic Spine Disease

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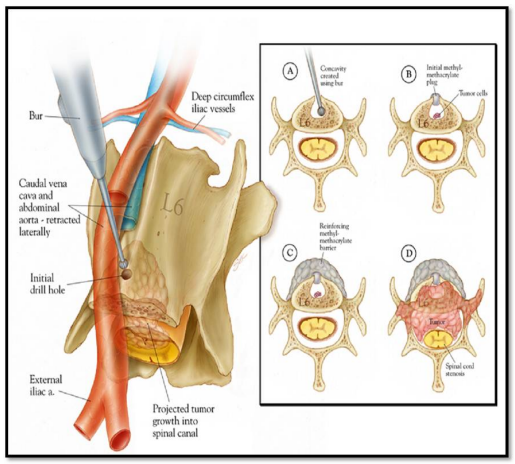
Introduction

Among the 1.5 million new cases of cancer diagnosed annually, 30-90% of patients experience spinal metastasis. [1,2] The purpose of this study was to use an animal model of metastatic spine disease to investigate nanoparticle-based tumor thermoablation as a treatment modality for metastatic spine disease.

Figure 1.



Artistic rendition demonstrating transperitoneal exposure and drilling of the L6 vertebral body with placement of tumor.

Hypothesis

Ferromagnetic nanoparticles induce intratumoral thermoablative necrosis when coupled with an alternating magnetic field (AMF) coil when the particles are injected directly into a metastatic mammary tumor in the rat spinal column. [3,4] These particles are visible on MRI imaging and may serve a therapeutic as well as diagnostic purpose.

Methods

Nanoparticle Delivery and Distribution Study Design:

Thirty-six female Fischer rats were randomized into control or nanoparticle (NP) injected cohorts. Three animals each for control and NP conditions were then randomized to each time point at 1, 3, 6, 12, 24, and 48 hours. All animals underwent L6 VB exposure and drilling of a 1mm vertebral body defect (Figure 1). On the 9th post-operative day, nanoparticles were injected at a concentration of 0.27 mg iron/cm3 of tumor under direct visualization.

Distribution Study Histological and Mass Spectrometry Analysis:

Liver, lungs, spleen, and blood were harvested for study of systemic particle distribution and processed using microwave digestion for ICP-MS to measure systemic nanoparticle distribution and concentration. Prussian Blue staining of all organs was also performed.

Intratumoral Thermodosimetry Study Design:

4 female Fischer rats were divided into two groups according to exposure of an 800 versus 600 G AMF. (Figure 2) Following nanoparticle injection, a fiber-optic temperature sensor (FISO Technologies Inc, Quebec, QC, Canada) was secured within the tumor. Animals were treated for 20 minutes in the AMF coil within 3 hours of nanoparticle injection.

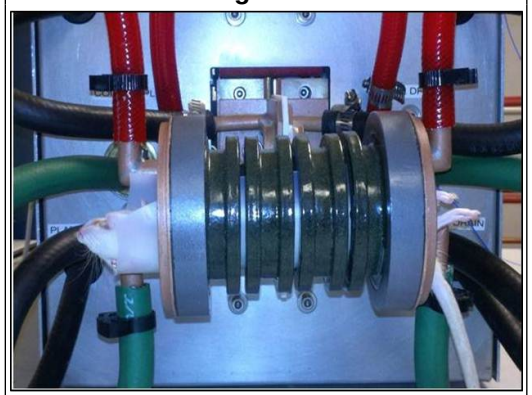
An additional cohort of 30 tumor-bearing fisher rats were randomly assigned to NP (n=16) or no NP (n=14), then placed in the AMF coil at 600 Gauss for 20 minutes. Fiber-optic rectal temperature probes monitored internal body temperature.

Results

Nanoparticle distribution. At one hour after nanoparticle injection, there was evidence of nanoparticle distribution throughout the tumor. ICP-MS analysis and Prussian Blue staining of the lymphoreticular organs did not demonstrate significant accumulation of nanoparticles at any time following surgery, however accumulation of nanoparticles in the meninges was found at 48 hours after injection.

Thermodosimetry study. Intratumoral temperature was consistently higher than rectal temperature for all animals tested at the 600G and 800 G conditions. Rectal thermometry of the NP and no NP group in the larger thermodosimetry cohort demonstrated an average rectal temperature of 36.3C and 36.6C respectively. The difference was not statistically significant (p=0.44). All animals were ambulatory at 24 hours following treatment.

Figure 2.



Rat placement in alternating magnetic field coil.

Conclusions

NP and AMF therapy to spinal column tumors is a safe treatment modality that results in limited systemic distribution, no immediate neurologic deficit and minimal change to core temperature in a rat intravertebral tumor model. Future imaging studies will better characterize ferromagnetic nanoparticles as a theranostic modality.

Learning Objectives

By the conclusion of this session, participants should be able to 1) describe the importance of improved animal models for metastatic disease, 2) Discuss in small groups the utility of thermoablation in spine tumors and 3) identify nanoparticle mediated therapy as an effective treatment for metastatic spine tumors.

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References

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