Session 8: Targeted imaging approaches and histologic correlations

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Novel Nano-Sized Manganese-based MRI CM Enhancing Tumours in an Oncogene-Driven Breast Cancer Model

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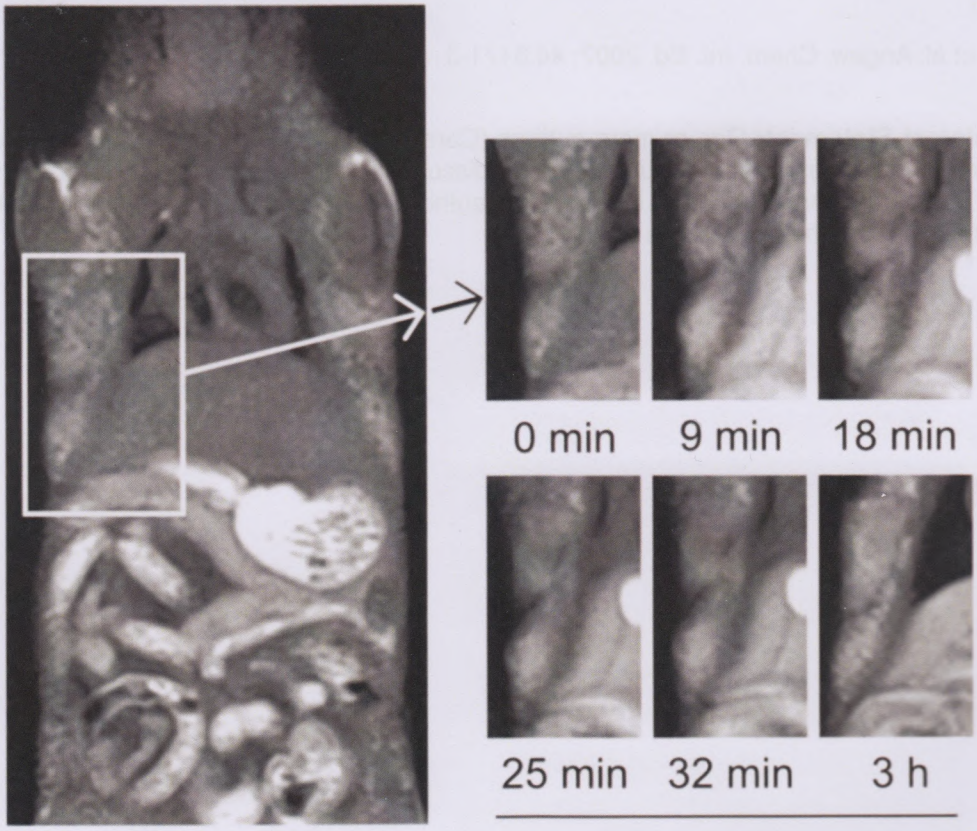
Purpose: Diagnostic imaging has a pivotal role in oncology and MRI is used to a high extent in combination with contrast media (CM) to improve sensitivity and specificity. In tumorous tissue the capillary bed is immature and an effect called enhanced permeability and retention (EPR-effect[ref 1]) has shown to be promising when nanomaterials are used as CM. In addition, there have been concerns of gadolinium as the magnetic moiety of MRI-CM as the metal may be retained in the body giving side effects.

Methods and Materials: In the present study a novel manganese based nanoparticle MRI-CM is presented[ref 2]. The CM nanomaterial has a globular shape, an average hydrodynamic diameter of 5 nm, and a relaxivity (r^1) of approximately 30 $(mM\ Mn)^{-1}\ s^{-1}$ (@60 MHz). The material consists of an organophosphosilane hydrogel with strongly chelated manganese (II) ions and a covalently attached PEG surface layer. The novel CM was studied in an MMTV-PyMT breast cancer model on a 3 T clinical scanner. Tissues were thereafter analysed for manganese and silicon content using inductively coupled plasma-atomic emission spectroscopy (ICP-AES). The presence of nanomaterial in tumour and muscle tissue was assessed using an anti-PEG monoclonal antibody.

Results: MRI of tumour bearing mice (n = 7) showed a contrast enhancement factor of 1.8 (tumour versus muscle) at 30 minutes post-administration. Contrast was retained and further increased 2–4 hours after administration. ICP-AES and immunohistochemistry confirmed selective accumulation of nanomaterial in tumour tissue. A blood pharmacokinetics analysis showed that the concentration of the CM gradually decreased over the first hour, which was in good agreement with the time frame in which the accumulation in tumour occurred.



Conclusions: In summary, the novel MRI-CM selectively enhances MR tumour contrast in a clinically relevant animal model. Based on the generally higher vascular leakiness in malignant compared to benign tissue lesions, the CM has the potential to significantly improve cancer diagnosis and characterization by MRI.

References:

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