

## Anti-VCAM-1 targeted MRI allows earlier detection of brain metastases in a xenograft melanoma mouse model

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### Abstract

**BACKGROUND:** Malignant melanoma frequently metastasises to the brain, with between 10% to 40% of patients estimated to develop intracranial metastases following diagnosis. Although treatments are available for managing brain metastases, their frequently late stage of detection limits the therapeutic potential. Anti-VCAM-1 antibody conjugated microparticles of iron oxide (VCAM-MPIO) have previously been shown to enable detection of early intracranial disease with a breast cancer model. **AIM:** To demonstrate the utility of VCAM-MPIO in a xenograft melanoma mouse model for detection of brain metastases. **METHODS:** 6 immunocompromised female SCID mice (age 8-9 weeks) were injected intracardially with  $1 \times 10^5$  cells of the human-derived melanoma cell line, H1\_DL2. Animals were imaged 21 days later by magnetic resonance imaging (MRI) with a multi-gradient echo 3D (MGE3D) sequence, following intravenous injection of VCAM-MPIO. Blood-brain barrier (BBB) integrity was confirmed on post-gadolinium  $T_1$ -weighted images. Control groups consisted of naïve SCID animals imaged with VCAM-MPIO and tumour-inoculated animals imaged with isotype IgG control antibody conjugated MPIO. Animals were perfusion-fixed, and brain sections assessed immunohistochemically for VCAM-MPIO binding and presence of metastases. **RESULTS:** Despite lack of BBB breakdown, VCAM-MPIO MRI of tumour bearing mice revealed multiple intracerebral hypointensities indicating specific binding of VCAM-MPIO to cerebral vessels. Both presence of intracerebral micrometastases and VCAM-MPIO binding to VCAM-1 positive vessels were confirmed immunohistochemically. Minimal intracerebral hypointensities were observed in the control groups. **DISCUSSION:** VCAM-MPIO MRI can detect melanoma micrometastatic disease in the brain before conventional (gadolinium enhanced) MRI techniques. The potential clinical implication of earlier detection is improved treatment response with reduced patient morbidity and mortality.

### Topics

- Cerebral Mets/ Other CNS Malignancies
- Imaging