# Ferumoxytol magnetic resonance imaging

Ferumoxytol is an FDA-approved iron supplement which can be used “off label” as a contrast agent: the nanoparticle-based drug is phagocytosed by tumor-associated macrophages (TAMs) and can be detected with magnetic resonance imaging (MRI).

## Indications

Ferumoxytol magnetic resonance imaging for intracranial arteriovenous malformation.

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Mohanty et al. evaluated if ferumoxytol-enhanced MRI can monitor TAM response to CD47 mAb therapy in osteosarcomas. Forty-eight osteosarcoma-bearing mice were treated with CD47 mAb or control IgG and underwent pre- and post-treatment ferumoxytol-MRI scans. Tumor enhancement, quantified as T2 relaxation times, was compared with the quantity of TAMs as determined by immunofluorescence microscopy and flow cytometry. Quantitative data were compared between experimental groups using exact two-sided Wilcoxon rank-sum tests. Compared to IgG-treated controls, CD47 mAb-treated tumors demonstrated significantly shortened T2 relaxation times on ferumoxytol-MRI scans ($p < 0.01$) and significantly increased F4/80+CD80+ M1 macrophages on histopathology ($p < 0.01$). CD47 mAb-treated F4/80+ macrophages demonstrated significantly augmented phagocytosis of ferumoxytol nanoparticles ($p < 0.01$). Thus, we conclude that ferumoxytol-MRI can detect TAM response to CD47 mAb in mouse models of osteosarcoma. The ferumoxytol-MRI imaging test could be immediately applied to monitor CD47 mAb therapies in clinical trials [1)].

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In a prospective study, adults with high-grade gliomas were enrolled between July 2015 and July 2017. Each participant was administered intravenous ferumoxytol (5 mg/kg) and underwent 3.0-T MRI 24 hours later. Two sites in each tumor were selected for intraoperative sampling on the basis of the degree of ferumoxytol-induced signal change. Susceptibility and the relaxation rates R2* (1/T2*) and R2 (1/T2) were obtained by region-of-interest analysis by using the respective postprocessed maps. Each sample was stained with Prussian blue, CD68, CD163, and glial fibrillary acidic protein. Pearson correlation and linear mixed models were performed to assess the relationship between imaging measurements and number of 400× magnification high-power fields with iron-containing macrophages. Results Ten adults (four male participants [mean age, 65 years ± 9 {standard deviation}; age range, 57-74 years] and six female participants [mean age, 53 years ± 12 years; age range, 32-65 years]; mean age of all participants, 58 years ± 12 [age range, 32-74 years]) with high-grade gliomas were included. Significant positive correlations were found between susceptibility, R2*, and R2' and the number of high-power fields with CD163-positive (r range, 0.64-0.71; $P < .01$) and CD68-positive (r range, 0.55-0.57; P value range, .01-.02) iron-containing macrophages. No significant correlation was found between R2 and CD163-positive ($r = 0.33$; $P = .16$) and CD68-positive ($r = 0.24$; $P = .32$) iron-containing macrophages. Similar significance results were obtained with linear mixed models. At histopathologic analysis, iron particles were found only in macrophages; none was found in glial fibrillary acidic protein-positive tumor cells. Conclusion MRI measurements of susceptibility, R2*, and R2' (R2* - R2) obtained after ferumoxytol administration correlate with iron-containing

macrophage concentration, and this shows their potential as quantitative imaging markers of macrophages in malignant gliomas [2].

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Malignant dural neoplasms are not reliably distinguished from benign dural neoplasms with contrast-enhanced magnetic resonance imaging (MRI). MRI enhancement in central nervous system (CNS) diseases imaged with ferumoxytol has been attributed to intracellular uptake in macrophages rather than vascular leakage.

Hamilton et al. compared imaging to histopathology and immunohistochemistry in meningiomas and dural metastases having ferumoxytol-enhanced MRI (FeMRI) and gadolinium-enhanced MRI (GdMRI) in order to correlate enhancement patterns to macrophage presence and vascular state. All patients having extraaxial CNS tumors were retrospectively selected from one of two ongoing FeMRI studies. Enhancement was compared between GdMRI and FeMRI. Diagnoses were confirmed histologically and/or by characteristic imaging. Tumor and vascular histology was reviewed. Immunohistochemical staining for CD68 (a macrophage marker), Connexin 43 (Cx43) (a marker of normal gap junctions), and smooth muscle actin (SMA) as a marker of vascularity, was performed in seven study cases with available tissue. Immunohistochemistry was performed on archival material from 33 subjects outside of the current study as controls: 20 WHO grade I cases of meningioma and 13 metastatic tumors. Metastases displayed marked delayed enhancement on FeMRI, similar to GdMRI. Four patients with dural metastases and one patient with meningioma showed similar enhancement on FeMRI and GdMRI. Five meningiomas with typical enhancement on GdMRI lacked enhancement on FeMRI. Enhancement on FeMRI was better associated with decreased Cx43 expression than intralesional macrophages. These pilot data suggest that FeMRI may better differentiate metastatic disease from meningiomas than GdMRI, and that differences in tumor vasculature rather than macrophage presence could underlie differences in contrast enhancement [3].

# Unclassified

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