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CMR 2005: 2.06**Ferumoxtran-10 enhanced MR imaging in detection of metastases outside the normal surgical area in prostate cancer**

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Rationale and Objectives: To evaluate whether, in prostate cancer patients, with Ferumoxtran-10 enhanced MR imaging lymph node metastases outside the normal surgical area (that is, the obturator fossa) will be detected.

Methods: A total of 150 consecutive patients with prostate cancer and at intermediate to high risk for nodal metastases (PSA >10 or Gleason <6 or at DRE stage T3) were enrolled in this study. At 1.5 T, T_1 - and T_2^* -weighted MR images of the pelvis were obtained, 24 h after administration of Ferumoxtran-10. The MR examinations were evaluated by one experienced reader.

Lymph node metastases were confirmed by lymph node dissection or CT-guided lymph node biopsy

Results: Thirty-one out of 150 patients (21%) had positive lymph nodes confirmed by histopathology. Of these 31 patients, 16 (52%) had positive lymph nodes only outside the normal surgical area (obturator fossa), eight (26%) had positive nodes inside and outside the obturator fossa and six (19%) only inside. Without Ferumoxtran-10 enhanced MRI, in 52% of the patients these positive nodes would not have been detected.

Conclusion: With Ferumoxtran-10 enhanced MR imaging, additional nodes will be found compared with obturator nodal dissection.

Session 3: Targeting; Tumor**CMR 2005: 3.01****MRI tumor characterization using Gd–GlyMe–DOTA–perfluorooctylmannose conjugate (Gadofluorine M), a novel protein-avid contrast agent**

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Rationale and Objectives: The aim was to define the pharmacokinetics and MRI tumor-enhancing characteristics of a new protein-avid

contrast agent, Gd–GlyMe–DOTA–perfluorooctylmannose conjugate (Gadofluorine M, Schering, Berlin, Germany) in a chemically induced tumor model of varying malignancy. Because of the unique properties of this agent, including a large effective *in vivo* hydrodynamic radius (5.5 nm) and strong binding to hydrophobic sites on extracellular proteins, it was hypothesized that patterns of dynamic enhancement in tumors could be used to measure abnormal tumor microvascular permeabilities and also could aid in the differentiation of viable and necrotic tumor components.

Methods: Gadofluorine M, 0.1 mmol Gd/kg, was administered intravenously to 32 anesthetized rats that had developed mammary tumors of varying degrees of malignancy over the 6 months following intraperitoneal administration of *N*-ethylnitrosourea (ENU), 45–250 mg. These tumors ranged pathologically from benign fibroadenomas to highly undifferentiated adenocarcinomas. Pre- and dynamic post-contrast T_1 -weighted MRI at 2.0 T (Bruker) was performed at short intervals for 40 min with region-of-interest analyses of whole tumor, tumor rim, tumor center and venous blood enhancement responses. These enhancement data were also post-processed using a two-compartment kinetic model to generate estimates of fractional plasma volumes (fPV) and the apparent coefficient of permeability–surface area product (K^{PS}). After killing the animals, the tumors were examined microscopically and scored by a pathologist, blinded to the MRI data, for tumor type, degree of malignancy (Scarff–Bloom–Richardson score), plus degree and distribution of necrosis. Pathological data were correlated with MRI observations.

Results: So far 26 tumor-bearing rats have now been successfully examined by dynamic MRI, with another 8–10 animals to be added by the time of presentation. Accumulated data show an immediate strong but gradually increasing tumor enhancement, with the late enhancement being concentrated in the tumor center, a zone of relatively greater necrosis. Complete data analyses with calculation of fPV , K^{PS} and paired tumor MRI–pathology correlations will be available at the time of presentation.

Conclusions: A novel MRI contrast agent, Gadofluorine M, strongly enhances tumors of varying pathology and on late images seems to highlight zones of necrosis, probably owing to a strong avidity for hydrophobic sites on extracellular proteins. Because this 1528 Da molecule tends to form aggregates with hydrodynamic diameters of >5 nm after intravenous administration, dynamic enhancement can also be used to assay tumor plasma volumes.

CMR 2005: 3.02**The stromal mechanism: an inherent link between necrosis-avid contrast agents and photodynamic therapy**

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Rationale and Objectives: Necrosis-avid contrast agents (NACAs) were discovered initially among porphyrin derivatives including gadophrin-2 that were intended to target neoplastic cells with the same principle adopted from cancer photodynamic therapy (PDT). Later, the NACAs of non-porphyrin chemicals including ECIII-60 and ECIV-7 were developed with demonstrated multifunctional features such as striking T_1 and T_2 dual-contrast enhancement of acute myocardial infarction, therapeutic assessment after tumor ablation, blood-pool effect for MR angiography and hepatobiliary tumor detection (1). Here we sought to investigate the underlying mechanisms of NACAs and to formulate consequent new diagnostic and therapeutic strategies.

Methods:

1. Summarizing experimental results derived from MRI, SPECT, autoradiography, radioactivity counting and fluorescent and optical microscopy studies in animal models of induced tumors and necroses