Differentiation of benign fibroadenomas from breast cancer with dynamic MRI: comparison of a novel macromolecular contrast agent and gadoteridol

H. J. Raatschen[1,2], Y. Fu[2], D. M. Shames[2], and R. C. Brasch[2]

[1]Radiology and Nuclear Medicine, Charite Campus Benjamin Franklin, Berlin, Berlin, Germany, [2]Radiology, University of California San Francisco Medical Center, San Francisco, CA, United States

Purpose:

To evaluate the suitability of two gadolinium-based contrast agents, the FDA-approved gadoteridol, and a new macromolecular polyethylene glycol (PEG)-based dendrimer, intended for clinical development, for differentiation of benign from malignant breast tumors in an animal model.

Method and Materials:

Chemically induced fibroadenomas and malignant breast tumors were imaged in 31 female Sprague-Dawley rats by dynamic MRI at 2.0 T after i.v. administration of PEG_{12000}-Gd-DO3A$_{26}$. The experiment was repeated 24 hours later in the same animals using gadoteridol. Vascular endothelial leakiness (K^{PS}; µl min^{-1} cm^{-3}) and fractional plasma volume (fPV; %) were calculated for all mammary tumors and normal soft tissue using a simple bidirectional pharmacokinetic model. The resulting estimates were evaluated statistically for their potential to differentiate fibroadenomas from malignant breast tumors, as determined by histology, and to differentiate tumors from normal soft tissue.

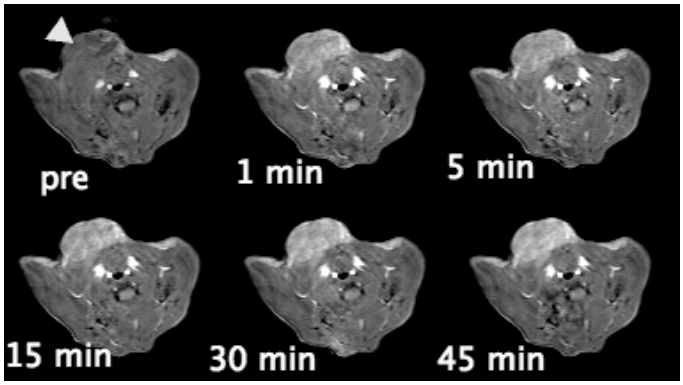

Figure 1: Dynamic PEG_{12000}-Gd-DO3A$_{26}$-enhanced MRI of a malignant breast tumor (arrowhead) demonstrating the strong and persistent tumor enhancement for 45 min.

Results:

Estimates for fPV (7.5 ± 2.7 vs. 5.4 ± 2.1%, mean ± SD) and K^{PS} (1.13 ± 0.74 vs. 0.45 ± 0.28 µl min^{-1} cm^{-3}) based on PEG_{12000}-Gd-DO3A$_{26}$-enhanced dynamic MRI were significantly higher in malignant breast tumors than in fibroadenomas ($p < 0.05$). In addition, PEG_{12000}-Gd-DO3A$_{26}$-based estimates for fPV (2.3 ± 1.6%) and K^{PS} (0.0 µl min^{-1} cm^{-3}) in normal skeletal muscle were significantly smaller than in neoplastic tissues ($p < 0.05$).

Gadoteridol-enhanced MRI did not yield significant differences between benign and malignant lesions, neither for fPV (28.2 ± 18.8 vs. 25.3 ± 8.9%) nor for K^{PS} (7911 ± 4994 vs. 8692 ± 6092 µl min^{-1} cm^{-3}), $p > 0.05$. However, gadoteridol-based estimates for fPV and K^{PS} in muscle (11.1 ± 12.2 % and 3664 ± 2883 µl min^{-1} cm^{-3}, respectively) differed significantly ($p < 0.05$) from benign and malignant mammary tumors.

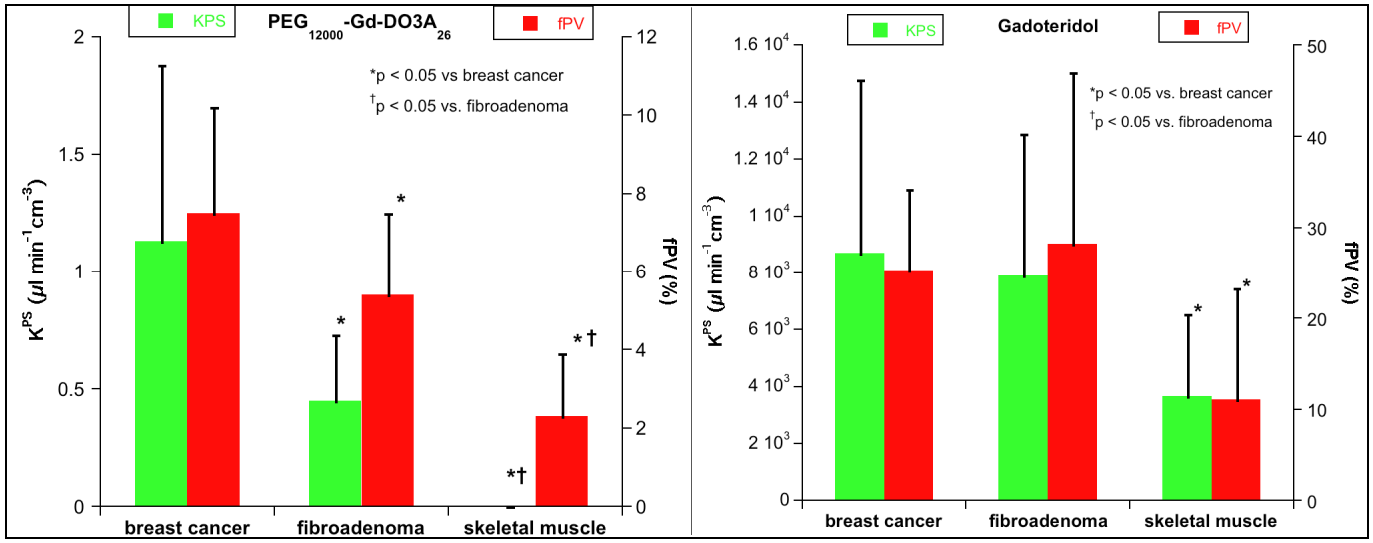

Figure 2: Microvascular characteristics of malignant and benign breast tumors as well as normal skeletal muscle based on macromolecular PEG_{12000}-Gd-DO3A$_{26}$- (left) and small-molecular gadoteridol-enhanced dynamic MRI (right). Of note, only the macromolecular contrast agent was suitable to differentiate malignant from benign breast tumors, whereas both contrast agents could be used to differentiate normal skeletal muscle from neoplastic tissue.

Conclusion:

The Gd-DO3A-conjugated PEG-core dendrimeric contrast medium PEG_{12000}-Gd-DO3A$_{26}$ is superior to the FDA-approved gadoteridol for differentiating benign fibroadenomas from breast cancer by tumor fractional plasma volume, fPV, and vascular endothelial leakiness, K^{PS}. The potential for differentiating normal tissues from mammary tumors is similar for both contrast agents.