MR IMAGING OF BREAST CANCER USING THE FOLATE-RECEPTOR TARGETED CONTRAST AGENT P1133

R. Meier[1,2], T. D. Henning[1], S. Boddington[1], S. Tavri[1], S. Arora[1], C. Corot[3], E. J. Rummeny[2], and H. E. Daldrup-Link[1]

[1]Radiology, University of California San Francisco, San Francisco, CA, United States, [2]Radiology, Technical University Munich, Klinikum Rechts der Isar, Munich, Germany, [3]Research, Guerbet, Paris, France

PURPOSE

Due to its over-expression on cancer cells, the Folate-Receptor (FR) presents a promising target for tumor-specific contrast agents. The purpose of this study was to assess the uptake of a new FR-targeted USPIO in breast cancers.

METHODS

The FR-targeted USPIO P1133 (Guerbet, France) was incubated for 24h with six different FR-positive human breast cancer cells, with and without free folic acid (FFA) as competitor. Labeling efficiencies were evaluated by MR imaging and ICP-mass-spectrometry. Subsequently, 12 athymic rats with implanted MDA-MB-231 breast cancers underwent MR imaging at 3T before, up to 1h and 24h p.i. of P1133 (n=6), P1133+FFA (n=3) or the non-FR-targeted USPIO P904B (n=3). Tumor signal-to-noise-ratios (SNR) were compared before and after USPIO-injection and between different animal groups using generalized estimating equations. MR-data were correlated with histopathology.

RESULTS

MR and spectrometry data showed different levels of P1133 uptake in tumor cells with different levels of FR-expression. The P1133-uptake was highest in MDA-MB-231 cells and was inhibited in vitro by adding FFA. In vivo studies demonstrated a progressive enhancement of central tumor areas with both, P1133 and P904B. Corresponding SNR data were significantly higher for P1133 compared to P904B, indicating at least a component of FR-specific enhancement with P1133. The P1133 tumor uptake was not significantly inhibited by FFA in vivo, most likely due to the rapid FFA metabolism in the liver.

CONCLUSION

The FR-targeted USPIO P1133 provides a significant and specific enhancement of FR-positive MDA-MB-231 breast cancers.

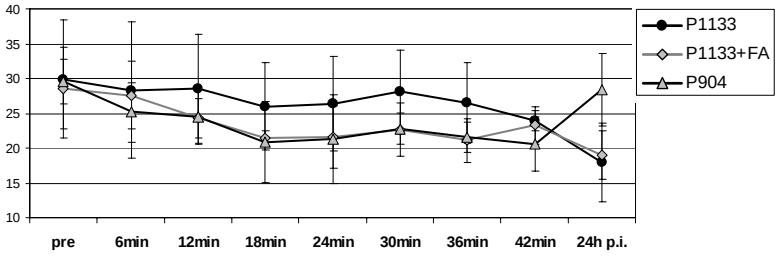

Figure 1: SNR data of the in vivo kinetics of the FR-targeted USPIO P1133 with and without competition of free folic acid (FFA) and the non-FR-targeted USPIO P904B.

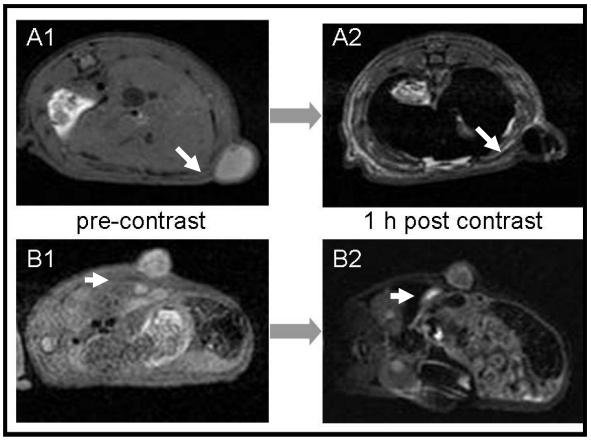

Figure 2: FSE T2-weighted MR images of rats with implanted FR-positive MDA-MB-231 tumors (white arrows) show a decline in signal intensity after injection of the FR-targeted USPIO P1133, indicating a specific enhancement in the tumor tissue (A1, A2). After injection of the non-FR-targeted USPIO P904B, the MDA-MB-231 tumors (white arrows) show no significant change in signal intensity.