

Application of a biodegradable macromolecular contrast agent in dynamic contrast enhanced MRI to assess the efficacy of indocyanine green enhanced photothermal cancer therapy

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INTRODUCTION

An accurate and timely evaluation of tumor response to treatment is critical to optimize cancer patient management. Dynamic contrast enhanced MRI (DCE-MRI) derives physiologically meaningful tumor vasculature parameters and are valuable to assess the efficacy of anti-cancer therapy. Macromolecular contrast agents are better than small molecular contrast agents in assessing the efficacy of anti-cancer therapy but are hindered by their high toxic Gd (III) tissue retention due to their prolonged blood circulation. Biodegradable macromolecular contrast agents (BMCA) alleviate this toxicity problem by in vivo degradation (accelerated excretion and minimum Gd (III) deposition). A BMCA, (Gd-DTPA)-cystamine copolymers (GDCC at 40 KDa, the renal filtration cutoff size), was used to assess the efficacy of indocyanine green enhanced photothermal therapy (DyeLA).

MATERIALS AND METHODS

MDA-MB-231 tumor (500 mm³) bearing mice, DenLaser 800 ($\lambda = 810$ nm) laser machine, DyeLA at 5 W x 10 min with intratumoral injection of 100 μ L 1.5% indocyanine green solution 4 hrs before treatment. GDCC was injected via a tail vein cannulation at a dose of 0.05 mmol-Gd/kg b.w. 4 hrs and 7 days after treatment and Gd-(DTPA-BMA) was used as a control 10 days after treatment at a dose of 0.1 mmol-Gd/kg b.w. 2D FLASH for DCE-MRI: TR /TE = 104 /4.46 ms, $\alpha = 30^\circ$, 0.5 * 0.5 * 1.5 mm, n=1, 11 sec. Osirix and home-made MATLAB program were used for image analysis. A two-compartment model was used to calculate tumor vascular parameters from DCE-MRI: fractional tumor plasma volume (f^{PV}), endothelium transfer coefficient (K^{PS}), and permeability surface area product (PS).

RESULTS and CONCLUSIONS

DyeLA treated tumors were significantly smaller than those untreated (1.1 ± 0.2 vs. 3.1 ± 1.2 , normalized size) 12 days after treatment. Values of f^{PV} and PS significantly dropped 4 hr after treatment and returned to close to normal values 7 days later (Fig. 1). Parameter mappings demonstrate the inhomogeneous tumor response to treatment when enhanced by GDCC and Gd-(DTPA-BMA) (Fig. 2). The values estimated by Gd-(DTPA-BMA) are unrealistic too high due to its quick perfusion into extracellular and extravascular space. Therefore response assessed by DCE-MRI using GDCC is promising in timely and accurately evaluation of anti-cancer treatment.

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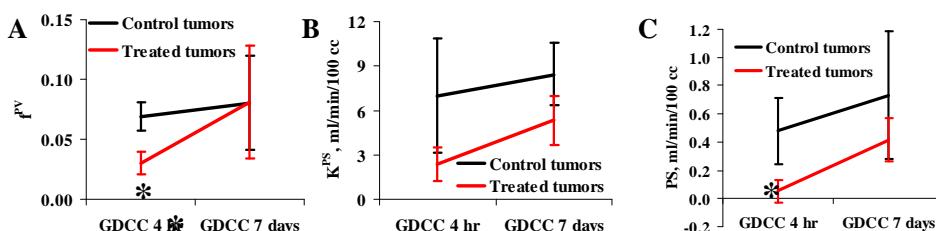


Fig.1. f^{PV} (A), K^{PS} (B, in ml/min/100 cc), and PS (C, ml/min/100 cc) for control and treated tumors using by GDCC. n =3 for each data point.

* $p < 0.05$ between control and treated tumors 4 h after treatment.

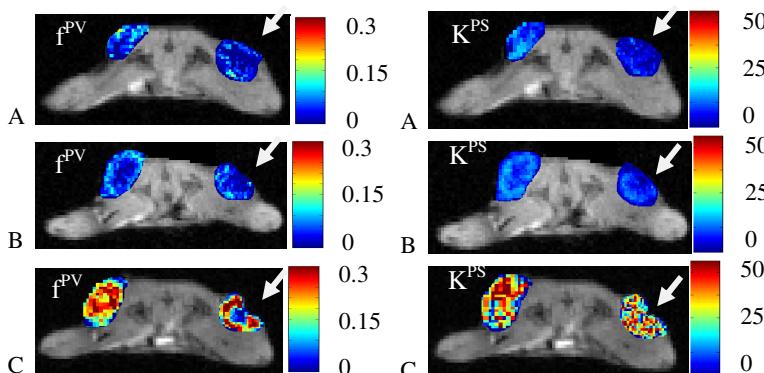


Fig.2. Representative f^{PV} and K^{PS} mapping (ml/min/100 cc) of control (left tumor in the images) and treated tumors (right tumor, pointed by white arrows) enhanced by GDCC (0.05 mmol-Gd/kg) 4 hr (A) and 7 days after treatment (B), and enhanced by Gd-(DTPA-BMA) (0.1 mmol-Gd/kg) 10 days after treatment (C).