Assess Tumor Acute Response to Photothermal Therapies by DCE-MRI Using Biodegradable Macromolecule Contrast Agent

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INTRODUCTION

MRI is the ideal imaging modality for anti-cancer photothermal therapies due to its compatibility, non-invasiveness, and superior soft tissue contrast. Dynamic contrast enhanced MRI (DCE-MRI) provides quantitative physiologically meaningful parameters, therefore are useful for accurate evaluation of efficacy of anti-cancer therapy. An accurate and timely evaluation of tumor response is critical in assessing drug efficacy or treatment in order to optimize cancer patient management. Macromolecular contrast agents are better than clinically approved small molecular contras agent in assessing the efficacy of anti-cancer therapy but are hindered by their high toxic Gd (III) tissues retention due to their prolonged blood circulation. Biodegradable macromolecular contrast agents (BMCA) alleviate this toxicity problem by in vivo degradation to accelerate their excretion, therefore only result in minimum Gd (III) accumulation. A BMCA, (Gd-DTPA)-cystamine copolymers (GDCC at 40 KDa, the renal filtration cutoff size), was used to assess the acute response from tumor and to correlate it with residual tumor.

MATERIALS AND METHODS

Mice bearing MDA-MB-231 tumor (50uL); DenLaser 800 (λ = 810 nm) laser machine; laser ablation (LA) at 2 W x 6 min; dye enhanced LA (DyeLA) at 5 W x 12 min with intratumoral injection of 30 uL 1.5% indocyanine green solution 4 hrs before treatment. GDCC was injected via a tail vein cannulization at a dose of 0.05 mmol-Gd/kg b.w. 4 hrs and 7 days after treatment. 2D FLASH for DCE-MRI: TR /TE = 104 /4.46 ms, flip angel 30º, 0.5 * 0.5 * 1.5 mm, average 1, 11 sec. 2D spin echo (SE): TR/TE = 400 /10 ms, flip angle 90º , 0.4 * 0.4 * 2 mm. Osirix and home-made MATLAB program were used for image analysis. A two compartmental model was used to calculate plasma volume (PV), fractional leakage rate (FLR), and permeability surface area product (PS).

RESULTS

Size of LA treated and DyeLA treated tumors are significantly smaller than those untreated (0.1 ± 0.1 and 0.4 ± 0.3 vs. 1.6 ± 0.4) 7 days after treatment. Bright area from inflammation in 2D SE images 4 hrs after treatment introduces confusion. PV and PS mapping revealed suspicious area with contrast agent uptake which could be correlated with residual tumor.

CONCLUSIONS

Acute response assessed by DCE-MRI using GDCC-40 is valuable in timely and accurately evaluation of anti-cancer treatment. It is functionally more useful than traditional snapshots of contrast enhanced MR.

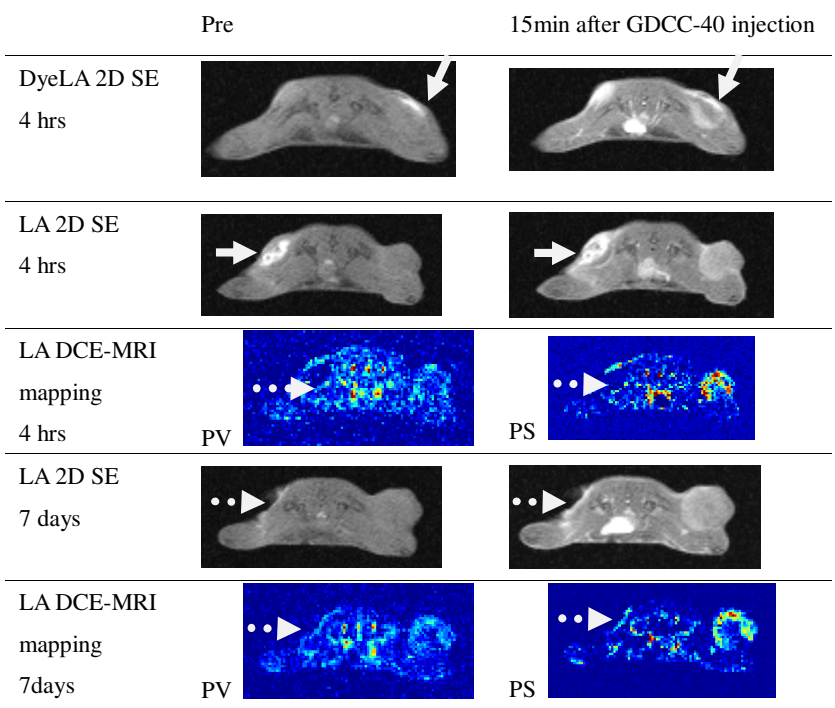

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Figure 1. Tumor acute response to LA and DyeLA. LA treated tumor 4 hrs after treatment was correlated with residual tumor 7 days later, using both 2D SE images and DCE-MRI parameter mapping. Solid arrows point to bright area (inflammation) in 2D SE images. Dotted arrows point to tumor area with suspicious contrast agent uptake, which turns out to be residual tumor.