



## Enhancement of recombinant adeno-associated virus mediated transgene expression by targeted echo-contrast agent

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**ABSTRACT.** Ultrasound-targeted microbubble destruction (UTMD) has been recently developed for destroying bubbles carrying drugs or genes, thereby permitting local release of these target molecules. We investigated whether SonoVue<sup>®</sup>, a new contrast agent that contains phospholipid-stabilized microbubbles filled with sulfur hexafluoride vapor, is effective at delivering a recombinant adeno-associated viral (rAAV) vector to the rat heart by UTMD. Serotype-2 (rAAV2) marked with green fluorescent protein (GFP) as a reporter gene was attached to the surface of sulfur hexafluoride-filled microbubbles. Microbubbles were infused into the tail vein of rats with or without simultaneous echocardiography. Additional controls included ultrasound microbubbles that did not contain virus, virus alone, and virus plus ultrasound. One group underwent echocardiographic destruction of microbubbles followed by rAAV2-GFP infusion. Rats were killed after 4 weeks and examined for GFP expression. Green fluorescence was detected in all groups that received the rAAV2-GFP vector, indicating expression of the rAAV2

transgene; however, GFP expression in the UTMD group was significantly higher than that in control groups. We conclude that ultrasound-mediated destruction mediated by SonoVue is a promising method for delivery of rAAV2 to the heart *in vivo*.

**Key words:** Ultrasound; Recombinant adeno-associated virus; Microbubble; Green fluorescent protein