In vivo acoustic manipulation for thrombolysis in-stent thrombosis: Concept validation

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Background, Motivation, Hypothesis/Goal, and Objectives

The treatment of patients with in-stent thrombus (IST) remains a challenge and represents a major clinical problem. Using poly lactic acid (PLA) with good biocompatibility and biodegradability, in this study, we designed a kind of PLA stent with an interesting acoustic trapping of microbubbles (MB), and validated its trapping effect *ex vivo* and *in vivo*. Further *in vivo* experiments demonstrated that with the help of acoustic manipulation, the blood flow interrupted by IST was recovered again even under the condition of low doses of thrombolytic drugs. The stent with the acoustic manipulation function may be an effective and powerful tool for inhibition of IST and avoid the bleeding risk due to excessive dosage.

Statement of Contribution/Methods

The PLA stent was fabricated by the additive manufacturing, and it was excited at its primary resonance frequency of 1.5 MHz by a single element transducer for acoustic manipulation. The stents were inserted into the abdominal aortas of 33 rabbits by a standard stent implantation. The trapping and thrombolytic processes were monitored by a 40 MHz commercial ultrasound (US) scanner vevo2100^{TM}. When the distal blood flow velocity was decreased by 50% due to IST, commercial SonoVue^{TM} MBs and a low dose of thrombolytics (recombinant tissue plasminogen activator, RTPA) were immediately injected intraveneously.

Results, Discussion, and Conclusion

We experimentally observed that the microbubbles were trapped and accumulated onto the surface of the stent at the driving frequency of 1.5 MHz. The mechanism originated from the acoustic radiation force induced by the Stoneley wave-excited localized field on the surface of a single resonant PLA strut. During the same exposure time of 9 min, the blood flow velocity of group of US+RTPA was still decreased slowly. In contrast, for US+MB+RTPA group, the thrombus adjacent to the stent was gradually dissolved and unstuck from the resonant stent with the trapped microbubbles, and the blood flow velocity gradually increased from 300 mm/s to the initial value of 633 mm/s by using Doppler ultrasound. In conclusion, this *in vivo* study confirmed that the acoustic trapping effect of the resonant PLA stent could be potentially used to inhibit IST.

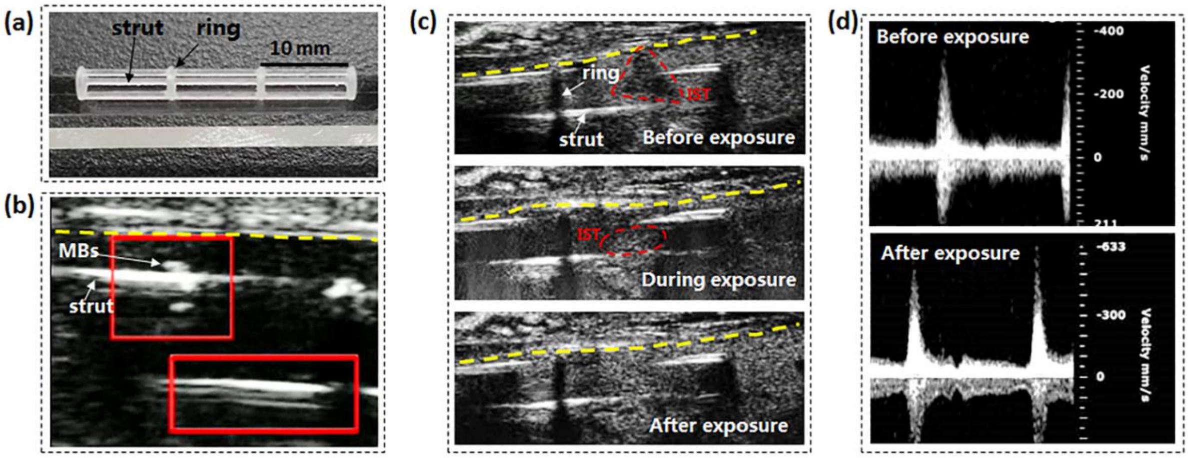

Figure 1 (a) PLA stent; (b) Ultrasound image of a population of microbubbles trapped by a resonant PLA stent at the driving frequency 1.5 MHz. The red rectangles represented the trapping positions. The yellow dotted lines represented the walls of abdominal aorta. (c) IST before, during and after ultrasound exposure. (d) Blood flow velocity before and after ultrasound exposure.