Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Appendix E1

VX2 rabbit liver cancer model for interventional therapy

Rabbit VX2 liver cancer model was processed according to the standard protocol (reference 21). Briefly, frozen rabbit VX2 tumor samples were defrosted and injected into the hind limb muscle of donor New Zealand white rabbits (3.0±0.5 kg) for incubation. Approximately 2–3 weeks after implantation, the donor rabbits were anaesthetized, the hind-limb tumors were excised and transected into several 1–2 mm pieces of the tumor for liver implantation. As following, Liver tumor implantation surgeries were performed according to the standard protocol (reference 21). For these surgeries, recipient rabbits were medicated for anesthetic induction with ketamine and dexmeditomidine, followed by intubation and maintenance with 1%–3% isoflurane. One preprocedural dose of enrofloxacin (5 mg per kilogram of body weight, administered subcutaneously) antibiotic prophylaxis was provided. Under aseptic conditions, a mini-laparotomy was performed in the subxiphoid area to expose the liver. Tumor fragments of 1–2 mm were freshly harvested from donor rabbits and implanted in the left hepatic lobe of recipient rabbits. With the use of a scalpel blade, two stab wounds were made 2–3 cm apart and approximately 5 mm deep in the liver parenchyma. Tumor pieces were then placed into both stab wounds. Wounds were closed with a small (0.5 cm^2) piece of hemostatic surgical sponge (BloodSTOP iX; PRN Pharmacal, Pensacola, Fla). The abdomen was then closed in two layers by using 3-0 polydioxanone suture (Ethicon, Somerville, NJ) for fascial repair and 5-0 Vicryl suture (Ethicon) for cutaneous apposition. After the procedure, the animals were aroused and recovered, returned to their cages, and monitored daily for wound healing and appetite until TACE. Liver tumors were incubated for 10-14 days before TACE until measurement by ultrasonic imaging.

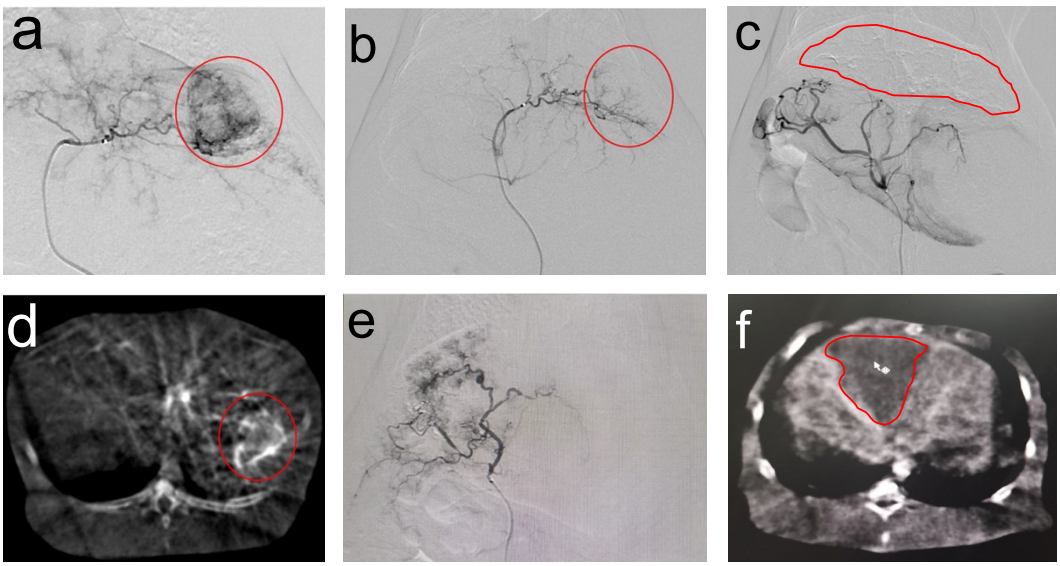

Figure S1. A typical DSA images and DynaCT images of the high dosage (1.2 mg) group. Before NDEB was transarterially administered, tumor staining was evidenced by DSA imaging technique (a). (b)

tumor staining disappears after a partial dose of NDEB was injected. After the whole ND-ATCE was completed hepatic artery and its branches were occluded(c) and heavily deposit in the liver (d). The overdose caused serious arterial embolization even one week after ND-ATCE(e) and severely ischemic necrosis on the liver lobe (f).

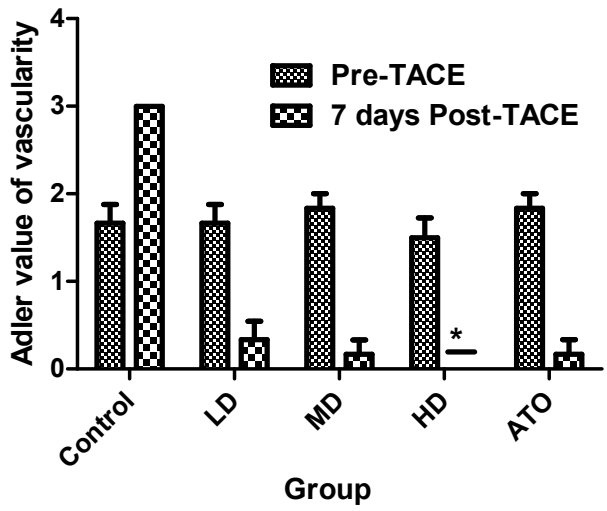

Figure S2. The vascular grade values according to Adler classification method calculated the color Doppler flow imaging of the whole tumor.

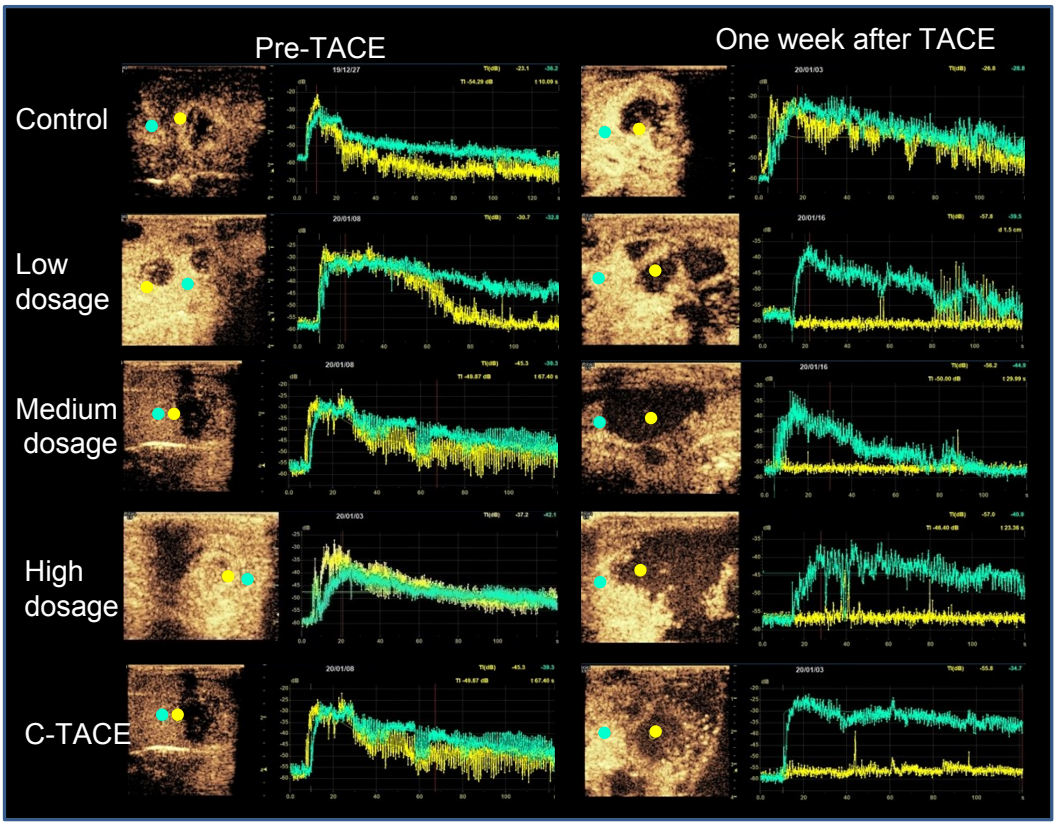

Figure S3. Time-Intensity curves of the dynamic CEUS of the sham and four tested groups. For individual curved intensity was recorded on the tumor (yellow spot) and neighbored liver lobe (green spot), and monitoring time recorded is 120 seconds after microbubbles injection.

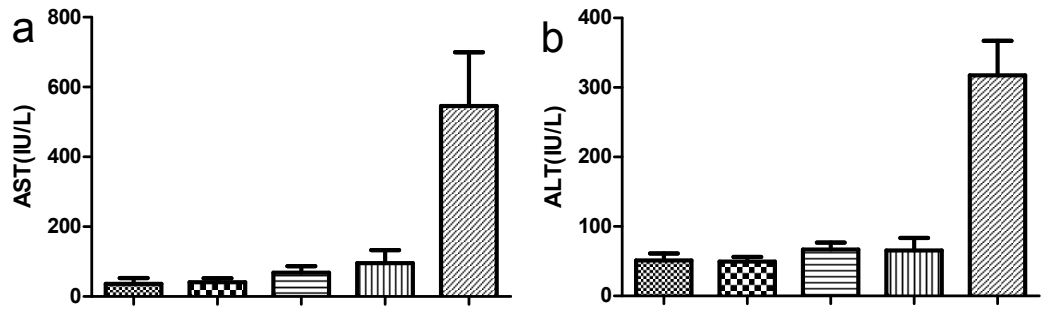

Figure S4. Serum hepatotoxicity evaluation by measurements of plasma levels ALT (a, normal range 27.4-72.2IU/L) and AST (b, normal range 10-78IU/L)) at 7 days after TACE procedure.

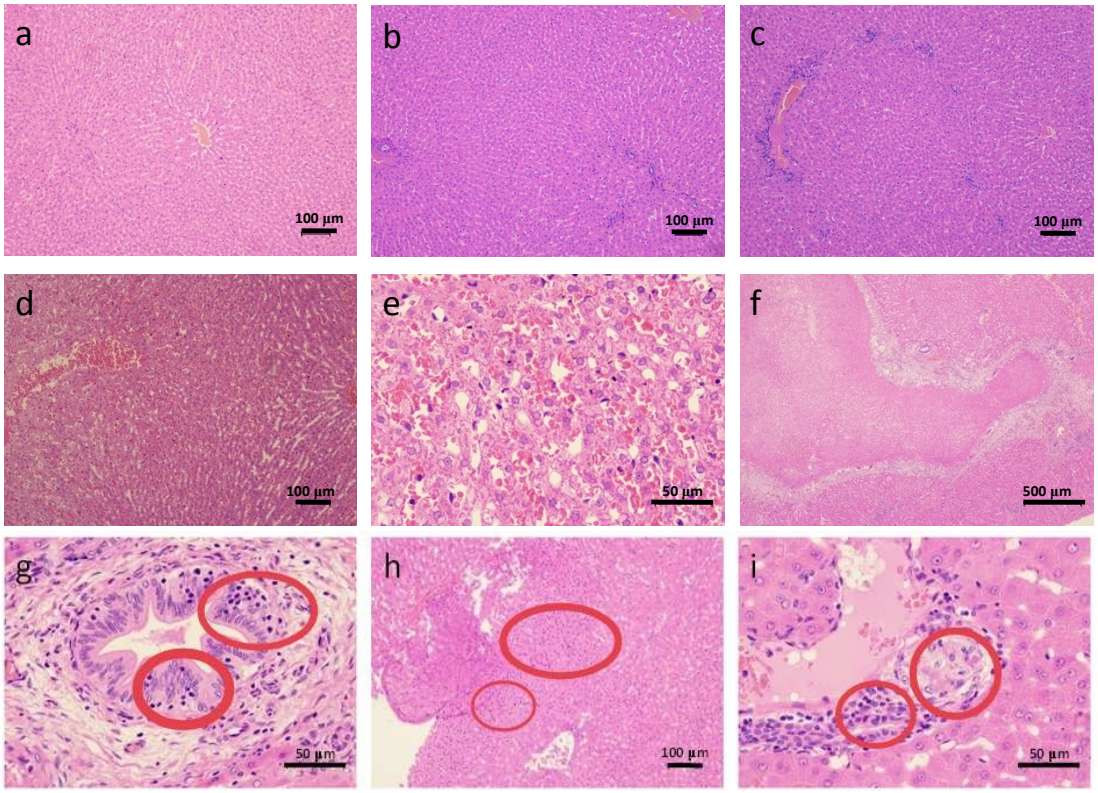

Figure S5. Representative fields of H&E stained non-tumors lobe of VX2 rabbits treated with saline TACE (a), C-TACE (b), low dose ND-TACE (c), medium dose of ND-TACE (d, e) and high dose of ND-TACE (f-i). Infiltration of inflammatory cells around the bile duct and ductal cell proliferation were observed in figure g; Vascular necrosis and inflammatory cell infiltration in the portal area can be found in figure h; elevated neutrophil infiltration in figure I was also detected.