Capillary Microfluidics-Derived Doxorubicin Containing Human Serum Albumin Microbeads for Transarterial Chemoembolization of Hepatic Cancer
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Purpose
Unfortunately, most patients with hepatocellular carcinoma (HCC) are not suited for a curative treatment such as resection and transplantation. Therefore, management of unresectable HCC requires alternative interventional therapies. Among them, transcatheter arterial chemoembolization (TACE) using microbeads has been an effective clinical practice in HCC therapy, and it avoids the toxic effect of chemotherapy. The injected microbeads occlude the tumor’s blood supply, resulting in necrosis of the tumor cells. In this study, we prepared doxorubicin (DOXO)-containing albumin microbeads as new TACE modality, using a capillary microfluidic device and evaluate the efficacy in animal models.

Methods
Albumin droplets containing DOXO was formed via a capillary microfluidic device and cross-linked with glutaraldehyde. In vitro evaluation of the fabricated microbeads, SEM imaging and DOXO release, were performed. And in vivo therapeutic efficacy was estimated on xenograft hepatic cancer models. The localization and distribution of DOXO beads in hepatic vessel was confirmed after intra-portal injection of DOXO beads on rats.

Results
The DOXO-MBs showed narrow size distribution (i.e., 183.2±2.2 μm) and the size was easily controlled by changing the flow of fluidic solutions. DOXO released in controlled manner for a month and the maximum release rate was around 15% and 46% in pH 5.4 and 7.2 buffer. Portal injection of DOXO-MBs in rats proved DOXO-MBs accumulated in the hepatic vessels. Hepatic tissues, recovered at 24 days after portal injection, showed that the DOXO released from DOXO-MBs penetrated surrounding hepatic tissues at a depth of 200 μm and induced a change of cellular morphology. In the xenografted tumor model, DOXO-MBs more efficiently inhibited tumor growth than I.V. injection (p<0.01).

Conclusion
Albumin DOXO micro-beads, fabricated via a capillary microfluidic device, showed a therapeutic potential for TACE treatment of human hepatic cancer.