Supporting Information

Microfluidic droplet-assisted fabrication of vessel-supported tumors for preclinical drug discovery

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Supporting figures

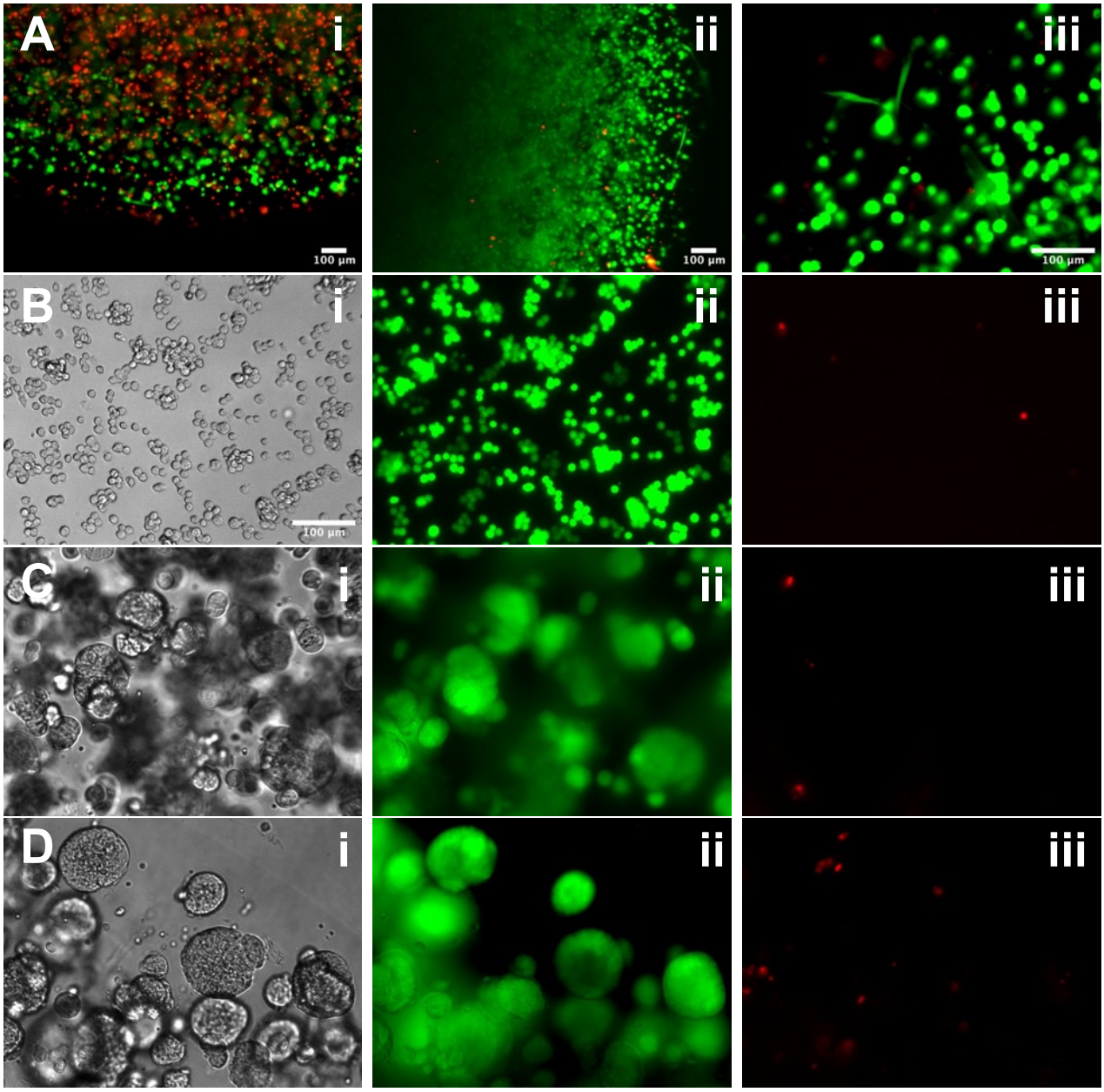


Figure S1. Cell viability test in GelMA hydrogel. A) The fibroblast viability test in GelMA after different exposure time. The live cells were labeled with Calcein AM (Bii), and dead cells were labeled with Propidium Iodide, after 24 hours culture. Ai) After treatment with 35 seconds of UV light, the survival rate of the cells was about 50%. Aii) After treatment with 15 seconds of UV light, the survival rate of the cells was above 90%. Aiii) After 15-s-UV exposure, the fibroblasts' viability was well maintained, and some cells began to stretch in the gel. B) The HCT-116 cell viability test in GelMA after 15-second-UV exposure. The live cells were labeled with Calcein AM (Bii), and dead cells were labeled with Propidium Iodide (Biii). The cell viability was above 90% after one day culture. C) The cells kept proliferating and tumor clusters was formed on Day 3. The live cells were labeled with Calcein AM (Cii), and dead cells were labeled with Propidium Iodide (Ciii). D) The tumor spheroids were formed on Day 5 (Di). Although dead cell cell number increased a little bit (Diii), the overall cell viability was well maintained. The scalebar in B, C and D is 100 microns.

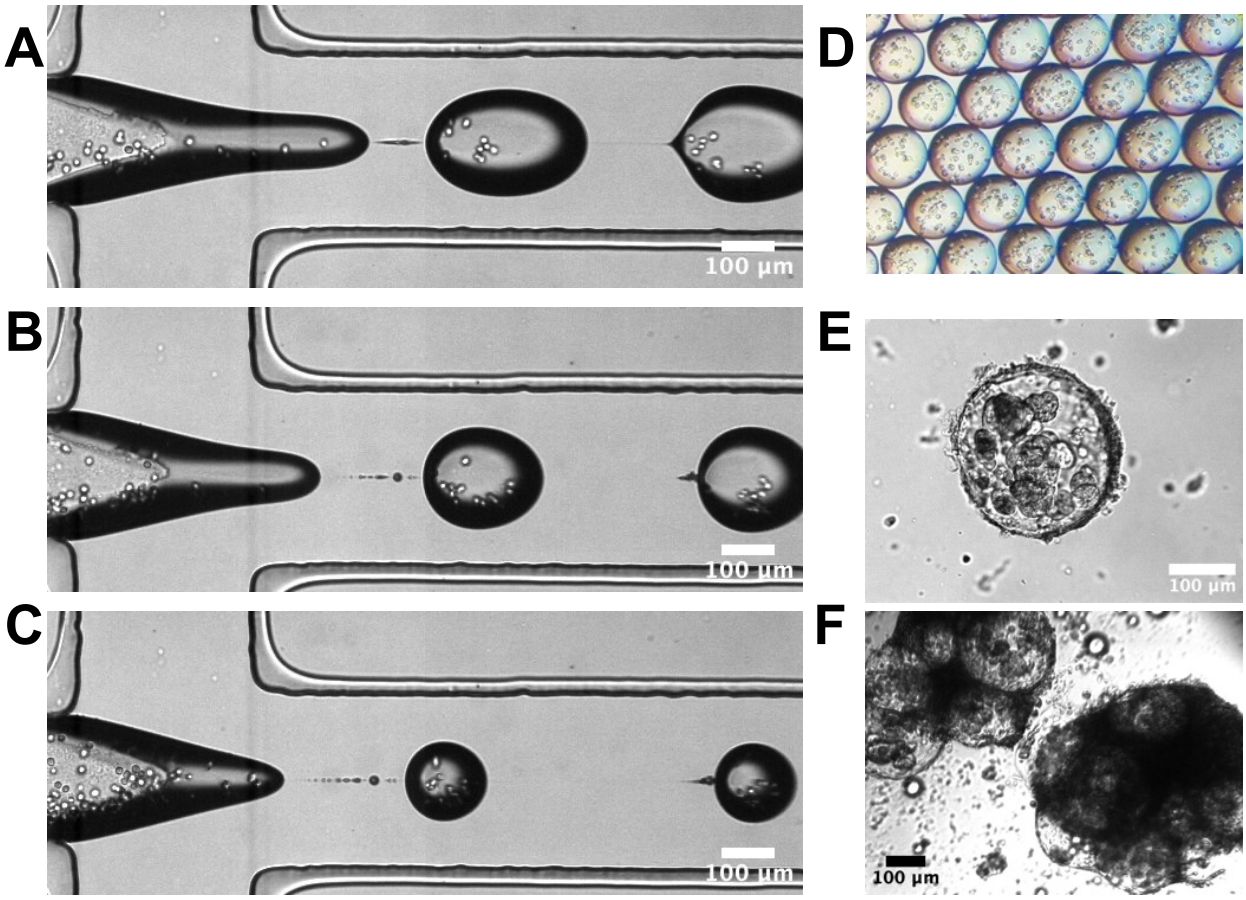


Figure S2. A-C) Cell-laden droplets of different size were generated by the microfluidic droplet generation device. D) The cell-laden droplets were recollected in a petri dish. E) The core-shell heterotypic tumor beads were developed *in vitro*. F) During the following culture, the fibroblast monolayer on the individual beads assembles the individual tumor beads together into a large tissue.

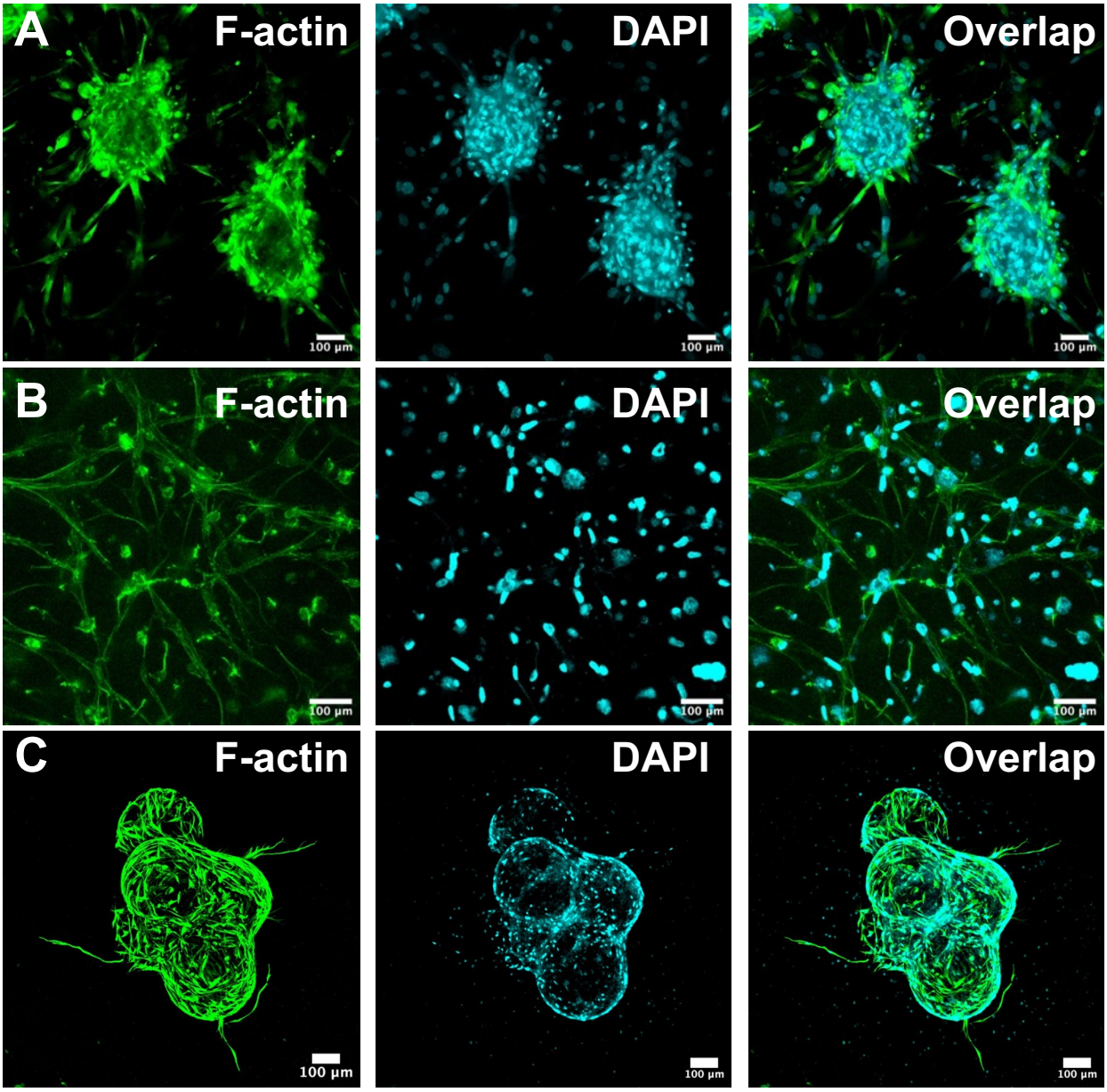


Figure S3. Fibroblast morphologies in different GelMA constructs. A) The fibroblasts were seeded in 3% w/v GelMA and self-assembled into spheroids after overnight culture. B) The fibroblasts were seeded in 8% w/v GelMA. After one week culture, the fibroblasts stretched and formed interconnected network. C) The fibroblasts were loaded into 5% w/v GelMA microbeads. After one week culture, the fibroblasts migrated to the beads surface. The individual fibroblast beads were bonded together into a large tissue.

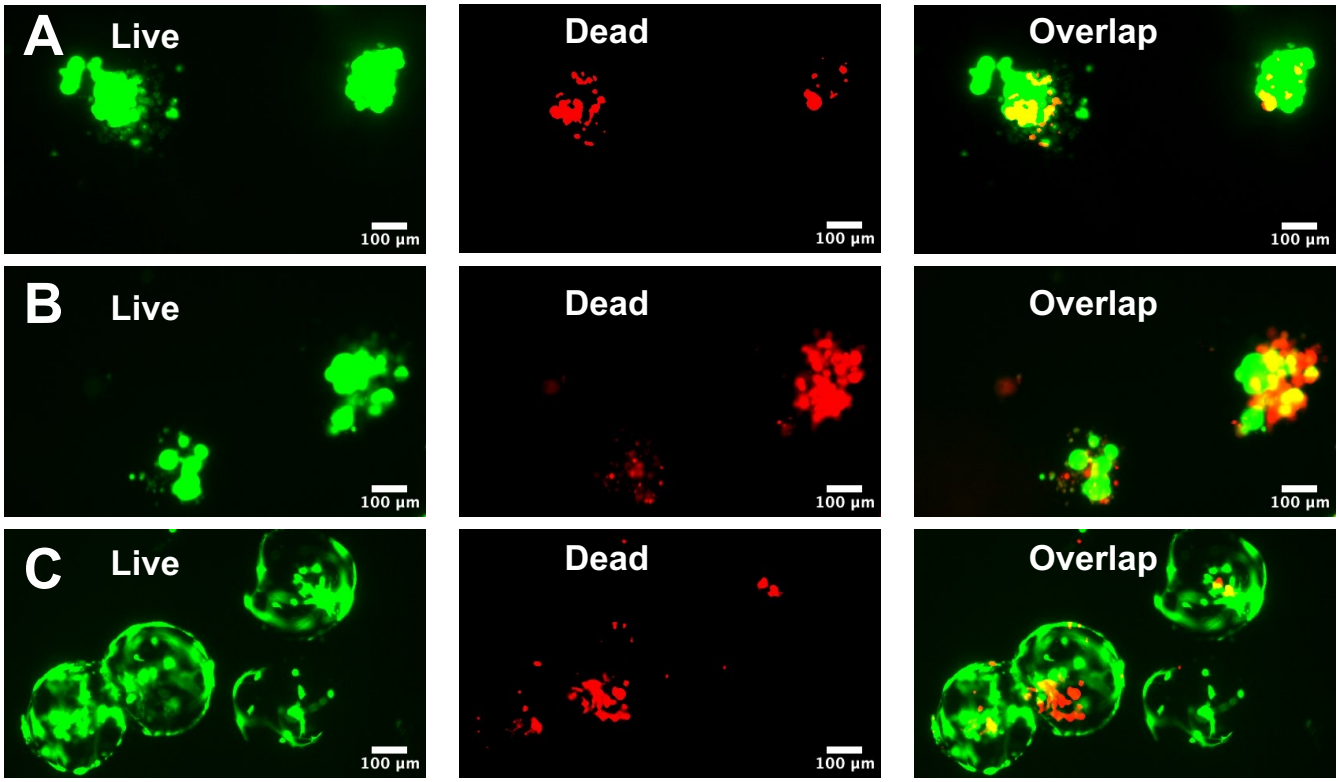


Figure S4. The live/dead stanning of cell laden micro beads after drug test. The alive cells were labeled with Calcein AM, and the dead cells were labeled with PI. A) The HCT-116 laden beads after 100 nM drug test. B) The HCT-116 laden beads after 1000 nM drug test. C) The fibroblast laden beads after 1000 nM drug test. The scalebar in A, B and C is 100 microns.

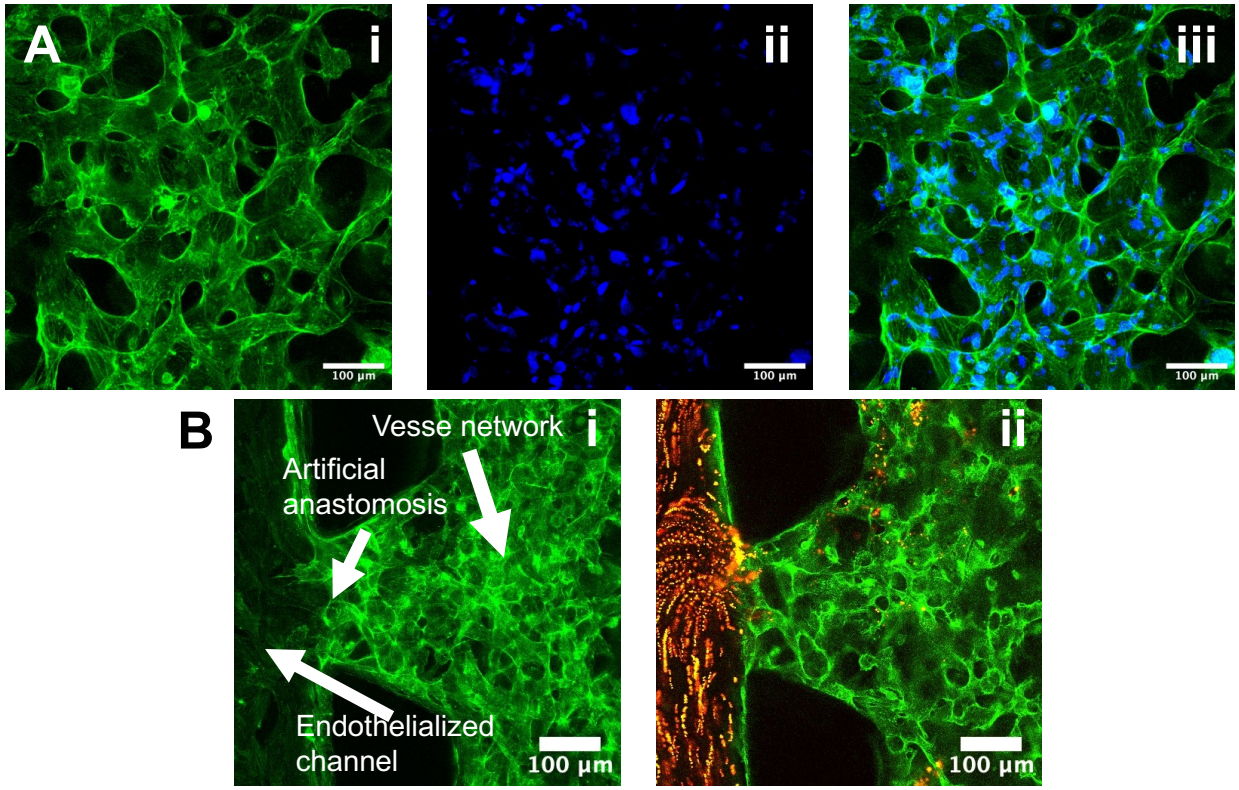


Figure S5. Confocal scanning of the functional on-chip vessel network. The 3D vessel network was characterized with FITC conjugated F-actin (Ai), and the nuclei were labeled with DAPI (A ii). (A iii) shows the overlap image. B) The confocal scanning shows the artificial anastomosis zone bridging the endothelialized channel and the capillary vessel network (i). The 2 um beads were flowed from the endothelialized channel into the vessel network to demonstrate the functionality of the whole vessel system (ii).

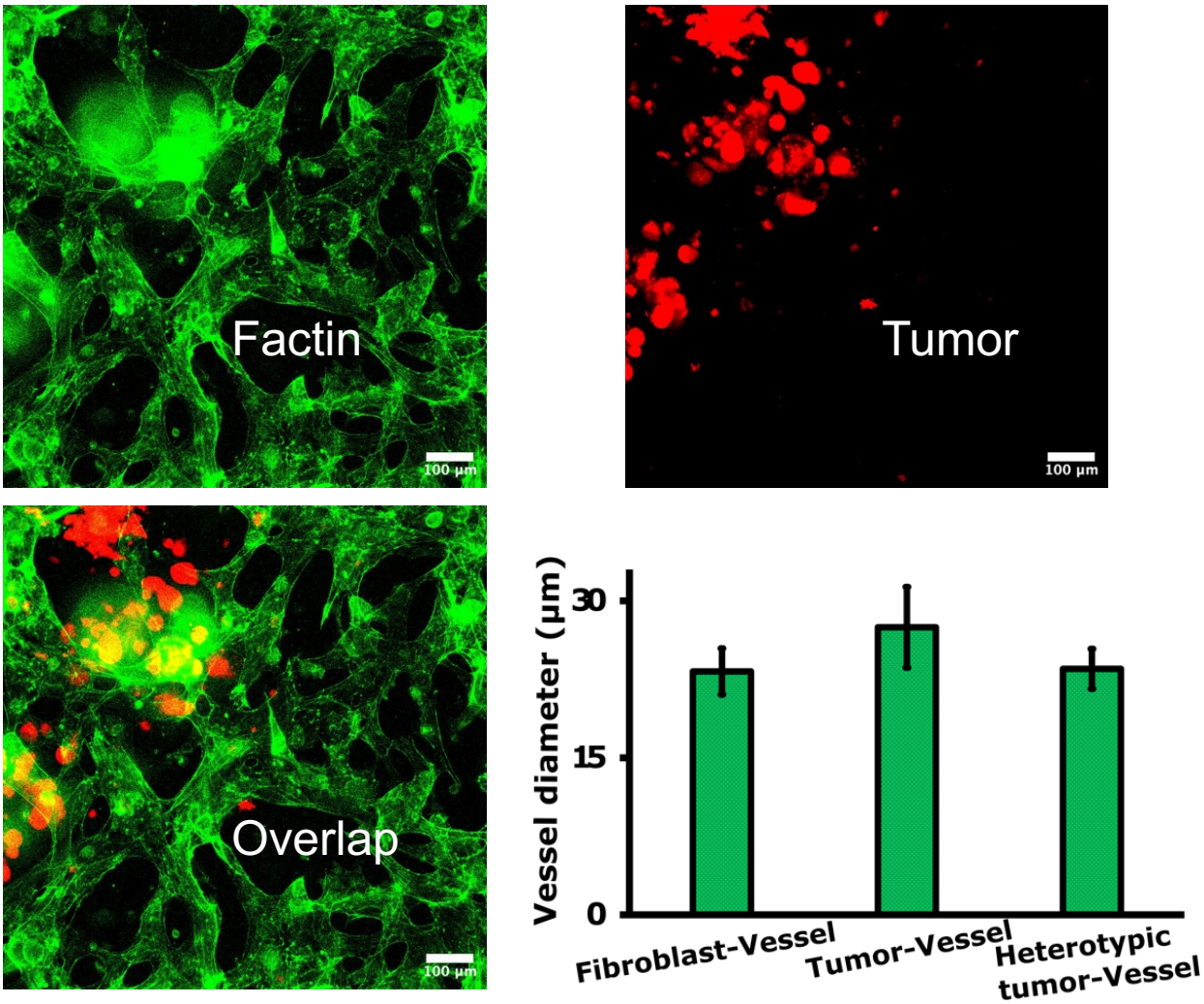


Figure S6. The confocal scanning of the Vessel-supported HCT116 laden micro beads. The vessel network was labeled with FITC-conjugated F-actin. The tumor beads were labeled with CellTracker™ Red. The histogram shows the mean effective vessel diameter.

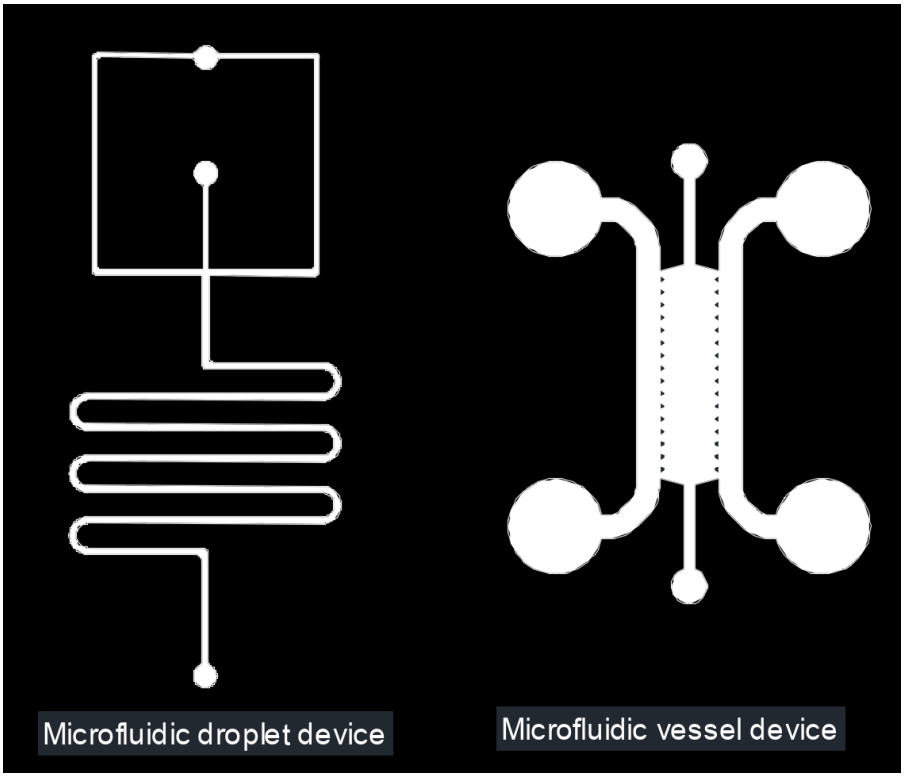
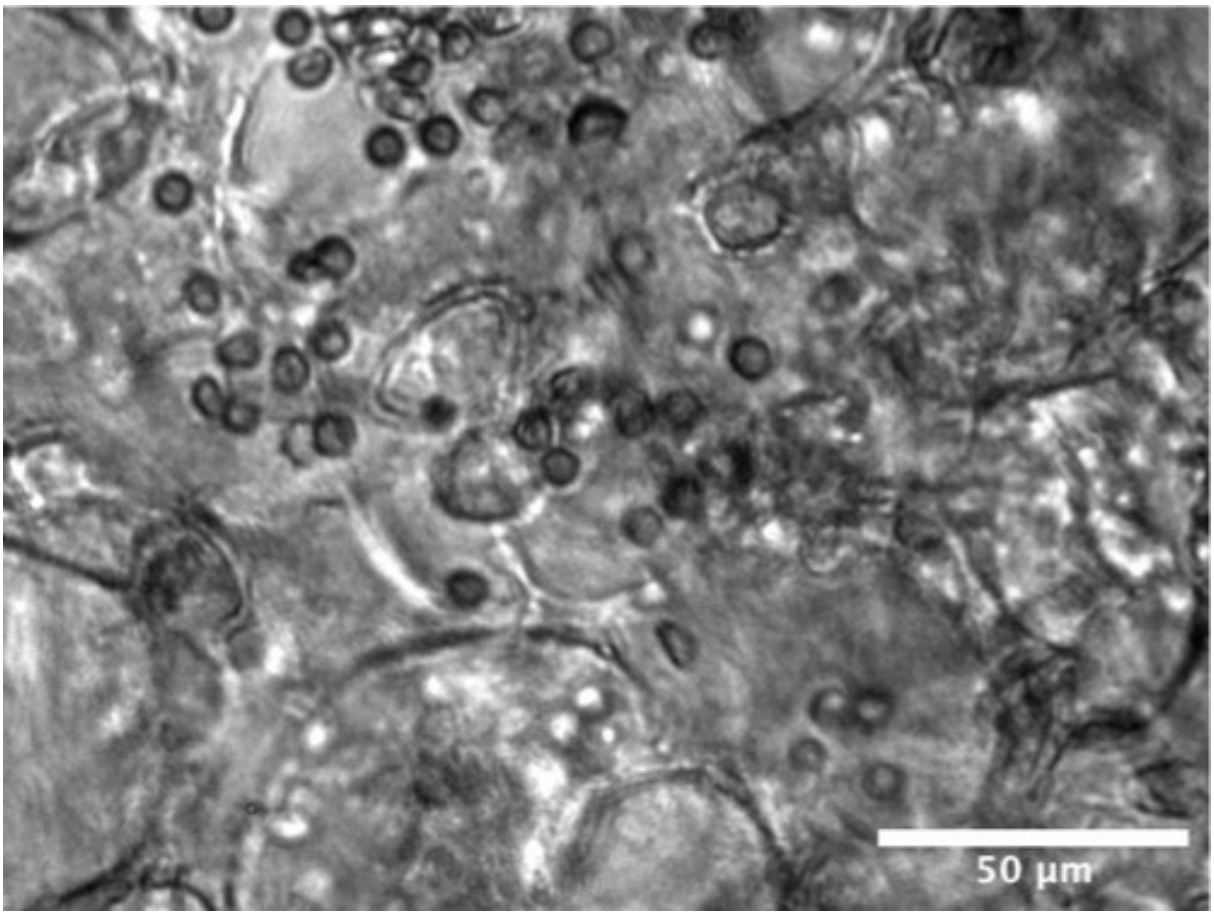
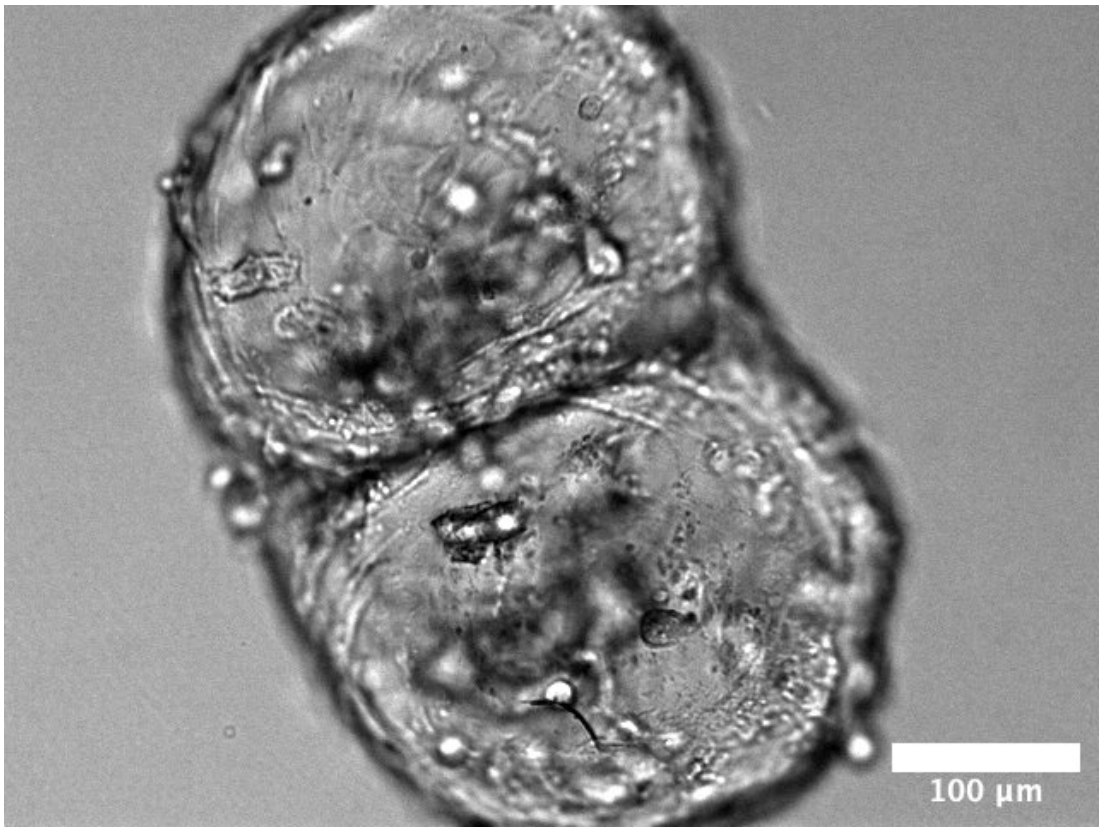


Figure S7. Snapshot of the microfluidic droplet device and vessel device in AutoCAD.

Supporting video



Supporting video 1. The suspended RBCs were perfused through the on-chip vessel network.



Supporting video 2. Bright field scanning of the fibroblast laden beads. The fibroblasts migrated to beads surface and expressed the bondage like morphology and trussed up the nearby beads together.