Electronic Supplementary Material (ESI) for Lab on a Chip.

Supplementary Information

A 96-Well Microplate Bioreactor Platform Supporting Individual Dual Perfusion and High-Throughput Assessment of Simple or Biofabricated 3D Tissue Models

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Drawings for bioreactor components are provided in the accompanying archive file.

1. 3-well standalone air panel
2. 3-well standalone imaging sample housing (stereolithography and PMMA versions)
3. 3-well standalone non-imaging sample housing
4. 3-well standalone media panel
5. 24-channel reservoir (stl file only)
6. 96-well plate (stereolithography version)
7. Well inserts for perfused constructs (stl file only)

To accompany the section entitled “Particle tracking in hydrogel-based constructs”, Video S1 captures 13 µm silvered glass microspheres flowing through a stepwise cast gelatin construct. Particles are resolved in both the top and bottom channels, at 8 mm and 5.5 mm above the videoscope probe, respectively. A screenshot may be found in Fig. 4B.

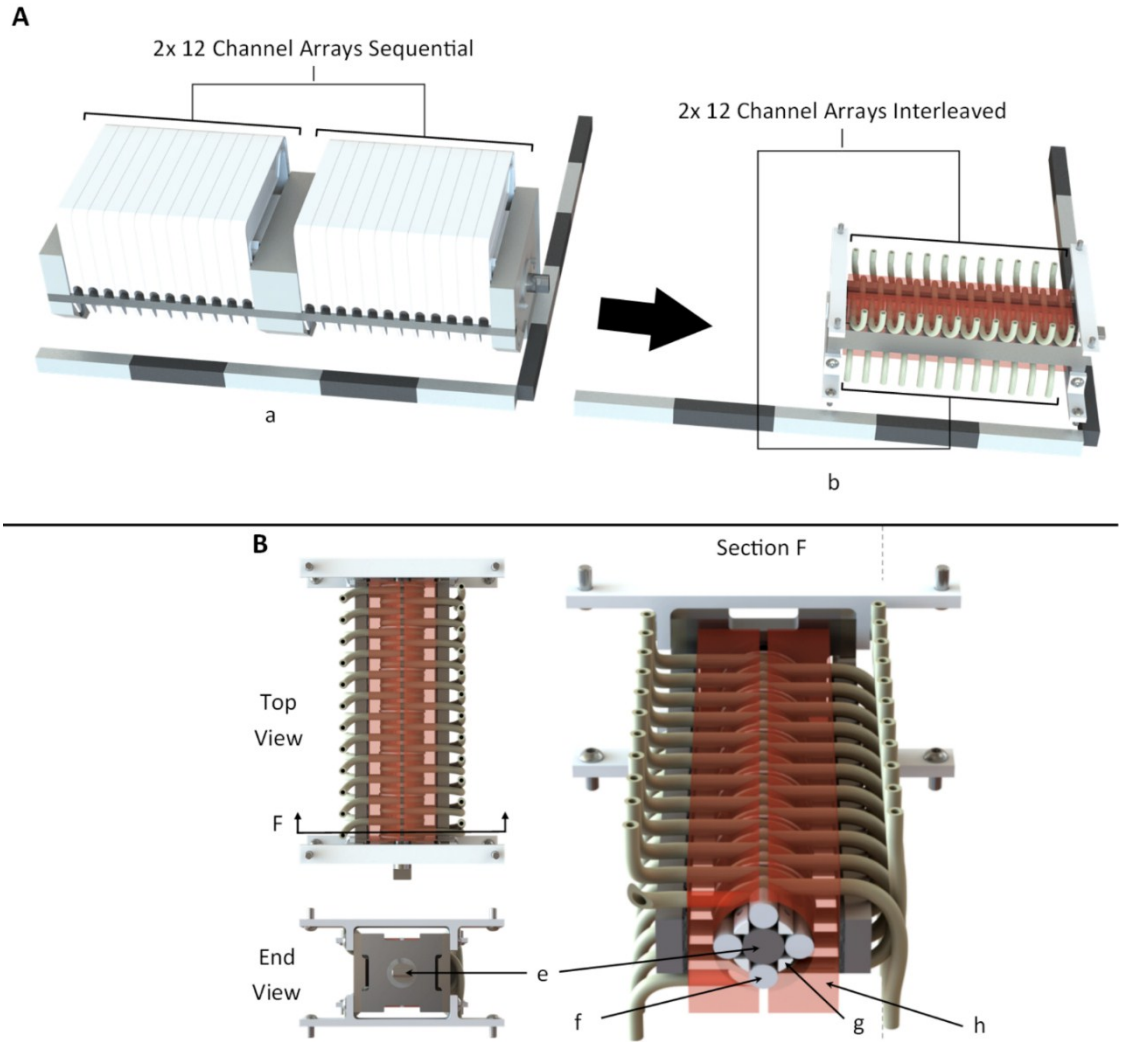

Fig. S1. Comparison of a standard microplate pumphead with the new microplate-footprint design. (A) Reduction in peristaltic pumphead size through the use of standard (a) to microplate (b) formats achieve by interleaving the tubing to use both sides of the rotor. Rulers are graduated in 50 mm increments. (B) Closer views of the microplate pumphead noting the Ø8 mm 304 stainless steel keyed shaft (e) fully supporting the four Ø5 mm PTFE rollers captured by an SLA-printed carrier (g). Tubing is compressed against both sides of the rotor (e,f,g) for 15% occlusion through fixed SLA-printed clamps (h).

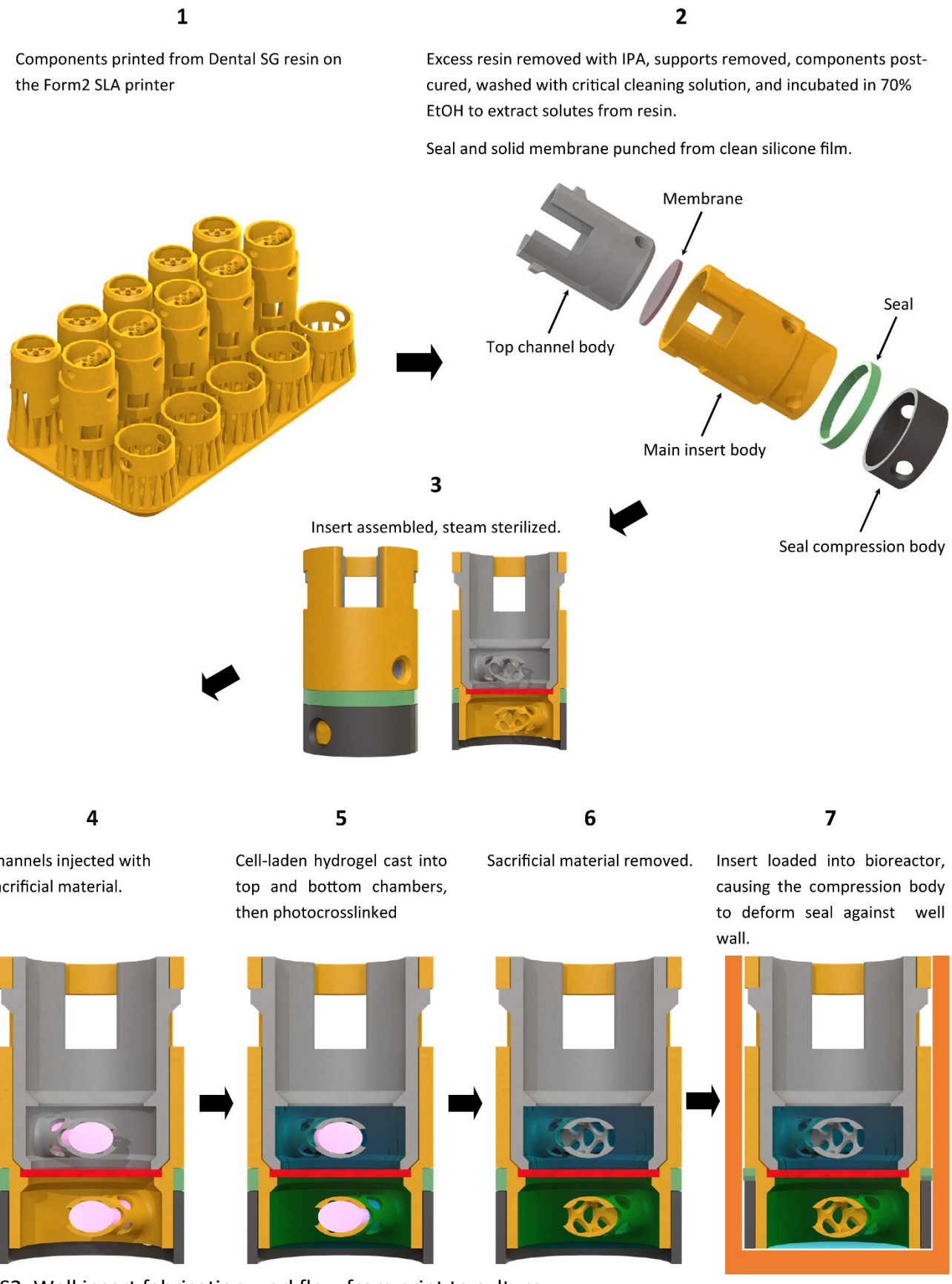

Fig. S2. Well insert fabrication workflow from print to culture.

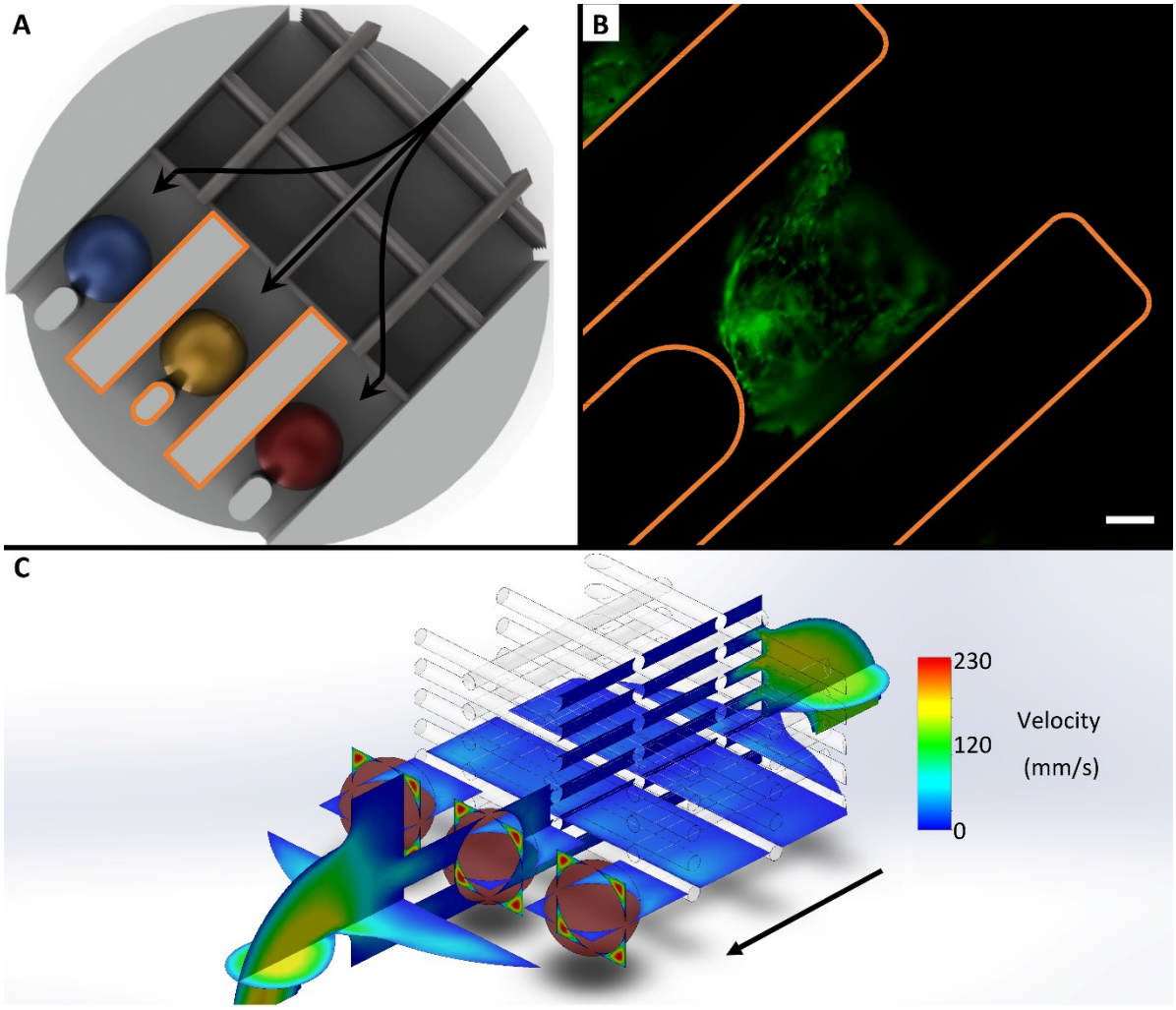

Fig. S3. Ovarian cancer construct to recreate native-like flow velocities around cell-laden microspheres. (A) Representation of the scaffold with lattice region to equalize flow across the three channels containing a single microsphere each. Arrows indicate flow direction. (B) Fluorescent image depicting live (green) and dead (red) cells with channel walls in orange. Scale bar is 200 µm. (C) Computational fluid modeling cut plots indicating native-like flow velocity at the microsphere surface. Arrow indicates flow direction.

Maximum flow velocities in the perfused cultures for the metabolic activity study were calculated via computational fluid dynamic (CFD) simulations performed in Solidworks using ideal system geometry and non-permeable samples at 37°C. Fluid was modeled as water. Walls were adiabatic with a surface roughness of 5 µm. Laminar and turbulent flows were permitted. Sections of tubing on the bioreactor inlet and outlet were used to create the non-uniform flow profile on the inlet, and the backpressure from the outlet. Inlet flow of 2.5 mL/min was considered uniform across the surface. The outlet surface was set to 1 atmosphere of pressure.

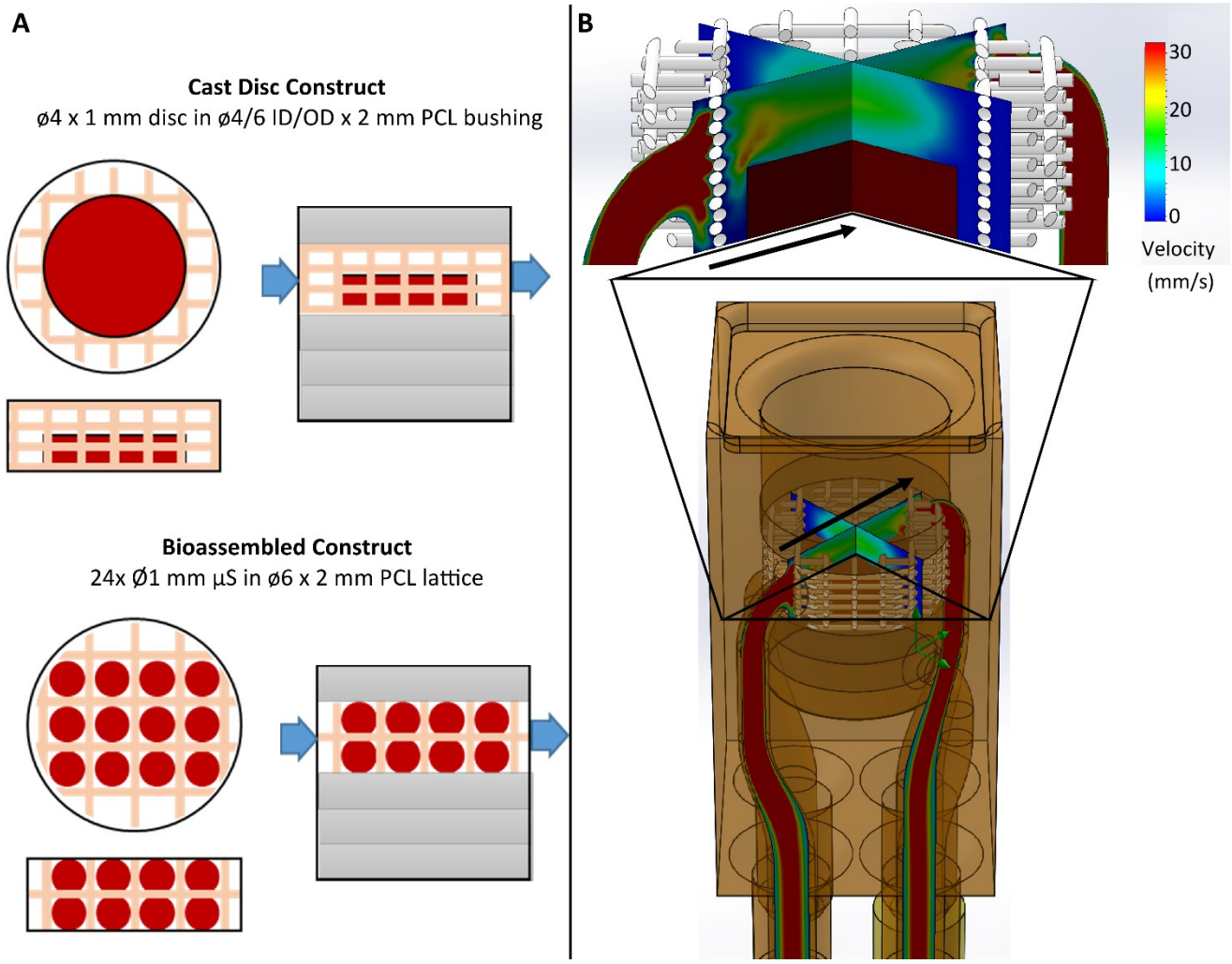

Fig. S4. Ovarian tissue construct details for the perfused metabolic activity assay. (Panel A) Disc and bioassembled construct formats where SKOV3-HFF cocultures are encapsulated in 10 w/w% gel-MA (red) and supported by PCL scaffold (beige), then aligned to the top flow channel in the bioreactor by silicone discs (grey). (Panel B) Cut plots of the linear flow velocity at a volumetric flow rate of 2.5 mL/min at the pumphead. Arrow indicates direction of flow.

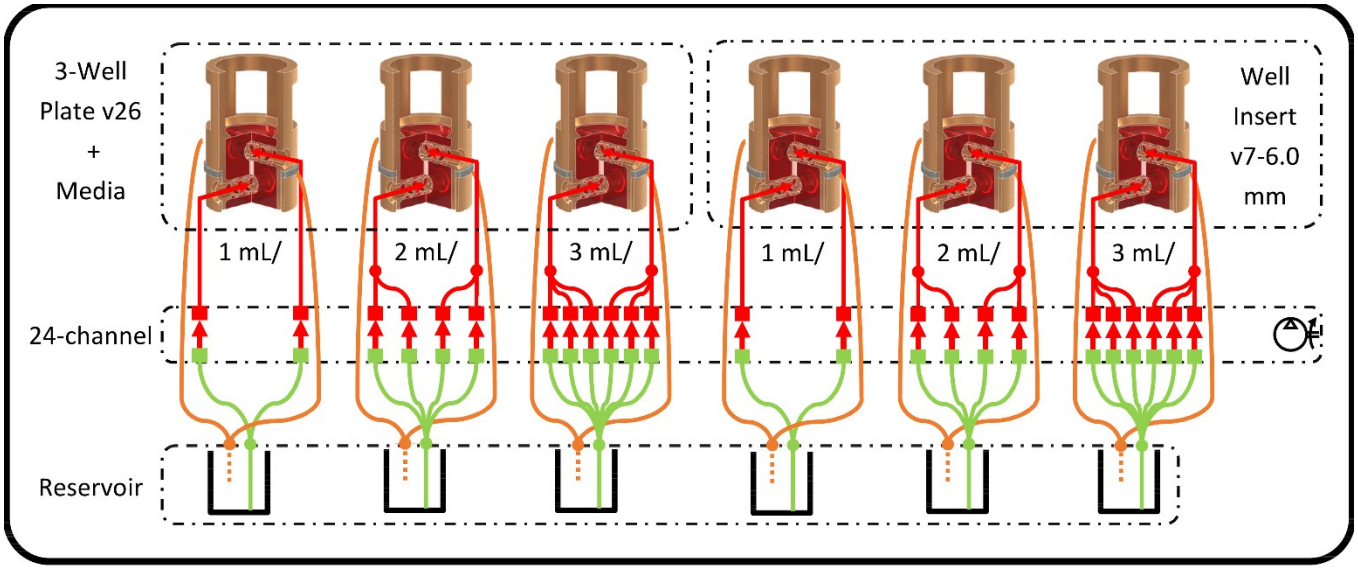

Fig. S5. Culture conditions for the perfused (top) and static (bottom) samples. Static samples were in individual wells.

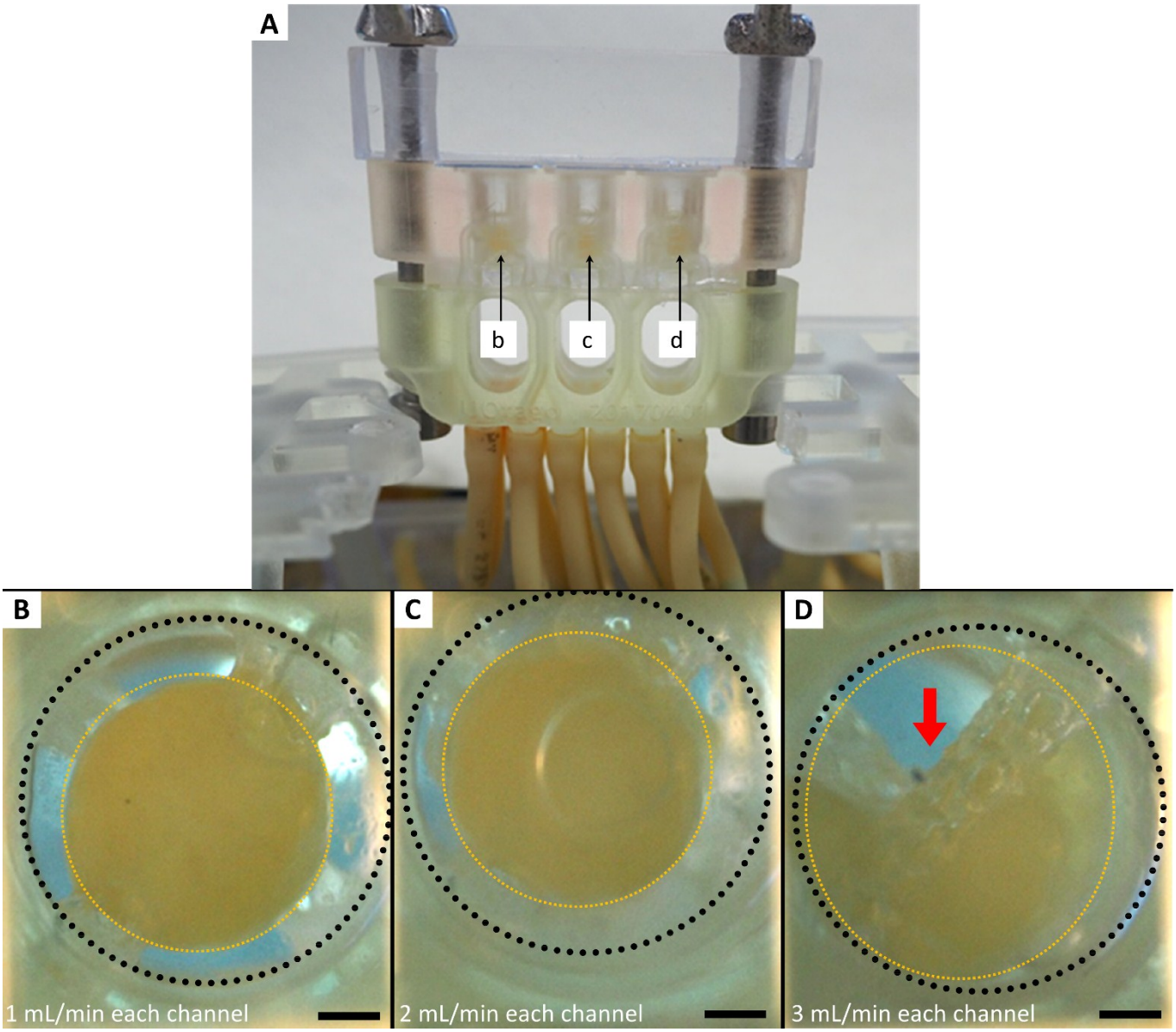

Fig. S6. Vascular inserts imaged in situ after 14 days of culture. (A) 3-well culture assembly viewed from the side to indicate relative positions of the samples cultured at different flow rates. (b-d) correspond to panels C-E. (B-D) Samples cultured at 1 mL/min (C), 2 mL/min (D), and 3 mL/min (E) per channel. Yellow circle marks outer boundary of the hydrogel. Black circle marks the well wall. All scale bars are 1 mm. Red arrow marks location of damage due to flow.