

**Supplementary Movie 1: Cellular compartmentalization in a Sk-Br-3-based VTS.**

The VTS was harvested and stained for CD31 (PV, red) and CD11b (yellow) after nine days of cultivation. Sk-Br-3 tumor cells expressed GFP (green outlines, after compartmentalization), and fibroblasts were identified by DsRed expression (blue outlines, after compartmentalization).

**Supplementary Movie 2: Segmentation of the PV.**

Original CD31-fluorescence signal (red) and PV surface segmented from this signal (yellow, transparent and solid). MCF7-based VTS. 3D grid spacing: 50  $\mu\text{m}$ .

**Supplementary Movie 3: Tracing of the PV.**

Original CD31-fluorescence signal (red) and PVs traced along this signal (colored according to PV mean diameter). MCF7-based VTS. 3D grid spacing: 50  $\mu\text{m}$ .

**Supplementary Movie 4: Segmentation of TCs.**

Original GFP-fluorescence signal (green) and TC surfaces segmented in rendered from this signal (transparent yellow). MDA-MB-468-based VTS. 3D grid spacing: 50  $\mu\text{m}$ .

**Supplementary Movie 5: Time course of PV remodeling during cultivation.**

MDA-MB-231-based VTSs were harvested and processed after 3, 6, 9, and 12 days of cultivation, respectively.

**Supplementary Movie 6: Distribution of Fibroblasts (blue) and MDA-MB-435s tumor cells (green) with respect to CD31 IF-stained PV (red).** Coronal cut through a VTS harvested and processed after nine days of cultivation.

**Supplementary Movie 7: Density and distribution of CD11b<sup>+</sup> macrophages in an MCF7-based VTS.** CD31<sup>+</sup> PV in red. CD11b<sup>+</sup> macrophages in yellow.

**Supplementary Movie 8: Density and distribution of CD11b<sup>+</sup> macrophages in a Sk-Br-3-based VTS.** CD31<sup>+</sup> PV in red. CD11b<sup>+</sup> macrophages in yellow.

**Supplementary Movie 9: Col IV-sleeve in MDA-MB-435s- and MCF7-based VTS.** Rendered CD31<sup>+</sup>- PVs are shown in red, Col IV in blue.

**Supplementary Movie 10: Structures within an MDA-MB-435s-based VTS cultivated at 20% O<sub>2</sub>.** CD31<sup>+</sup>-PVs in red, fibroblasts as transparent blue structures, and tumor cells in green.

**Supplementary Movie 11: Structures within an MDA-MB-435s-based VTS cultivated at 2% O<sub>2</sub>.** CD31<sup>+</sup>-PVs in red, fibroblasts as transparent blue structures, and tumor cells in green.

**Supplementary Movie 12: Structure of an MDA-MB-435s-based VTS treated with a control substance.** CD31<sup>+</sup>-PVs in red, the position of tumor cells is shown as green orbs of 10 μm diameter.

**Supplementary Movie 13: Structure of an MDA-MB-435s-based VTS treated with axitinib.** CD31<sup>+</sup>-PVs in red, the position of tumor cells is shown as green orbs of 10 μm diameter.

**Supplementary Movie 14: Structure of an MDA-MB-435s-based VTS treated with LDC 1267.** CD31<sup>+</sup>-PVs in red, the position of tumor cells is shown as green (outside VTS shell) or yellow (inside VTS shell) orbs of 10 μm diameter.

**Supplementary Movie 15: Structure of an MDA-MB-435s-based VTS treated with DesOH LY-411575.** CD31<sup>+</sup>-PVs in red, the position of tumor cells is shown as green (outside VTS shell) or yellow (inside VTS shell) orbs of 10 μm diameter.

**Supplementary Movie 16: Hypoxic cells within an MDA-MB-468-based VTS treated with a control substance.** CD31<sup>+</sup>-PVs in red, the position of Hif1a<sup>+</sup>-cells shown as turquoise orbs of 5 μm diameter.

**Supplementary Movie 17: Hypoxic cells within an MDA-MB-468-based VTS treated with a UK 383367.** CD31<sup>+</sup>-PVs in red, the position of Hif1a<sup>+</sup>-cells shown as turquoise orbs of 5 μm diameter.