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Application of 3D kidney-on-a-chip for contrast-induced nephropathy

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Objectives: Contrast-induced nephropathy (CIN) is one of the major causes of hospital-acquired acute kidney injury. However, because actual estimated incidences of CIN are reported on a much lower basis than expected, substantial costs and subject numbers are required for clinical trials. Animal models are less predictive due to the difference in renal concentration ability and glomerular filtration rate. Furthermore, conventional in vitro cell culture studies can not reflect physiologic microenvironments and rheologic properties of contrast media. To complement these limitations, we applied the 3D kidney-on-a-chip model to the evaluation of CIN.

Methods: Renal proximal tubule epithelial cells (RPTEC, Ronza) were cultured in OrganoPlate (Mimetas) with a channel width of 400 μm and a height of 220 μm , applying time-averaged shear stress of 0.13 dyne/cm². Three-dimensional tubular structure of RPTEC was formed after a 5-6 day application of fluid shear stress. After 24hr treatment with two types of iodine contrast media, low - osmolar agent (iopromide) and iso-osmolar agent (iodixanol), we evaluated cell viability with WST assay. The results of cell viability in 3D kidney-on-a-chip were compared with those in static conditions (conventional culture dish). TUNEL assay was performed to identify the extent of apoptosis in each group and reactive oxygen species production was also assessed using CELLROX reagents (Invitrogen).

Results: Both low-osmolar and iso-osmolar agents showed decreased cell viability compared with the negative control, and cell death was increased in high concentrations. In particular, low-osmolar agents showed much lower viability in higher iodine concentrations (50.1% vs. 75.1%, $P < 0.05$). These results are similar to the assessments of conventional cell cultures. ROS intensity after 2 hours of contrast media exposure was higher in iso-osmolar agents, but not to a significant amount.

Conclusion: Low-osmolar radiocontrast agents revealed more cytotoxic effects in 3D-kidney-on-a-chip compared with iso-osmolar agents, which is similar to the result in static conditions. Further elaborate assessments and mechanistic interpretations are required.