

## Guest editorial:

### HIGHLIGHT REPORT: SOFTWARE FOR TISSUE ANALYSIS AND RECONSTRUCTION

Mohie A.M. Haridy<sup>1\*</sup>, Yasser S. El-Sayed<sup>2</sup>

<sup>1</sup> Department of Pathology and Clinical Pathology, Faculty of Veterinary Medicine, South Valley University, Qena, Egypt

<sup>2</sup> Department of Veterinary Forensic Medicine and Toxicology, Faculty of Veterinary Medicine, Damanshour University, Damanshour, Egypt

\* Corresponding author: Dr. Mohie A.M. Haridy;  
e-mail: mohieharidy@vet.svu.edu.eg

<http://dx.doi.org/10.17179/excli2015-587>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>).

Recently, novel image processing and analysis software named TiQuant has been published that allows for reconstruction and quantification of biological tissue from common confocal laser scans (Friebel et al., 2015). Although the software can be applied for analysis of many types of tissue, its reconstruction and analysis methods are specifically tailored to liver tissue. For example, TiQuant permits reconstruction and quantification of the bile canaliculus as well as sinusoidal networks of liver lobules. Additionally, a novel 3D surface reconstruction algorithm allows for automated detection, reconstruction and quantification of liver cell boundaries and the three-dimensional shape of liver lobules. TiQuant is able to analyze the volume of hepatocytes, thereby permitting differentiation between mono- and binucleated cells. Moreover, the hepatocyte surface can be analyzed to quantify which fraction of the hepatocyte membrane forms a bile canaliculus or is in contact with a sinusoid. A particular strength of TiQuant is that the position of each cell in relation to larger tissue structures, e.g. central veins or portal veins and bile ducts can be detected, thereby

allowing the analysis of individual cell features in relation to lobular position.

TiQuant opens additional perspectives for spatio-temporal modelling, a discipline of systems biology (Drasdo, 2014a, b; Widera, 2014; Ahmed et al., 2014). Understanding the principles and mechanisms that orchestrate the complex coordination of individual cells in an organ requires quantitative 3D and time-resolved analysis of all cells in a tissue (Hammad et al., 2014).

Previous studies in this field combining image analysis and spatio-temporal modeling have for example identified a previously not recognized order principle by showing that the endothelial cells of the liver sinusoids represent major guide rails for hepatocytes during liver regeneration (Höhme et al., 2007; Hoehme et al., 2010). Moreover, spatio-temporal models have been integrated with metabolic models, and predicted the metabolic performance of healthy and damaged tissues (Schliess et al., 2014). Spatio-temporal models also represent a promising concept to extrapolate between *in vitro* systems and the *in vivo* situation (Godoy et al., 2013; Heise et al., 2012; Mielke et al., 2011;

Braeuning et al., 2010; Schug et al., 2013; Ghallab, 2013; Hammad, 2013; Hammad and Ahmed, 2014; Reif et al., 2015). TiQuant will be a valuable tool in this field of research and will facilitate 3D tissue analysis. It is freely available for non-commercial use at <http://www.msysbio.com/tiquant>. Windows, OSX and Linux are supported.

## REFERENCES

- Ahmed H, Omar MA, Abdou AM. Quantification of three-dimensional structures in liver tissue: bile canalicular and sinusoidal networks. *EXCLI J.* 2014;13:548-50.
- Braeuning A, Singh Y, Rignall B, Buchmann A, Hammad S, Othman A, et al. Phenotype and growth behavior of residual  $\beta$ -catenin-positive hepatocytes in livers of  $\beta$ -catenin-deficient mice. *Histochem Cell Biol.* 2010;134:469-81.
- Drasdo D, Hoehme S, Hengstler JG. How predictive quantitative modelling of tissue organisation can inform liver disease pathogenesis. *J Hepatol.* 2014a;61:951-6.
- Drasdo D, Bode J, Dahmen U, Dirsch O, Dooley S, Gebhardt R, et al. The virtual liver: state of the art and future perspectives. *Arch Toxicol.* 2014b;88:2071-5.
- Friebel A, Neitsch J, Johann T, Hammad S, Hengstler JG, Drasdo D et al. TiQuant: Software for tissue analysis, quantification and surface reconstruction. *Bioinformatics.* 2015;31:3234-6.
- Ghallab A. In vitro test systems and their limitations. *EXCLI J.* 2013;12:1024-6.
- Godoy P, Hewitt NJ, Albrecht U, Andersen ME, Ansari N, Bhattacharya S, et al. Recent advances in 2D and 3D in vitro systems using primary hepatocytes, alternative hepatocyte sources and non-parenchymal liver cells and their use in investigating mechanisms of hepatotoxicity, cell signaling and ADME. *Arch Toxicol.* 2013;87:1315-530.
- Hammad S. Advances in 2D and 3D in vitro systems for hepatotoxicity testing. *EXCLI J.* 2013;12:993-6.
- Hammad S, Ahmed H. Biomarker: the universe of chemically induced gene expression alterations in human hepatocyte. *EXCLI J.* 2014;13:1275-7.
- Hammad S, Hoehme S, Friebel A, von Recklinghausen I, Othman A, Begher-Tibbe B, et al. Protocols for staining of bile canalicular and sinusoidal networks of human, mouse and pig livers, three-dimensional reconstruction and quantification of tissue microarchitecture by image processing and analysis. *Arch Toxicol.* 2014;88:1161-83.
- Heise T, Schug M, Storm D, Ellinger-Ziegelbauer H, Ahr HJ, Hellwig B, et al. In vitro - in vivo correlation of gene expression alterations induced by liver carcinogens. *Curr Med Chem.* 2012;19:1721-30.
- Höhme S, Hengstler JG, Brulport M, Schäfer M, Bauer A, Gebhardt R, et al. Mathematical modelling of liver regeneration after intoxication with CCl<sub>4</sub>. *Chem Biol Interact.* 2007;168:74-93.
- Hoehme S, Brulport M, Bauer A, Bedawy E, Schorrmann W, Hermes M, et al. Prediction and validation of cell alignment along microvessels as order principle to restore tissue architecture in liver regeneration. *Proc Natl Acad Sci USA.* 2010;107: 10371-6.
- Mielke H, Anger LT, Schug M, Hengstler JG, Stahlmann R, Gundert-Remy U. A physiologically based toxicokinetic modelling approach to predict relevant concentrations for in vitro testing. *Arch Toxicol.* 2011;85:555-63.
- Reif R, Karlsson J, Günther G, Beattie L, Wrangborg D, Hammad S, et al. Bile canalicular dynamics in hepatocyte sandwich cultures. *Arch Toxicol.* 2015;89:1861-70.
- Schliess F, Hoehme S, Henkel SG, Ghallab A, Driesch D, Böttger J, et al. Integrated metabolic spatial-temporal model for the prediction of ammonia detoxification during liver damage and regeneration. *Hepatology.* 2014;60:2040-51.
- Schug M, Stöber R, Heise T, Mielke H, Gundert-Remy U, Godoy, et al. Pharmacokinetics explain in vivo/in vitro discrepancies of carcinogen-induced gene expression alterations in rat liver and cultivated hepatocytes. *Arch Toxicol.* 2013;87:337-45.
- Widera A. Integrated spatiotemporal-metabolic modelling bridges the gap between metabolism on the cellular level and organ function. *EXCLI J.* 2014;13:1289-91.