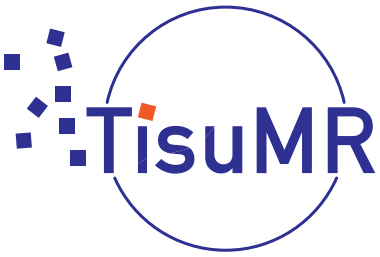
Project Number: 737043

Project Acronym: **TISuMR**

Project Title: **Integrated Tissue Slice Culture and NMR Metabolomics — A Novel Approach Towards Systemic Understanding of Liver Function And Disease**

TISuMR Device Specification



Document version: 0.0.0
Last modified: May 21, 2019

1 Executive Summary

2 Change History

Version	*Mod. Date*	*Summary of changes*	*Author*
0.0.0	22/5/2019	Initial discussion version	ms, mu

3 Scope of this document

TISuMR is a collaboration project between University of Southampton, University of Groningen and Karlsruhe Institute of Technology. The aim of the project is to develop technologies for NMR (nuclear magnetic resonance) compatible microfluidic perfusion culture of PCLS (precision cut liver slices). The devices that are being developed at the three project partner sites are built for different aims (high-resolution liquid NMR spectroscopy of the perfusion fluid, high-resolution magic-angle spinning NMR spectroscopy, or conventional analysis using HPLC and other techniques). These different approaches lead to different interfacing requirements for the perfusion system. In order to ensure comparability of the results, it is necessary to standardise certain aspects of the design. This will ensure identical culture conditions, as well as a common standard to judge the performance of the culture system and basic viability of the tissue slices.

This document defines the specifications for a device design to be qualified as a TISuMR device. All the TISuMR personnel will follow these requirements for device design if the device is used for TISuMR research. Possible variations are also given to cater to specific experimental needs.

Changes to this document will be decided in the TISuMR meetings. The intended changes will be communicated to all the partners before the meeting to think upon. All the partners should agree for a change to be made final. This document will be available on https://github.com/marcel-utz/tisumr-device to obtain the latest version of the document. Marcel Utz will own the master copy and will be responsible to implement the changes. A drawing of the proposed device is shown in Fig.1

4 Required Specifications

- **Culture chamber geometry:** The culture chamber is cylindrical in shape with a diameter of 7 ± 1 mm and a depth of 500 ± 100 μm.
- **Perfusion geometry:** The perfusion fluid flows around the PCLS. There can be more than one inlets and outlets. The inlet and outlet channels have cross sectional dimensions of $200\pm100\times200\pm100$ μm^2.
- **Chip or device material:** Polycarbonate is used for the chip or device fabrication.
- **Temperature:**. The PCLS culture is performed at $37\pm0.5^\circ$.
- **Gas composition:** Either carbogen (95 % O_2 + 5 % carbon dioxide) or a mixture (80 % O_2+ 10 % nitrogen +5 % carbon dioxide) is used for the culture.
- **Viability standards:** Adenosine tri(phosphate) (ATP) content in the tissue slice after culture is used as a measure of viability. As a rule, tissue slices can be considered viable if they contain at least 6 pmol of ATP per mg of protein. The protocols for ATP determination are given in section ...
- **Medium composition:** William E with Glutamax + Glucose (1.375 g/500mL William E medium) + Gentamycine (500μL/500mL)
- **Sterilization:** Ethanol will be used for sterilization. Provide ethanol concentration and minimum exposure time. Define internal vs external sterilisation. How are ancillary perfusion equipment to be sterilised (e.g., tubing, syringes, connectors, gaskets?)

5 Allowed variations

- **Detailed fluidic paths:** Fluidic network can be designed freely.
- **Flow protocol:** The media can be flowed by different types of pumps or centrifuge.
- **Fabrication method:** The devices can be made through machining or bonding layers by different protocols.
- **Flow rates:**. Range of flow rates will be decided through optimization.

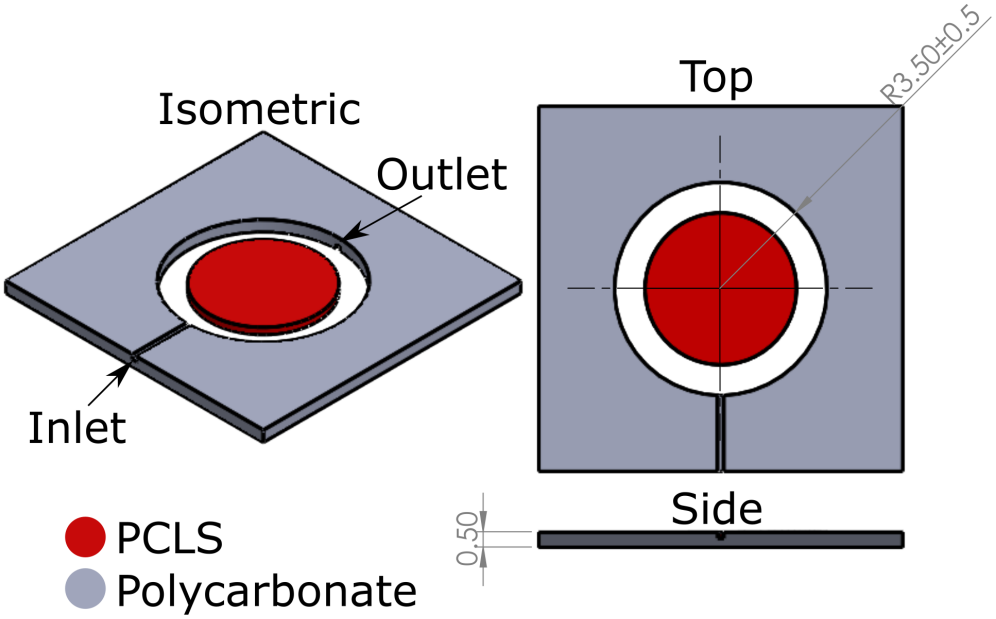


Figure 1: *Isometric, top and side views of the device. The diameter of the PCLS chamber is 0.7 mm. The thickness of the chamber is 0.5 mm.*