Characterization of the aerosol applied for Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC)

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Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) is a new approach for the treatment of peritoneal carcinomatosis (Solass et al., 2012). During PIPAC, the chemotherapeutic solution is delivered as an aerosol, which is generated within the capnoperitoneum by an approved single fluid nozzle (Fig. 1) called micro injection pump (MIP®, Reger Medizintechnik, Germany). At standard operation conditions, 150 mL of the chemotherapeutic solution is supplied with a volumetric liquid flow rate of 30 mL/min at a fixed MIP® position with a distance to the peritoneum of 5 cm – 15 cm.

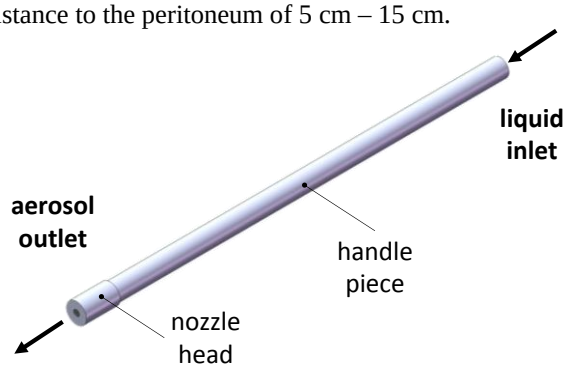

Figure 1. CAD-model of the MIP®, length = 250 mm, nozzle head diameter = 15 mm, nozzle head orifice diameter = 0.2 mm.

Performed in-vivo animal experiments by tissue penetration depth measurements (Khosrawipour et al., 2015) have shown that the local drug distribution is not as homogenous as predicted previously (Solass et al., 2012) and that can be explained by unsuitable aerosol properties. Based on the lack of knowledge regarding the operating principle of the MIP® and the corresponding aerosol characteristics ex-vivo granulometric analyses on the performance of the MIP® were performed by means of laser diffraction spectrometry (HELOS/KR-H2487, Sympatec GmbH, Germany). The conclusions based on laser diffraction spectrometry regarding the droplet deposition were verified by additional gravimetric analyses.

Results show, that the aerosol generation process consists of an initiation phase, a steady state phase and a shutdown phase whose duration strongly depend on the adjusted liquid flow rate. At standard operation conditions in steady state phase, the MIP® provides a bimodal aerosol (see Fig. 2) with volume-weighted median droplet diameter of $x_{50,3}$ = 25 µm. Considerations regarding the deposition mechanisms lead to fact that more than 97.5 vol.-% of the supplied chemotherapeutic solution directly deposits in spray direction with the peritoneum due to gravitational settling and inertial impaction, whereas less than 2.5 vol.-% of the supplied solution forms an aerosol cloud that can reach lateral and upper regions within the capnoperitoneum.

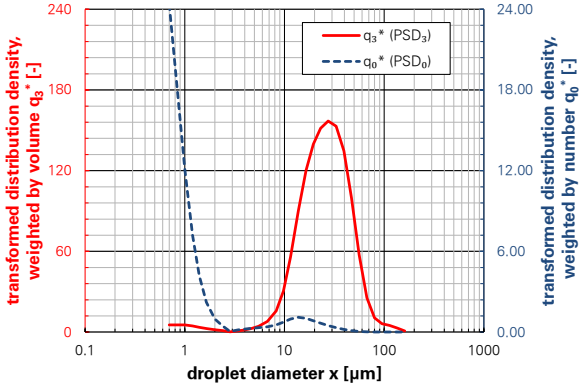

Figure 2. Droplet size distribution weighted by number and volume in steady-state phase at standard MIP® operation conditions.

The presentation will give detailed information on the PIPAC-approach, the operation principle and performance of the MIP® based on granulometric and gravimetric analyses.

Khosrawipour et al. (2015) *Ann. Surg. Oncol.* **23**, 1220-1224.
Solass et al. (2012) *Surg. Endosc.* **26**, 1849-1855.