PLATINUM DISTRIBUTION AFTER CLINICAL (HYPERTHERM) INTRAPERITONEAL CHEMOPERFUSION USING LASER ABLATION – INDUCTIVELY COUPLED PLASMA – MASS SPECTROMETRY

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Objective: Cytoreductive surgery (CRS) followed by intraperitoneal chemoperfusion (IPEC) with platinum (Pt) – based drugs benefits selected patients with peritoneal carcinomatosis (PC). However, little is known about the tumor tissue penetration of these drugs after IPEC, and on the effect of combined hyperthermia on Pt distribution. Highly sensitive bioimaging with laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) may allow detailed insight in the tissue distribution of Pt.

Methods: Tumor tissue samples were obtained from two patients with PC from gastric and ovarian cancer, who underwent CRS followed by 90min. of IPEC (38°C) or HIPEC (40°C) with cisplatin (120mg/m²), respectively. A single tumor nodule from each patient was removed after (H)IPEC and freeze-dried in liquid nitrogen. To analyze penetration depth, distribution and concentrations of Pt within these tumors, LA-ICP-MS was used. Ablation was performed with an Analyte G2 193nm ArF* excimer laser, coupled to an XSeries 2 ICP-quadrupole-MS. Calibration of the system was achieved using four gelatin standards, spiked gravimetrically by 1001 ± 5µg/ml Pt and 1000 ± 5µg/ml Indium standards.

Results: Figure 1 depicts LA-ICP-MS and showed that the distribution of Pt can be observed with high sensitivity (5.1x10³ counts per seconds /µg g⁻¹). In general, distribution, penetration and concentrations of Pt are limited to the outer layer of the tumor and influenced by tumor type, temperature and tissue density. While the dense tumor derived from ovarian cancer treated with
HIPEC demonstrate a Pt-gradient, a more uniformly Pt-distribution can be observed in the less dense tumor derived from gastric cancer treated with IPEC.

**Conclusion:** LA-ICP-MS is a highly sensitive technique for the analysis of Pt distribution in human tumor sections. Additionally, these images can be correlated to histological images and may be of particular interest in the future for investigating the influence of tumor microenvironment on drug delivery.

![Figure 1](image1.png)

Figure 1. LA-ICP-MS images of the Pt distribution in peritoneal tumor nodules derived from a patient with gastric cancer treated at 38°C (A) and from a patient with ovarian cancer treated at 40°C (B), both for 90min. with cisplatin (120mg/m²). A logarithmic colorscale was employed to highlight the distributions at all concentration levels simultaneously. An adapted sigmoidal curve was fitted using the Levenberg-Marquardt algorithm and linear regression was used for selected regions (C). The solid bold lines represent the averages across all images, the transparent lines indicate the average profile within a single image.