EUROPEAN SYNCHROTRON RADIATION FACILITY
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Experiment Report Form

	Experiment title: Comparison of Intraperitoneal Cisplatin Protocols for Treatment of Peritoneal Carcinomatosis through XRF Imaging	**Experiment number**: LS 2935
Beamline: ID16B	**Date of experiment**: from: 1/12/2020 to: 6/12/2020	**Date of report**:
Shifts: 15	**Local contact(s)**: Remi Tucoulou and Jaime alberto Segura ruiz	*Received at ESRF:*

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Report:

Scientific Backgroud

When treating patients with cancer of the peritoneal surface (peritoneal carcinomatosis, PC), intraperitoneal drug delivery (IPDD) is increasingly used. In this procedure the chemotherapy is administered into the peritoneal cavity of the patient, directly targetting the tumors and minimizing the stystemic absorption of the drugs. However, IPDD has a limited (1 mm) tissue penetration of the instilled platinum (Pt) compounds (mainly cisplatin and oxaliplatin). Recent efforts to enhance tissue penetration include delivery as an *aerosol*, and use of Pt containing *nanoparticles*.
Advanced nanoscale imaging would allow to gain important insights in the relative efficacy of these novel strategies. Therefore we used XRF imaging to study the Pt distribution in tumor tissue at the nanometer scale after intraperitoneal treatment of tumor bearing animals with either liquid instillation or aerosolized drug, and using either the standard commercially used drug formulation or a novel nanoparticle.

Experimental Work

The experiment consisted of two major parts, being linescans in order to get a feeling on the penetration depth of the different drug formulations and imaging to get an idea of how the drugs are distributed throughout the tumor tissue.

Figure 1 gives an example of a line scan. For each sample, four such scans were performed in order to get more statistical relevant information. Further data processing and comparison with other data sets will lead to insights in which protocol for drug administration yields the largest penetration depth and hence which protocol can target the largest tumor nodules.

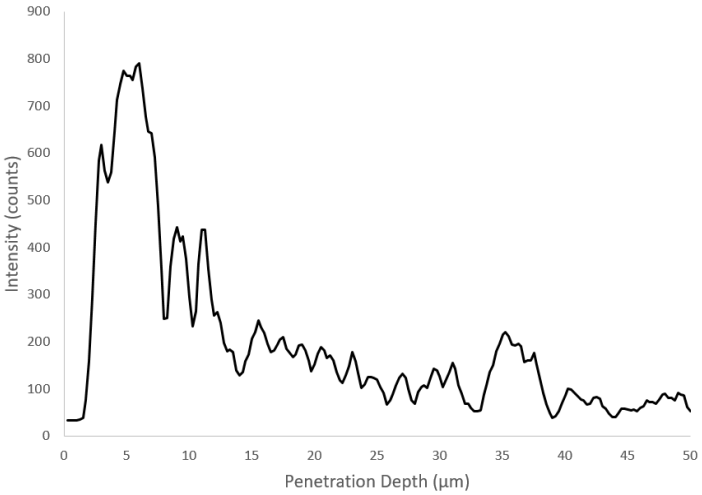

Figure 1 Line scan through a tumor section, intensity of the Pt-L_α line plotted against the depth in the tumor; 0.05s dwell time 250nm step size

Two types of mappings were taken. The first are relatively coarse overview scans, used to locate interesting areas and to get a good general view of the tumor section. Since the sections are much larger than the area that can be realistically imaged in ultra-high resolution during a beamtime, these scan are crucial to get both relevant information and a general overview. All overview scans used the same scan setting, being 50 ms dwell time and 200 nm step size. An example of such an overview scan is given in Figure 2, with an RGB color map showing Pt, Ca and Zn.

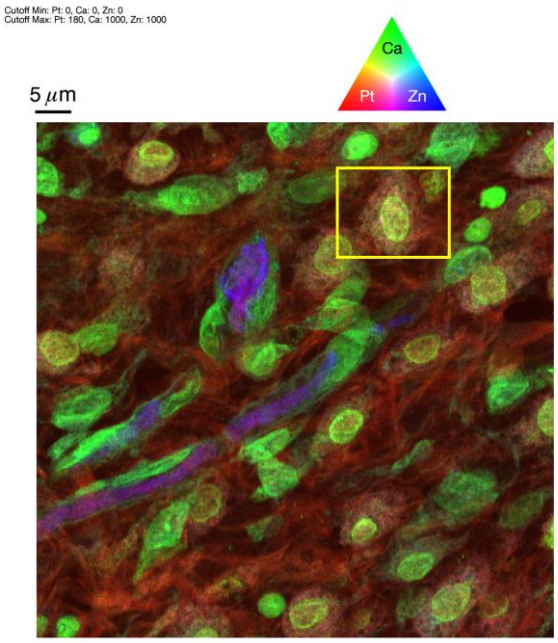

Figure 2 RGB (Pt, Ca, Zn) image of an overview scan, 0.05s dwell time, 200nm step size. The region for the scan of Figure 3 is indicated in yellow

Using the overview scans, regions of interest for more detailed imaging were selected. These focussed on cancer cells, regions in the tumor with elevated Pt concentration and regions with anomalous morphology. These images could teach us a lot on how the chemotherapy interacts with the tumor tissue. Figure 3 gives an example of a detail scan with the elemental mapping for the 9 main elements found in the studied tissues.

Depending on the studied region, these detailed scans used two set of scan conditions. The dwell time was kept constant at 50ms, but the step sized varried from 50nm (~beamsize) to 25nm (double oversampling) when ultra-high resolution was desired.

During the beamtime, a total of 15 samples was investigated using line scans, amounting to 60 scans.
11 samples were used for imaging purposes, yielding 21 overview scans and 38 detail scans.

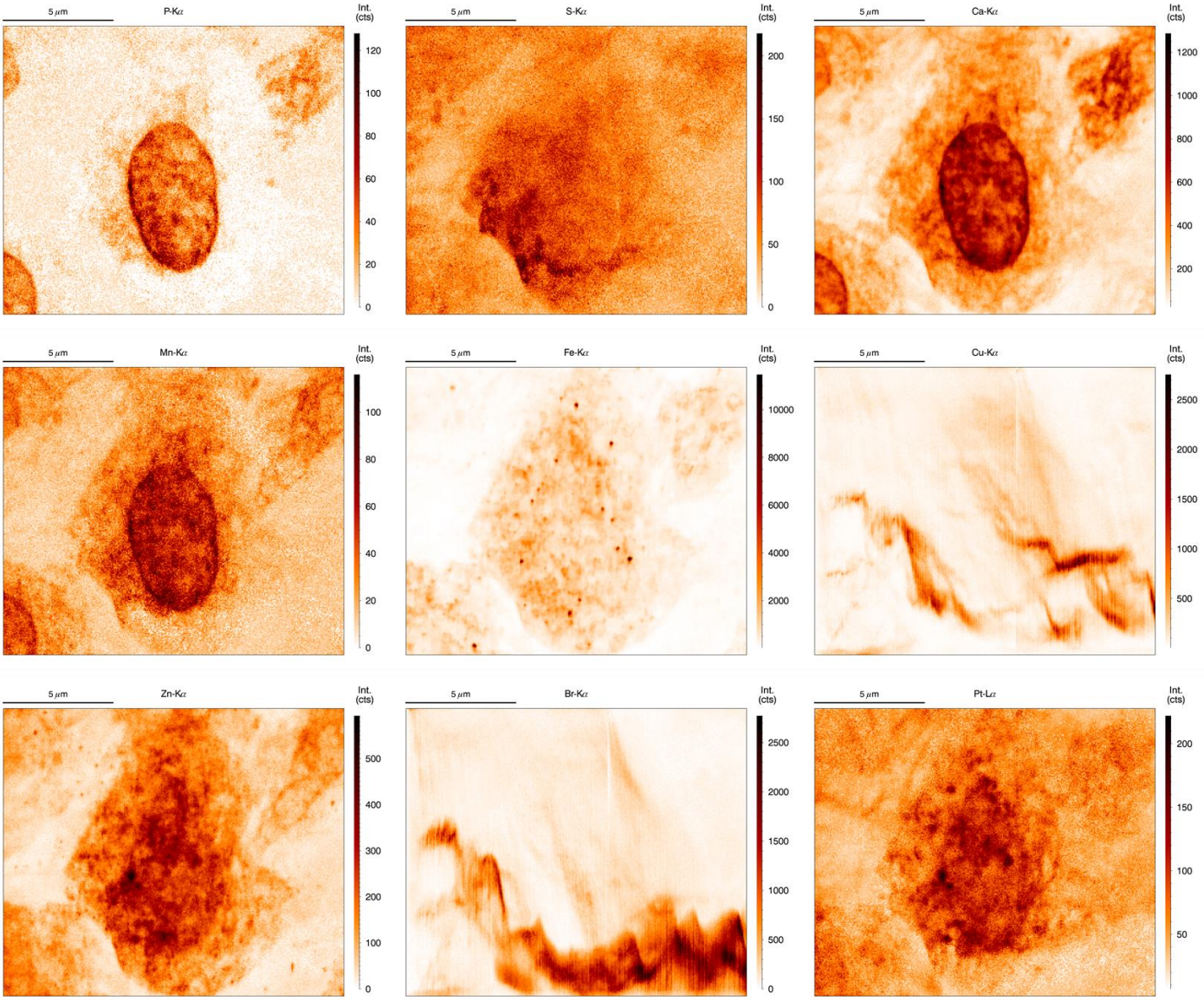

Figure 3 Elemental mappings for the 9 main elements found in the studied tissue, being from top left to bottom right: P, S, Ca, Mn, Fe, Cu, Zn, Br and Pt; 0.05s dwell time, 50nm step size