EUROPEAN SYNCHROTRON RADIATION FACILITY
INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

Experiment Report Form

	Experiment title: Nano-XRF and nano-XANES analysis of resistance mechanism and drug-tissue interactions in cisplatin treated ovarian cancer tumors	**Experiment number**: LS 2711
Beamline:	**Date of experiment**: from: 6/6/2018 to: 11/6/2018	**Date of report**:
Shifts:	**Local contact(s)**: Remi Tucoulou	*Received at ESRF:*

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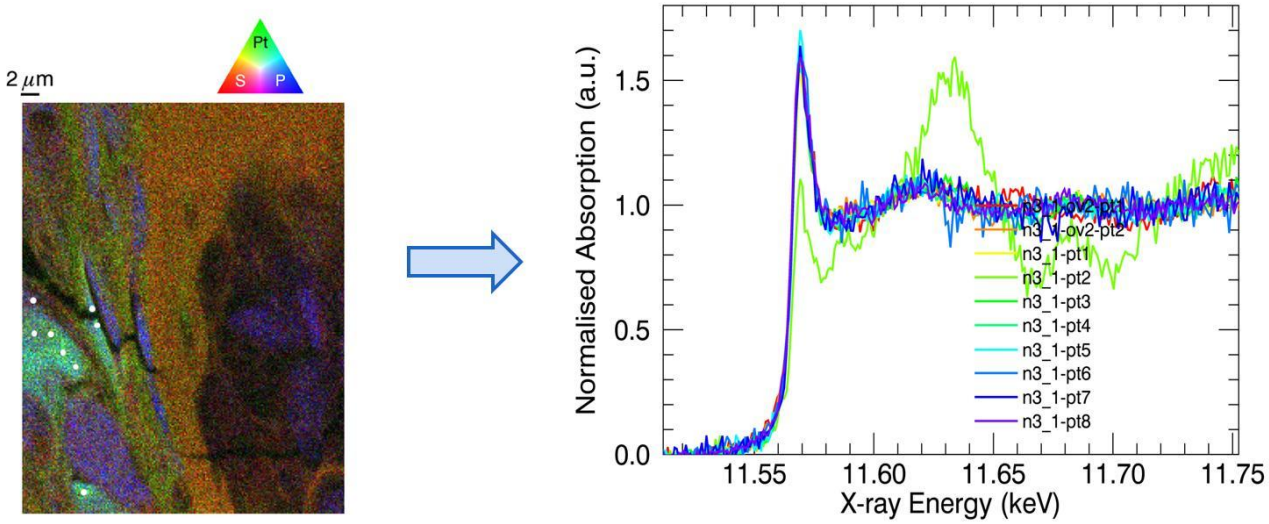
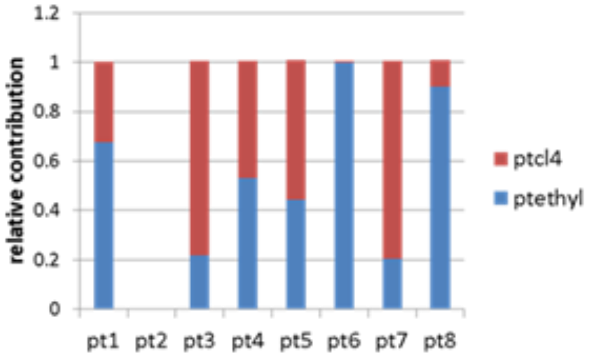
Report:

As continuation of previous experiments at ID16B (LS2444 and LS2559), the resistance phenomena in human ovarian cancer tumors to cisplatin intraperitoneal chemotherapy (IPC) has been evaluated.
Detailed analysis by nano-XRF, nano-XANES and immunohistochemistry (IHC) techniques will add valuable information on tumor-drug interactions, next to the knowledge we already gathered during previous experiments (e.g. the prevalent presence of Pt in the ECM of the tumors)[1-2]. Nano-XANES measurements were used to shed light on the chemical state of Pt (e.g. oxidation state and molecular geometry) and on the protein adducts and DNA-protein cross-links of Pt, clarifying the action mechanisms of Pt as well as the effect of the Pt-coordinating groups on the chemical activity. Pt XRF-maps could be compared to the classic immunohistochemistry (e.g. caspase-3, Ki67) to correlate tumor cell apoptosis/necrosis, repair and proliferation with the Pt concentration, offering detailed info on the behaviour of these cytotoxic drugs in tumor tissues. The Pt distribution, coupled with its chemical state, within cells could enhance our knowledge on drug resistance mechanisms playing a major role in disease progression of ovarian cancer.

The experiments were performed in two steps. First, overview scans were made, localizing regions with increased Pt signal. In the second step, local XANES point measurements were taken to assess the chemical state of this Pt. The focus in these cases lay on regions where Pt and S both had elevated concentrations, due to the results of our previous beamtimes, indicating their is a connection between Pt residing outside the tumor cells' nucleus and S-rich structures in the ECM.

The study clearly showed different forms of Pt were present in the investigated cells, some of which was still in the cisplatin arrangement, while other regions had Pt linked to organic groups.





References

1. Carlier, C.; Laforce, B.; Van Malderen, S. J. M.; Gremonprez, F.; Tucoulou, R.; Villanova, J.; De Wever, O.; Vincze, L.; Vanhaecke, F.; Ceelen, W., Nanoscopic tumor tissue distribution of platinum after intraperitoneal administration in a xenograft model of ovarian cancer. *Journal of Pharmaceutical and Biomedical Analysis* **2016,** *131*, 256-262.

2. Laforce, B.; Carlier, C.; Vekemans, B.; Villanova, J.; Tucoulou, R.; Ceelen, W.; Vincze, L., Assessment of Ovarian Cancer Tumors Treated with Intraperitoneal Cisplatin Therapy by Nanoscopic X-ray Fluorescence Imaging. *Scientific Reports* **2016,** *6*, 29999.