

P409 Analysis of specific platinum - DNA adducts after clinical intraoperative intraperitoneal chemoperfusion of ovarian cancer patients

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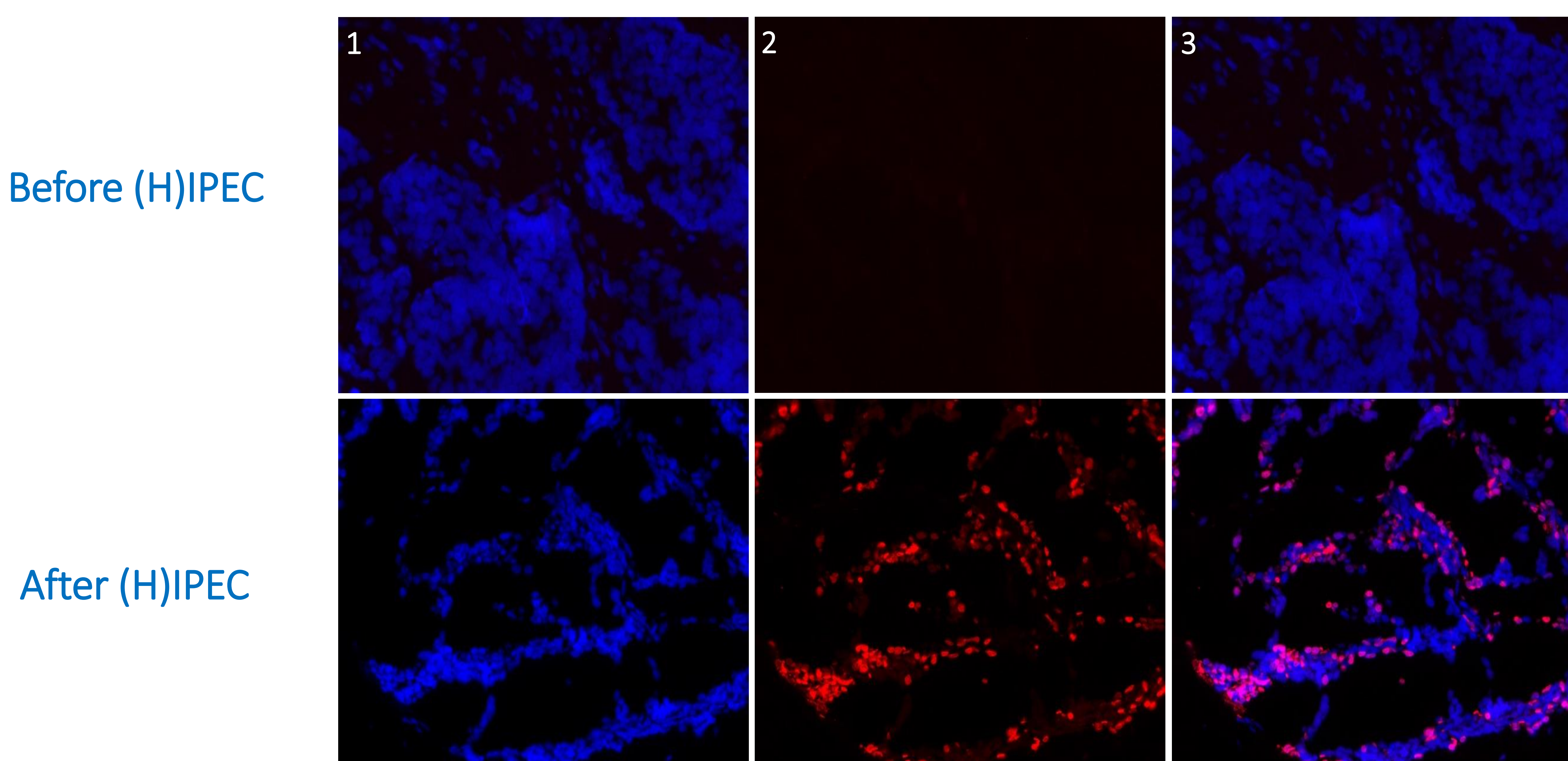
Background and purpose

Cytoreductive surgery (CRS) followed by intraperitoneal chemoperfusion (IPEC) with platinum (Pt) – based drugs benefits selected patients with peritoneal carcinomatosis (PC). Nevertheless, despite the initially successful response to the chemotherapy, 80% of women will eventually develop recurrent peritoneal disease, which can only arise from minimal residual disease left after primary CRS, and resistant tumor cells. However, little is known about the amount and distribution of cisplatin-DNA adducts and the influence of combined hyperthermia. Therefore, we want to analyze the relative contribution of structurally defined cisplatin-DNA adducts.

Experiment

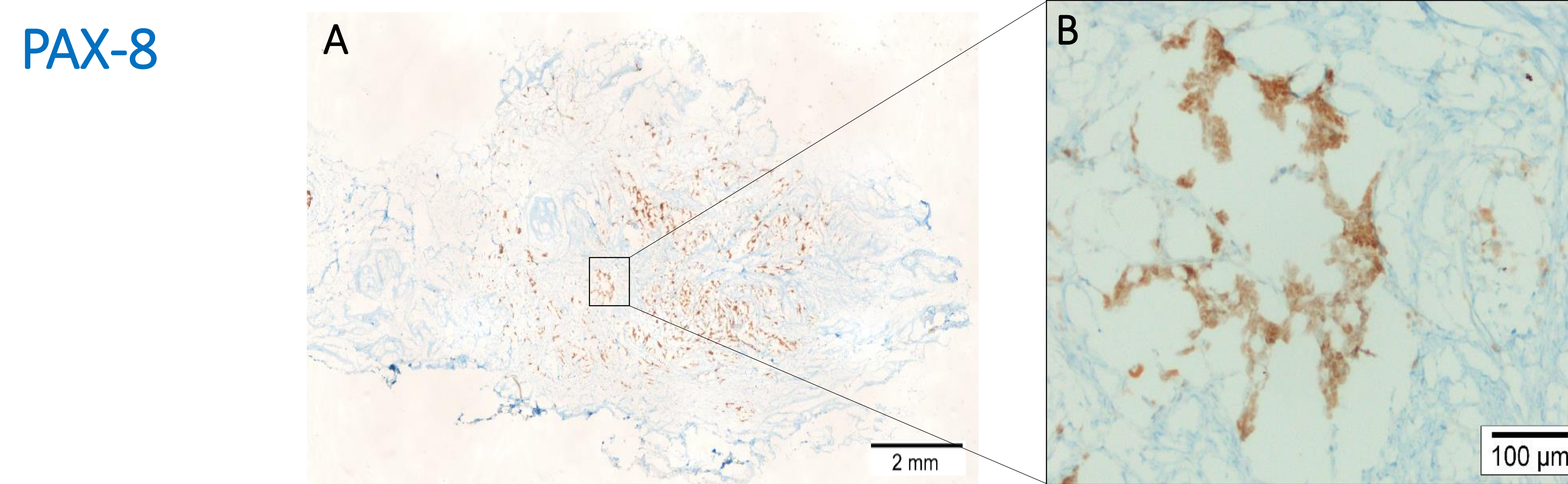
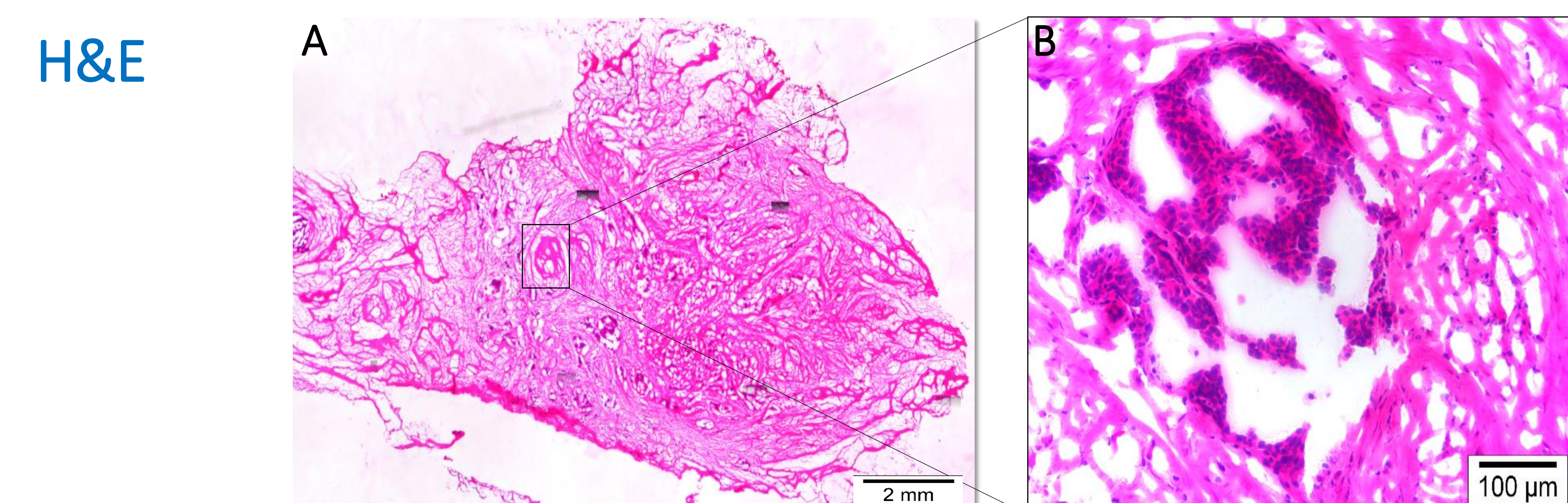
Tumor tissue samples were obtained from patients with PC from primary or recurrent serous epithelial ovarian cancer (OC), who underwent CRS immediately followed by 90 min. of chemoperfusion. Concerning the chemoperfusion, patients were randomized into 4 different groups: IPEC (37-38°C) or hyperthermic IPEC (40-41°C; HIPEC) treatment with a cisplatin dose of 120 or 75 mg/m². Tumor nodules were removed from each patient after (H)IPEC and snap-frozen in liquid nitrogen. Tumor tissue sections of 5 µm were cut and stained with the monoclonal antibody R-C18 to investigate the amount and distribution of 1, 2 Pt- guanine, guanine adducts (1, 2 Pt-[GpG]) in the nuclear DNA of individual cells. Additionally, Haematoxylin and Eosin (H&E) and Paired Box gene 8 (PAX-8) stainings confirmed the presence of epithelial ovarian cancer cells in the tissues.

Results



Cryo-sections of tumor tissues excised before and after (H)IPEC were stained with the ICA protocol. DAPI staining showed DNA content (1); IF staining with Mab R-C18 showed 1, 2 Pt-[GpG] DNA adducts (2); Overlay of 1 and 2 (3). Magnification 40X

Consecutive cryo-sections of tumor tissues excised after (H)IPEC were stained with H&E and PAX-8. Overview of the tumor tissues (A); Region of interest, which corresponds to image 3 of the ICA assay (B). Magnification: A = 40X; B = 200X



Conclusions

ICA staining:

- is a highly sensitive and specific staining method
- made it possible to visualize and quantify the 1, 2 Pt-[GG] adducts in human tumor tissues after (H)IPEC
- can be correlated to other histological images, which may be of particular interest when investigating the influence of e.g. transport mechanisms in the acquisition of Pt resistance.