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# Doxorubicin, mitoxantrone and irinotecan drug eluting beads and free drugs for the treatment of experimental peritoneal carcinomatosis in pancreas cancer

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Peritoneal carcinomatosis is a late, but severe, complication of many solid tumors. In 20% of all cases, the peritoneal carcinomatosis is caused by pancreatic carcinoma. Patients with peritoneal carcinomatosis (all tumor entities) have a median survival time of 3.1 months.

In this metastatic stage of the disease, few patients show a sustained response to chemotherapy or radiation therapy. In palliative therapy, targeted delivery offers the opportunity to focus drugs directly to the tumor site, which is a prerequisite for avoiding toxic side effects. We aimed to demonstrate the therapeutic efficiency of biocompatible polyvinyl-alcohol hydrogel drug eluting beads (DEBs) containing doxorubicin, mitoxantrone and irinotecan in a model of experimental pancreatic cancer *in vitro* and *in vivo.* Herefore, Panc02 murine pancreatic carcinoma cells were exposed to Doxorubicin, mitoxantrone and irinotecan DEBs and free compounds. The effect on cell proliferation and apoptosis induction was compared. Using these cells peritoneal carcinomatosis was induced inC57 black6 mice. Mortality, tumor load and therapy-associated weight loss were compared after treatment of tumor bearing mice with DEBs or free compounds

*In vitro* treatment with DEBs decreases tumor cell proliferation and induces apoptosis. The effect is less pronounced than corresponding doses of the free drug.

Repeated applications of the free drugs *in vivo* induce significantly higher lethality and weight loss than corresponding doses of DEBs. No relevant differences in antitumoral activity were observed. No systemic spread of the beads could be found after subcutaneous injection of radiopaque beads using computer tomography and HE-histology of post-mortem organ specimens after intraperitoneal injection. DEBs remained within the injected cavity or at the injected site.

It can be concluded that DEBs show the advantage of low systemic toxicity while at the same time inducing significant antitumoral activity. Our study offers experimental proof as to the efficiency and safety of the intraperitoneal use of DEB-beads and they may represent a future therapeutic option for pancreatic cancer patients with peritoneal carcinomatosis.