Evaluation of chemoradiotherapy with carbon ions and the influence of p53 mutational status in the colorectal carcinoma cell line HCT 116.

Aims and background. Heavy ion therapy has shown promising results in the treatment of recurrent colorectal carcinoma. The present study evaluates the effect of five different cytostatic agents in combination with radiotherapy with carbon (C12) ions and photons in two isogenic colorectal cancer cell lines differing in p53 status. Methods and study design. Clonogenic survival analyses were performed using the human colon cancer cell lines HCT 116 wt and the isogenic p53 deficient cell line HCT 116 p53 -/-.. Single photon doses (6 MV X-rays) up to 10 Gy were applied using a linear accelerator. Carbon ion irradiation up to 3 Gy was performed at the Heidelberg Ion-Beam Therapy Center with the horizontal beamline delivering an extended Bragg peak with an average linear energy transfer of 103 keV/µm. Five different cytostatic agents were applied in combinations with photon and carbon ion radiotherapy. Results. Both cell lines showed a similar response to photons and carbon ions, whereas treatment with carbon ions resulted in a superior relative biological efficiency. Irinotecan and paclitaxel alone showed high toxicity in the treatment of wildtype cells. A notable difference was observed on the cell death of p53 -/- cell lines. Here, single treatment with paclitaxel and gemcitabine resulted in good response rates.
Combinations of carbon ions with gemcitabine, irinotecan or paclitaxel revealed high response rates. After irradiation with carbon ions and temozolomide, cell survival rates depended on p53 status, with a decreased survival rate in wildtype cells. Conclusions. Irinotecan and paclitaxel are an effective treatment for HCT 116 wt cells, whereas HCT 116 cells with p53 deficiency can be treated successfully with paclitaxel and gemcitabine. Combined treatment modalities with carbon ions and chemotherapy provide great effectiveness that may offer new treatment opportunities for recurrent colorectal cancer in the future.