Carbon ions and protons elicit an equal amount of late effects in irradiated rat lungs*

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The application of charged particles such as carbon ions and protons in modern radiotherapy represents an important step towards a successful treatment of surgically untreatable tumors, such as in the head and neck region. A beneficial feature of charged particles is the *inverted depth dose profile,* which spares the normal tissue in the entrance channel, but deposits high doses inside the tumor [1]. As the development of particle therapy continues, new applications are emerging, for instance irradiation of moving tumors in the thorax with scanned particle beams [2]. In Germany, lung cancer ranks among the top three cancers with the highest mortality [3]. Efforts are being made to treat lung cancer using charged particles, but the normal tissue response to these radiation qualities is not well investigated. Selection of the appropriate charged particle for therapy of a specific tumor type—carbon ions or protons—requires knowledge about possible differences in the normal tissue response such as fibrosis in the patient. Here we investigated the response of lung tissue to doses of carbon ions and protons and scored the amount of fibrosis 10 months after irradiation in order to determine possible differences in the effect of both particles.

Materials and Methods

Groups of 3 (C-ions) or 5 (protons) adult male albino Wistar rats of the Hsd/Cpb:WU strain weighing 300 ± 10 g at the beginning of the experiment were irradiated at a physical dose of 18 Gy with 150 MeV/u protons or 270 MeV/u carbon ions. 50% of the lung volume was irradiated. After 42 weeks, animals were sacrificed and 5 µm lung slices were Hemotoxylin-Eosin (HE) stained and scored as described in [4]. Significance between datasets was assessed with the Mann-Whitney-U test, null hypothesis (protons and carbon ions elicit an equal amount of fibrosis) was rejected at $p < 0.05$.

Results and Discussion

Both radiation qualities elicited a fibrotic reaction in the radiation field (Fig. 1). A disorganization of the lung parenchyma was visible, with strongly damaged alveoli. Infiltrates containing inflammatory cells were visible in the tissue, which indicates a chronic inflammation. Blood vessels showed signs of edema and thickening of the *tunica media*. Qualitative assessment of the histological features did not reveal a difference of the morphology after exposure to carbon ions or protons.

Scoring of the lungs substantiated this assessment, as both qualities elicited an equal amount of fibrosis in the lung parenchyma (Fig. A, inset). Scoring for inflammation and vascular damage did not reveal a difference between both radiation qualities (not shown). The differences were also not significant in other dose ranges of carbon ions and protons (13–15 Gy physical dose).

We conclude that, comparing the same physical doses of carbon ions and protons, typical late radiation damage is elicited in the rat lung at a comparable severness, which predestines both radiation qualities for lung cancer treatment. This first result provides a basis for further studies of late effects of both radiation qualities, where more doses and additional endpoints will be taken into account.

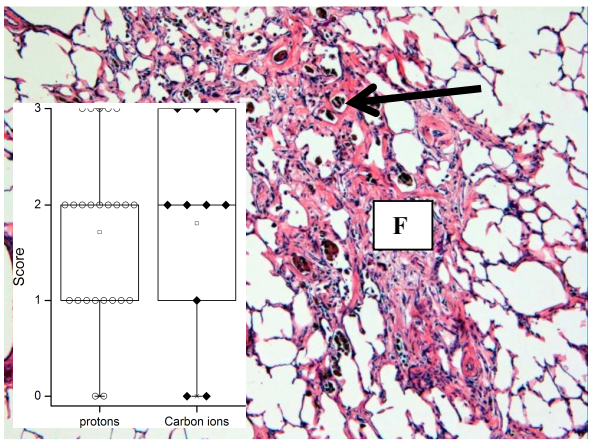

Fig. 1: Representative example of a fibrotic reaction in HE stained lung tissue irradiated with 18 Gy carbon ions. The alveolar structure is disrupted by a fibrotic clot (F). Inflammatory cells can be observed (arrow). Inset: Scoring results for fibrosis in tissue irradiated with protons (left) and carbon ions (right).

References

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* *Supported by HGS-HIRe and grant CBR-754842 from the University of Groningen*