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The pathology and the pathogenesis of late radiation-induced heart diseases after low and high radiation doses

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Contrary to historical concepts of the radioresistance of organs with slow cell turnover, the heart is one of the most radiosensitive organs in the human body. The risk of death from radiation-induced heart diseases is significantly increased after high radiation doses (>40 Gy in Hodgkin's disease), after intermediate doses (<10 Gy mean heart dose in breast cancer) and after low doses (<1 Gy in Japanese A-bomb survivors). Despite a plethora of in vivo studies performed in experimental animals (dogs, rabbits, rats and mice) during the last 40 years, neither the precise pathology, nor the pathophysiology or the pathogenesis of fatal radiation-induced heart diseases have been clarified. The wide range of radiation doses to the heart which have been proven to cause fatal radiation-induced heart diseases suggests that different pathogenic mechanisms are involved. After high radiation doses to large parts of the heart, pericarditis has been the most frequent radiation-induced heart disease in the past, yet this complication is very rare with modern treatment plans. High local doses to coronary arteries have been suggested to increase the risk of atherosclerosis and myocardial infarction, however, this could not be reproduced in rodent experiments. The most common pathology after local irradiation of the heart of rodents is progressive general and focal rarefication of the microvasculature. The different pathogenic mechanisms depend strongly on anatomical dose distributions in the heart. As long as these are not well understood, any plan based on NTCP models is unsafe. Future research in experimental animals should concentrate on in vivo and ex vivo correlations of molecular and cellular alterations with histopathological damage in the irradiated heart in relation to local dose. Experiments on cell lines in vitro are of limited value unless integrated into a comprehensive in vivo/ex vivo research programme. The most promising approach would be prospective studies in radiotherapy patients correlating anatomical dose distribution in the heart to the distribution of alterations quantified with advanced functional imaging procedures.

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