Contribution ID: **110** Type: **poster preferred**

Preliminary results from mechanistic modelling of X-ray promoted atherosclerosis in ApoE-/- mice

Thursday, 18 October 2012 16:33 (1 minute)

Mechanistic models may help to determine how ionising radiation promotes the development of atherosclerosis. For this purpose a model has been formulated that allows for radiation to contribute to the process of atherosclerosis in several ways. The model is based on what is known from the scientific literature on plaque formation and the possible influences of radiation on this process. The current formulation has been tailored to experiments carried out at the Dutch National Cancer Institute (NKI) with ApoE-/- mice. Plaque formation in this genetically modified mouse model is considered to partly mimic the process of atherosclerosis as it occurs in humans. At NKI the carotid arteries of groups of ApoE-/- mice were exposed to 0, 2, 8 or 14 Gy X-ray doses. After approximately half a year the arterial tree was removed from these mice and examined for plaques. It was observed that the number and surface area of plaques grew with increasing dose. Moreover, exposed mice demonstrated plaques of a more inflammatory phenotype that is prone to intraplaque haemorrhage. At the Dutch National Institute for Public Health and the Environment (RIVM) mechanistic modelling was therefore aimed at adequately predicting number, size and phenotype of the observed plaques. Preliminary results from this model fitting process will be shown. The fact that possible radiation effects are included in several steps of the model helps to indicate where radiation action is required to explain the data and where it is not. This is important for the more accurate determination of radiation risk for vascular disease, but it also constitutes significant input for new, tailored experiments aimed at advancing our knowledge on the influence of radiation on atherosclerosis.

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Session Classification: Poster Session 3

Track Classification: Charged Particles in Medicine and Space Research