Contribution ID: **24** Type: **not specified**

Therapeutic efficacy of 225Ac-containing polymersomes

Cancer, still presenting one of the major challenges in modern healthcare, leads to more than 8.8 million deaths annually. While the main treatment options include surgery, chemotherapy, and radiotherapy, increasing attention is given to brachytherapy in e.g. the treatment of prostate cancer. Advantages of brachytherapy, as compared to radical prostatectomy and external beam radiation therapy, lie in the much higher radiation doses which can be given to the tumour tissue whilst spearing healthy tissue. Whereas in classic brachytherapy careful placement of the seeds is still essential for optimal irradiation of the tumour, recently a movement towards the use of micro and nano particles for intratumoural administration has begun. These particles are able to distribute themselves to and within the tumour tissue, and can be labelled with either beta or alpha emitters. We have shown in the past that polymersomes are ideal candidates to be used in alpha therapy, as they are able to retain the recoiling daughter nuclides of 225Ac to a large extent, thus limiting the renal toxicity caused by recoiling daughters1.

We have evaluated the suitability of 225Ac-containing polymersomes composed of polybutadiene-polyethylene oxide as intratumoural therapeutic agents. Polymersomes containing 10 kBq and 50 kBq 225Ac have been injected intratumourally in MDA-MB-231 tumour-bearing BALB/c nude mice. At 1 and 7 days p.i. the biodistribution and tumour retention has been assessed. Polymersomes were retained very well in the tumour tissue, whereas 225Ac-DOTA was rapidly cleared. This observed retention in the tumour tissue together with an increase in double-strand DNA breaks, determined by -H2AX staining, in the tumours treated with 225Ac-polymersomes indicates that vesicles containing alpha-emitters like 225Ac will be suitable agents for long-term irradiation of tumours. The overall survival of the treated and control animals as well as the tumour growth has been followed in time. We have found a definite tumour growth inhibition for the tumours injected with 225Ac-polymersomes, showing that these vesicles can be used for intratumoural cancer therapy.

Acknowledgements
The present study was funded by the ZonMw Early Career Scientist Hotel grant, project nr 43500401I

(1) de Kruijff, R. M.; Drost, K.; Thijssen, L.; Morgenstern, A.; Bruchertseifer, F.; Lathouwers, D.; Wolterbeek, H. T.; Denkova, A. G. Appl. Radiat. Isot. 2017, 128.

Email Address

r.m.dekruijff@tudelft.nl

Presentation Type

Contributed Oral

Primary author: Dr DE KRUIJFF, Robin (Delft University of Technology)

Co-authors: Dr MORGENSTERN, Alfred (European Commission, Joint Research Centre, Directorate for Nuclear Safety and Security, Karlsruhe, Germany); Ms KIP, Annemarie (Radiology and Nuclear Medicine, Radboud university medical centre; Nijmegen, the Netherlands); Dr DENKOVA, Antonia (Radiation Science and Technology, Delft University of Technology, Delft, the Netherlands); Dr BRUCHERTSEIFER, Frank (European Commission, Joint Research Centre, Directorate for Nuclear Safety and Security, Karlsruhe, Germany); Ms MOLKENBOER-KUENEN, Janneke (Radiology and Nuclear Medicine, Radboud university medical centre; Nijmegen, the Netherlands); Dr RAAVÉ, Rene (Radiology and Nuclear Medicine, Radboud university medical centre; Nijmegen, the Netherlands); Dr HESKAMP, Sandra (Radiology and Nuclear Medicine, Radboud university medical centre; Nijmegen, the Netherlands)

Presenter: Dr DE KRUIJFF, Robin (Delft University of Technology)