Contribution ID: **58** Type: **Verbal**

In vivo study of 111In-loaded polymersomes

Tuesday, 13 May 2014 16:30 (15 minutes)

In the fight against cancer, it is of utmost importance to damage diseased cells whilst leaving healthy tissue unaffected. Vesicles composed of amphiphilic block copolymers have been proven to be promising nano-carriers, which are capable of transporting a variety of pharmaceuticals to tumour sites [1]. Their application can be extended to the field of nuclear medicine by designing ultra stable polymersomes, although such studies are scarce. Here, we present a study demonstrating the radiolabeling of polymer vesicles with the molecular imaging agent 111In, and their in vivo pharmacokinetics in mice. This has been examined using microSPECT, the most powerful pre- clinical imaging technique in terms of spatial resolution.

The vesicles are composed of poly(butadiene-b-ethylene oxide) block copolymers, and the labelling has been achieved by transportation of the radionuclide, complexed to a lipophilic ligand, through the hydrophobic bilayer into the aqueous cavity containing a strong hydrophilic chelate [2]. A sufficient amount of the radionuclides was successfully encapsulated in the polymersomes (>90 % loading efficiency) with a negligible loss of radiolabel upon incubation in serum (<5 % in 24 hours at 37 ˚C), allowing their safe application in in vivo studies. The 111In containing 80 nm polymersomes have been subsequently used in pharmacokinetic and bio-distribution studies using microSPECT. Both healthy and tumour bearing female Ncr nude mice were injected intravenously or subcutaneously with 80 nm polymersomes loaded with 20 MBq 111In. Periodic microSPECT images were taken, and a biodistribution was performed 24 and 48 h p.i.

The polymersomes have been observed to circulate a considerable time in vivo (longer than 6 h) in healthy mice, and are primarily cleared by the spleen, which complies with the circulation time obtained in other in vivo polymersome studies [3]. This in contrast to a much shorter circulation time observed for polymersomes intravenously injected in tumour bearing mice, where the liver and spleen removed the polymersomes from circulation within 1.5 h. Saturation of the RES by saturation with a higher polymersome concentration is expected to prolong the blood circulation time of the vesicles. Very promising results were obtained for subcutaneously injected mice, where a high retention rate of polymersomes in the interstitial tissue surrounding the tumour site was observed, whereas unencapsulated 111In-DTPA was cleared immediately. This makes subcutaneously injected polymersomes a valuable option for loco-regionally targeted tumour therapy.

References:
[1] B.M. Discher, Y.Y. Won, D.S. Ege, J.M.C. Lee, F.S. Bates, D.E. Discher and D.A. Hammer, Polymersomes: tough vesicles made from diblock copolymers, Science 1999, 284, 1143
[2] G. Wang, R.M. de Kruijff, M.C.A. Stuart, E. Mendes, H.T. Wolterbeek and A.G. Denkova Polymersomes as radionuclide carriers loaded via active ion transport through the hydrophobic bilayer, Soft Matter 2013, 9, 727-734.
[3] P.J. Photos, L. Bacakova, B. Discher, F.S. Bates, and D.E. Discher, Polymer vesicles in vivo: correlations with PEG molecular weight, J. Controlled Release 2003, 90, 323-334

Primary authors: Dr DENKOVA, Antonia (Delft University of Technology); Mr WANG, Guanglin (Delft University of Technology); Ms DE KRUIJFF, Robin (Delft University of Technology)

Co-authors: Prof. WOLTERBEEK, Bert (Delft University of Technology); Dr ABOU, Diane (Johns Hopkins Hospital); Dr MENDES, Eduardo (Delft University of Technology)

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

Session Classification: Radiopharmaceutical Chemistry, Labelled Compounds 1

Track Classification: Radiopharmaceutical Chemistry, Labelled Compounds