BIODISTRIBUTION OF RA-224 AND ITS PROGENY PB-212 AFTER INTRAPERITONEAL INFUSION OF RA-224 LABELED MICROPARTICLES IN RATS

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Background and Objectives

- This novel alpha-therapy Radospherm®, consisting of biodegradable radium-224 labelled calcium carbonate (CaCO₃) microparticles, was developed with the intent to treat micrometastases located in the abdominal cavity
- Designed to be administered intra-peritoneally (IP) following cytoreductive surgery
- Designed to confine radiation exposure to the peritoneal cavity while treating both the linings of the peritoneal surfaces and liquid volumes
- The distribution of the Ra-224 labeled microparticles was examined using planar gamma imaging, SPECT and CT
- The ex vivo biodistribution of Ra-224 and its progeny Pb-212 was determined

Materials and methods

- Fifteen female Wistar rats were infused IP with Ra-224-labeled microparticles (200-400 kBq, 1 mg CaCO₃, 1 mL + 3 mL Plasmalyte flush) via a multi-hole pigtail catheter
- Four female Wistar rats were infused IP with free Ra-224 (200-400 kBq, RaCl₂) as a reference for uptake of released Ra-224
- The Ra-224 labeled microparticles were imaged using both planar gamma imaging, SPECT and CT to evaluate the distribution over time in the abdominal region
- Longitudinal ex vivo biodistribution was performed after microparticle infusion and organs were harvested for activity measurements

Results

- Planar gamma imaging was successful in visualizing the IP distribution of microparticles, with the hotspots identified as aggregates both in SPECT and under visual inspection as vivo. Figure 2A shows a representative image with little aggregation in the SPECT. The planar gamma image of the same animal showed fairly uniform emission (top left). Figure 2B shows high levels of aggregation seen in only one set. In the planar gamma image (bottom left), this shows Ra-224 uptake in the background. All three modalities, planar gamma imaging, SPECT and CT were able to visualize the microparticle distribution.

Conclusion

- High peritoneal retention of both Ra-224 and its progeny Pb-212 after IP injection of Ra-224 labeled CaCO₃ microparticles, was found in rats with assumed high translational value to the clinical setting
- SPECT and planar imaging demonstrated that distribution of the Ra-224 labeled microparticles occur to the entire peritoneal lumen in the animals. SPECT and CT revealed some clusters of the labeled microparticles
- Due to the short range of the therapeutically active alpha particles, the clusters are not expected to have an impact on safety of the product