Aim

Radiosynovectomy or radiosynoviorthesis (RSO) is a common therapeutic treatment of arthritis in Germany with more than 70,000 treated joints per year. In this regard, ^{169}Er-colloid (^{169}Er) is universally used for the therapy of small joints due to its low range beta particles and the small thickness of synovium in small joints. The use of ^{169}Er in RSO is essential especially in rheumatoid arthritis, because the fingers are the most commonly affected joints. Unfortunately, because ^{169}Er is not available outside of Europe, the use of RSO in Asia and America is primarily reserved for the treatment of hemophilic arthritis in large joints using other isotopes. ^{117m}Sn colloid (^{117m}Sn) is an interesting candidate to replace ^{169}Er in the treatment of small joints since the dosimetry characteristics and the range of conversion electrons of ^{117m}Sn are very similar to those of the beta particles of ^{169}Er.

Materials & Methods

In a previous safety trial, 5 dogs were injected in the left elbow using 93 ± 2 MBq of ^{117m}Sn. The animals were followed at baseline and multiple subsequent time points for various safety parameters (blood work, excretion radiation analysis, radiation field measurements, scintigraphy, MRI/PET and joint fluid analysis), and were sacrificed after 49 ± 1 days (>3 $t^1/_{2\ phys}$) at which time the amount of radioactivity was measured in the dissected organs/tissue, followed by histopathology and autoradiography of the joint. A subsequent pivotal, prospective, multi-dose trial for safety and efficacy in 48 client-owned dogs with grade 1/2 osteoarthritis (OA) is underway. Subjects are randomized into three dosing groups (37MBq, 65MBq or 93MBq) of ^{117m}Sn (normalized to a 22.7kg dog) intra-articular.

The treated joints are compared with the untreated contralateral joints at baseline, 1, 3, 6, 9, and 12 months evaluating for safety (blood work, radiation field, excretion analysis, scintigraphy) and efficacy (PET/MRI, video recordings, and the Canine Brief Pain Index [a validated measurement of activity]). For evaluation of ^{18}F-FDG-PET the change in SUV average MAX was analyzed, and for MRI the quantitative thickness of synovium and qualitative fluid volume in joints was analyzed. The pain/activity level was estimated by the owners of dogs using an 11 question survey, question 11 of which is an overall evaluation of the dog's state of activity ranging from poor, fair, good, very good, or excellent. Results for 6 dogs at 6 month follow-up at one site are available.

Results

In the safety study, 99.19 ± 0.36% of administered activity (%ID) was retained in the synovium of the treated joints despite multiple prior synovial punctures related to the study. The majority of the radiocolloid that was found outside the treated joint was in the liver (0.70 ± 0.36%ID), with a significantly lower %ID in local lymph nodes (0.07 ± 0.03%ID) and spleen (0.01 ± 0.07%ID). Over the follow-up period 0.06 ± 0.02%ID was found in blood, feces and urine within the first 14 days, and 0.75 ± 0.38%ID was found in organs outside the joint after 45 days. In postmortem autoradiographic studies the vast majority of activity was found in the synovial macrophages and infrequently in other locations (synovial lining cells, macrophage-like cells and macrophages).

In the pivotal study, follow-up over 6 months was available in 6 dogs (3 with 37MBq, 1 with 65MBq, and 2 with 93MBq ^{117m}Sn).

- **Results in ^{18}F-FDG-PET:**
  4 dogs demonstrated a decrease in SUV average MAX values in the injected joint (1 at 37MBq, 1 at 65MBq, and 2 at 93MBq).

- **MRI results:**
  5 dogs showed qualitative improvement at 6 months over baseline (decrease of symovium thickness and joint volume) in the injected joint (2 at 37MBq, 1 at 65MBq, and 3 at 93MBq).

- **Canine Brief Pain Index overall score**
  4 dogs demonstrated an overall decrease of pain/increase in activity (2 at 37MBq, 1 at 65MBq and 1 at 93MBq).

Conclusion

^{117m}Sn colloid is useful in RSO of small-medium joints, with excellent joint retention and very limited dose outside the joint. Autoradiographic studies documented a fixed uptake in synovial macrophages by phagocytosis. These macrophages were found in all layers of the synovium, which showed transportation of ^{117m}Sn colloid from the surface to varying depths. This opens up the possibility of treating larger joints.

In the pivotal studies, clinical improve of arthritis was observed in the first 6 treated dogs at the 6 month follow-up. The higher dose of 93MBq ^{117m}Sn may be more effective than the low dose of 37MBq. After completion of this pivotal dog study, we will extrapolate the optimal applied activity in RSO for human use in various size joints.