Evaluation of Homogeneous Sn-117m Colloid Radiosynovectomy in Normal Dogs Using Scintigraphy, PET-MRI and Other Modalities

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Introduction

Late stage osteoarthritis (OA) causes severe, chronic joint pain. Patients who have failed medical therapy can be treated using radioactive colloids by radiosynovectomy/ radiosynoviorthesis (RSV/RSO), a procedure approved outside of the US. A limitation of RSV/RSO is the suboptimal characteristics of some existing radioactive colloids that can leak from the joint or may have high enough beta energies that result in irradiation of tissues beyond the joint synovium. To overcome these limitations a novel radioactive Sn-117m homogeneous colloid was developed and tested in normal dogs to determine safety and joint retention.[1,2] Sn-117m ($t_{1/2}$=14d) decays by isometric transition, producing both gamma rays (159 keV, 86% abundant), as well as monoenergetic conversion elections (~140 keV; >110% abundant) with a range of ~ 290µm in tissue. This provides the therapeutic advantage of depositing energy in the synovium with minimal or no effect to surrounding tissue.

Objective

In previous studies using rat models, homogeneous Sn-117m colloid (HTC) demonstrated average knee joint retention of >99.0%, safety, and efficacy.[3] Our new objectives were to (1) validate the safety of the HTC in dogs using imaging and other modalities, and (2) validate the radiation field and radioactive excretion levels in dogs.

Materials & Methods

Five normal, purpose bred hounds received an injection of 25mCi of HTC in the left elbow and were followed for 3 half-lives before sacrifice. Baseline and subsequent evaluations included: Fused PET-MRI, scintigraphy, roentgenogram, blood chemistries, synovial fluid, radiation field measurements, excretions, physical examination and a log of activity. Dogs were sacrificed at 3 half-lives. Pending analyses include histopathology and auto-radiography.

Results

Joint retention of the HTC was 99.1% at six weeks. Scintigraphy and PET-MRI demonstrated high concentration in the injected joint with minimal uptake in other tissues (*Figures 1 and 2)*. Radiation in blood and fecal/urine excretion generally was at or near background within 24 hours, and radiation fields were below Nuclear Regulatory Commission (NRC) release criteria at the time of injection. Chemistries and roentgenograms were unremarkable. Arthrocentesis showed mild elevation in some parameters which generally returned to or trended toward normal. Activity and physical exam remained unremarkable.

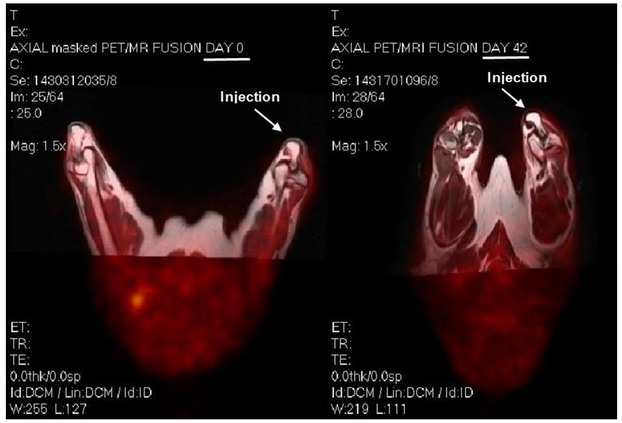

Figure 1. Fused PET-MRI showing injected left elbow is unremarkable vs. the right elbow, and unchanged from baseline vs. day of sacrifice 42 days later. Injection of HTC resulted in no anatomic or physiological joint abnormalities.

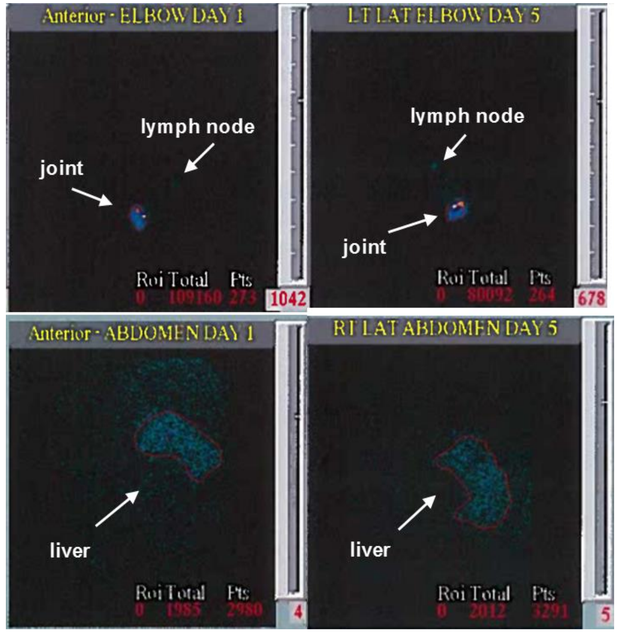

Figure 2. Lateral decubitus scintigraphy views enhanced with color lookup table of left elbow and abdomen in the highest uptake dog at day 1 and day 5. A super majority of HTC remains in the elbow.

Conclusion

These results demonstrate that HTC delivered intra-articular has exceptionally high retention in the joint space of normal dog elbows, is safe and well tolerated, produces radioactive excretions that generally are at or close to background within 24 hours, and produces a radiation field at the time of injection that is below NRC release criteria. These results have led to the initiation of a randomized study of the HTC in dogs with naturally occurring elbow OA, with a plan to study human OA in the future. Our study using PET-MRI demonstrated that the use of HTC produces no physiologic or anatomic joint abnormalities.

References

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