Retention and Biodistribution of Sn-117m Colloid in Intra-Articular Injections

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Abstract

Radiosynoviorthesis (a.k.a. radiosynovectomy) employing the theranostic isotope, Sn-117m (t½ 14 d, γ 159 keV, 86%), is well suited to treat smaller arthritic joints since the therapeutic conversion electrons (~140 keV, 112%) have a range of about 300 µm. This allows for treatment of the synovium without affecting the surrounding tissues. Retention of the colloidal product in the synovial cavity is highly desirable. We describe the joint retention and biodistribution trial measurements of Sn-117m colloid injected into normal canine elbows.

Background

Radiosynoviorthesis (RSO) has been used for over 60 years to successfully treat arthritis and synovitis. In RSO a radioactive colloid is injected directly into the synovial cavity, The resulting intracavitary radiotherapy reduces pain, effusion, perfusion and inflammation (synovitis). The isotopes that have been employed are shown in Table 1 of which Er-169, Re-186 and Y-90 are in common clinical use.

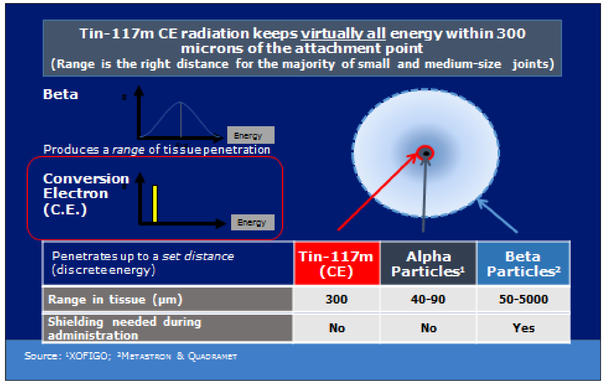
Table 1: Radiosynoviorthesis isotopes

Isotope	$t_{1/2}$ (d)	Imaging Particle	Energy (keV)	Therapy Particle	Maximum Energy (keV)	Range (mean) in Tissue (mm)	Range (max) in Tissue (mm)	Typical Dose (mCi)	Joint Size
Sn-117m	13.6	γ	159	C.E.	151	0.27	0.29	0.5-1.0	Small
Er-169	9.3	None	-	β-	350	0.14	1.1	1	Small
Re-186	3.7	γ	137	β-	1070	1.1	4.4	2.5	Medium
Y-90	2.7	None	-	β-	2280	4.1	11	4	Large
P-32	14.3	None	-	β-	1711	2.8	8.4	2	Large
Au-198	2.7	γ	412	β-	960	0.9	4.2	7	Large/Med
Sm-153	1.9	γ	103	β-	808	0.55	3.3	5	Medium
Re-188	0.7	γ	155	β-	2120	3.1	10.4	10	Large
Ho-166	1.1	γ	81	β-	1855	2.6	9.2	10	Large
Dy-165	0.1	γ	95	β-	1289	1.3	5.9	270	Large
Tm-170	129	γ	84	β-	968	0.9	4.2	1.6-4.8	Medium

Objective

Tin-117m (Sn-117m) is a novel RSO radioisotope with characteristics summarized in Table 1 and Figure 1. While similar to Er-169, it's conversion electrons (~140 keV, 112%) restrict the therapeutic range to 300 µm in tissue thereby avoiding irradiation of non-targeted tissues such as bone marrow. The photons (159 keV, 86%) are easily detected in any gamma camera and can be used to confirm correct placement of the product.

Figure 1: Characteristics of tin-117m



Tin forms excellent colloids and is even used as a scaffold for several RSO products. We have created a unique stable homogeneous Sn-117m colloid (HTC) with a narrow size range (7+/- 4 µm). This product is too large to leak from the synovial cavity yet it is small enough to be phagocytosed and incorporated into the synovial surface. An objective of this study involves determining the suitability of the HTC as a RSO agent initially in canine elbows. This includes measuring retention (and any biodistribution) and external radiation levels.

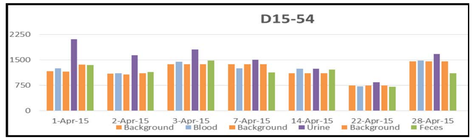
Materials & Methods

Five normal purpose-bred hounds were injected with ~2.5 mCi of a homogeneous preparation of Sn-117m colloid (~6 µm) in the intra-articular space of the left elbow. The animals were sacrificed after six weeks (3 half-lives) and the amount of radioactivity in the dissected tissues was measured. Urine, blood, feces and synovial fluid samples were taken periodically during the trial and analyzed for radioactive content.

Results

Average joint retention of the colloid was 99.1% of the administered dose at three-half-lives. When integrated over the study period the activity in blood, urine and feces was <0.1%. The majority of the extra-synovial activity was found in the liver (<0.7%) and spleen (<0.1%). Activity also was detected in the left prescapular lymph node (<0.03%). Some of the leakage might be attributed to the multiple synovial fluid taps performed over the duration of the trial. Figure 2 displays an example (study dog D15-54) of the fluid and organ biodistribution data.

Figure 2: Typical biodistribution of HTC injected in normal canine elbows. All fluids are at or near background.



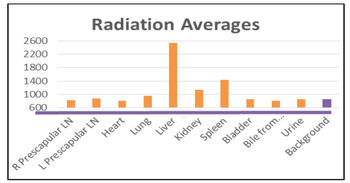
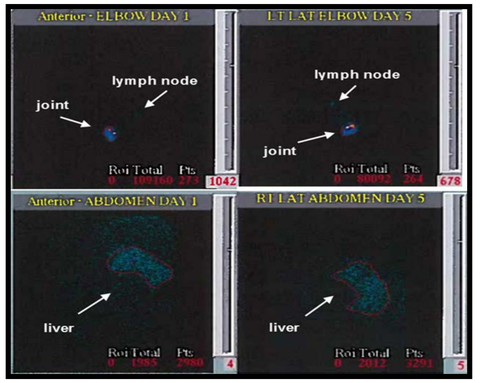


Figure 3 compares typical images of the injected site with the liver (highest non-targeted organ uptake). Note the very high gain difference that reflects the minute uptake in the liver or any other organ. In addition, external radiation measurements immediately after injection were ~20 mR/h near the joint surface and ~330 µR/h at 1 m which is well below the typical animal release criteria (< 500 µR/h at 1 m).

Figure 3: Images of the injection site and liver demonstrating high retention in the synovial cavity



Summary

These results demonstrate a high degree of retention of the Sn-117m homogeneous colloid delivered intra-articularly. Other than minimal transient leakages possibly due to synovial punctures the results are consistent with a gradual removal of the colloid through the lymphatic system. The high joint retention supports the use of Sn-117m colloid in treating arthritis.

Disclosures

Stevenson and Doerr: Employment/ownership in R-NAV, LLC (trial sponsor)

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