

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

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Disclosures

Lattimer: None

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Simon: None

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Ketring: None

Manson: None

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

Radiosynoviorthesis

- A.k.a. Radiosynovectomy
- Treatment for arthritis
- Used worldwide for over 60 years
- Radioactive colloid injected directly into the synovial cavity
 - Intracavitary radiotherapy to reduce pain, effusion, perfusion and inflammation (synovitis)
- Commercial isotopes are Y-90, Re-186, Er-169
 - Y-90 for large joints (knee)
 - Re-186 for mid-size joints (elbow, wrist, ankle)
 - Er-169 for small joints (fingers)
- Issues with Er-169
 - Replacement isotope desirable
 - Sn-117m and Er-169 have very similar tissue dosimetry profiles (presentation by R. Wendt)

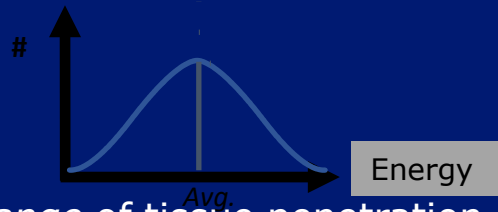
Radiosynoviorthesis Isotopes

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

Characteristics of Sn-117m

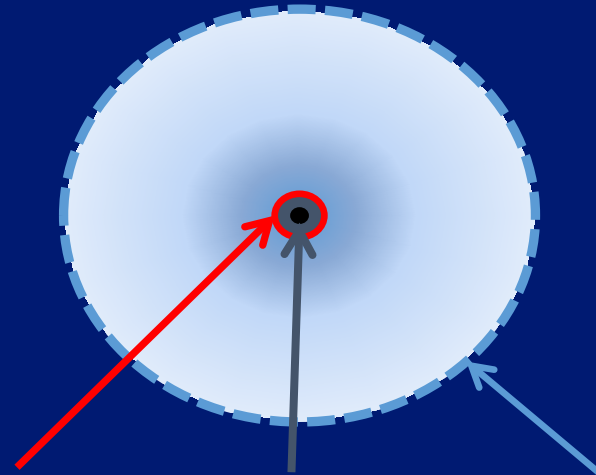
Tin-117m CE radiation keeps virtually all energy within 300 microns of the attachment point
(Range is the right distance for the majority of small and medium-size joints)

Beta



Produces a *range* of tissue penetration

Conversion Electron (C.E.)

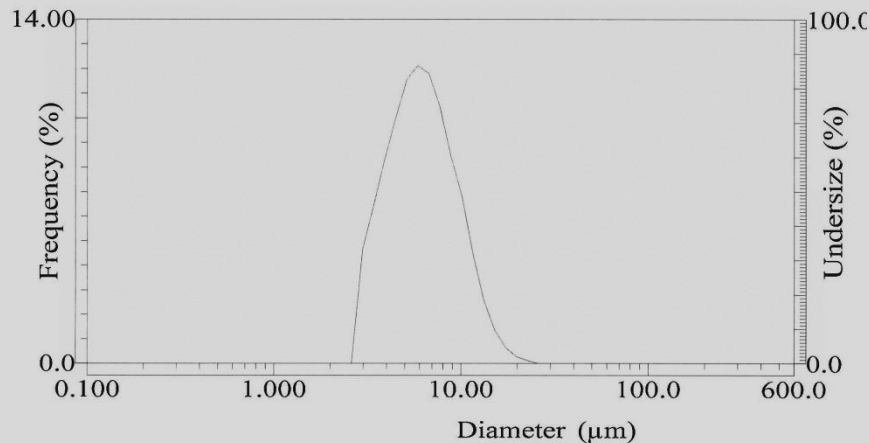


	Tin-117m (CE)	Alpha Particles¹	Beta Particles²
Penetrates up to a <i>set distance</i> (discrete energy)			
Range in tissue (μm)	300	40-90	50-5000
Shielding needed during administration	No	No	Yes

Sn-117m Colloid

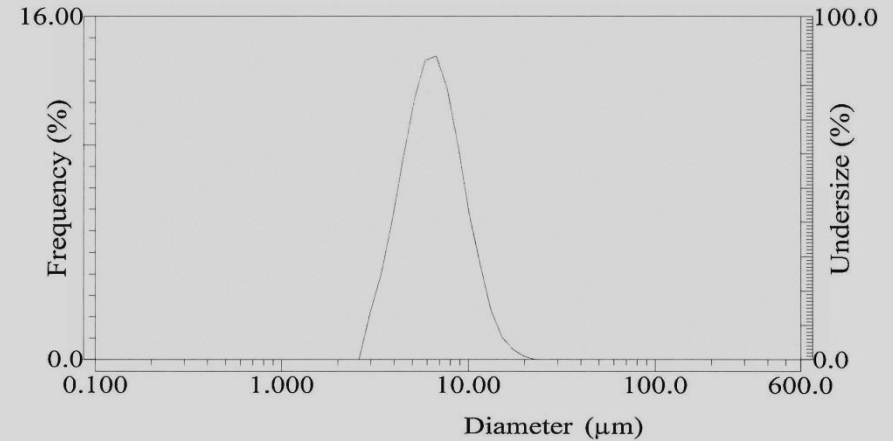
Retention of colloid in normal rat joint:

Time	7 days	2 weeks	6 weeks
Retention	>99.9%	>99.9%	99.8%



Stability studies – colloid size
particle distribution at manufacture

Mean = 6.28 μm SD = 2.76 μm



Stability studies – colloid size
particle distribution at 5 weeks in
room temperature

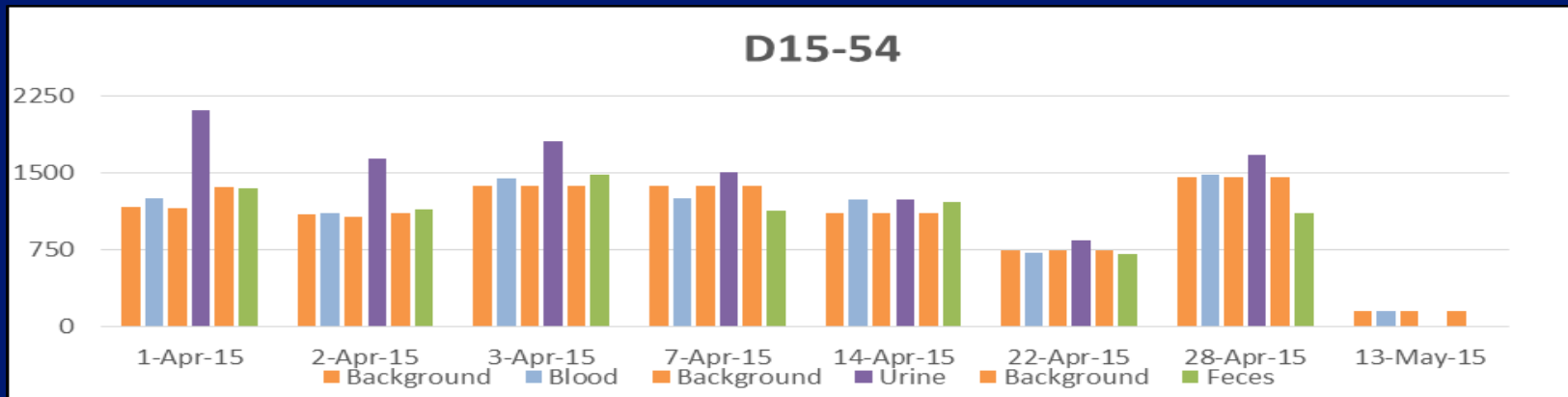
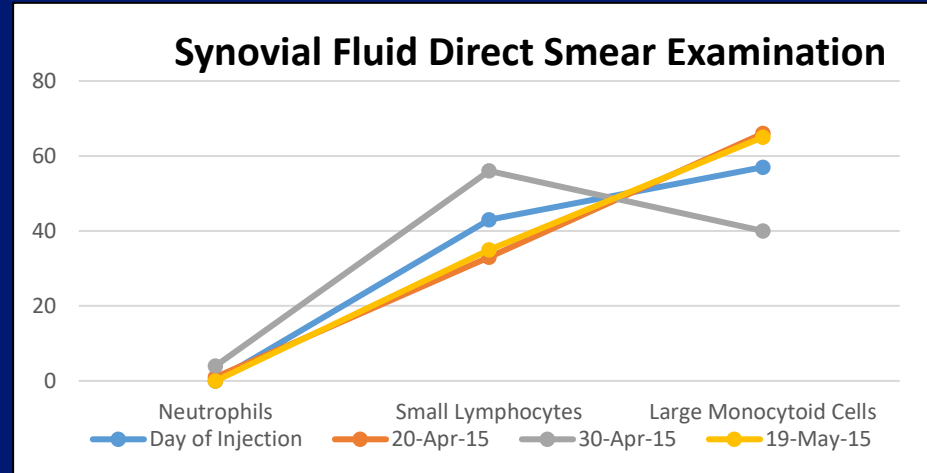
Mean = 6.43 μm SD = 2.47 μm

Trial Design

- Prior GLP OA rat trials determined approximate dosage (1.0-2.5 mCi) for canine elbows (presentation by C. Doerr)
- GLP **Safety** trial in **5 normal purpose bred hounds (50 lb.)**
- University of Missouri College of Veterinary Medicine
 - Jimmy Lattimer DVM (PI) and Kimberly Selting DVM (Alt. PI)
- Highest anticipated dosage (**2.5 mCi**)
- Followed to 3 $t_{1/2}$ (March-May, 2015)
- Data collected includes:
 - Histopathology, PET/MRI, x-ray, excretion, **distribution**, autoradiography, **dosimetry**, synovial fluid analyses, physical examinations, **radiation field**

Biodistribution – Fluids/Excreta

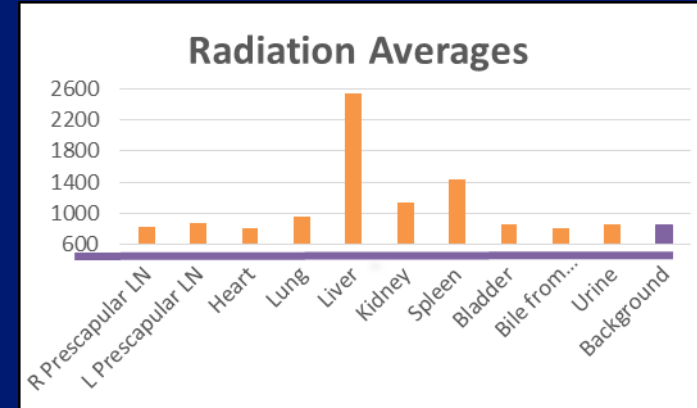
- Urine, blood and fecal samples were taken from each dog for several weeks after injection
- Radioactivity in the samples was measured using a solid NaI detector. Background and back-decay corrections
- Efficiency and sample size corrections applied



- Synovial fluid @ 6 weeks had < 1% of initial colloid content - majority had been incorporated into the synovial membrane

Biodistribution - Organs

- Tissue/Fluid samples were counted on a NaI crystal attached to a multichannel analyzer for 20 seconds. Background subtracted and back-decayed
- Detector efficiency and sample size corrections applied

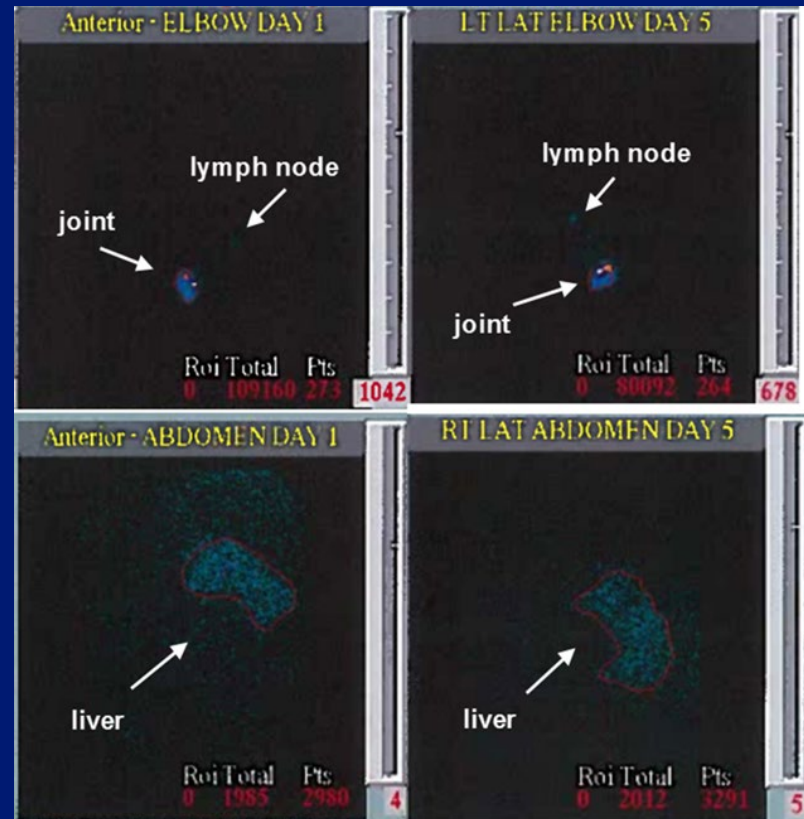


Dog Number	% in Organs	% in blood, urine and feces	% Left at site of injection
971227	0.40	0.10	99.50
973246	1.13	0.05	98.82
972916	1.39	0.05	98.56
968676	0.50	0.07	99.43
970824	0.75	0.06	99.19

- Injected elbow joint retained almost all of the activity (**99.1%**) (confirmed by direct measurements)

Retention

- **Retention = 99.1%**
(Despite multiple synovial punctures during the 42 days of the study)
- External radiation fields immediately after 2.5 mCi injection:
 - Surface ~ 20 mR/h*
 - @1 m ~ 330 μ R/h
- Agrees with Monte Carlo modeling (R. Wendt)
- Typical animal release criteria:
 - Field @ 1 m < 500 μ R/hr
 - Excreta low (exempt = 27 μ Ci)



* Use of a shielded syringe recommended to reduce hand dose during procedure

Conclusions

- Sn-117m colloid can be safely and easily injected into canine elbow joints
- High retention (>99%) after six weeks (3 half-lives)
- Minimal biodistribution or excreta
- Uptake into synovial tissue by phagocytosis
- Migration through synovial tissue (confirmed by autoradiography) and eventual removal via lymphatic system
- Continued irradiation of the deep and more superficial synovial tissue due to 14 d half-life
- **→ Potential to treat small and larger joints**

Questions?