PRECLINICAL EVALUATION OF $^{117m}$Sn COLLOID AS A RADIOSYNOVIOORTHESIS AGENT FOR TREATMENT OF CANINE ELBOW JOINT OSTEOARTHRITIS

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Osteoarthrosis/Osteoarthritis
Most common clinical disorder

- Result of joint injury
  - Trauma
  - Instability
- Infection – bacterial, viral, rickettsial
- Autoimmune disease
Osteoarthrosis/Osteoarthritis
Most common clinical disorder

- Progression
  - Synovial inflammation – earliest stage of joint degeneration
  - Ligamentous and capsular injury
  - Cartilage injury
  - Subchondral and perichondral bone injury – latest stage of disease

Progression rate
Radiosynoviorthesis

- Use of a radioisotope preparation to partially ablate the synovium and reduce inflammation in a joint thereby slowing progression of osteoarthritis

- Challenges
  - Retention of the isotope in the joint tissues
  - Minimal intrinsic chemical toxicity to joint structures
  - Minimal radiation dose to cartilage, bone and ligaments/tendons
  - Minimize radiation dose to rest of patient and others
$^{117m}$Sn Colloid (Synovetin OA™)

- **Half-life**: 14 days
- **Emissions**
  - Conversion electrons – 140 keV – <300 micron range in tissue
  - Insufficient energy to reach bone and tendons
  - Gamma photons – 158 keV – imageable on gamma camera
- **Colloid size**: ~3 – 15 µm
  - Promotes retention in joint through engulfment by joint macrophages
  - Stable in suspension for 5 weeks
  - Easily suspended and injected
Prior studies

- Prior studies performed in rats
  - Lewis rat meniscal tear model > 150 rats
  - A range of doses were treated
  - Duration of trial was 42 days
  - Confirmed decrease in inflammation
  - Minimal adverse effects on synovium except high dose group
  - No cartilage, bone or ligamentous injury
  - > 99% of isotope retained in the joint
Study design

- Five young adult purpose-bred female hounds
- Minimum 5 days acclimation
- CBC, serum chemistries, urinalysis
- Radiographs, PET/MRI, post injection nuc. med. scan
- Joint fluid cytology and analysis
- Injection of left elbow with $^{117}\text{mSn}$ colloid
  - 2.5 millicuries – normalized to 22.75 kg BW by BSA
- Daily observation for lameness
Study Design Continued

- 24 hours after injection – NM scan of elbow and abdomen
- Collection of blood, urine and feces for 5 days
  - Standard size samples counted in swipe counter
  - Total excreted urine and feces activity calculated
- 42 days after injection - all clinical pathology and imaging studies repeated
- 43 days after injection – euthanasia & postmortem
  - All major organs collected and counted for total activity
  - Histopathology of all major organs
  - Histopathology and autoradiography of joint tissues
Results

- No dog exhibited any lameness after injection
- NM confirmed retention in joint at 24 hours
- Urine and feces collection indicated > 99% average retention
- Imaging studies were normal and static between studies
- Post mortem studies
  - Organ and elbow activity indicated > 99% retention in elbow
  - No histologic abnormalities were found in organs or joints
  - Micro autoradiography confirmed synovial localization
PET/MRI images – day 0 & 42
Post mortem autoradiography of synovium
Conclusions

- $^{117m}$Sn colloid (Synovetin) should be evaluated as a radiosynoviorthesis agent in dogs
  - It was retained in the elbow joints with > 99% localization
  - The agent was well tolerated by the animals
  - No adverse reactions to the injection were detected
  - Further trials in dogs with naturally occurring clinical arthritis are needed to evaluate the efficacy of this agent
Future Studies

- $^{117}\text{mSn}$ colloid (Synovetin™) is currently being evaluated in a multicenter trial for treatment of clinical lameness in dogs with grade 1 or 2 elbow arthritis.

- Trials are currently being planned for evaluation of this agent in the treatment of osteoarthritis in a limited equine study.

- Evaluation of efficacy in other joints and more advanced osteoarthritic conditions in dogs


Role of inflammation in the pathogenesis of osteoarthritis: latest findings and interpretations, Sololove J, Lepus C; Ther Adv Musculoskel Dis, 2013 5(2) 77-94