Comparison of the Effect of $^{99m}$Tc-DPD and $^{99m}$Tc-MDP on Experimentally-induced Osteoarthritis in the Stifle Joint of the Dog

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Abstract. This study was designed to evaluate the effect of $^{99m}$Technetium-dicarboxypropane diphosphonate ($^{99m}$Tc-DPD) and $^{99m}$Technetium-methylene diphosphonate ($^{99m}$Tc-MDP) on bone scan image quality and time in dogs with osteoarthritis. The left cranial cruciate ligament (CrCL) in ten healthy adult Beagle dogs was transected under general anesthesia. The dogs were assigned to $^{99m}$Tc-DPD-injected or $^{99m}$Tc-MDP-injected groups. Stifle joint scintigraphy was performed after intravenous injection of 10 mCi $^{99m}$Tc-DPD or $^{99m}$Tc-MDP. Scintigraphy was conducted before CrCL transection and 2, 4, 6, 8, 10 and 12 weeks after the procedure. There were no significant differences in density, sensitivity and pathological foci between the $^{99m}$Tc-DPD and $^{99m}$Tc-MDP groups of experimentally-transected CrCL dogs. A comparison of the images obtained with Pinhole type and low energy general purpose type collimators of the stifle joint of normal dogs and after CrCL transaction revealed no significant differences in bone radioactivity. Scintigraphs were obtained 3 h after $^{99m}$Tc-MDP and 2 h after $^{99m}$Tc-DPD injection. In conclusion, application of $^{99m}$Tc-DPD and $^{99m}$Tc-MDP in experimentally-induced osteoarthritis of the stifle joint in dogs results in similar effects on radioactive uptake ratio and image quality. $^{99m}$Tc-DPD is more efficient than $^{99m}$Tc-MDP in reducing the overall time of scintigraphy.

The radionuclide $^{99m}$Technetium ($^{99m}$Tc) emits gamma radiation with an energy of 140 KeV, ideal for diagnostic purposes. It is particularly useful for gamma cameras with thin crystals that absorb over 90% radiation (1). $^{99m}$Tc has excellent physical properties for nuclear medicine imaging due to its application in the gamma camera (2). The short half-life of the radionuclide allows the injection of several mCi of activity, leading to images with high information density (3, 4). The development of $^{99m}$Tc-labelled phosphorous compounds has made bone scintigraphy one of the most useful nuclear medicine scintigraphy techniques available (5). Until the introduction of the $^{99m}$Tc-tripolyphosphate complex, there was no major choice of radiopharmaceutical for skeletal imaging (6). Radio pharmaceuticals have been utilized for several years, and a number of studies comparing the different $^{99m}$Tc-labelled phosphorous compounds has been conducted (7-8). To date, no unanimously preferred radiopharmaceutical is available for skeletal imaging studies. The majority of the present data suggest that $^{99m}$Tc-methylene diphosphonate ($^{99m}$Tc-MDP) (9), $^{99m}$Tc-HMDP (10) and/or $^{99m}$Tc-dicarboxypropane ($^{99m}$Tc-DPD) (11) offer the best combination for skeletal localization and soft tissue clearance.

At present, $^{99m}$Tc-labelled phosphonate compounds are frequently employed, but their mechanism of bone uptake remains to be determined (12-14). Most of the bone-seeking agents operate on the basis of the P-O-P bond (pyrophosphate) and the P-C-P bond (diphosphonates) (15, 16). $^{99m}$Tc-MDP and $^{99m}$Tc-DPD contain the P-C-P bond (17, 18). $^{99m}$Tc-MDP is currently the most widely used bone imaging agent. Following the recent commercial introduction of $^{99m}$Tc-DPD, the clinical importance of bone scintigraphy has increased significantly. In Korea, the frequency of its use is increasing continuously in humans, but not in animals. Analysis of the early stages of osteoarthritis in humans presents numerous difficulties, since the patient generally does not seek medical attention until pathologic changes are far

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advanced and articular cartilage is already extensively lost (19). Consequently, researchers employ animal models to obtain information about the early changes in the articular cartilage, bone and synovium (20, 21). Among these, the cruciate-deficient dog is the most widely studied model (1, 22). Cranial cruciate ligament (CrCL) transection in the dog serves as a standard experimental representation of osteoarthritis (20). In an osteoarthritis model of the stifle joint of dogs, $^{99m}$Tc-labelled phosphorous complexes accumulate mainly at the osteochondral junction of the osteophytes (20, 23-25). The primary objective was the detailed evaluation of the clinical efficacy of $^{99m}$Tc-DPD for detecting osteoarthritis in the knee joint, compared to $^{99m}$Tc-MDP (7, 26-28).

Care should be taken not to misinterpret abnormalities resulting from technical factors, that is, differences in uptake resulting from poor positioning of the patient, and focal regions of increased activity caused by radioactive contamination (2). The efficacy of single-head Pinhole bone scintigraphy is well established (29), and the technique is increasingly used to diagnose a broad spectrum of skeletal diseases (30). Pinhole magnification delineates both anatomic and pathologic signs in detail and enhances diagnostic efficacy (31, 32).

The main purpose of the present study was to assess bone uptake changes and image quality, using scintigraphy of nuclear medicine, in a dog model of osteoarthritis with experimentally-transected CrCL. In addition, we compared the uptake ratios and image times with $^{99m}$Tc-DPD and $^{99m}$Tc-MDP agents. All statistical computations were made using the SAS system. Differences in the distribution of values between $^{99m}$Tc-DPD and $^{99m}$Tc-MDP agents. All statistical computations were made using the SAS system. Differences in the distribution of values between $^{99m}$Tc-DPD and $^{99m}$Tc-MDP were assessed with the Wilcoxon rank sum test. The data are expressed as means±S.D. Probability values of less than 0.05 were considered statistically significant.

**Results**

**Clinical appearance.** All experimental dogs recovered well from the anesthesia and surgical interventions, and demonstrated no signs of distress throughout the observation period. In particular, no complications, such as sequels to the surgical interventions, abscess, consequential diseases or infections, were observed throughout the entire study period.

**Comparison of the uptakes of $^{99m}$Tc-DPD and $^{99m}$Tc-MDP.** Stifle joint scintigraphs revealed increased uptake in the left transected CrCL dogs as early as 2 weeks. In contrast, no increased uptake was evident in the normal right stifle joint. At 8 weeks after the procedure, more radioactivity uptake was observed in the left stifle joint relative to the non-operated stifle joint. In general, following CrCL transection, $^{99m}$Tc-MDP uptake was slightly higher than that of $^{99m}$Tc-DPD. However, there were no significant differences between the activity ratios of the $^{99m}$Tc-DPD and $^{99m}$Tc-MDP groups (data not shown). Scintigraphs were obtained 2 hours and 3 hours after $^{99m}$Tc-DPD and $^{99m}$Tc-MDP injection, respectively (Figure 1).

**Comparison of the LEGP collimator and Pinhole collimator.** Stifle joint scintigraphs of $^{99m}$Tc-DPD and $^{99m}$Tc-MDP, at all weeks after CrCL transaction, disclosed that the Pinhole...
uptakes were slightly higher than the LEGP uptakes (Figure 2). However, no significant differences were evident between the data obtained with the two types of collimator (data not shown).

**Discussion**

The quality of ⁹⁹ᵐTc-radiopharmaceutical may be affected by many factors, including: chemical purity and stability of the initial chemicals, the production procedure, radionuclide and radiochemical purity of ⁹⁹ᵐTc-eluate (5) and the time interval between labelling and analysis (17, 33). Users claim that new bone-seeking radiopharmaceuticals have higher bone uptake, faster or similar blood clearance and, therefore, better image quality and shorter minimum time between administration and imaging, compared with traditional ⁹⁹ᵐTc-MPD agents (7). In the routine skeletal imaging procedure, the patient is usually evaluated 4 to 5 minutes (early phase) and 2.5 to 3.5 hours (late phase) after the intravenous administration of 10-25 mCi of ⁹⁹ᵐTc as a diphosphonate or diphosphonate complex (34-36).

Bone scintigraphy is a sensitive and frequently used method in the early detection and follow-up of reactive articular changes in experimental animal models for osteoarthritis (1). CrCL injury is one of the most common orthopedic diseases in the dog hind limb (37). This model shows that progressive structural changes develop in the articular cartilage and subchondral bone of the unstable joint that are typical of osteoarthritis in humans (21). The juxtaarticular bone is the focus of bone-seeking isotopes in osteoarthritis (1). The crystalline structure of the bone salt mineral is hydroxyapatite, Ca₁₀(PO₄)₆(OH)₂. The localization

![Figure 1. Scintigraphs of stifle uptake 8 weeks after left cranial cruciate ligament transection. LEGP collimator scintigraphs were obtained 2 h after ⁹⁹ᵐTc-DPD (A) and 3 h after ⁹⁹ᵐTc-MPD (B) injection. Images A and B show concentrated abnormal increased activity in the left stifle joint.](image1)

![Figure 2. Scintigraphs at 8 weeks after left cranial cruciate ligament transection. LEGP (A) and Pinhole (B) views of ⁹⁹ᵐTc-DPD in the left stifle joints. Pinhole uptake was slightly higher than LEGP uptake.](image2)
of intravenously-administered ionic radioactive tracers primarily involves their selective concentration by hydroxyapatite crystals (2, 15). Although the mechanism of 99mTc-labelled phosphate and diphosphonate localization remains to be clearly defined, several observations strongly suggest that the mineral phase of bone is the primary site of deposition of these materials in the skeleton. The majority of evidence suggests that these materials localize in the bone on the surfaces of hydroxyapatite crystals and amorphous calcium phosphate by chemisorption (2).

Osteoarthritic joints have been identified from animal data (22, 25). Some display increased uptake of bone-seeking agents (21), even in the very early stages of disease (38, 39), and may thus be employed to obtain a better image of the bones, since the lower blood and tissue concentration (38, 39), and may thus be employed to obtain a better image of the bones, since the lower blood and tissue concentration

...contrast to transfer rates were slightly higher for 99mTc-MDP (17). Computer analysis of the activity ratios of 99mTc-DPD and 99mTc-MDP in osteoarthritis models with 99mTc-DPD and 99mTc-MDP, respectively. 99mTc-DPD is obtained 3 hours and 2 hours after the intravenous injection of 99mTc-DPD and 99mTc-MDP, respectively. 99mTc-DPD is more effective than 99mTc-MDP in reducing the overall procedure time.

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### References


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