

Nuclear Scintigraphic Examination in Veterinary Medicine

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Abstract

The present review will discuss the information of nuclear scintigraphic examination in veterinary medicine. The main focus is on the introduction of nuclear medicine procedures in animal patients and describes conventional nuclear medicine (brain scintigraphy, bone scintigraphy, thyroid scintigraphy, inflammation and oncological scintigraphy). Single photon emission scintigraphy (SPECT) and positron emission tomography (PET) have recently been developed using for nuclear scintigraphic examination to provide functional and physiological imaging, the quantification of biochemical processes, molecular interactions, and neoplasias. Radiopharmaceuticals or radionuclides have a longer physical half-life allowing that need longer acquisition times used for specific investigation purposes. In veterinary medicine, scintigraphy can be the basis of a sensitive, specific and non-invasive diagnostic method, which information has been applied to support the diagnostic process and treatment planning for animal patients.

Keywords: Nuclear Scintigraphy, Radionuclides, SPECT, Veterinary Medicine

การตรวจภาพกัมมันตรังสีทางเวชศาสตร์นิวเคลียร์ในทางสัตวแพทย์

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บทคัดย่อ

การทบทวนวรรณกรรมนี้ กล่าวถึงข้อมูลเบื้องต้นของการตรวจทางเวชศาสตร์นิวเคลียร์ ในทางสัตวแพทย์ จุดประสงค์หลักเพื่อที่จะแนะนำวิธีการตรวจทางเวชศาสตร์นิวเคลียร์ในสัตว์ป่วย และอธิบายการตรวจสมอง กระดูก ต่อมไทรอยด์ การอักเสบ และเนื้องอก ด้วยวิธีดังกล่าว ปัจจุบันนี้เครื่อง single photon emission computed tomography (SPECT) และ positron emission tomography (PET) ได้ถูกพัฒนาขึ้น เพื่อให้ใช้สำหรับการตรวจรับภาพของสารกัมมันตรังสี โดยให้ภาพของข้อมูลที่เกี่ยวข้องกับการทำงานและลักษณะโครงสร้างของระบบหรืออวัยวะนั้นๆ การประเมินขบวนการทางชีวเคมี ปฏิกริยาในระดับโมเลกุล และภาพของเนื้องอกในทางสัตวแพทย์ สารเภสัชรังสีหรือสารกัมมันตภาพรังสีมีค่าครึ่งชีวิตค่อนข้างยาว จึงสามารถสร้างภาพได้นาน และสามารถใช้ตรวจดูโครงสร้าง การทำงานของระบบต่างๆ ได้อย่างจำเพาะเจาะจง ในทางสัตวแพทย์นั้น วิธีการตรวจวินิจฉัยด้วยภาพกัมมันตภาพรังสี สามารถที่จะให้ข้อมูลพื้นฐานได้เป็นอย่างดี มีความจำเพาะและเป็นเทคนิคการวินิจฉัยที่ไม่ก่อให้เกิดความเจ็บปวด ซึ่งข้อมูลที่ได้ยังสามารถนำมาประยุกต์ เพื่อที่จะช่วยในขบวนการวินิจฉัยโรคของสัตวแพทย์ และวางแผนการรักษาสัตว์ป่วย

คำสำคัญ : ภาพกัมมันตรังสี สารเรดิโอไอโนวไคลด์ เครื่อง SPECT เวชศาสตร์ทางสัตวแพทย์

Introduction

Nuclear scintigraphy in veterinary medicine

Nuclear medicine techniques offer a non-invasive alternation to investigate biological processes *in vivo*. These techniques in veterinary medicine have recently been increasing in popularity for clinical work and research applications. Veterinary nuclear medicine techniques similar to human medicine by using radionuclide can be provided information about the physiological functions of specific organs in either a diagnostic or therapeutic manner. Scintigraphy is a diagnostic branch in nuclear medicine. There is one basic difference from the other methods for example radiography, ultrasound, and endoscopy. By all the other methods can be imagined only morphological matters whereas scintigraphy has revealed physiological imaging. The advantages of scintigraphy are able to visualize and quantitate the distribution of different substances in the living organism indicating the processes of the body.

Scintigraphy procedures use radiopharmaceuticals or radionuclides (radioactive elements called isotopes or tracers), which emit gamma radiation. These are generally short physical half-life linked to chemical characteristics are suitable for stable labeling of different materials and can be applied by injection, orally and inhalation. Radiopharmaceuticals transport the radioactive atoms to specific organs of the living organism. The gamma radiation emitted from the radiopharmaceutical will be available for external detection and measurement. The most frequently used isotope is Technetium-99m (^{99m}Tc) in both veterinary and human scintigraphy procedures.

The instruments (a gamma camera) have been developed using for detection are called single photon emission computed tomography (SPECT) and positron emission tomography (PET), which three-dimensional versions of planar two-dimensional nuclear medicine images. These instruments establish imaging of the distribution of radiopharmaceutical and a better

sensitivity, resolution of image quality. Moreover, the biochemical properties of radioisotopes are important for this technique, which make them uniquely powerful probes of biological systems. SPECT cameras suffer from lower detection sensitivity by a factor 50-100 and lower spatial resolution by a factor 3-4 compared with PET (Wirrwar et al., 2001). Recently, small-animal devices have been constructed with resolutions of 0.8 mm or better (Stickel and Cherry 2005).

The development of nuclear medicine in veterinary medicine, planar scintigraphy (bone, thyroid, and renal scintigraphy) has continued a clinical practice used in a variety of orthopedic, thyroid, and renal disorders in veterinary patients (Daniel and Brawnier 2006). The previously listed examinations are the most widely performed scintigraphical methods in the veterinary clinics. The standard protocols used for veterinary nuclear medicine had been described by Daniel and Berry (2006). Nevertheless, there are a few others used rather rarely (bone marrow, splenic sequestration, lymphoscintigraphy).

Although, disadvantages of nuclear medicine in the practice of veterinary medicine are the lack of suitable equipment (veterinary gamma camera), costs, personnel, specific software, and other techniques resulting in these techniques have not become a widespread primary imaging modality in veterinary medicine (Enserink et al., 2007). However, the concept of "One Medicine" has provided for translational research in the field of disease in veterinary patients as it relates to human disease. Therefore, this review article will discuss information of nuclear scintigraphic examinations in veterinary medicine, which described following the radiopharmaceuticals by using SPECT, indications, and their present clinical applications. Further, scintigraphic techniques will prove to be used a great opportunity investigation tool for research applications, human medicine and veterinary medicine.

Brain scintigraphy

Brain scintigraphy is one of the most common nuclear medicine applications. SPECT brain scintigraphy can be performed using conventional radiopharmaceuticals such as ^{99m}Tc hexamethylpropylene amine oxine (^{99m}Tc HMPAO) and ethylcysteinate dimer (^{99m}Tc ECD) can be used in dogs and cats (Martle et al., 2009). Brain scintigraphy of dog by using ^{99m}Tc ECD with SPECT (Figure 1).

Indications for brain scintigraphy in the field of veterinary medicine differ from human medicine. The most frequent indications are suspected intracranial lesions such as brain tumors, cysts, abscess, hemorrhage, and vascular lesion, whereas cranial nerve disorders seizures, epilepsy or behavioral changes are much less frequently examined in animals than in humans. However, the regional brain perfusion was performed in dogs with idiopathic epilepsy and revealed a significant

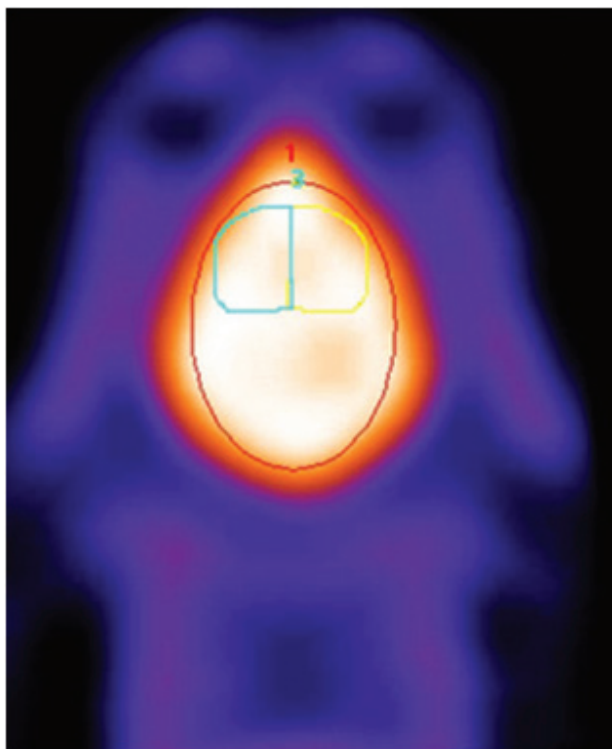


Figure 1 Horizontal SPECT image of the dog's brain that ^{99m}Tc -ECD providing brain perfusion data. Notice the high symmetrical striatal binding and the clear head and eye contour (Vermeire et al., 2011).

hypoperfusion in the subcortical region (Martle et al., 2009; Vermeire et al., 2009).

Brain scintigraphic studies were the measurement of local cerebral blood flow (CBF) in cats (Hassoun et al., 2003; Zimmer et al., 2003). The regional brain perfusion evaluated in normal dogs could be used as a reference to evaluate different canine pathophysiological changes (Peremans et al., 2001; Martle et al., 2009; Vermeire et al., 2009). The method of brain imaging has been used for anesthetic agents in small animal imaging therefore will likely alter the brain function that one is trying to measure. Waelbers et al. (2011, 2012) demonstrated that the effect of medetomidine on the regional cerebral blood flow in dogs and cats.

Bone scintigraphy

Bone scintigraphy is the most frequently performed veterinary nuclear medicine procedure used in the evaluation of the skeletal system (Lamb 1991; Chambers 1996) and useful for diagnosing conditions such as infections, tumors, and arthritis. There are several commercially available radiopharmaceuticals ^{99m}Tc methylene diphosphonate (^{99m}Tc MDP) and ^{99m}Tc -disodium oxidronate (HDP) (Debruyne et al., 2013). Bone scintigraphy in a lame dog by using ^{99m}Tc MDP as shown in Figure 2. Major advantage of bone scintigraphy opposed to radiological examination is that it is able to detect abnormalities at a very early stage within a few hours after injury incomplete bone fractures while radiological abnormalities are detectable after days.

The bone scintigraphic examination is usually performed into three phases (Three-phase bone scintigraphy) including vascular phase or blood flow phase (phase I), extracellular or soft tissue phase (phase II), and bone phase (phase III). After intravenous injection of a radiopharmaceutical, the first phase imaging is showing larger blood vessels (both arteries and veins) immediately (within one minute). The second phase takes 2-20 minute after application, which this images represent the

radiopharmaceutical biodistribution in the extracellular fluid space of tissues after delivery through the vascular system. The third phase imaging begins 2-3 hour after injection when theradiopharmaceutical localizes in bone on the surface of the exposed hydroxyapatite crystals while the remaining radiopharmaceutical is excreted by the urinary tract.

Indications for bone scintigraphy in phase I imaging are a susceptible test for ischemic injury, vascular infarction, and detecting acute inflammatory processes where significant local capillary recruitment in acute localized cellulitis has occurred. Phase II imaging is useful in detecting and evaluating inflammatory diseases in soft tissues surrounding the skeleton in tendon or ligament injuries, synovitis, myositis. Phase III imaging detects and evaluates acute or chronic bone disease that involves an increased rate of bone turnover (fractures, osteoarthritis, osteomyelitis, enthesopathies



Figure 2 Ventral planar images acquired 3 hours following injection of ^{99m}Tc MDP in a lame dog. There is a symmetrical uptake associated with the elbows, with the left elbow being more intense (Le Blanc et al., 2014).

and primary or metastatic malignancies), and it also localizes dead bone tissue as a result of bone infarcts, sequestrum formation or previous trauma (Zhuang et al., 2000).

Recently, ^{99m}Tc MDP bone scintigraphy is a very sensitive tool reported by Van Bruggen et al. (2010) that semiquantitative evaluation of planar bone scintigraphy could be provide valuable information enabling the diagnosis of abnormalities of the coronoid process in lame dogs.

Thyroid scintigraphy

Thyroid scintigraphy is one of the most frequently performed in veterinary nuclear medicine (Brawner 1996; Balogh et al., 1999). Thyroid scintigraphy is most generally used to helping in the diagnosis and treatment management of feline hyperthyroidism, hypothyroidism and canine thyroid carcinoma (Gutptill et al., 1995; Peterson et al., 1989). It is performed in dogs and cats whereas it has been used to a limited degree in other species such as the horse.

Actually, the measurement of thyroid function in nuclear medicine occurred the late 1930s (Sawin and Becker 1997), almost immediately on the discovery of fission-derived radioisotopes such as ^{131}I (nonradioactive iodine is ^{127}I). Radioiodine has specific affinity for thyroid cells and other tissues and it is the choice of treatment for feline hyperthyroidism. Recently, ^{99m}Tc pertechnetate ($^{99m}\text{TcO}_4$) has been used more widely for thyroid imaging than radioiodine because of its availability, low cost and radiation safety (Fischetti et al., 2005). Thyroid scans in a normal cat by using $^{99m}\text{TcO}_4$ as shown in Figure 3a.

Recently, thyroid scintigraphy is one of the most used additional information for evaluating the functional status of the thyroid glands, detection and localization of ectopic thyroid tissue, and differentiation between benign and malignant thyroid diseases. Morphological data is particularly important before surgical excision and

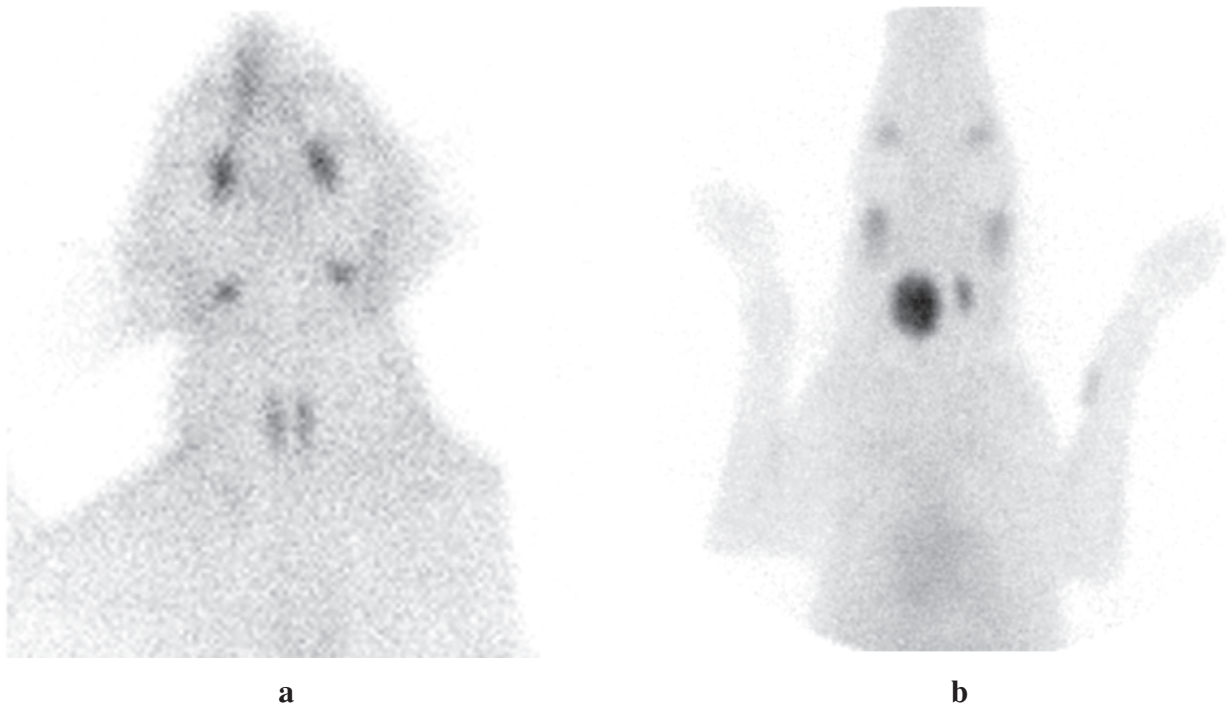


Figure 3 (a) Thyroid scans in a normal cat (b) Thyroid scans in dog with thyroid carcinoma. Image was acquired 20 minutes following injection of $^{99m}\text{TcO}_4$. Dog has a thyroid carcinoma of the right thyroid lobe. The tumor has increase pertechnetate uptake but is not producing excess T4 and therefore the left lobe is not suppressed (Daniel and Neelis. 2014).

evaluating response to therapy especially when suspected malignancy is diagnosed. Additionally, radioiodine therapy is routinely used in veterinary medicine, most commonly for the treatment for feline hyperthyroidism (Peterson 2006).

Inflammation and oncological scintigraphy

Scintigraphic procedures have the potential occasional to detect inflammation or oncological processes in the examined organs but there are especially designed scintigraphical methods for detecting inflammation foci (Moon et al., 1989; Tucker et al., 1992) and malignancies (Steyn and Ogilvie 1995; Balogh et al., 1997).

There is widely variability available of radiopharmaceuticals for inflammation scintigraphy. However, only a few agents are currently in general use for inflammation imaging. Some examples of these include ^{18}F -fluorodeoxyglucose (^{18}F -FDG), ^{99m}Tc -labeled bisphosphonates such as methylene-

diphosphonate or hydroxymethylene diphosphonate, ^{67}Ga -citrate, ^{99m}Tc -labeled nanocolloids, and ^{99m}Tc or ^{111}In dium (oxine or tropolone), agents for the detection of increased blood flow and capillary permeability, such as Immunoglobulin G (IgG) or albumin.

Radioactives used for oncological scintigraphy are ^{99m}Tc methoxyisobutyl-isonitrile (^{99m}Tc MIBI), pentavalentdimercaptosuccinic acid (^{99m}Tc DMSA (V)) and monoclonal antibodies (^{99m}Tc MoAbs). ^{99m}Tc MIBI is found to be useful in canine parathyroid and adenoma malignant lymphoma. Gallium citrate is a sensitive but not specific radiopharmaceutical. It has been used both for inflammation and oncological scintigraphy (Balogh et al., 2001). Thyroid scans in dog with thyroid carcinoma by using $^{99m}\text{TcO}_4$ as shown in Figure 3b.

Indications for inflammation scintigraphy are several in the veterinary practice as well. Examinations are carried out to identify or localize any inflammatory or septic focus in animals with known or suspected

inflammatory disease such as septicemia or multisystem infections, inflammatory bowel diseases, osteomyelitis, septic arthritis, rheumatoid arthritis. Furthermore, it is retained to evaluate surgical sites or implants in orthopedic patients, examine lesions identified by radiography or ultrasonography.

Recently, inflammation scintigraphy is an increasing interest for the clinicians to detect inflammation processes and malignancies as early as possible, using a sensitive, specific and non-invasive method. Oncological scintigraphy, ^{99m}Tc MIBI and ^{99m}Tc DMSA (V) scintigraphy is useful for the detection of soft tissue malignancy in dogs (Balogh et al., 2001).

Conclusion

In Thailand, the field of veterinary nuclear medicine has a few in clinical practices because of the limitation of radiotracer synthesis, the lack of equipment, facilities, personal, and budgetary facilities. Nevertheless, the author believe that nuclear scintigraphy is gaining in popularity because of value in the non-invasive technique of early diagnosis, underlying diseases, prognostic consequences and further probably also for therapy evaluation in veterinary medicine.

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