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REVIEW

Application of Advanced Imaging Modalities in Veterinary Medicine: A Review

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Abstract: Veterinary anatomy has traditionally relied on detailed dissections to produce anatomical illustrations, but modern imaging modalities, now represent an enormous resource that allows for fast non-invasive visualizations in living animals for clinical and research purposes. In this review, advanced anatomical imaging modalities and their applications, safety issues, challenges, and future prospects of the techniques commonly employed for animal imaging would be highlighted. The quality of diagnostic imaging equipment in veterinary practice has greatly improved. Recent advances made in veterinary advanced imaging specifically about cross-sectional modalities (CT and MRI), nuclear medicine (PET, SPECT), and dual imaging modalities (PET/CT, PET/MR, and SPECT/CT) have become widely available, leading to greater demands and expectations from veterinary clients. These modalities allow for the creation of three-dimensional representations that can be of considerable value in the dissemination of clinical diagnosis and anatomical studies. Despite, the modern imaging modalities well established in developed countries across the globe, it is yet to remain in its infancy stage in veterinary practice in developing countries due to heavy initial investment and maintenance costs, lack of expert interpretation, a requirement of specialized technical staff and need of adjustable machines to accommodate the different range of animal sizes. Therefore, veterinarians should take advantage of these imaging techniques in designing future experiments by considering the availability of these varied imaging modalities and the creation of three-dimensional graphical representations of internal structures.

Keywords: application, computed tomography, magnetic resonance imaging, nuclear medicine, combined-modality, imaging modalities

Introduction

In veterinary medicine, diagnostic and therapeutic radiography were the sole imaging tools for getting an image in the process of diagnosis. Radiographs, unfortunately, only display a shadow of organs and reveal little information about interior anatomical structures. Endoscopy is a specialized procedure that provides full-color views of tissues within the body, while ultrasonography allows veterinarians to have a better imaging alternative when it became accessible. Although ultrasonography and endoscopy have improved the ability of veterinarians to make more accurate diagnoses, additional imaging options are needed for a broader array of conditions using noninvasive methods.[1] Three-dimensional computer modeling can now provide morphological, anatomical, and pathophysiological information in a far less minimal-invasive and faster fashion.[2] In addition to static images or movies, computer graphics enables the creation of naturalistic interactive three-dimensional models of the anatomy, in which dynamic processes can be simulated and visualized, allowing the researcher to extract the skeleton, internal organs, and vascular structures, among other things.[3]

There have been major advancements in the development of and access to advanced imaging in veterinary medicine. Even though, radiography and ultrasonography will remain mainstays in veterinary medicine due to availability, cost and ease of use, advanced diagnostic imaging will continue to become more utilized due to its increased diagnostic capability. Cross-sectional and nuclear imaging modalities enable clearer depiction of anatomy, particularly in parts of the body with relatively complex internal anatomy that is not well suited to conventional imaging. Hence, advanced imaging modalities

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are inherently better detectors of diseases than radiography and planar imaging, despite having lower spatial resolution. Some of the increasingly common advanced diagnostic imaging in animals include computed tomography (CT), magnetic resonance imaging (MRI), nuclear medicine, and combined imaging modalities that were the preserve of veterinary medicine establishments or research facilities.[4] The development of such advanced imaging technologies improves the quality of anatomical imaging that enables for better diagnosis and treatment of various animal diseases. This review discusses the growing number of applications in morphological and physiological perspectives, as well as safety concerns, obstacles, and future opportunities. This will help professionals working in the field of veterinary medicine or biomedical research, veterinary diagnostic and teaching hospitals and laboratories, and designing future experiments by considering the availability of these varied imaging modalities.

Computed Tomography

Computed tomography (CT) is a diagnostic imaging modality that is widely used in veterinary medicine as it can provide axial sectional or slice-oriented imaging of the patient.[5] It works as an x-ray tube that moves around the body and continuously projects a thin fan of x-rays through the body. Electronic detectors opposite the tube continuously monitor the number of x-rays passing through the body and the angle at which the beam is being projected. The number of x-rays reaching the detector changes as the beam passes through different tissues because of the tube movement. A computer mathematically evaluates the data and determines the most probable density of any point within the volume of tissue scanned.[6] This assists in the detection of anomalies in places where plain radiography shows a lot of superimpositions. The use of CT in veterinary medicine has risen dramatically in recent years, owing to lower costs, accessibility, and advances in expertise and technology. In addition to diagnosing and treating many disorders, CT is currently being utilized to study areas ranging from drug delivery and surgical breakthroughs to anatomical and educational uses across the world.[7]

Application of Computed Tomography

CT scans were first used in clinical practice in the early 1970s and were originally designed as a brain scanner. In the 1980s, the application in veterinary medicine for clinical use was initially reported for the investigation of central nervous system disorders, normal CT brain anatomy, and various forms of malignancies found in dogs and cats.[8–10] CT has become continually being explored and accessible CT imaging centers are emerging due to technological advancements and its increased availability in general practice in veterinary medicine.[7] In many cases, CT imaging can provide valuable information that cannot be obtained with ultrasound and radiography.[11]

Some of the current researches in both the clinical and laboratory settings have been influenced by the development of CT techniques and their applications.[12] The use of contrast-enhanced CT for dynamic imaging of cerebral and tumor microvasculature is becoming incredibly common.[13] The application of such techniques has the potential to transform our understanding of complicated disorders in a variety of anatomical locations and pathological situations.[7] The exploitation of the unique characteristics of synchrotron radiation-based μCT facilities could render dynamic experimentation possible, enabling the full elucidation of the pathogenic mechanisms involved in different diseases and disorders in addition to understanding basic anatomical structures. The use of CT images to produce 3D reconstructions is an important and growing application of CT in veterinary medicine and research. This could be useful for teaching young children, undergraduates, or surgeons, teaching anatomy and physiology using 2D pictures, 3D movies, virtual museums, or even 3D printed models, as well as providing virtual dissection experiences are all possibilities.[14] In forensics and archaeology, CT has also risen in line with the technologies available, it has included identifying tool marks on bones, age determination, assessing gunshot wounds, analyzing teeth, understanding the pathology of bones, and estimating post-mortem intervals.[15]

In different species of animals, CT diagnostic information on the location, extent, and characterization of lesions in the nasal cavity, paranasal sinuses, retrobulbar region, jaw, dental arcade, diagnostic lameness workups, the appendicular skeleton, skull, temporomandibular joints, and tympanic bullae are the most routinely assessed structures and are more accurate than conventional radiographs.[16–19] For the lumbosacral area, evaluation of bone remodeling, evidence of cauda equina compression by either soft tissue or bone remodeling within the spinal canal, and comparison of size and density of intervertebral foramina, both between right and left sides at the same space and between different intervertebral disc spaces is possible.[6] For the abdominal cavity, a CT examination is normally performed after an abdominal ultrasound to investigate the margins and resectability of an abdominal mass or to confirm suspected ectopic ureters. Investigation of the invasiveness of an adrenal tumor to the surrounding blood vessels is also an important indicator for an abdominal CT. The investigation of portosystemic shunts using dynamic contrast study has become more common with the availability of a multislice CT machine.[5]

Several bone and growth diseases have been investigated using CT. The benefit of CT scanning is that it can show micro-fractures, bone thickness, trabecular bone distortion and architecture, and bone curvature and angles in situ, in addition to gross anatomy-like fractures and general morphology.[7] When considering the extensive range of activities that can be applied to the normal body, CT has a wide range of applications in diseases, pathologies, and other investigations. Localized mechanical strain can be detected by measuring cortical bone thickness and trabecular bone deformation,[20] and it is likely linked to many bone disorders in addition to fractures and trauma incidents. CT examination of intervertebral disc disease (IVDD) has been used widely to replace the use of myelography. It has also become the first choice of imaging modalities to investigate IVDD when the cost and availability of MRI prohibit the use of MRI.[5] Besides, the use of CT is most commonly indicated in patients with thoracic and abdominal disease, intracranial and extracranial lesions, and disorders of the musculoskeletal system including the appendicular skeleton and spine.[21,22] As the generation of images in CT is so rapid, this diagnostic modality is important in cases where anesthesia and sedation are not an option.[23]

CT has also been given detailed anatomical descriptions of the bones, show where weaker areas might occur in guinea pigs.[24] Recent studies have shown visible thinning and fractures within bones of chronically laminitis horses, using µCT and histopathology in parallel.[25] µCT studies have also given enormous insights into bovine lameness by combining clinical data with µCT images and measurements, direct correlations between bone damage, remodeling, and growth were made, thus giving new insights into the mechanisms behind bovine lameness.[26] In addition to visualizing bone measurements such as thickness, trabeculation, and anatomical size, CT is an excellent platform for understanding bone angle and rotation, useful in understanding deformities, dysplasia, neoplasia, osteopathy and degenerative diseases in addition to normal anatomy or trauma situations.[7] CT scanners can also provide images at an almost cellular level of resolution and have been employed for cardiac, pulmonary, hepatic, splenic, renal, and tumor imaging and to study gene expression.[27] In general, the cross-sectional description of anatomy in CT images eliminates the problem of the super-imposition of body parts. Therefore, CT has a higher sensitivity for detecting disease and enables a more accurate assessment of the extent of lesions and anatomical clarities.

Safety Concerns in CT

The significant rise in CT utilization has drawn a lot of attention to the dose of ionizing radiation given to animals during exploration. Ionizing radiation causes damage at the cellular level. When x-ray photons pass through human/animal tissue, ion pairs are formed. Interaction between ionic pairs and DNA can cause irreversible damage to the DNA.[28] A recent research outputs revealed that continuous exposure to radiation has oncogenic effects. Thus, the overuse of CT has a cancer risk, which veterinarians, imaging professionals, and patients must be aware of. Employing safe imaging parameters is the responsibility of the CT technologist; it is crucial that veterinarians understand the relationships between imaging parameters to properly implement ALARA (As Low As Reasonably Achievable) in each examination.[29] Besides, veterinarians base their imaging decisions, and they must be educated about the risks of CT to make the decision. Furthermore, the ionizing radiations regulations for the safe use of ionizing radiations in veterinary Practice should be provided in accordance with the countries that employed the imaging equipment, which is crucial when dealing with CT in veterinary practice.[30] Therefore, understanding the characteristics of CT will provide more effective and accurate patient and veterinary care in the fields of diagnosis, radiotherapy and research, and may lead to improved optimization of imaging exposure dose.

Challenges and Future Prospects

When computed tomography became available, it enabled veterinarians to establish diagnosis with unprecedented speed and accuracy. However, the costs, availability, expertise and technology are very challenging to its widespread usage and clinical use and it affects the way they practice and teach veterinary medicine.[31] Naturally, the expense and space requirement needed for such high caliber machines and experimental set up restricts the possibilities in the normal clinical setting but is increasingly possible under research conditions.[7] Several studies use this technique simultaneously to achieve insights and science. For instance, Nano-CT, which can currently achieve resolutions of 400 nm, and new software and algorithms, which are also being designed and advance the current uses of existing devices, are illustrations of the future generation of imaging techniques.[32] The key to advancing clinical techniques is the sharing of world-class research alongside the financial ability to provide a service according to the needs of the patient. These applications, as well as the use of CT in a variety of other circumstances, are critical to the advancement of the veterinary profession and research.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a type of advanced imaging modality that is used in radiology to create images of the body's anatomy and physiological processes. MRI was first exhibited in 1973 and is now a mature analytical modality that is widely employed in clinical practice and research as a diagnostic tool. It generates images of the body's organs using powerful magnetic fields, magnetic field gradients, and radio waves.[33] The images were created by using radio waves to stimulate magnetized tissues and then capturing the returned radio waves from the stimulated tissues. Different sequences can be obtained depending on the type of emitted radio wave (duration, phase, and frequency) and the time at which the returning wave is captured. For the diagnosis of most neurologic, orthopedic, oncologic, and other illnesses, it is the imaging modality of choice. In most cases, the sequences used for examinations in large animals are similar to those employed in small animals. MRI investigations often comprise multiple different acquisition planes, including transverse, dorsal, and sagittal planes, in addition to varied sequences.[34] Thus, the application of MRI for imaging the different body regions and provides a practical guide for their use in different anatomical structures and clinical indications. This allows the veterinarian to make an informed decision on why to choose MRI.

Application of Magnetic Resonance Imaging

Because of its capacity to provide high-contrast, anatomically detailed tomographic pictures, magnetic resonance imaging (MRI) is being employed more frequently in veterinary medicine.[35] MRI is a relatively new imaging modality with considerable potential for visualizing soft tissues. It has a wide spectrum of application. This has enhanced our ability to study anatomy and pathologic changes in vivo. Today, MRI is often available in veterinary medicine and has proven its value in the detection of neurologic, orthopedics, oncologic, and other diseases.[16] Many issues about musculoskeletal diseases in animals, such as the pathophysiology of navicular disease, traumatic arthritis, and osteochondrosis in equines, and wobbler syndrome in dogs, could be addressed with it. Magnetic resonance angiography (MRA) and Magnetic resonance spectroscopy (MRS) are two emerging MRI applications. It is notably useful for distinguishing between an inflammatory process and a neoplastic mass, as well as tumors and peritumoral edema. It is good at detecting osteomyelitis, cellulitis, and abscesses since it is more specific and sensitive.[36,37]

The clinical application of magnetic resonance imaging in veterinary ophthalmology was investigated in clinical cases of a feline orbital melanoma, a feline optic nerve meningioma, and a canine orbital fibrosarcoma. Because of its higher soft-tissue contrast and multiplanar and multislice imaging capabilities, it reveals excellent anatomical information of the canine and feline eye, orbit, and optic nerves.[38] Although MRI has traditionally been used for diagnosing various diseases affecting the central nervous system, CNS neoplasia, Inflammation of nervous tissue in animals and humans, in recent years the range of clinical applications has broadened considerably.[39] MRI is now being used for diagnosis in areas such as nasal neoplasia, eye and orbital diseases, and musculoskeletal diseases, including shoulder osteochondrosis, canine elbow dysplasia, and cranial cruciate ligament injuries.[35]

MRI also identified the optic, trigeminal, and in part, the facial, vestibulocochlear and trochlear nerves in the rabbit. The absolute and relative size of the pituitary gland, midline area of the cranial and caudal cranial fossa, and height of the telencephalon and diencephalon, 3rd and 4th ventricles were also determined.[40] In the horse, MRI enabled detection of changes with an acute onset of severe unilateral forelimb lameness originating from the heel portion of the foot, and is the gold standard for studying orbit, lymph nodes, blood vessels, muscles, and salivary glands.[34,41] MRI also plays a crucial role in the diagnostic work-up of head disorders particularly useful in avoiding problems associated with superimposition of multiple structures in the head.[34]

Large animals can be scanned with today's scanners, which are becoming more widespread in clinical and research settings. For these reasons, the use of MRI in large animal models for fundamental or translational neuroscientific research has been growing tremendously.[42] MRA enables for the noninvasive visualization of vascular malformations such as aneurysms, and thrombi, as well as the precise anatomic location of Portosystemic shunts. Additional diagnostic roles for MRI and MRA will almost certainly emerge as experience with these techniques improves.[35] The diagnostic usefulness of MRI in cases of dental disease is limited to lesions involving the pulp cavity, the periodontal space, the lamina dura, and the bone marrow of the surrounding alveolar bone.[34] Although the majority of studies are still conducted in a clinical setting, with significant constraints such as equipment availability and safety measures, specialized MRI platforms with high-quality holding facilities are beginning to appear.

Safety Concerns in MRI

The behavior of ferromagnetic objects when exposed to a strong magnetic field is one of the most important patient safety factors related with magnetic resonance imaging (MRI). Forces on a ferromagnetic implant could cause it to move, resulting in harm and possibly death. Strong magnetic fields can also cause external ferromagnetic objects to become airborne and travel rapidly towards the magnet's center. This "missile" or "projectile" effect could result in damage or death once more.[43] Magnetic fields, whether static or gradient, can affect medical devices, whether implanted or external, and cause them to dysfunction. Tissue heating due to RF energy deposition, which is measured as the specific absorption rate, is one of the radio frequencies (RF)-related risks (SAR). Due to the higher frequency of the RF pulses, this becomes more pronounced with increasing field strengths. Skin patches, tattoos, cables, and wires can all absorb RF energy, causing them to heat up and potentially burn the patient. Acoustic noise, which is associated with rapidly switching gradient coils, is also a concern to patients that can be avoided by using hearing protection and noise reduction techniques.[44]

MRI is, in general, a safe technique, although injuries may occur as a result of failed safety procedures or human error.[45] Contraindications to MRI include most cochlear implants and cardiac pacemakers, shrapnel, and metallic foreign bodies in the eyes. Magnetic resonance imaging in pregnancy appears to be safe, at least during the second and third trimesters if done without contrast agents.[46] Since MRI does not use any ionizing radiation, its use is generally favored in preference to CT when either modality could yield the same information. Amplitude and rapid switching of gradient coils during image acquisition may cause peripheral nerve stimulation.[47] However, as millions of MRIs are performed globally each year,[48] fatalities are extremely rare.[49]

Challenges and Future Prospects

Despite MRI's shortcomings, incorporating technology into veterinary practice appears to be tough. This is exacerbated by the fact that the techniques involved are highly specialized and, necessitate specialized training, specialized software, and professional computer capability by today's standard. Again, administering of prolonged anaesthesia for veterinary patients for effective handling during the imaging procedure is costly. While the MRI market in the developing world has a lot of potential, it also has a lot of problems, such as the unclear outcomes of healthcare reforms, a shortage of appropriately educated employees, and high costs. Another big obstacle to the rapid growth of MRI in veterinary clinical applications and research is a shortage or complete lack of properly trained personnel. Veterinarians who are interested in MRI are that many of them have limited knowledge of MR physics and limited experience in MRI clinical applications and research.[35] Therefore, the financial implications for training and marketing become a key focus, outweighing the need in practice. In most developing countries, the use of MRI, its availability for diagnostic, teaching, or research purposes in any of the government-owned veterinary establishments or any of the institutions engaged in the residency training program is limited. Recently, there has been a rapid increase in the availability of MRI modality as the increment of economy.[50]

The development of nanoparticles-based target-specific contrast agents and innovative contrast mechanisms such as CEST is expected to further take small animal MRI research into a new horizon.[51] To keep up with the rapid advancement of this imaging technology, the diagnostic imaging community should work hard to develop MRI training programs and degree programs in universities and research centers. The demand, however, outweighs the expense, and knowledge should be developed and improved, as well as correct and accurate diagnosis and staying up with the trend.

Veterinary Nuclear Medicine Imaging

Nuclear medicine is a distinct diagnostic imaging technique. Its use in veterinary medicine has been increasing over the last two decades. It mirrors the use in human health, but lags behind significantly. It is thought that animals are capable of undergoing almost any diagnostic or therapeutic procedure from human medicine.[52] The application of *Atomic Energy for Peace* through implementation of knowledge of nuclear energy for medical use has developed after the United States dropped atomic bombs on the Japanese cities of Hiroshima and Nagasaki in Second World War.[53] After the Second World War, the attack on Pearl Harbor, the United States developed nuclear reactors to produce atomic bombs, which were subsequently dropped on the Japanese cities of Hiroshima and Nagasaki. After the end of the war, the United States was involved in the campaign for the application of *Atomic Energy for Peace*, which stimulated the implementation of knowledge of nuclear energy for medical applications, among other beneficial actions.[53] This technique allows us to administer a radioactive substance (radionuclide) either by injection or by mouth and observe the activity within the patient, providing both morphologic and functional information.[54]

Nuclear imaging is currently experiencing broad application in the filling of several gaps in veterinary medicine, in which radioactive substances are used for diagnostic and therapeutic purposes. They rely on the in-vivo detection and quantification of the radiotracer distribution and binding to specific biological targets.[55] The two most common nuclear imaging modalities are single photon emission computed tomography (SPECT) and positron emission tomography (PET) scans.[56] In both PET and SPECT, a small amount of a radioactive compound (tracer) is administered to a subject, and images are acquired with a highly sensitive camera that can detect the small amount of radioactivity emanating from the body. The resultant images are 3-dimensional spatial reconstructions of the tracer location at the time of imaging.[57]

Image quality in SPECT and PET is mainly determined by spatial resolution and sensitivity.[58] As opposed to traditional radiography or computed tomography, which provides a static picture at a point in time, nuclear medicine can visualize dynamic processes over time. Importantly, this modality provides not only morphologic but also patho-physiologic information. This is very important, where different diseases may have the same appearance on other modalities and more specific tests would be valuable.[59] In both imaging modalities, clinical application and diagnostic imaging have been applied in the same perspective. Availability of a variety of probes and strategies confer PET a high degree of versatility. The ability to detect multiple probes simultaneously and the availability of radioisotopes with longer half-lives are some of the advantages of SPECT over PET.[27]

Positron Emission Tomography

Positron Emission Tomography (PET) is a type of imaging that gives functional information in addition to structural information received through other imaging techniques. It is one of the quickest-growing fields of medical imaging, with enormous potential for evaluating metabolic processes in the body. The mechanism of action is based on infusing a radioactive isotope of glucose (most often 18F-fluorodeoxyglucose, 18F-FDG) into the body and measuring its accumulation in various organs and tissues.[60] Thus, PET imaging is used to visualize, characterize, and measure biological processes at the cellular, subcellular, and molecular levels in living subjects using noninvasive procedures.[61] It enables researchers to assess the metabolic nature of malignancies in addition to anatomical information.[62] This technique is now mostly used in oncology, neurology, and cardiology researches for a detailed evaluation of many diseases.[63]

Applications of PET

Positron Emission Tomography (PET) is increasingly being used as an imaging modality for clinical and research applications in veterinary medicine. It plays an important role in the diagnosis, staging, image-guided treatment planning, and monitoring of malignant diseases,[64] detecting the margin of oral neoplasia, in particular for tumors arising from highly vascularized tissue, such as the lingual and laryngeal areas, and assessment of inflammation and pain,[65] and diagnosis of cognitive dysfunction syndrome,[66] arterial sampling-based kinetic analysis,[67] diagnosis and tracking of primary and metastatic tumors, to study the normal physiology of glucose uptake, metabolism, and muscle activity during and after exercise, evaluation of patients presenting with indistinct or intermittent clinical signs of musculoskeletal inflammation or injury.[68]

Even though PET's application mainly focused on oncogenic diseases, there are also reports evaluating the use of PET in nononcologic applications such as for the staging of several canines and feline tumors,[69] detection of inflammation relates to neurologic disease,[70] and lameness evaluation in a dog.[68] Nowadays, orthopedic uses of PET have gained interest, equine lameness imaging with the use of 18F-NaF PET for assessment of active bone remodeling and 18F-FDG is also utilized for cardiac imaging and neuroimaging purposes.[65,71]

Among the several imaging technologies applied to in-vivo studies of research animals, PET permits the spatial and temporal distribution of compounds labeled with a positron-emitting radionuclide to be determined.[72] In conjunction with measures of blood flow, PET can be used to study the balance between flow and metabolism in chronic models of coronary artery disease.[73] Some small animal PET scanners permit gating of the heart, which allows systolic and diastolic myocardial images of the rat heart to be obtained.[74] PET provides not only precise anatomical positioning and quantification but also longitudinally studies of the spatial and temporal dynamics of disease-specific functions and molecular events in a complete organism. It also assists to track a liposomal glucocorticoid level, at visible and occult inflamed sites thereby for the prediction of therapeutic response.[75] Scientists in the field of invertebrate neuroscience and regenerative medicine also used PET for addressing questions in the area.[76]

Single Photon Emission Computed Tomography

Single-photon emission computed tomography (SPECT) is a nuclear medicine imaging modality where two-dimensional projections are acquired with a gamma camera and the projections are used for the reconstruction of a three-dimensional image volume. The gamma camera is rotated around the patient and multiple images from multiple angles are obtained. A computer can then reconstruct the images. Radiopharmaceuticals used for SPECT are labeled with gamma-emitting radionuclides.[77] The projections are distorted by several factors, including attenuation and scattering of gamma-ray, collimator structure, data acquisition, reconstruction method, and organ motions. The collimator in SPECT is a crucial component of the imaging chain that controls the noise, resolution, and sensitivity of the final functional image.[78,79]

Although planar gamma camera images have been used in veterinarians for decades, SPECT was initially used primarily for the diagnosis of lameness in horses and later for small animals. However, SPECT have not received much enthusiasm in veterinary medicine. This may be partially explained by the lack of suitable equipment (many veterinary gamma cameras are used for both large and small animal imaging but have been rebuilt to meet the specific requirements for equine imaging), specific software, and the necessity for anesthesia.[62] Nowadays, SPECT imaging in veterinary medicine is gaining in popularity for clinical and research applications. In this part, the practical application of SPECT in different clinical settings, its diagnostic and treatment implications applied in veterinary medicine has been included.

Applications of SPECT

Single-photon emission computed tomography (SPECT) is an important imaging modality for various applications in veterinary medicine. Among its numerous applications, SPECT is useful for noninvasive investigation of renal function in the mouse by means of dynamic imaging, parenchymal scanning, and quantification of filtration, secretion, and reabsorption events,[80] comparison of regional cerebral blood flow (rCBF) in dogs with congenital portosystemic shunt (PSS) and hepatic encephalopathy (HE) with rCBF in healthy control dogs with a 99mtechnetium-hexamethylpropylene amine oxime (99mTcHMPAO) tracer,[81] in vivo assessment of the dopamine transporter (DAT) availability in healthy dogs,[82] non-invasive assessment of neuroinflmmation, blood–brain barrier alterations, and neurotransmitter systems, provision of better insight into the neurobiology of epilepsy in human and dogs that is desirable for veterinary epilepsy patients these promising developments in the medium term,[83–85] to screen thoracic metastasis and is recommended in dogs with thyroid neoplasia,[86] and also used extensively to study cardiac health-like blood flow to the heart through myocardial perfusion imaging and to image blood flow to the brain.[77]

In recent times, imaging technologies have been increasingly applied to animals to study biological processes in real-time and at the molecular level. In this way, SPECT is extremely useful in animal studies, therapeutics, and diagnostics.

Many researchers had assessed local changes in neurotransmitter release associated with the performance of a given behavioral task in laboratory animals for the development of new potential drugs for psychiatric and neurological disorders, which could be useful to better understand brain functioning and allow translation of preclinical results into clinical applications,[87] offering functional insight into brain alterations for a better understanding of the pathophysiology of underlying epilepsy syndromes as well as to forecast disease risk after epileptogenic brain insults;[83] assessing the accuracy of a scout dose of holmium-166 poly(L-lactic acid) microspheres (^{166}Ho-PLLA-MS) in predicting the distribution of a treatment dose of ^{166}Ho-PLLA-MS. In the porcine model, a scout dose of ^{166} Ho-PLLA-MS can accurately predict the biodistribution of a treatment dose;[88] investigating neurotransmission, metabolism, regional cerebral blood flow, and pharmacology in vivo. Consequently, SPECT imaging can also assist in diagnosing multiple neurodegenerative and neuropsychiatric disorders. It also provides imaging biomarkers to track disease development and monitor the effects of drugs on disease progression and used to determine optimal dosing for new drugs via microdosing experimental setup and can aid with accelerating the implementation of personalized medicine.[89,90]

Safety Concerns in Nuclear Medicine

The International Atomic Energy Agency (IAEA) continues to be the global authority on the use of radioactive materials for medical reasons. "The IAEA is empowered to create or adopt safety standards for the protection of health and the minimization of danger to life and property, and to provide for the application of these standards," according to its Statute. The International Atomic Energy Agency (IAEA) recently developed a new Safety Report for veterinary practitioners who use radiation and national regulatory agencies, which includes recommendations and tips to help professionals do their work safely.[91] The International Atomic Energy Agency (IAEA) believes that the same laws and regulations should apply to the use of nuclear energy in veterinary medicine as they do in human nuclear medicine. Some aspects of veterinary nuclear medicine must be considered, such as the animals' lack of conscious cooperation and strict control, temporary confinement or isolation of animals from the general public after nuclear procedures, dose adjustments for diagnostic or therapeutic purposes, use of anesthesia, and equipment adjustments due to the patient. From the point of radiation safety, exposure to ionizing radiation should be as low as achievable, ie, obtaining an interpretable diagnostic image or treatment of a disease, recommended doses of radioactive isotopes, reduced time of exposure, keep the distance and use personal protective equipment like gloves, sleeves, and aprons.[52,91]

Challenges and Future Prospects of Nuclear Medicine

Although nuclear imaging modalities can be used to reveal molecular events, they cannot provide any information about molecular structure. Other techniques such as high-performance liquid chromatography (HPLC) are required for the characterization of the molecular structure. Further developments in detector technology and image reconstruction algorithms for nuclear imaging modalities are desired to overcome the limitations such as very low detection sensitivities and spatial resolutions. Development of highly target-specific ligands is desired to radiolabel the radionuclides.[92] Due to the high cost of PET scanners and the short half-life of radionuclides, small animal PET imaging has been limited only to the most advanced centers. Because PET radionuclides have such a short half-life, a cyclotron should be located near the PET imaging system. Pharmacologic restrictions and prerequisites, as well as interspecies differences in metabolism and mass effects of PET ligands, continue to be challenges to translating animal research findings into clinical practice. PET has required a great deal of work to create as a result of radiochemical, radiopharmacological, and imaging studies. However, several biological, methodological, and technological issues remain the difficulties in the interpretation of the images, the effects of anesthesia, the need for anatomical references, the constraint of the injected mass of radiotracer and, finally, progress concerning the microPET camera, particularly in terms of spatial resolution.[93]

To date, PET appears to be developing rapidly as a viable tool for animal research. It allows noninvasive measurement of many different biological processes and permits longitudinal calculations of animal models. High-resolution dedicated animal PET scanners are available, and additional improvements in performance, cost, and ease of use can be anticipated. Nevertheless, several challenging issues still must be addressed for PET to become a routine part of the biological sciences.[94] In SPECT, the use of specialized collimators is viewed as a technique for improving sensitivity without degrading image resolution. Furthermore, pinhole SPECT technology is seen as an area of intense recent interest, particularly due to its ability to enhance resolution capabilities in SPECT and to offer the possibility of stationary small animal SPECT imaging.[95] If further innovation can increase the effectiveness of animal nuclear imaging systems while also lowering their complexity and expense, these technologies may find their way into large research institutes as well as the pharmaceutical and biotechnology companies. As technology advances, costs decline, and the availability of high-resolution PET scanners increases, this method may become the gold standard for veterinary diagnostic imaging. Furthermore, advancements in image reconstruction software, the potential for two-way imaging, and the use of specific collimators in the case of SPECT can all help existing PET and SPECT technologies.

Combined-Modality Imaging

Nuclear imaging modalities are particularly valuable for disease diagnosis, staging, and treatment response evaluation since they allow highly sensitive detection of biological activities in vivo.[96] To synergize the information provided by different kinds of images, images produced by two or more techniques are often combined.[97] Molecular imaging combines anatomic and molecular information by employing SPECT, PET, MRI, and CT in combination with specific imaging modalities. They all provide complementary views of normal and diseased tissues, with PET and SPECT offering quantitative functional information and MRI and CT scans providing high-resolution anatomical information.[77] The latest hybrid nuclear imaging machines representing the top imaging technologies include PET/CT, SPECT/CT, and PET/MRI. The power of combined-modality imaging will increase dramatically as molecularly targeted radiotracers with high specific activity are developed and as the sensitivity and resolution of PET increase to allow for high-resolution, temporal imaging.[77]

The combination of PET and computed tomography (CT) into PET/CT has heralded a new era of hybrid imaging driven by the rapid ascend of PET/CT and the decline of stand-alone PET. The integration of PET and CT into a hybrid system provided added value that exceeds the sum of its parts, in particularly fast and accurate attenuation correction and the combination of anatomical and molecular information.[98] PET/CT was previously performed by acquiring a PET scan and CT scan on different machines at different times; but more recently, new machines acquire images on a dual PET/CT scanner as part of one imaging examination. Combined PET/CT scanners provide automatic image fusion, whereas PET and CT studies obtained independently require appropriate software for fusion.[99] PET is now routinely acquired with CT (PET/CT), and more recently, PET/MR has become more available.[100]

The addition of SPECT to planar images helps to localize the abnormal uptake, improves diagnostic accuracy, and assessment of the disease extent.[101] However, despite this improvement, SPECT does not provide the exact location. CT can be obtained for attenuation correction and anatomical localization resulting in hybrid imaging: SPECT/CT, which further improves detection of abnormal radiotracer accumulation.[102] Moreover, SPECT/CT improves reader confidence compared with planar imaging.[103] SPECT/CT is superior compared with SPECT alone with multiple established indications and emerging new applications.[104] The addition of SPECT also results improved sensitivity and accuracy. Acquisition of both SPECT and CT further improves accuracy and provides an anatomic reference.[100]

Applications of Combined-Modality Imaging

Before a decade, various dedicated dual-modality imaging systems have been designed for small animal imaging. In dedicated SPECT-CT and PET-CT systems,[105] structural data from CT images are also used to generate attenuation correction maps for SPECT and PET image reconstruction, respectively. Dedicated SPECT-CT systems have found applications for oncology research, development of radiolabeled nanobodies[106] and gene therapy vectors,[107] and investigation of various disease models.[108] PET-CT is principally employed for oncologic imaging.[109] MRI compatible optical imaging systems have been developed.[110] Dedicated PET-MRI, SPECT-MRI, and optical-PET systems have also been developed for small animal imaging.[111–113] PET–MRI imaging would be particularly useful for animal research. It provides an opportunity to combine functional information from PET with anatomical as well as various other kinds of information (ie, functional, metabolic, or perfusion) from MRI.[114]

Recently, special imaging equipment and appropriate nuclear medicine facilities are required to perform the studies, which are most commonly performed on patients with cancer;[99] diagnosis and initial staging of malignancy, assessment of response to therapy, and detection of recurrent disease after treatment and have many applications as research tools in studying spontaneous cancer development in animals and aiding in novel radiotracer development.[104] It offers synergies of functional and anatomic information, allows precise anatomic localization of radioactivity foci, and is mainly applied in oncology, cardiology, and for the diagnosis of bone lesions and infections.[115] Thus, the role of hybrid imaging systems is growing, both in research and clinical practice and new combinations of modalities are being developed, inspired by the success of PET/CT, SPECT/CT, and PET/MR.

Challenges and Future Prospects

Recent advancements in detector technology have the possibility for improved spatial and energy resolution, as well as increased stability and device compactness. However, these new detectors must be integrated into entirely new systems.-[116] PET/CT with 18F-FDG for tumor imaging will ultimately replace SPECT/CT; advances in SPECT instrumentation, CT technology, and development of radiotracers have the potential to advance SPECT/CT beyond its current level of performance. The horizon for SPECT/CT imaging lies in the development of new tumor-specific agents that can improve oncologic clinical diagnostic and therapeutic applications. Future SPECT/CT developments will also be undergo a full diagnostic procedure in a single location, as well as reduced radiation exposure over time. In the near future PET/MRI may emerge as a new powerful multimodality technique, offering considerable potential for imaging applications beyond correlation of functional and anatomic images. Future developments will also include the simultaneous acquisition of multifunctional data such as PET tracer uptake, MR spectroscopy, or fMRI along with high-resolution anatomic MRI. As the number of clinical applications grows, it is projected that the use of combined imaging modalities in clinical practice will increase in importance.

Conclusion

It is evident that the latest advances in imaging technology have revolutionized veterinary diagnosis, treatment planning, and preclinical research. It provides accurate anatomical and pathophysiological information, images of any body plane, good contrast and spatial resolution, and can make diagnostic recommendations. The correct use of appropriate imaging technology can help to detect pathologies, physiological activities and positioning structures, and ultimately help diagnose and carry out the research so far. Using more than one method to fully understand the condition may bring great benefits. The future of imaging in veterinary facilities is full of possibilities; however, space limitations, financial restrictions, and technical issues may hinder the use of advanced imaging techniques for diagnosis and clinical applications. The physics of imaging modes is very complex and a detailed discussion of this field is beyond the scope of this article. However, for proper application in clinical and preclinical settings, basic knowledge is required. To better perform preclinical and clinical tasks and improve the overall standard of care, today's veterinarians should also be familiar with these advanced imaging modalities.

Disclosure

The authors report no conflicts of interest in relation to this work.

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