Review Article

Cancer Diagnostic and Therapeutic Considerations in Dogs: A Review

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ABSTRACT

Cancer presents a significant health concern in dogs, akin to its impact on humans, and stands as a primary contributor to canine mortality. The elevated incidence of cancer in dogs, relative to other domesticated animals, may be attributed to their intimate companionship with humans, advanced medical diagnostics, and elevated healthcare standards that have extended their lifespans beyond typical expectations, albeit accompanied by a heightened susceptibility to cancer. Effective diagnosis and treatment of canine cancer hinge upon a comprehensive understanding of tumor varieties, their underlying pathophysiology, and molecular alterations affecting genes and proteins. A range of diagnostic tools is employed for detecting cancer in dogs, encompassing blood profiles, cytological evaluations, histopathology, immunohistochemistry, and various imaging methods such as computed tomography, magnetic resonance imaging, positron emission tomography, and single-photon emission computed tomography. Additionally, molecular techniques play a crucial role. Therapeutic options for addressing canine cancer encompass chemotherapy, surgical procedures, and radiation therapy. Furthermore, promising developments including cancer vaccines and novel anti-cancer medications are currently undergoing clinical trials, aiming to enhance the management of cancer in dogs. This article provides an overview of both current and emerging diagnostic and treatment approaches, whether currently available or in the experimental stage, for effectively managing cancer in dogs.

Keywords: Dog cancers, Cancer biomarkers, Cancer vaccines, Chemotherapy, Nanoparticles, Surgery

1. INTRODUCTION

The term "tumor" denotes the uncontrolled growth and proliferation of cells, often resulting from the loss of contact inhibition phenomena (Lisanti *et al*., 2010). The alteration in DNA due to several factors leads to the development of cancers (Fig. 1). In the canine world, cancer is a pressing health issue, affecting approximately four million dogs annually (Gardner *et al*., 2016). Tumors are classified into two primary categories: benign and malignant (Sarver *et al*., 2022). Benign tumors remain localized at their site of origin and refrain from invading surrounding tissues, blood vessels, or lymph nodes. In contrast, malignant tumors display invasive behavior, spreading to nearby tissues, blood vessels, or lymph nodes. Malignant tumors are commonly referred to as "cancer" (Chow, 2010). The incidence of cancer in dogs is influenced by several predisposing factors, including breed, gender, age, and geographical location. Older dogs, particularly those aged ten or older, exhibit a higher susceptibility to cancer (Gardner *et al*., 2016). Gender also plays a role, with female dogs experiencing a higher incidence due to the prevalence of mammary cancer (Merlo *et al*., 2008).

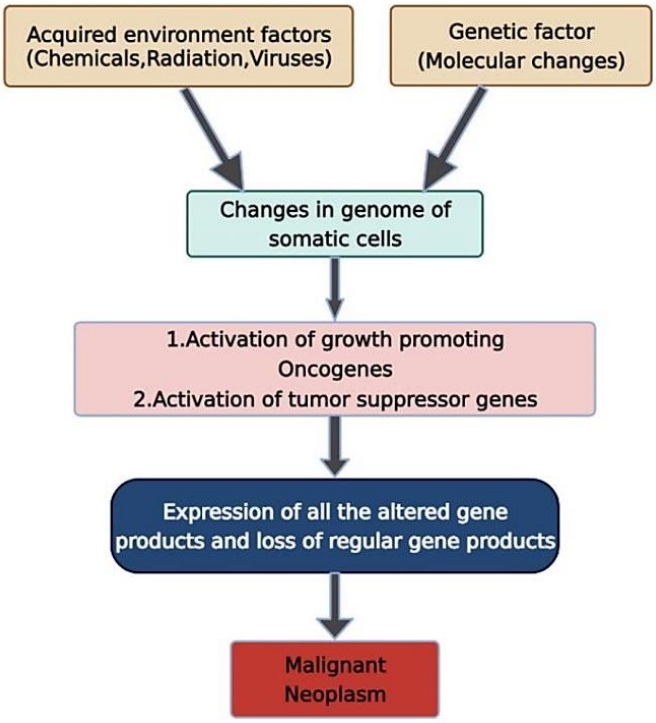

Fig. 1. Cancer development. Overview of factors and mechanisms inducing development of neoplasm

Specific dog breeds are at a higher risk of developing particular types of cancers (Table 1) (Raghavan *et al*., 2005; Dobson, 2013; Erich *et al*., 2013; Seim-Wikse *et al*., 2013; Edmunds *et al*., 2021; Labadie *et al*., 2022). Common tumor types include meningiomas, gliomas, hemangiosarcoma, pituitary tumors, lymphoma, metastatic carcinoma, and histiocytic sarcoma (Fig. 2) (McGrath, 1962; Song *et al*., 2013). The accurate and early diagnosis of cancers is very important to choose appropriate therapeutic measures. At present, a wide range of diagnostic and therapeutic considerations are available for the management of cancers in dogs. This review article summarized different diagnostic and therapeutic considerations in dog cancers including both traditional as well as more advanced ones.

Table 1. Dog breeds with a higher incidence of certain cancers

Dog breed	Susceptibility for cancer
Boxer	Mast-cell cancer and Gliomas
Rottweilers and Greyhounds	Osteosarcoma
Golden Retrievers	Lymphoma and Osteosarcoma
Scottish Terriers	Transitional-cell carcinoma of the bladder
Flat-Coat Retrievers, Bernese	Histiocytic sarcomas

Mountain Dogs	
Chow Chows	Gastric carcinoma and Melanoma.

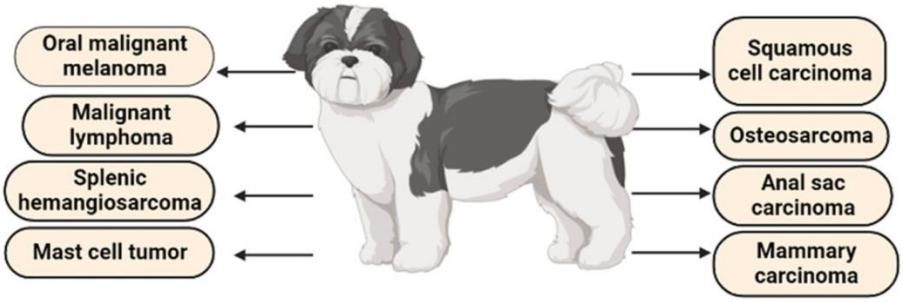

Fig. 2. Common cancers in dogs. The highly prevalent common cancers in dogs irrespective of their breeds.

2. DIAGNOSTIC JOURNEY: FROM BLOOD PROFILING TO MOLECULAR TOOLS

Accurate and timely cancer diagnosis plays a pivotal role in enabling clinicians to select appropriate treatment modalities (such as surgery, chemotherapy, radiation therapy, etc.), thereby influencing the cancer prognosis. The process of diagnosing a suspected cancer case commences with a comprehensive patient history review and a thorough physical examination of the canine, encompassing meticulous scrutiny for any external growths on the dog's body surface, alongside hematological and biochemical profiling—a straightforward and economically viable testing procedure. Nonetheless, these diagnostic assessments are rudimentary and cannot provide definitive and early confirmatory diagnosis. Certain cancers manifest subtly, necessitating more advanced diagnostic techniques such as cytology, histopathology, detection of cancer biomarkers, immunohistochemistry, molecular tools (such as PARR assay for diagnosis of lymphoma), flowcytometry (for detection of the type of cancer), etc. (Fig. 3 & Fig. 4). These diagnostic modalities are discussed below in succeeding sections.

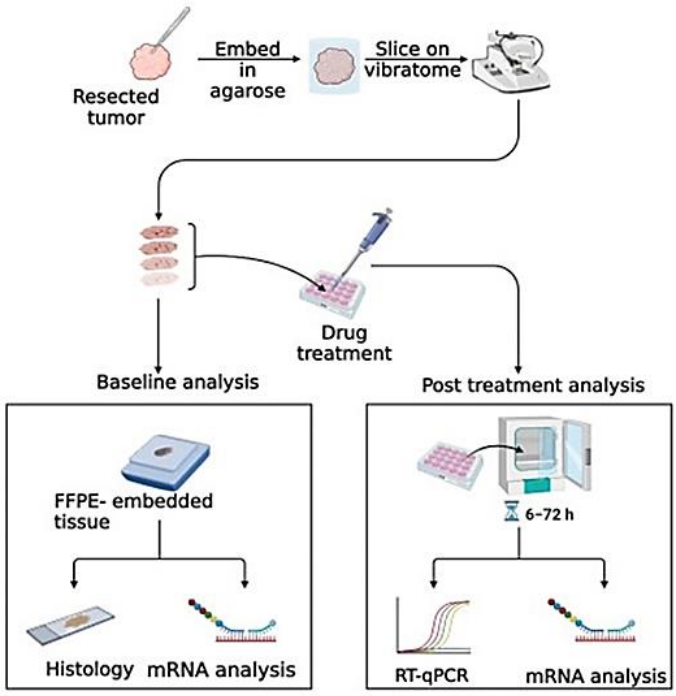

Fig. 3. Overview of tumor analysis. Common methodologies applied across different labs for analysis of tumors

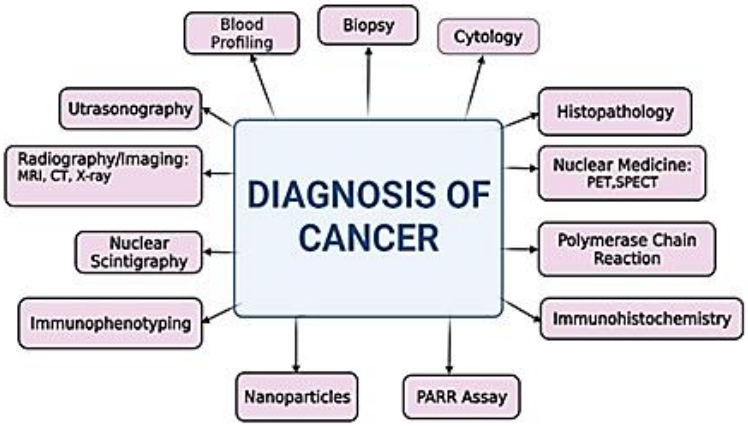

Fig. 4. Diagnosis of cancer. Different sets of techniques available for diagnosis of cancers in different settings

2.1 Blood Profiling

Blood profiling includes both hematological (blood cells and bone marrow) and biochemical examination. Blood profiling is crucial to diagnose blood malignancies, particularly leukemia. Before approaching another diagnosis, the initial complete blood count of a dog can provide valuable details about the overall health of the patient and potential recommendations for

further investigation (Wilson-Robles *et al*., 2020). In this test, blood cancers are diagnosed by assessing the number of blood cells or abnormal cells whether increasing or decreasing in blood. Later, a bone marrow biopsy can help in confirming the diagnosis of blood cancer.

The VDI TKcanine+ test measures thymidine kinase (TK1) and canine C-reactive protein (cCRP) levels, shedding light on both cancer and inflammation. The Nu.Q Vet Cancer test detects nucleosomes, a marker associated with various cancers, including lymphoma and hemangiosarcoma (McAnena *et al*., 2017).

2.2 Cytological Examination

Cytology involves the microscopic examination of cells obtained through fine needle aspiration (FNA) or smear impression. It offers fundamental information about tumor type and assists in classifying tumors as mesenchymal or epithelial in origin (Ayele *et al*., 2017). Cytological examinations have numerous advantages, including minimal sample requirements, no need for sophisticated equipment, and the ability to perform tests without sedation or anesthesia. Veterinarians often use cytology for on-the-spot assessments to determine the necessary steps (Chibuk *et al*., 2021). The section covers cytological examination applications, sensitivity, and specificity for various cancers.

2.3 Biopsy

Biopsies involve the microscopic examination of tissue samples obtained through various techniques for cancer diagnosis (Howlett *et al*., 2016). A biopsy sample should ideally contain both normal and tumor tissue to evaluate microscopic invasiveness accurately. The fast and cost-effective fine needle aspiration biopsy technique, which does not require anesthesia, is highlighted. The importance of histological evaluation in mammary tumor diagnosis is discussed, emphasizing its gold standard status. Liquid biopsy, a non-invasive technique, detects circulating tumor DNA (ctDNA) in the blood. Its applications in diagnosing urinary tract cancers and c-kit gene mutations in mast cell tumors are examined (Schillaci *et al*., 2019). The concept of ctDNA, its significance, and its potential use for early cancer detection are explored. Liquid biopsy's role in challenging cases where tissue biopsies are impractical, such as lung and brain cancers, is emphasized (Flory *et al*., 2022).

2.4 Histopathology

Histopathology involves the examination of excised tissue samples under a microscope after various processing steps. This method provides detailed insights into tissue architecture and is particularly valuable for distinguishing between benign and malignant tumors (Withrow *et al*., 2013). Histological examination is considered the gold standard for cancer diagnosis and provides a definitive diagnosis compared to cytological methods. Pathologists identify tumor cell histogenesis based on microscopic features, such as nuclear shape, cytoplasmic characteristics, and the presence or absence of stromal components (Prasad *et al*., 2021). Histochemical stains, including methyl green, toluidine blue, and periodic acid-Schiff, are commonly employed to determine the cell of origin in cancer development. While histopathology offers unparalleled accuracy, it requires substantial time for tissue fixation and preparation, particularly in the case of bone tumors necessitating decalcification. In contrast, cytopathology through fine needle puncture allows for quicker diagnoses.

2.5 Immunohistochemistry (IHC)

IHC is a valuable adjunct to histopathology, aiding in the confirmation of histological diagnoses and determining the origin of poorly differentiated tumors. IHC involves the use of labeled monoclonal or polyclonal antibodies to identify specific antigens on cell surfaces. These antibodies bind to target antigens, forming antibody-antigen complexes that can be visualized, often using enzyme-based reactions or fluorophores (Berg and Fishman, 2020). In cancer diagnosis, IHC helps pathologists verify histological diagnoses made from standard stained sections. It also plays a crucial role in identifying the cell of origin for poorly differentiated tumors. Specific biomarkers, as listed in Table 2 (Altmannsberger *et al*., 1985; Ramos-Vara *et al*., 2007; Rao, 2010; Nieves *et al*., 2014; Paździor-Czapula *et al*., 2015; Usman *et al*., 2021), assist in characterizing various cancers.

Table 2. Tumour markers that are commonly identified using IHC

Marker (antigen)	Significance and usage
Vimentin	Identifies all mesenchymal cells. Often used to help confirm diagnosis of a tumour of mesenchymal origin.
Cytokeratin	Identifies most epithelial cells. Often used to help confirm diagnosis of a tumour of epithelial origin
CD3	A marker of T-cell origin. Together with CD79a, used to help distinguish between T- and B-cell lymphomas.
CD79a	A marker of B-cell origin. Used in a similar manner to CD3. Most plasma cells do not express CD79a, making it of less use in diagnosing plasmacytomas
CD18	A marker of leucocytes. Very useful in helping to diagnose tumours of monocyte/macrophage origin.
Desmin	A marker of muscle origin. Is expressed in most tumours of smooth muscle or striated muscle origin.

2.6 Radiographs/Imaging

Radiographic and imaging techniques have evolved significantly, offering diverse modalities for cancer detection. Conventional methods, such as X-ray, ultrasonography (USG), CT-scan, and magnetic resonance imaging (MRI), provide information on cancer location, anatomical changes, and tissue appearance alterations (Edmunds *et al*., 2021). Functional imaging techniques, including dynamic CT, functional MRI, PET, SPECT, contrast-enhanced ultrasound, and more, detect cancers at earlier stages by assessing pathophysiological changes within tumors. These changes encompass altered blood flow, increased glucose metabolism, and changes in cellularity (Marcus *et al*., 2009; Bai *et al*., 2023). Functional imaging also supports monitoring the therapeutic response in cancer patients.

2.7 Immunophenotyping

Immunophenotyping relies on flow cytometry (FC) to identify and categorize cell populations based on specific protein expression. FC rapidly and accurately assesses the presence or absence of cell-surface markers (Song *et al*., 2012). While immunophenotyping is valuable in diagnosing various diseases, including blood malignancies like lymphoma and leukemia, it is often used in conjunction with other diagnostic tools (Ghisleni *et al*., 2006). FC enhances the accuracy of diagnosis by evaluating cell lineage, antigen levels, clonality, and minimal residual disease. It is also instrumental in monitoring treatment responses and aiding in the development of new therapeutic strategies (Ghisleni *et al*., 2006; Kruse *et al*., 2014).

2.8 Molecular diagnosis

In response to limitations associated with conventional diagnostic techniques like imaging, histology, and biochemical evaluation, molecular and immunophenotyping methods have gained prominence for early-stage cancer diagnosis. These methods are facilitated by user-friendly molecular analysis tools, enabling applications in cancer diagnosis, staging, immunophenotyping, and the detection of minimal residual disease (MRD) genes (Regan, 2017). Notable molecular tools in cancer diagnosis include PCR-based detection of c-kit gene mutations, PARR assay for lymphoma detection (Burnett *et al*., 2003), real-time PCR for identifying low BRCA2 gene expression in canine mammary tumors (Yoshikawa *et al*., 2015), and FISH for detecting BCR-ABL chromosomal abnormalities in chronic myeloid leukemia (Culver *et al*., 2013). These tools have significantly contributed to accurate early cancer diagnosis and represent the evolution of cancer diagnostic techniques (Mochizuki *et al*., 2015; Settawongsin *et al*., 2016).

3. THERAPEUTICS FOR DOG CANCERS

Effective therapeutic strategies for treating dog cancers encompass chemotherapy, surgery, radiation therapy, immunotherapy, electro-chemotherapy, gene therapy, and nanoparticles (Fig. 5) (Rassnick *et al*., 2000). Each of these therapeutic approaches is discussed below.

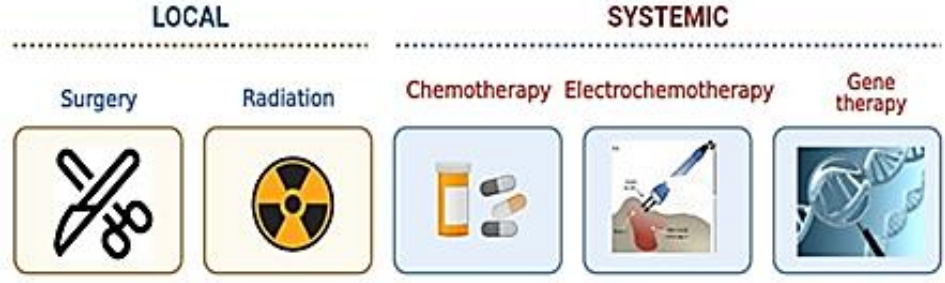

Fig. 5. Methods of cancer therapy. Various modalities available to the clinicians/researchers for therapeutic interventions against different cancers

3.1 Chemotherapy

Recent decades have witnessed significant progress in canine cancer chemotherapy, targeting rapidly dividing cells. While these drugs effectively kill cancer cells, they also harm rapidly dividing normal cells, leading to side effects such as nausea, vomiting, and anemia (Kamble *et al*., 2021). Noteworthy drugs include Toceranib phosphate (Palladia®, Zoetis) for

mast cell tumors, Vinorelbine for various malignancies, and histamine-receptor blockers like diphenhydramine. Combination therapy, such as cyclophosphamide, vincristine, and prednisolone, is used for multicentric lymphoma (Addissie and Klingemann, 2021). Chemotherapy is administered through three methods. First, conventional chemotherapy follows maximum-tolerated doses, leading to serious complications. Second, metronomic chemotherapy, administered continuously at low doses, offers unique benefits including anti-angiogenic properties and fewer side effects. Third, targeted chemotherapy, such as tyrosine kinase inhibitors like Toceranib phosphate and Masitinib mesylate, focuses on specific cellular pathways (Simeonov and Stoikov, 2006). Tyrosine kinase inhibitors target abnormal cell proliferation and have shown promise in treating canine cancers, with drugs like Ibrutinib (Imbruvica®) approved for various hematopoietic malignancies (Robak *et al*., 2022). Verdinexor (KPT-335) inhibits nuclear export protein Exportin 1 in canine osteosarcoma (Breitbach *et al*., 2021), while STA-1474 has exhibited biological activity in dogs with various tumors (Weissleder *et al*., 1989).

3.2 Surgery

Surgical interventions aim to remove tumors with surrounding healthy tissue. Factors like tumor type, location, and invasiveness dictate surgical approaches. These include complete tumor removal, debulking (if total removal poses risks), and alleviating pain due to tumor pressure. Surgical interventions may complement chemotherapy for better prognosis (Nordlinger *et al*., 2009). Achieving curative-wide surgical margins (>5cm) is crucial to prevent tumor recurrence (Hao *et al*., 2018).

3.3 Radiation Therapy

Radiation therapy is an increasingly accessible treatment option, using ionizing radiations like X-rays, gamma rays, electron beams, or protons. These radiations harm cancer cells or alter their genetic makeup, leading to cell death. It is used as a standalone treatment for certain tumors like skin cancers, prostate carcinomas, and lymphomas, but often works best when combined with surgery or chemotherapy. Radiation therapy has shown success in treating mast cell tumors, lymphomas, and thymoma (Meleo, 1997; Ladue *et al*., 1998; Mayer, 2006). In some cases, radiation therapy can reduce tumor size and improve neurological symptoms, as seen in pituitary tumors (Dow *et al*., 1990; Bley *et al*., 2005; Mayer, 2006). However, the prognosis depends on the tumor's severity, histopathologic grade, clinical stage, location, and the patient's overall health. Side effects may manifest after treatment completion (Bateman *et al*., 1994).

3.4 Immunotherapy for Canine Cancer

Immunotherapies designed to harness the immune system's potential to combat tumors and employ tumor-associated antigens as vaccines have emerged as a promising approach in canine oncology. In particular, CD4+ and CD8+ T cells play pivotal roles in orchestrating anticancer immune responses (Hammerstorm *et al*., 2011).

One notable example of an anticancer vaccine is sipuleucel-T, FDA-approved for prostate cancer treatment in humans. It consists of autologous T-lymphocytes incubated with a fusion protein linking a common prostate cancer antigen (prostatic acid phosphatase) to an adjuvant (granulocyte-macrophage colony-stimulating factor) (Hammerstorm *et al*., 2011). In dogs, the USDA-approved Oncept vaccine, a DNA vaccine, is used specifically to treat stage II or III oral melanoma (Wouda *et al*., 2015). Further enhancing T-lymphocyte efficacy, researchers are exploring chimeric antigen receptors (CARs) that specifically recognize

tumor-associated surface antigens. Although the FDA has approved six CAR T-cell treatments for human blood malignancies, such as lymphomas and leukemias, the application of CAR-T cells in canine cancer treatment is still in its early stages (Lucroy *et al*., 2020).

Natural Killer (NK) cells, which are gaining attention as cellular therapeutics for canine cancer, hold potential as well (Comiskey *et al*., 2018). While only one clinical trial using NK cells in dogs has been reported to date, it yielded promising results. In this trial, NK cells were isolated from blood lymphocytes, and dogs with locally advanced, non-metastatic osteosarcoma received radiation followed by intra-tumor NK cell injections. Some dogs also received human IL-2. Tumor shrinkage was observed, with no pulmonary metastasis in 5 out of 10 patients at the 6-month endpoint (Stoica *et al*., 2009). The combination of pre-treatment radiation with NK cell therapy enhances its antitumor effects, inducing adhesion molecules on tumor cells that bind to NK cells. Additionally, intra-tumor injection of NK cells has demonstrated efficacy in inducing tumor regression and lasting responses (Suzuki *et al*., 2018).

Researchers are exploring various avenues, including the development of a Listeria vector vaccine for osteosarcoma in both dogs and humans. This vaccine uses an attenuated strain of Listeria monocytogenes carrying tumor-associated antigens. Attenuated Listeria strains are preferred for their ability to trigger potent CTL (cytotoxic T lymphocyte) responses (Oladejo *et al*., 2021). This vaccine is currently undergoing clinical trials and has shown promise in treating malignancies.

3.5 Electro-Chemotherapy (ECT)

Electrochemotherapy (ECT) is an innovative treatment approach that aims to enhance the uptake of chemotherapy drugs within tumor cells by applying electric pulses. These electric pulses significantly increase drug toxicity and efficacy, potentially by up to 1000 times (Probst *et al*., 2018). ECT has demonstrated remarkable effectiveness against various tumors, particularly those located in or just under the skin, including melanoma, squamous cell carcinoma, soft tissue sarcomas, and localized cutaneous lymphoma in dogs (Yeom *et al*., 2021).

ECT was first introduced in veterinary medicine in Europe in 1997 (Tellado *et al*., 2022). A study comparing ECT to surgery for mast cell tumors in dogs found that ECT achieved complete responses in 70% of patients, while surgery achieved complete responses in only 50% of cases, highlighting ECT's efficacy as a treatment comparable to surgery (Leibman *et al*., 2001).

ECT is particularly effective in cases of drug-resistant tumors, as it enhances the permeability of tumor cell membranes to chemotherapy drugs (Tellado *et al*., 2022). Commonly used drugs in electrochemotherapy include bleomycin and cisplatin (De Virgilio *et al*., 2018). Unlike physical methods like surgery, high-frequency focused ultrasound, hyperthermia, or radiotherapy, which cannot differentiate between malignant and healthy cells, ECT offers a precise and selective approach to killing tumor cells when combined with electro-permeabilization and appropriate drugs (Vižintin *et al*., 2021).

ECT has been successfully applied in the treatment of various primary cancers and metastases in both dogs and cats (Tozon *et al*., 2016). It can be used as a curative treatment or as an adjunct to surgery for solitary, multiple, or subcutaneous tumor nodules. Recent developments in electrode designs and technological breakthroughs show great

promise in treating deep-seated cancers through electro-chemotherapy (Tozon *et al*., 2016). While ECT achieves up to 80% local tumor control, its impact on distant metastases is limited (Kotnik *et al*., 2019). Thus, combining ECT with other therapies may be necessary to achieve a systemic response.

3.6 Gene Therapy in Canine Cancer

Gene therapy has emerged as a promising approach in treating cancer, targeting both inherited and somatic mutations in proto-oncogenes and tumor suppressor genes (Matlashewski *et al*., 1984; Wiman, 1993; Vogelstein *et al*., 2000; Shanker *et al*., 2011). The core idea behind gene therapy is to replace defective genes with functional copies, thereby restoring normal cellular function. Compared to other treatment modalities, gene therapy offers a more specific approach (Das *et al*., 2015).

The foundation for gene therapy was laid in the 1960s when it was observed that viruses could integrate their genetic material into the genomes of infected cells, potentially leading to malignant transformation. Edward Tatum outlined the therapeutic potential of using viruses for genetic modification of somatic cells in 1966 (Das *et al*., 2015). Various approaches are under investigation for gene therapy in cancer treatment, including: a) Expressing genes to induce apoptosis or increase tumor sensitivity to conventional therapies. b) Introducing wild-type tumor suppressor genes to compensate for their loss or deregulation. c) Using antisense (RNA/DNA) techniques to prevent oncogene expression. d) Enhancing tumor immunogenicity to promote immune cell activity (Das *et al*., 2015).

Viruses, particularly morbilliviruses and adenoviruses, have been widely studied as vectors for gene therapy due to their restricted host range and the availability of species-specific subtypes (Arendt *et al*., 2009). The mechanism of action of gene therapy against cancer cells using adenovirus is illustrated in Fig. 6. However, it's important to consider the toxicity associated with viral vectors in gene therapy (Arendt *et al*., 2009).

Clinical trials have shown promise, with nine lung cancer patients directly injected with a retroviral vector containing the p53 gene exhibiting tumor regression in some cases (Roth *et al*., 1996). Similarly, intratumoral injection of an adenovirus vector encoding wild-type p53 complementary DNA (Ad-p53) led to tumor regression in preclinical investigations in animal models (Swisher *et al*., 1999). The use of interleukin-12 (IL-12) gene therapy has demonstrated potent anticancer effects in various tumors in animal models (Cross and Burmester, 2006; Pavlin *et al*., 2012). While the results of ongoing clinical trials for gene therapy in cancer treatment are promising, further validation is required before it can be widely used in the treatment of cancer in both dogs and humans.

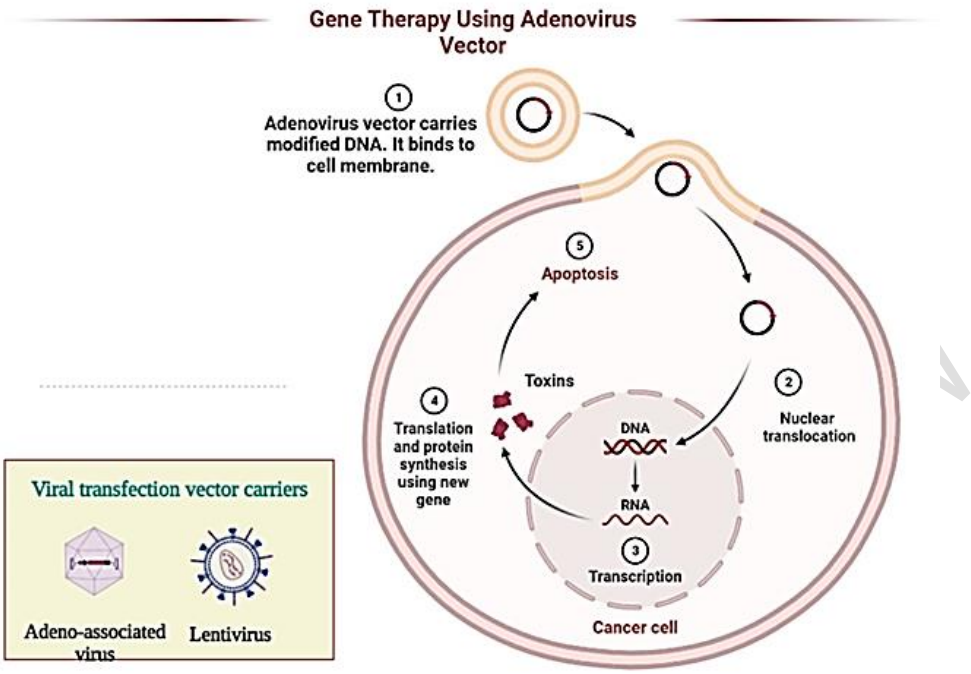

Fig. 6. Gene therapy for treatment of cancer using adenovirus vector. Different viruses are being tested for viral-vector based gene therapy modalities. These vectors may carry therapeutic transgene to target and eliminate cancer cells

3.7 Nanoparticles in Cancer Therapy

Nanoparticles have shown significant potential in cancer treatment, primarily as vehicles for the targeted delivery of chemotherapy drugs to tumor sites. Key properties of nanoparticles, including size, charge, and surface chemistry, impact their uptake, intracellular fate, and cytotoxicity (Abbasi *et al*., 2023).

Nanotechnology's role in cancer treatment is still in its early stages of research and development. Promising clinical trials have been conducted with hyaluronan cisplatin nanoparticles, nanocrystals of cisplatin, and paclitaxel for the effective treatment of various canine cancers, such as oral melanoma, oral sarcoma, and anal gland adenocarcinoma (Zabielska-Koczywas and Lechowski, 2017).

One noteworthy example is liposome-encapsulated muramyl tripeptide-phosphatidylethanolamine (L-MTP-PE), a synthetic analog of muramyl tripeptide found in mycobacterium cell walls (Nardin *et al*., 2006). L-MTP-PE enhances the anticancer activity of monocytes and macrophages by inducing the release of inflammatory cytokines such as TNF-α and IL-6 (Asano and Kleinerman, 1993). Clinical trials in dogs with hemangiosarcoma have shown significantly longer survival periods for those receiving L-MTP-PE compared to dogs receiving chemotherapy and placebo liposomes (Barnes *et al*., 2022). Mifamurtide, a liposomal muramyl tripeptide phosphatidyl ethanolamine, is licensed in Europe for the treatment of cancers in humans (Barnes *et al*., 2022).

Other liposome-based nanoparticles have been employed for delivering various chemotherapy drugs, including curcumin, doxorubicin, cisplatin, and untargeted tumor RNA (Ambrosio *et al*., 2022). Additionally, doxorubicin conjugated to glutathione-stabilized gold nanoparticles demonstrated higher cytotoxicity against canine osteosarcoma cell lines compared to the free drug (Malek *et al*., 2021).

Although several studies have explored nanoparticle-based cancer therapies in dogs, none of these nano-drugs are currently FDA-approved for canine cancer treatment. In contrast, a few nano-drugs have gained approval for cancer treatment in humans in the USA and Europe (Dang and Guan, 2003).

4. CONCLUSION

Dogs face a heightened susceptibility to cancer compared to other domesticated animals, mirroring the cancer incidence seen in humans. This presents a significant challenge for veterinary oncologists striving to effectively manage these malignancies in canines. Traditional diagnostic tools, such as X-rays, ultrasonography, cytology, and histopathology, prove effective in identifying larger tumors or those with evident structural and morphological changes. However, they fall short in detecting early-stage, cell-originating, or inconspicuous cancers. To overcome these limitations, advanced diagnostic techniques, including functional imaging methods, molecular tools, and immunophenotyping, play a crucial role.

In the realm of canine cancer treatment, three primary avenues—chemotherapy, surgery, and radiation therapy—are at the disposal of veterinary professionals. The most remarkable outcomes are achieved when these modalities are combined rather than used in isolation. Nonetheless, these therapies lack the ability to distinguish between healthy and cancerous cells. In contrast, cutting-edge therapeutic approaches like electrochemotherapy (ECT), gene therapy, cancer vaccines, and nanoparticle-based treatments show promise in precisely targeting and eliminating cancer cells while sparing healthy ones. However, the majority of these advanced therapeutic techniques are still in various stages of clinical trials, holding the potential to revolutionize canine cancer management in the future.

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