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Review Article

CLINICAL APPLICATION OF ELECTRON BEAM THERAPY IN VETERINARY MEDICINE

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ABSTRACT

Electron beam radiotherapy is a teletherapy technique utilizing megavoltage electron beams produced by a linear accelerator. These electrons interact with tissue, reaching their maximum dose at shallow depths and rapidly decreasing beyond the target area, minimizing radiation exposure to distal tissues and organs. The clinical application of high-energy electron beams (up to 20 MeV) allows for effective treatment of superficial tumors while preserving deeper healthy tissues. Due to these advantages, electron beam therapy plays a crucial role in both human and veterinary oncology. In veterinary oncology, radiotherapy has become an essential modality for tumor treatment, with two primary techniques: teletherapy and brachytherapy. Teletherapy, including electron beam radiation, is the most commonly used approach in veterinary radiotherapy, offering significant advantages in treating superficial tumors while minimizing radiation exposure to surrounding healthy tissues. Recent studies highlight the growing role of electron beam therapy in the management of tumors in dogs and cats, particularly for oral tumors, soft tissue sarcomas, mast cell tumors, nasal carcinomas, and brain tumors. Additionally, hypofractionated radiation protocols (8–10 Gy per fraction, with total doses of 16–30 Gy) have been explored for palliative treatment in companion animals with short life expectancy, where the risk of late radiation side effects is low. This technique provides symptom relief and improves the quality of life for affected animals. Despite advancements in veterinary radiotherapy, treatment outcomes depend on factors such as total radiation dose, fractionation schedule, and tumor type. While electron beam radiotherapy has demonstrated efficacy in various oncological applications, further studies are needed to optimize treatment protocols and enhance long-term tumor control while minimizing adverse effects.

Keywords: Megavoltage radiation, Linear accelerator, Superficial tumors, Veterinary oncology

INTRODUCTION

Electron beam radiotherapy is a teletherapy technique that utilizes megavoltage electron beams produced by a linear accelerator. The essence of this teletherapy technique lies in the interaction of electrons with tissue, where electrons rapidly (at shallow tissue depths) reach their maximum dose, which then decreases rapidly. Megavoltage electrons have the property of a short range and do not deliver significant radiation doses to distally located tissues. Therapy with megavoltage electron beams ensures relative dose uniformity from the body surface to a specific depth of target tissues, after which the dose rapidly declines to negligibly small, almost zero values, resulting in minimal irradiation of distal tissues and organs. The treatment depth is controlled by selecting the appropriate radiation energy and, if necessary, applying a bolus. The clinical application of high-energy electron beams up to 20 MeV enables effective radiotherapy of pathological changes located from the body surface to approximately 6 cm in depth, preserving deeper healthy tissues and organs. Therefore, megavoltage electron beam therapy is suitable for treating superficial tumors (Valve et al., 2023). From this perspective, this type of teletherapy has a significant clinical advantage over other forms of radiotherapy. Fletcher (1976) states that there is no alternative to electron beam therapy and that even the strongest advocates of photon radiation therapy acknowledge that electron beam teletherapy is essential for completing every radiotherapy program.

Electron beam therapy is widely used in human medicine for treating skin and lip cancer, upper respiratory and digestive tract tumors, head and neck tumors, breast cancer, and various other localizations (Placidi et al., 2024).

Treated skin areas included the eyelids, nose, and auricle, scalp, and widespread skin conditions such as melanoma and lymphoma affecting entire limbs (Wooden et al., 1996) or the entire skin in cases of mycosis fungoides (Jones et al., 1995).

The treated areas of the upper respiratory and digestive tract included the floor of the mouth, soft palate, retromolar region, and salivary glands (Wang, 1991).

Chest treatments included irradiation of the chest wall after mastectomy (Perkins et al., 2001) as well as irradiation of corresponding lymph nodes, such as internal mammary nodes and, less frequently, axillary nodes, and their post-surgical treatment following mastectomy or lymphadenectomy (Shrivastava et al., 2013).

In addition to the aforementioned application sites of megavoltage electron beams, this teletherapy technique has also been used for treating malignant changes in the retina (Hogstrom et al., 2017), orbit (Donaldson & Findley, 1991), spine (craniospinal irradiation), paraspinal muscles, pancreas,

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and other abdominal organs (intraoperative radiotherapy), vulva and cervix (intracavitary radiotherapy) (Park et al., 2016).

CLINICAL APPLICATIONS

Radiotherapy in Veterinary Oncology of Small Animals

Radiotherapy is becoming widely available for the treatment of tumors in veterinary patients. In veterinary oncology, two primary radiotherapy techniques are distinguished—teletherapy and brachytherapy (Šehić, 2002).

Brachytherapy is the therapeutic use of radioisotopes, which are applied to the tumor surface, implanted within tumors, or systemically administered to accumulate in a specific organ or tumor. This technique mainly involves beta and gamma radiation (e.g., strontium-90, gold-198, iridium-192, cesium-137, iodine-125, iodine-131, and phosphorus-32). The primary advantage of brachytherapy is the ability to deliver higher radiation doses directly to malignant tissues, thereby minimizing unwanted irradiation of surrounding healthy tissues. Interstitial brachytherapy, which involves implanting temporary or permanent high-energy radioactive sources within the tumor, is one method of this technique. However, such implants pose a radiation hazard to anyone in contact with the patient, making this aspect of interstitial brachytherapy a practical challenge and limiting its availability and application in veterinary oncology (Farrelly & McEntee, 2003).

Teletherapy, or external beam radiation therapy (EBRT), is described as radiation therapy using a radiation beam directed from a source positioned at a certain distance from the patient. This technique represents the most commonly used clinical approach to radiotherapy in veterinary oncology. Teletherapy techniques include the use of orthovoltage X-ray devices and megavoltage sources such as cobalt-60 and linear accelerators (Šehić, 2002; Farrelly & McEntee, 2003).

Orthovoltage X-ray radiation is based on the same principles of radiation beam production as conventional diagnostic X-ray devices, with beam energies ranging from 150 to 500 kV. When this type of radiation beam interacts with a patient, the maximum radiation dose is deposited in the skin, with a tendency for rapid dose attenuation as the beam penetrates deeper tissues. Consequently, this technique has been used primarily for the radiotherapy of superficial tumors. However, it also results in higher radiation deposition in tissues with a high atomic number, such as bone, which can lead to undesirable radiation-induced bone damage. Additionally, the deposition of maximum radiation doses on the skin intensifies radiation-induced skin reactions. Over recent decades, megavoltage radiotherapy, utilizing cobalt-60 and linear accelerators, has largely replaced orthovoltage radiotherapy in veterinary oncology (Farrelly & McEntee, 2003).

Megavoltage radiotherapy involves the use of high-energy photon and electron beams, typically in the megavolt (MV) range. High-energy photon beams have greater tissue penetration capability,

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enabling the treatment of deeply situated tumors. Megavoltage radiotherapy allows for the deposition of the maximum radiation dose at a specific depth below the body surface (Table 1), thereby reducing skin damage side effects. This technique includes the application of cobalt-60 and linear accelerators (LINAC), with the main difference between them being the method of radiation production. Machines using cobalt-60 generate radiation through its radioactive decay, requiring source replacement approximately every five years. Linear accelerators, on the other hand, produce high-energy electron beams across a range of energies. For example, a 6-MV linear accelerator can generate six different electron beams ranging from 5 to 14 MeV.

Electron beam radiation is characterized by low penetration and a uniform distribution within tissues, making it particularly useful for radiotherapy of superficial tumors such as skin cancers. Additionally, electron beam radiotherapy is frequently employed in veterinary oncology for postoperative treatment of patients with relatively superficial residual microscopic disease associated with surgical scar tissue. The advantage of this teletherapy technique lies in the rapid dose fall-off with increasing tissue penetration depth (Table 1), ensuring that significant radiation doses are not delivered to adjacent or deeper healthy tissues, thereby preventing adverse effects on deeper normal tissues (Farrelly & McEntee, 2003).

Table 1: Approximate Depth Dose Distribution of Different Radiotherapy Techniques in Veterinary Medicine (Farrelly & McEntee, 2003).

Radiotherapy Type	Energy	Maximum Dose Depth (cm)	50% Dose Depth (cm)	25% Dose Depth (cm)
Orthovoltage X-rays	280 kV	Surface	7,5	11,8
Cobalt-60	1,25 MV	0,5	11,6	21
LINAC (Photons)	4 MV	1,0	14	25
	6 MV	1,5	15,6	28
LINAC (Electrons)	5 MeV	1,0	2	2,4
	8 MeV	1,5	3,2	3,6
	12 MeV	2	4,7	5,3

The goal of radiotherapy is to maximize tumor cell destruction without increasing the severity of radiotherapy side effects. Acute radiation effects may occur but are generally manageable without significant complications. However, late radiation effects are dose-dependent, and their likelihood increases with higher per-fraction doses. Radiotherapy protocols that use lower per-fraction doses reduce the risk of late effects, allowing for higher total doses and improved tumor control rates (Lundberg et al., 2022).

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When evaluating the outcomes of veterinary oncology radiotherapy, factors such as median survival and tumor control rates should not be the sole considerations. Long-term survival rates and the incidence of acute and late radiotherapy complications should also be assessed. Early veterinary studies using low total doses (Lazo et al., 2022) demonstrated poor long-term tumor control and short survival times, making late radiation effects rarely a concern. Treatment scheduling was primarily dictated by difficulties in repeatedly anesthetizing patients rather than radiobiological necessity, and reported acute radiation effects were generally mild and transient. The availability of newer, safer short-acting anesthetics now permits more frequent treatments with lower per-fraction doses, allowing for higher total doses while reducing individual fraction sizes (Debreuque et al., 2020). Differences in tumor control rates depend on the total dose, fraction size, and radiation course duration. Many veterinary radiation therapy studies have used relatively high per-fraction doses (≥ 4 Gy), delivered every other day (Monday, Wednesday, Friday) to moderate total doses (40–48 Gy) (Moore, 2002). Such coarse fractionation may provide good tumor control for radiosensitive tumors with moderate rates of late effects. Recent studies have explored the use of higher total doses (typically 3 Gy per fraction daily up to a total dose of 51–60 Gy) and long-term patient follow-ups, reporting sustainable control of various tumor types. These definitive fractionation protocols have shown curative potential for dogs with certain oral tumors, mast cell tumors, and brain tumors, as well as for dogs and cats with soft tissue sarcomas. The application of so-called hypofractionated radiation protocols, i.e., the delivery of very high fractions (8–10 Gy per fraction) with a moderate total dose of 16–30 Gy, has been described in the palliative treatment of companion animals with a short life expectancy, where the risk of late radiation side effects is therefore low. The most commonly described tumors in small animals include oral tumors, thyroid carcinoma, mast cell tumors (Cray et al., 2020), soft tissue sarcomas (Forrest et al., 2000), nasal carcinomas (Northrup et al., 2001), brain tumors, osteosarcomas, and cutaneous squamous cell carcinomas. The radiotherapy of these tumors has involved the less frequent use of orthovoltage X-rays and the more common application of megavoltage radiation, including electron beam radiotherapy, which has gained significance in clinical veterinary radiotherapy practice only in recent decades (Moore, 2002; Šehić, 2002).

RADIOTHERAPY OF TUMORS IN DOGS

Oral Tumors

In a study by Theon et al. (1997), a total megavoltage radiation dose of 48 Gy was used to treat 105 dogs with squamous cell carcinoma, fibrosarcoma, and oral melanoma. The three-year survival rates after treatment were 55% for squamous cell carcinoma, 40% for fibrosarcoma, and 20% for oral melanoma. Acute skin reactions were observed in 8% of dogs during the last week of fractionated treatment. In another study (Blackwood & Dobson, 1996), 36 dogs with oral melanoma were treated with megavoltage teletherapy at a total dose of 36 Gy. Tumor reduction

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was observed in all dogs, while 25 dogs achieved complete tumor remission. The median survival time was 21 weeks, with only 10 dogs surviving longer than one year. Observed acute radiation effects were moderate in severity.

Thyroid Carcinoma

A study by Theon et al. (2000) was conducted on 25 dogs treated with a total dose of 48 Gy, with 72% achieving complete tumor remission. Acute reactions were very common, mainly in the form of mucositis.

Mast Cell Tumors

A study by Al Sarraf et al. (1996) demonstrated that mast cell tumors were effectively treated with a total dose of 48–54 Gy in 3–4 Gy fractions per week following surgery, achieving a 90% cure rate. The tumor did not recur in the next three years. Acute radiation effects became visible as early as the first week after radiation therapy cessation.

Soft Tissue Sarcomas

Soft tissue sarcomas (STS) were traditionally considered radioresistant. However, higher total radiation doses have been shown to provide long-term tumor control in most dogs. In a study, 48 dogs with STS underwent a post-surgical extended fractionation regimen, receiving 3 Gy per fraction every other day up to a total dose of 63 Gy. One year after treatment, 86% of dogs were alive, and five-year survival was 76%. However, most deaths were unrelated to tumor progression. Acute effects were mild, eliminating the need for treatment delays. The only recorded late effect was an osteosarcoma that developed in the irradiated field six years after radiation (Forrest et al., 2000).

Nasal Carcinomas

Adams et al. (1998) described an accelerated radiotherapy protocol for nasal tumors in 21 dogs. A total dose of 42 Gy was fractionated into 9–10 fractions over 11–13 days. All treated animals exhibited acute radiation changes, including severe mucositis lasting up to five weeks, while one dog developed acute skin necrosis. Only 15 dogs survived six months post-treatment, and all experienced late effects such as blindness, osteonecrosis, and three deaths directly caused by therapy. Another study using an accelerated fractionation protocol (Thrall et al., 1993) treated 18 dogs with nasal tumors using a total dose of 48 Gy in 16 × 3 Gy daily fractions. After three days, an additional 3 Gy was administered daily for three days, resulting in a total dose of 57 Gy. Severe acute effects were observed in 11 of 18 dogs, including mucositis, desquamation, and edema. Two dogs died due to severe acute reactions in irradiated tissues. The high incidence of unacceptable

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acute effects likely resulted from the short overall treatment time, which did not allow for normal tissue healing.

In addition to the described radiotherapy treatments for various tumors in dogs, different radiotherapy protocols have also been used for brain tumors (Theon et al., 2000) and osteosarcomas (Ringdahl-Mayland et al., 2022). However, these publications did not extensively analyze acute tissue damage dynamics and severity.

RADIOTHERAPY OF TUMORS IN CATS

Radiation therapy in cats differs significantly from radiation treatment of malignancies in dogs in terms of both tumor response to therapy and normal tissue response to radiation (Moore, 2002). The probability of developing acute radiation-induced reactions in normal tissues is significantly lower in cats than in dogs when similar doses are applied. However, comparing late tissue reactions remains challenging. In cats, only a few tumor types allow for prolonged survival with radiotherapy. For example, oral tumors in cats are almost exclusively squamous cell carcinomas, which are characterized by poor radiosensitivity (Theon et al., 1995). Studies on the treatment of cutaneous squamous cell carcinoma (Theon et al., 1995) and soft tissue sarcomas with high total radiation doses are among the few extensive studies on cats that provide a clearer assessment of late radiotherapy effects. This suggests that in predicting radiotoxicity in cats, total dose size and fractionation protocol are less critical than the difficulty of protecting surrounding normal tissue (Moore, 2002).

Soft Tissue Sarcomas

Early studies (Dommert, 1961; Hilmas & Gillette, 1976; Odenall et al., 1983) reported very low efficacy of radiotherapy in reducing recurrence rates of soft tissue sarcomas in cats. More recent studies suggest aggressive surgical intervention combined with high-dose pre- or post-operative radiotherapy. Coarse fractionation was described in a study of 31 cats treated with orthovoltage radiation to a total dose of 52–60 Gy, administered in 4 Gy fractions three times per week after incomplete surgical excision. Acute skin toxicity was mild, but systemic acute side effects were severe, leading to euthanasia of six cats due to subsequent acute pneumonia and renal insufficiency caused by the adverse effects of orthovoltage radiotherapy on deeper tissues and organs. In such cases, electron beam therapy would likely have been the preferred choice, as it ensures rapid dose fall-off in deeper normal tissues. Cronin et al. (1998) studied megavoltage radiotherapy in 33 cats that received a preoperative total dose of 48 Gy over 16 days in 3 Gy fractions. Surgery was performed 2–4 weeks after radiotherapy, and the median survival time was 2.6 years. Acute skin reactions, including dry desquamation and transient pneumonia, were observed in only a few patients, but no late radiation effects were reported in any cat.

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Cutaneous Squamous Cell Carcinoma

A study on the effectiveness of orthovoltage treatment for squamous cell carcinoma of the facial skin in 90 cats, receiving a total dose of 40 Gy over 10 fractions, was described by Theon et al. (1995). Results showed that cats positive for the feline immunodeficiency virus were more prone to radiation-induced skin reactions, including severe ulceration, especially in cases of nasal tumors.

COMPARATIVE ANALYSIS

Electron Beam vs. Other Radiotherapy Techniques

When compared to other radiotherapy modalities, electron beam therapy offers unique advantages:

- Lower penetration depth, making it ideal for superficial tumors
- Sharp dose fall-off, minimizing radiation exposure to deeper tissues
- High precision, reducing the risk of late radiation effects

Orthovoltage radiation, which was traditionally used for superficial tumors, has been largely replaced by megavoltage radiotherapy due to its superior depth-dose distribution and reduced risk of radiation-induced complications.

Comparison with IMRT and Proton Therapy

- **Intensity-Modulated Radiation Therapy (IMRT):** IMRT provides highly conformal dose distribution by modulating beam intensity, making it superior for treating deep-seated tumors. However, IMRT delivers a low dose of scattered radiation to surrounding healthy tissues, which may lead to secondary malignancies over time. Unlike IMRT, electron beam therapy is optimal for superficial lesions where dose uniformity and sharp dose fall-off are essential.
- **Proton Therapy:** Proton therapy delivers precise radiation doses using charged protons, allowing for better dose deposition with minimal exit dose beyond the tumor. This makes it highly effective for deep-seated and complex tumors. However, its high cost and limited availability make it less practical for veterinary applications compared to electron beam therapy, which remains more accessible and cost-effective for treating superficial tumors in small animals.

FUTURE DIRECTIONS

Despite the proven benefits of electron beam radiotherapy, there is a need for further research to optimize:

- **Treatment protocols** to improve tumor control while minimizing side effects

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- **Fractionation schedules** to balance efficacy and safety
- **Combination therapies**, such as integration with chemotherapy or immunotherapy

Advancements in veterinary radiotherapy are expected to further refine treatment outcomes and expand indications for electron beam therapy in small animal oncology.

CONCLUSION

Electron beam radiotherapy represents an essential component of modern veterinary oncology. Its unique physical properties allow for effective treatment of superficial tumors while minimizing radiation exposure to deeper tissues. Future research should focus on optimizing treatment parameters to maximize therapeutic efficacy and minimize adverse effects, ensuring improved quality of life for veterinary patients.

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