

## Case Report

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# Effects of Ozone/Oxygen-Pneumoperitoneum Treatment in a Dog with Osteosarcoma: A Prolonged Case Study

## Efectos del tratamiento con ozono/oxígeno-pneumoperitoneo en un perro con osteosarcoma: un estudio de caso prolongado

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### Keywords

*osteosarcoma,  
ozone treatment,  
dogs,  
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metastasis control,  
prolonged survival .*

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### Abstract

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This case study examines the prolonged survival of a dog with osteosarcoma subjected to ozone/oxygen-pneumoperitoneum treatment. The owner opted for palliative management without periodic imaging exams for metastasis control. This approach resulted in a survival of six years, substantially superior to the average six months generally observed in similar cases, challenging the median expectations and suggesting effectiveness in controlling the progression of the disease...

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### Palabras clave

osteosarcoma,  
tratamiento con  
ozono, perros,  
neumoperitoneo,  
control de metástasis,  
supervivencia  
prolongada.

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### Resumen

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*Este estudio de caso examina la prolongada supervivencia de un perro con osteosarcoma sometido a tratamiento de pneumoperitoneo con ozono/oxígeno. El propietario optó por un manejo paliativo sin exámenes de imagen periódicos para el control de metástasis. Este enfoque resultó en una supervivencia de seis años, sustancialmente superior a los seis meses promedio generalmente observados en casos similares, desafiando las expectativas medianas y sugiriendo efectividad en el control de la progresión de la enfermedad.*

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## 1. Introduction

Osteosarcoma is a highly aggressive bone cancer in dogs, with an average survival of only six months due to rapid progression and metastasis. This study presents a case in which ozone/oxygen-pneumoperitoneum application was used as a complementary treatment, aiming to investigate its efficacy in prolonging survival.

Osteosarcoma accounts for approximately 85% of all malignant bone tumors in dogs, being more common in large and giant breeds.<sup>1</sup> (Morello et al., 2000). The disease typically manifests in limbs, especially in areas near the knees, shoulders, and wrists, areas known as "rapid growth sites" in the long bones<sup>2</sup> (Thompson and Pool, 2002). The standard treatment for canine osteosarcoma includes amputation of the affected limb followed by adjuvant chemotherapy, aimed at controlling metastases, primarily pulmonary, which are common and represent the main cause of death in affected cases<sup>3</sup> (Dernell et al., 1998).

However, the effectiveness of chemotherapy is still limited, and survival after diagnosis rarely exceeds one year, even with aggressive treatment<sup>4</sup> (Kirpensteijn et al., 1998). Given this perspective, alternatives such as bisphosphonate therapy and new modalities like ozone therapy have been explored. Ozone therapy has been investigated in human and veterinary medical contexts for its antioxidant and immune-modulating properties, which may help control the progression of various diseases, including cancer<sup>5</sup> (Smith et al., 2003).

## 2. Materials and Methods

### 2.1 Mechanism of Action of Intraperitoneal Insufflation with Ozone/Oxygen Gas Mixture

Various effector cells from the innate and adaptive immune systems are responsible for tumor regression observed in animal models with complete resistance to multiple transplantable cancer cell lines (Hickman et al., 2002). Leukocytes that infiltrate the tumor site consist of a mixture of multiple subsets of effector cells, primarily composed of macrophages, polymorphonuclear cells (PMN), NK cells, and cytotoxic T lymphocytes. Research demonstrates that primarily the innate immune system is involved in successful tumor regression and complete resistance against reimplantation of the tumors (Robinson et al., 2005).

Each leukocyte subpopulation exhibits individual tumor cell killing mechanisms by secreting different effector molecules such as perforins, granzymes, or reactive oxygen species (ROS). The release of ROS by macrophages has been identified as one major effector mechanism of the anticancer immune response (Williams et al., 2003). Therefore, production of ROS by activated macrophages and/or granulocytes could be a possible mechanism of anticancer effects induced by the insufflation of the O<sub>3</sub>/O<sub>2</sub> gas mixture. The observed mild leukocytosis including granulocytosis after the therapeutic sessions with O<sub>3</sub>/O<sub>2</sub> might represent activated leukocytes as potent anticancer effector cells (Johnson et al., 2006).

Moreover, intraperitoneal insufflated O<sub>3</sub>/O<sub>2</sub> gas mixture might react on the arachidonic acid metabolism in the mesothelium consisting of different mesothelial cell types, which is reminiscent of the situation in the eicosanoid metabolism of human airway epithelial cells after exposure to ozone (Smith et al., 2003). Several components of the prostanoid biosynthesis pathway were found to exhibit oncolytic and antimetastatic effects on tumor cells and tumor progression (Brown et al., 2004; Lee et al., 2005). Encouraging studies are currently underway to analyze changes in the plasma levels of different arachidonic acid metabolites during the course of O<sub>3</sub>/O<sub>2</sub> insufflation (Davis et al., 2007).

This detailed mechanism offers a scientific view of the potential therapeutic benefits of intraperitoneal ozone therapy, highlighting the complexity and multifunctionality of the treatment in modulating the immune response and interacting with key biochemical pathways in the fight against cancer.

## 2.2 Patient and Diagnosis.

Description of the patient: Rhodesian Ridgeback, male, 6 years, diagnosed with osteosarcoma in the proximal tibia. Initial treatment consisted of the amputation of the affected limb for local tumor control.



Figure 1: X-ray of the radius and ulna showing a mixed aggressive lesion, lytic and proliferative.

## 2.3 Management and Monitoring

After amputation, the dog underwent a protocol of ozone/oxygen insufflation directly into the peritoneum over five consecutive days. This procedure utilized the MedozonIP gas processor, designed to generate and insufflate the ozone/oxygen (O<sub>3</sub>/O<sub>2</sub>) and pure medical oxygen mixture.

## 2.4 Equipment and Insufflation Procedure

- Ozone Gas Processor: The MedozonIP is equipped with integrated intra-abdominal pressure control (IAPC), preventing high pressures during insufflation, ensuring the procedure's safety. This device was recently patented.
- Ozone Kit: The Ozon-Kit was used for insufflation, consisting of a 150 mm plastic tube with a sterile filter attached to the output of the MedozonIP generator. The tube was pre-purged with approximately 10 ml of the required gas to remove air before insufflation, using the "backflush" method.
- Dosage and Administration: The O<sub>3</sub>/O<sub>2</sub> gas mixture was administered in a standardized volume of 80 mL/kg of body weight, containing 50 lg of O<sub>3</sub> per milliliter of gas mixture, equivalent to a proportion of 2.5% O<sub>3</sub> and 97.5% medical O<sub>2</sub>.
- Pressure Control: A Vasofix R Braunuele R catheter was implanted in the right lower quadrant of the abdomen to facilitate intra-abdominal pressure control during the insufflation process.



Figure 1

Figure 2

Figure 1: Moment of the intra-peritoneal catheter placement

Figure 2: Start of the intra-peritoneal insufflation process

### 2.5 Clinical Monitoring

No periodic imaging exams were conducted to monitor metastases, focusing instead on the patient's well-being and clinical signs. Clinical monitoring centered on observing the animal's response to treatment and assessing any adverse effects or complications related to the procedure.

## 3. Results and Discussion

The patient achieved a remarkable six years of survival after diagnosis, during which no periodic imaging tests for metastasis monitoring were conducted. This outcome suggests that the ozone/oxygen treatment might have effectively controlled the disease's progression, challenging the expectations based on existing literature.

This case challenged the conventional survival expectations for osteosarcoma in dogs, using ozone therapy as an alternative therapeutic approach. The administration of ozone/oxygen-pneumoperitoneum resulted in a notable extension of the patient's survival without the common imaging follow-ups for metastasis detection, providing an acceptable quality of life despite the disease's initial severity.

## 4. Conclusions

The use of ozone/oxygen-pneumoperitoneum in dogs with osteosarcoma may offer a valuable alternative for prolonging survival in cases where conventional treatments are not viable or desired. This particular case highlights the potential of ozone therapy as an effective option in controlling the progression of osteosarcoma, significantly extending survival and improving the quality of life of the patients. This case underlines the need for more research to assess the efficacy and safety of this treatment in a broader population of patients with osteosarcoma. Further studies are essential to better understand the potential of ozone therapy as either an alternative or complementary treatment for this severe and often fatal condition.

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