












## Acoustic radiation force Impulse elastography to aid diagnosis of two canine malignant peripheral nerve sheath tumors

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**ABSTRACT:** This report described the use of acoustic radiation force impulse (ARFI) elastography in the diagnosis of two cases of canine malignant peripheral nerve sheath tumors. Both patients presented with lameness in the thoracic limb and no response to previous clinical treatment or trauma history. Physical examination revealed muscular atrophy in one of the thoracic limbs, in both dogs. B-mode axillary ultrasound showed the presence of a predominantly hypoechogenic, heterogeneous, irregular, nonencapsulated nodule with adjacent reactivity, measuring approximately 20.1 mm x 15.4 mm in the first case and 18.3 mm x 10.7 mm in the second. ARFI elastography was performed, showing areas of significant stiffness, with an average shear wave velocity of 4.12 m/s (case 1) and 4.35 m/s (case 2), suggesting malignancy. In both cases, the affected limb was amputated, and the tumors sent for histopathological analysis, which were; subsequently, diagnosed as malignant tumors of the peripheral nerve sheath. The ultrasonographic methods used were essential in the diagnosis and therapeutic conduct.

**Key words:** neoplasm, diagnosis, ARFI elastography, peripheral nerves, dog.

### Elastografia Acoustic radiation force Impulse (ARFI) para auxílio no diagnóstico de dois tumores malignos da bainha dos nervos periféricos caninos

**RESUMO:** O objetivo deste relato é descrever o auxílio da elastografia por impulso de força de radiação acústica (ARFI) no diagnóstico de dois casos de tumores malignos da bainha dos nervos periféricos em canídeos. Ambos os pacientes apresentavam claudicação em membro torácico e já haviam sido tratados clinicamente por outros profissionais, sem resposta ao tratamento ou histórico de trauma. Ao exame físico, foi observada atrofia muscular em apenas um dos membros torácicos, nos dois casos. Foi realizado exame ultrassonográfico axilar. Na avaliação modo B, foi observada a presença de estrutura nodular, predominantemente hipocogênica, heterogênea, irregular, não encapsulada e com reatividade adjacente, medindo aproximadamente 20.1 mm x 15.4 mm no primeiro caso e 18.3 mm x 10.7 mm no segundo caso. Foi realizada elastografia ARFI, demonstrando a presença de áreas de maior rigidez, com velocidade de ondas de cisalhamento média de 4.12 m/s (caso 1) e 4.35 m/s (caso 2), sugerindo malignidade. Em ambos os casos, foi realizada amputação do membro afetado e os nódulos removidos foram encaminhados para análise histopatológica, na qual se obteve o diagnóstico de tumor maligno da bainha de nervo periférico. Os métodos ultrassonográficos realizados nesses casos foram essenciais para o diagnóstico e conduta terapêutica.

**Palavras-chave:** neoplasia, diagnóstico, elastografia ARFI, nervos periféricos, cão.

## INTRODUCTION

Primary peripheral nerve tumors are uncommon in veterinary medicine (ROSSMEISL et al., 2019). Malignant peripheral nerve sheath tumors (MPNSTs) are locally invasive soft tissue sarcomas that affect the spinal or cranial nerves, originating from Schwann cells, modified Schwann cells, perineural cells or intraneural fibroblasts (KNIGHT et al., 2022; SIRRI et al., 2016). Their locally aggressive

characteristics, such as invasion into surrounding tissues and infiltration into nerve roots and plexuses, even into the spinal cord or brain stem, usually lead to late diagnosis (SIRRI et al., 2016).

Establishing a diagnosis based solely on clinical findings and palpation is difficult, especially because most of the clinical signs, such as lameness, muscle atrophy and neurological and proprioceptive deficits, are nonspecific (LE CHEVOIR et al., 2012; ZHALNIAROVICH et al., 2014). A MPNST is suspected

in cases of lameness in which orthopedic causes are not identified and when the patient does not respond to conventional treatment (LE CHEVOIR et al., 2012).

ARFI (Acoustic Radiation Force Impulse) elastography allows qualitative and quantitative assessment of the potential for tissue deformity, based on the degree of tissue stiffness, resulting in estimated shear wave velocity (SWV) (waves that return from the target tissues). Moreover, this tool can be effective in differentiating between benign and malignant lesions, since the latter tend to increase tissue stiffness (ERCOLIN et al., 2024; FELICIANO et al., 2017).

Surgical removal is the treatment of choice, which involves excision of the neoplasm with appropriate surgical margins, typically through limb amputation (ROSSMEISL et al., 2019). However, the prognosis is guarded because these tumor cells tend to remain in the nervous tissues and there is a risk of local invasion (KNIGH et al., 2022; ZHALNIAROVICH et al., 2014).

Given the difficulties in establishing an early diagnosis so that appropriate therapeutic methods can be applied, the present study aims to present the ultrasonographic and elastographic features of two cases of canine MPNSTs and demonstrate their importance and relevance as a diagnostic aid.

Case 1. An 11-year-old Labrador retriever, weighing 36 kg, presented for consultation after lameness of approximately one month and was unable to bear weight on the right thoracic limb (RTL). According to the owner, the condition had worsened in the previous week after the oral administration of dipyrone 500 mg, which did not improve the patient's clinical condition.

Physical examination detected a moderate increase in volume in the axillary region, and intense muscle atrophy was observed in the RTL, associated with superficial pain, hopping and absence of withdrawal reflex, despite maintaining normal proprioception. After clinical assessment, a tumor or neuritis in the brachial plexus, or axillary lymphadenopathy, was suspected. Hematological profile, radiographic studies of the thorax and right scapulohumeral joint, and ultrasonography of the right axillary region were requested. According to the hematological profile, mild hypochromic normocytic anemia, neutrophilia with left shift and a slight increase in total proteins and alkaline phosphatase (FA) were detected, with no changes in the radiographic exams.

Ultrasonographic examination was performed with an ACUSON S2000™ ultrasound system (Siemens®, Munich, Germany), using a linear multifrequency matrix transducer, with frequencies

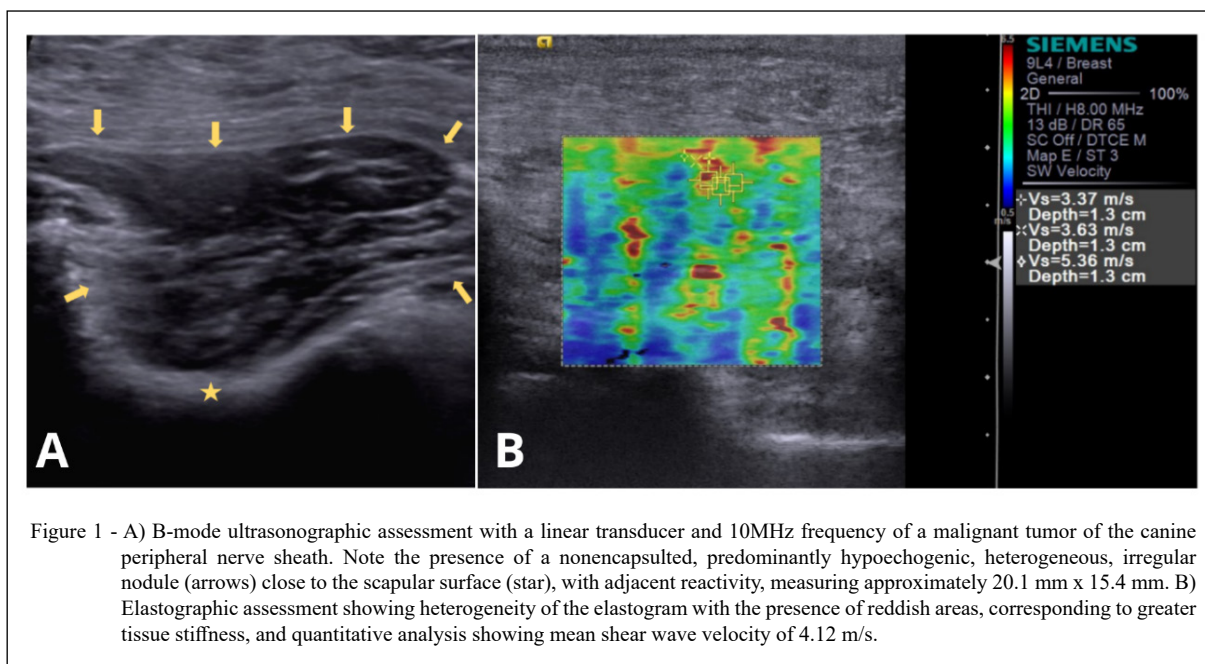
ranging from 4.0 to 9.0 MHz. The patient was placed in the supine and left lateral decubitus position, and trichotomy was performed. Irregular margins and contours of the right radial nerve were observed, with the presence of a single, apparently nonencapsulated, predominantly hypoechogenic and heterogeneous nodule (Figure 1A), measuring approximately 1.3 cm x 1.5 cm in the longitudinal section, with reactivity in adjacent tissues. The right axillary lymph node exhibited normal echogenicity and a regular surface, measuring approximately 1.4 cm x 0.68 cm in the longitudinal section, with no notable abnormalities, such as changes in size, echogenicity, echotexture and contours.

After B-mode, ARFI elastography of the nodule was performed (Figure 1B). The same ultrasound equipment was used, but with the aid of Siemens Healthineers Virtual Touch™ Quantification software, for qualitative and quantitative characterization of the ARFI method. Qualitative assessment was conducted by obtaining color scale images (elastogram), where bluer tones corresponded to more elastic tissues while reddish colors represented their more rigid counterparts. For quantitative assessment, three areas of interest were randomly selected by extending the nodule, where SWV values were expressed in m/s. Next, the mean was calculated to determine total shear speed: 4.12 m/s. Elastography showed that the nodule was rigid and non-deformable.

Ultrasound-guided aspiration cytology of the brachial plexus nodule was carried out, but the result was inconclusive due to the low cellularity of the sample. The limb was amputated, and a sample of the affected tissue was sent for histopathological assessment, confirming MPNST diagnosis, without metastasis to adjacent axillary lymph nodes.

Case 2. A 12-year-old female Shih Tzu, weighing 7kg, was seen due to left thoracic limb (LTL) lameness that had progressed over approximately two months with no history of trauma. Physical examination detected humeral and scapular muscle atrophy, associated with loss of withdrawal reflex and the presence of proprioceptive deficit. No increase in volume was detected in the axillary region, nor were any other changes reported in the other limbs.

After clinical assessment, a lower motor neuron lesion was suspected, with possible involvement of the brachial plexus, with the main differential diagnoses being tumor or neuritis. Hematological and biochemical tests (alanine aminotransferase, FA, albumin, creatinine, and urea) were requested, as well as a radiographic study of the scapulohumeral joint, and an ultrasound of the left axillary region. No changes were found in the hematological and radiographic studies.



Ultrasound examinations were performed with the same equipment, transducer and frequency used in case 1. The patient was placed in the right decubitus position, and trichotomy was performed in the left axillary region, revealing a single irregular, heterogeneous, and hypoechoic nodule in the brachial plexus region (Figure 2A). After B-mode ultrasound, ARFI elastography was performed on the nodule observed in the brachial plexus (Figure 2B). As in case 1, the same software was used to analyze ultrasound images qualitatively and quantitatively.

For quantitative assessment, three areas of interest were randomly selected by extending the nodule extension, for which SWV values (4.35 m/s) were obtained. Elastography showed that the nodule was rigid and non-deformable, like the lesion described in case 1. The patient was referred for an incisional biopsy, which returned a diagnosis of MPNST, with no signs of metastasis to adjacent axillary lymph nodes. The LTL was amputated seven days after diagnosis.

The present report provided important information on the ultrasonographic identification of two canine MPNSTs and, primarily, on the applicability of ARFI elastography in both cases. Most cases are difficult to diagnose because nodules cannot always be identified through palpation (ZHALNIAROVICH et al., 2014). Imaging diagnostic methods, such as ultrasonography, computed tomography and magnetic resonance, can be used for diagnosis, as

well as electromyography (CHATZISTEFANOU et al., 2012; ZHALNIAROVICH et al., 2014).

Given that MPNSTs can originate in cranial or spinal nerves, their clinical presentation may vary, depending on tumor location (ROSSMEISL et al., 2019). In the first case reported, a change in the brachial plexus was suspected because only one limb was involved, a common presentation in peripheral nerve injuries (LE CHEVOIR et al., 2012). In both cases the patients showed lameness and muscular atrophy, clinical signs previously reported in association with this type of neoplasm (ZHALNIAROVICH et al., 2014).

Ultrasonography has been used to identify and characterize different neoplasms, and although it is highly sensitive in detecting soft-tissue tumors, it is limited in detecting malignancy (CHATZISTEFANOU et al., 2012). Its characteristics include tubular, hypoechoic, and heterogeneous structures, with reactivity of adjacent tissues and the presence of tortuous blood vessels; although, they may exhibit no blood flow (DA CRUZ et al., 2021; ROSE et al., 2005). The findings reported in these two cases are consistent with those described by other authors (DA CRUZ et al., 2021; ROSE et al., 2005), but it is known that B-mode ultrasonography has low specificity for tumor differentiation and malignancy determination, requiring other more accurate examinations for better characterization (DA CRUZ et al., 2022).

Elastography is a new noninvasive ultrasonographic technique that complements B-mode

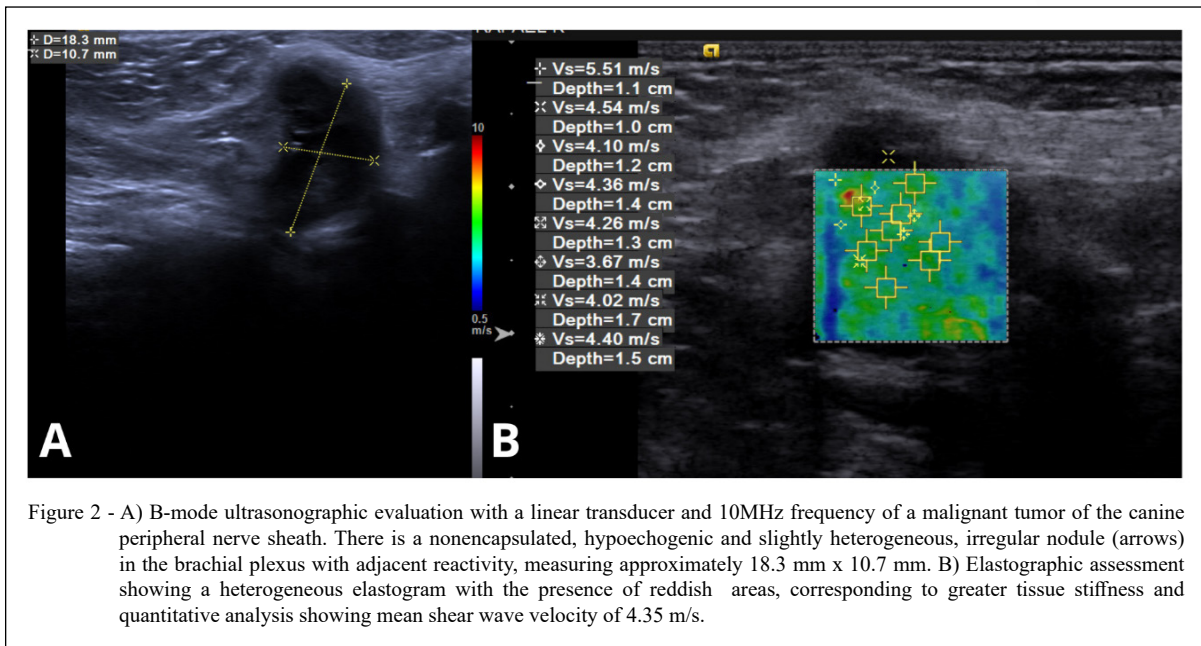


Figure 2 - A) B-mode ultrasonographic evaluation with a linear transducer and 10MHz frequency of a malignant tumor of the canine peripheral nerve sheath. There is a nonencapsulated, hypoechoic and slightly heterogeneous, irregular nodule (arrows) in the brachial plexus with adjacent reactivity, measuring approximately 18.3 mm x 10.7 mm. B) Elastographic assessment showing a heterogeneous elastogram with the presence of reddish areas, corresponding to greater tissue stiffness and quantitative analysis showing mean shear wave velocity of 4.35 m/s.

and can be used to predict tissue malignancy or benignity in different tumor types (ERCOLIN et al., 2024). In veterinary medicine, elastography has been the subject of study for the safe and noninvasive assessment of a variety of tumor tissues, including mammary glands (FELICIANO et al., 2017), lymph nodes (FEBO et al., 2023), cutaneous and subcutaneous tumors (DA CRUZ et al., 2022), as well as splenic (MARONEZI et al., 2022) and hepatic tissues (HUIJANTUG et al., 2020).

Qualitative assessment shows less specificity for this differentiation. A study carried out by LONGO et al. (2018), using strain elastography, reported that breast tumors had greater stiffness than their benign counterparts, with 100% sensitivity and 61% specificity. When quantitative analysis was carried out using the ARFI method, specificity reached 94.7% for differentiation between malignant and benign breast tumors and a cut-off point of 2.57 m/s (FELICIANO et al., 2017). Although, there is no specific study of MPNSTs, shear wave velocity was significantly higher than the cut-off point established for breast neoplasms, and highly suggestive of malignancy.

An increase in stiffness should be interpreted based on the individual characteristics of tumor growth and proliferation (DA CRUZ et al., 2022). In general, an increase in malignant tumor stiffness could be associated with areas of microcalcification or fibrosis, secondary to inflammatory processes and hemorrhage (FELICIANO et al., 2017). In the case of a MPNST in the brachial

plexus, histopathological analysis showed the presence of a moderate amount of fibromuscular bundles, with areas of intense multifocal hemorrhage and moderate hemosiderosis, intense multifocal coagulation necrosis and thrombin in blood vessels (MARTINS et al., 2015), findings that could justify the increase in tissue stiffness observed in the ARFI assessment of MPNST cases.

Given the strong suspicion of a MPNST in both cases, based on clinical and ultrasound findings, total amputation of the thoracic limb was recommended, despite the inconclusive cytological result, as mentioned in the first case. The decision was based on the aggressive behavior of this type of tumor, which exhibits a high risk of metastasis and a tendency to local invasion (KNIGH et al., 2022). As such, this procedure had both a therapeutic and diagnostic purpose, allowing the collection of neoplastic tissue for subsequent histopathological analysis.

In conclusion, ultrasound made it possible to identify the presence of a nodule in the brachial plexus in both cases, which, combined with elastographic assessment, provided more information about its potential malignancy. ARFI elastography proved to be an effective method in characterizing and predicting malignancy in these types of lesions, suggesting its important diagnostic value, since it was crucial in establishing the treatment protocol. However, further studies are needed to establish a correlation between ARFI characteristics and malignancy.

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## DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHORS' CONTRIBUTIONS

The authors contributed equally to the manuscript.

## BIOETHICS AND BIOSECURITY COMMITTEE APPROVAL

The authors of the article entitled "Use of ARFI elastography to aid diagnosis of two canine malignant peripheral nerve sheath tumors" declare, for all due purposes, that the project that gave rise to the present data has not been submitted for evaluation to the Ethics Committee of the University/Research Institute "Universidade Federal de Santa Maria (UFSM)", but are aware of the content of the Brazilian resolutions of the National Council for Control of Animal Experimentation - CONCEA "http://www.mct.gov.br/index.php/content/view/310553.html" if it involves animals.

Thus, the authors assume full responsibility for the data presented and are available for possible questions, should they be required by the competent authorities.

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