### DIAGNOSTIC ACCURACY OF SHEAR WAVE ELASTOGRAPHY IN COMPANION ANIMAL SOFT TISSUE INJURY: A SYSTEMATIC REVIEW

(D18B0006)

## A RESEARCH PAPER SUBMITTED TO THE FACULTY OF VETERINARY MEDICINE, UNIVERSITI MALAYSIA KELANTAN IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE DEGREE OF

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DOCTOR OF VETERINARY MEDICINE

UNIVERSITI MALAYSIA KELANTAN

# FYP FPV

#### **CERTIFICATION**

This is to certify that we have read this research paper entitled 'Diagnostic Accuracy of Shear Wave Elastography in Companion Animal Soft Tissue Injury: A Systematic Review' by Chin Yi Lin, and in our opinion it is satisfactory in terms of scope, quality and presentation as partial fulfillment of the requirement for the course DVT 55204 – Research Project.

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#### **DEDICATIONS**

I hereby dedicate my dissertation work to my family. Warmest thanks to my mother, Koh, for accepting me and lifting me up as who I am today. My siblings, J.W. and Wendy, who have loved me dearly.

I dedicate this dissertation to many lecturers who have guided me throughout the process. Thanks to Prof. Ibrahim who always have faith in me and keep me going on no matter what. Proving what I thought I could not have accomplished has been one of the most rewarding moments of my life. Thank you, Dr. Wakil and Dr. Goni who have shepherded me through the thesis writing process.

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I dedicate this work to myself. I will go further, farther and freer while upholding the honor of Hippocrates. I put my future in god's hands and in the love of god, all glory to Him who has given me all I have.

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#### **Abbreviation**

**ARFI** Acoustic radiation force impulse

**CEUS** Contrast-enhanced ultrasound

E Young's modulus

**EHBO** Extrahepatic biliary obstruction

**EHPSS** Extrahepatic portosystemic shunt

**FNA** Fine needle aspiration

**G** Shear modulus

LN Lymph node

MHPSS Multiple acquired portosystemic shunts

**pSWE** Point shear wave elastography

**ROI** Region of interest

**STE** Strain elastography

**SWE** Shear wave elastography

**SWV** Shear wave velocity

TE Transient elastography

#### **ABSTRACT**

An abstract of the research paper presented to the Faculty of Veterinary Medicine, Universiti Malaysia Kelantan, in partial requirement on the course DVT 55204 – Research Project

Shear wave elastography (SWE) is a novel diagnostic modality to evaluate tissue stiffness in relation to the tissue's molecular constitution and disease status. This imaging technique measures the propagation velocity of the shear wave in relation to the tissue's stiffness – the stiffer the tissue, the faster the waves are. This systematic review is conducted to identify the diagnostic accuracy and peculiar organ sensitivities towards SWE while evaluating if this technique is feasible in small animal clinical settings. Thus, a total of 15,339 publications from 2010 to 2022 were extracted from three databases, Google Scholar, PubMed, and Science Direct using different search strategies. A total of 17 studies have met the eligibility criteria after sequential screenings according to the inclusion and exclusion criteria. 25 examinations across 17 studies, 36.0% of studies discussed SWE in the canine or feline liver, specifically hepatic fibrosis, followed by 12.0% that discussed pancreatic lesions. Other parenchymatous organs were also discussed, including the mammary gland, kidney, spleen, peripheral lymph nodes, pancreas, prostate, kidney, thyroid, salivary glands, and muscles. Until now, the liver remained the most studied organ for the diagnostic accuracy of SWE in small animal practice. SWE was proven to positively correlate with other diagnostic standards including strain elastography, FNA biopsy, and histopathological examination, and is expected to be used as an adjunct diagnostic method in detecting tissue stiffness and parenchymatous organ injury with increased accuracy.

Keywords: Shear wave elastography, canine, feline, diagnostic accuracy, feasibility

#### **ABSTRAK**

Abstrak daripada kertas penyelidikan dikemukakan kepada Fakulti Perubatan Veterinar, Universiti Malaysia Kelantan untuk memenuhi sebahagian daripada keperluan kursus DVT 55204 – Projek Penyelidikan.

Shear wave elastography (SWE) adalah modality diagnostik baru bagi menilai kekerasan tisu yang berhubung dengan konstitusi molekul dan status penyakit. Teknik pengimejan ini mengukur halaju gelombang shear wave berhubung dengan kekerasan tisu – semakin keran tisu tersebut, semakin cepat gelombangnya. Semakan sistematik ini dijalankan untuk mengenalpasti ketepatan diagnostic teknik ini dan sensitiviti organ terhadap SWE, sementara menilai sama ada teknik tersebut boleh dilaksanakan dalam klinikal praktis haiwan kecil. Sejumlah 15,339 buah penerbitan dari tahun 2010 hingga 2022 telah diekstrak daripada tiga pangkalan data, termasuk Google Scholar, PubMed dan Science Direct dengan menggunakan strategi carian yang berbeza. Sebanyak 16 penerbitan telah memenuhi kriteria kelayakan selepas saringan berurutan dan penerbitan ini telah dipilih. Sebanyak Daripada 24 pemeriksaan, 36.0% daripada 16 penerbitan ini membincangkan SWE dalam hati anjing ataupun kucing, khususnya terhadap fibrosis hepatic, diikuti oleh 12.0% yang membincangkan lesi pada pancreas. Organ-organ lain termasuk limpa, nodus limfa periferal, pancreas, kelenjar prostat, kelenjar salivary, tiroid, buah pinggang dan otot turut dibincangkan. Sehingga kini, hati kekal sebagai organ yang paling banyak dikaji untuk ketepatan diagnostk SWE dalam amalan haiwan kecil. SWE telah terbukti mempunyai korelasi positif dengan piawaian diagnostik lain termasuk strain elastography, biopi FNA, dan pemeriksaan histopatologi. SWE dijangka untuk digunakan sebagai kaedah diagnostik tambahan dalam mengesan kekerasan tisu dan kecederaan organ dengan peningkatan ketepatan.

**Kata kunci:** Shear wave elastography, anjing, kucing, ketepatan diagnostic, kebolehlaksanaan.



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#### 1.0 INTRODUCTION

In recent decades, elastography has evolved as an innovative imaging technology. Using ultrasonography, the acoustic and mechanical characteristics of a region of interest can be assessed and displayed as a color-coded map. It is utilized to detect alterations in the organ's stiffness, which is correlated with the tissue's molecular composition, structural organization, and, most crucially, pathological condition (Figueira *et al.*, 2015). The elasticity and rigidity of tissue are frequently connected with pathological alterations involving inflammation, fibrosis, neoplasia, and calcification. When elastic tissue is subjected to mechanical excitation, the stiffness parameters of the tissue dictate the level of longitudinal displacement and deformation. These variations will then be monitored and recorded to provide images of elasticity. Furthermore, elastography can be divided into quasi-static and dynamic elastography, which pertains to strain imaging and shear wave imaging, respectively.

Shear wave elastography (SWE) is a dynamic elastography technology that generates low-velocity, lateral shear waves that can penetrate deeper layers of tissue. Shear waves can be produced by external vibration, physiologic motion, and acoustic radiation force (Shiina, 2015). There is a correlation between the propagation velocity of shear waves and tissue stiffness; the stiffer the tissue, the faster the waves travel. Using Doppler instruments, the wavelength at the vibration site can provide a real-time estimation of tissue stiffness in the area of interest (Figueira *et al.*, 2015). SWE is advantageous due to its more robust mechanical penetrating properties, which enable the detection of the lesion in obese patients or patients with ascites and pleural effusion. It has also been demonstrated to have more excellent reproducibility than other elastography procedures because the results are independent of the operator's skill. The fundamental principles of stress, strain, and elastic modulus should be understood to interpret the images generated from SWE. The differences in the elasticity of

soft tissues when experiencing shear and compression are expressed by Young's modulus (E) or shear modulus (G) (Shiina, 2015).

Since the early 1990s, elastography has been utilised to define localised lesions of numerous organs, particularly in the human prostate, liver, breast, lymph nodes, musculoskeletal system, and thyroid gland (DeJong *et al.*, 2017). SWE has, to the author's knowledge, acquired increasing interest among small animal practitioners. In veterinary practices, it has been shown efficient for measuring the stiffness of the liver, lymph nodes, muscles, pancreas, spleen, kidney, prostate gland, and mammary tissue. By monitoring strain levels and ratios, SWE gives crucial information for distinguishing malignant from benign lesions in parenchymal organs, according to numerous studies. As a result, SWE is anticipated to generate new diagnostic information regarding the elasticity of tissues.

#### 1.1 Research problem

In the past decade, noninvasive elastography has gained more attention in human and veterinary medicine and has become more commercially available. Studies have been carried out on the feasibility and reliability of SWE in diagnosing soft tissue injury in a human patient. However, there has been limited research that explored the level of diagnostic accuracy using SWE in small animals.

As the changes in tissue stiffness can help in the early detection and diagnosis of disease when morphological changes are not apparent, a thorough review of the available literature can contribute to understanding the principle and future of SWE in veterinary practices.

This study aimed to review the uses of SWE in small animal medicine to provide evidencebased information regarding the diagnostic accuracy of SWE compared to biopsy for the evaluation of tissue stiffness in the case of soft tissue injuries. The feasibility of the routine usage of SWE will also be discussed from the clients' and practitioners' perspectives.

#### 1.2 Research questions

- 1.2.1 What is the level of diagnostic accuracy using SWE in small animals?
- 1.2.2 What are the peculiar organ sensitivities to SWE diagnosis?
- 1.2.3 What is the feasibility of the routine usage of SWE in veterinary practices?

#### 1.3 Research hypothesis

- 1.3.1 SWE has better diagnostic accuracy for soft tissue injury than other diagnostic methods.
- 1.3.2 The liver is the most sensitive organ to SWE diagnosis.
- 1.3.3 SWE is feasible for routine use in the companion animal practices.

#### 1.4 Objectives

- 1.4.1 To determine the level of diagnostic accuracy of SWE in soft tissue injury from the available literature
- 1.4.2 To identify the organ which is more sensitive to SWE diagnosis.
- 1.4.3 To identify the feasibility of routine usage of SWE in veterinary practices.



#### 2.0 LITERATURE REVIEW

#### 2.1 Principle of shear wave elastography

Shear wave elastography (SWE) is a technique for dynamic elastography that creates transverse shear waves that cause particles to oscillate perpendicular to the wave's direction. As the shear wave velocity (SWV) propagates through the tissue, it is measured and shown on a color-coded map. Each color pixel in the elastogram represents the location-specific mechanical properties (DeJong et al., 2017). The stiffness of tissue within the area of interest (ROI) is compared to that of surrounding tissues. Each elastography's shear wave velocity is measured as Young's modulus (kPa) and shear wave velocity (m/s). Young's modulus quantifies the tissue's resistance to compressive deformation (strain) resulting from mechanical stimulation or forces (stress) put on the tissue. The greater Young's modulus, the greater the tissue's resistance to compressive deformation and, thus, the stiffer the material. Existing SWE techniques include 1-dimensional transient elastography (1D-TE), point shear wave elastography (pSWE), and 2dimensional shear wave elastography (2D-SWE). 1D-TE, which became commercially available in 2003, is the most popular method for evaluating liver fibrosis in human patients utilizing the FibroScanTM system without direct B-mode image guiding (Shiina, 2015). 2D-SWE is the most recent imaging approach for shear waves that employs acoustic radiation forces. The linear or curve transducer generates repeated push pulses within a brief time frame, causing tissue displacement. The returning echo pattern will change over time, and the same transducer is used to monitor these changes. 2D-SWE enables real-time display of a colour quantitative elastogram superimposed on a B-mode image, enabling the operator to make decisions based on anatomical and tissue stiffness data (Sigrist et al., 2017).

#### 2.2 Routine usage of shear wave elastography in veterinary practices

In SWE, all tissues are assumed to be viscoelastic, isotropic, and incompressible. When a mechanical force (stress) is applied, the tissue response in local displacement and deformation (strain) is known as their mechanical properties.

Young's modulus (E) represents the relationship between the applied pressure and the resulting strain. It quantifies how difficult it is to deform a tissue via compression or shear stress and can be calculated using the following equation after externally applying stress ( $\sigma$ ) and measuring the strain ( $\varepsilon$ ),

$$E = \sigma / \varepsilon$$

A study of human breast tissue samples demonstrates that E levels are much greater in diseased than in normal glandular tissues (Samani *et al.*, 2007).

SWE has acquired significant attention throughout the years as one of the emerging diagnostic modalities utilized in clinical settings because of its noninvasiveness, real-time capabilities, and greater penetration strength. The approach has supplied valuable information for analyzing the rigidity of lymph nodes, pancreas, spleen, thyroid, breast tissues, prostate gland, kidney, muscles, and most notably, the liver. Transient elastography has been proven to assess and predict the course of human liver cirrhosis (Kim *et al.*, 2019). SWE has also been shown to correlate renal parenchymal stiffness with renal function deterioration in feline studies (Thanaboonnipat *et al.*, 2019). Recent research indicates that in the musculoskeletal system, SWE can be used to measure the shear elastic modulus of the thoracolumbar multifidus muscle in dogs, and the results correlate positively with age-related changes (Tokunaga & Shimizu, 2021).

#### 2.3 Comparative diagnostic accuracy of SWE

The gold standard for detecting microscopic pathological changes in the tissue's molecular structure is a biopsy. It is a recognized difficult and invasive procedure that requires the patient to be under general anesthesia. Repeated biopsies may be necessary for certain circumstances to assess the progression of a disease or to account for the possibility of sampling error. SWE evolved gradually as a noninvasive and accessible diagnostic tool in human medicine for determining the severity of soft tissue injury, especially in the staging of hepatic fibrosis. Tamura et al. (2019) compared the liver shear wave velocity (SWV) of six dogs with clinically significant hepatic fibrosis, twenty-two without such fibrosis, and eight healthy dogs. Even though the SWVs of dogs with clinically relevant hepatic fibrosis were significantly greater than those without clinically relevant hepatic fibrosis, it is challenging to predict the absence or mild severity of hepatic fibrosis in dogs using 2D- SWE. The authors hypothesized that necroinflammatory activity within the hepatic parenchyma was difficult to stage and evaluate on SWVs because the necroinflammatory activity had a weaker effect on SWVs than hepatic fibrosis. Comparing the diagnostic accuracy of 2D-SWE to that of other diagnostic modalities, specifically biopsy, will require additional research.

#### 3.0 MATERIALS AND METHODS

This systematic review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

#### 3.1 Literature search and strategy

Three English electronic databases, Google Scholar, PubMed and Science Direct were used for literature searching. The search setting was fixed from 2010 to 2022 to identify all the literature published within the specific time frame. Specific search phrases include keywords of "shear

wave elastography" OR "sonoelastography" AND "feline" OR "cat" OR "canine" OR "dog" AND "soft tissue injury" OR "parenchymal organ injury" OR "healthy" AND "diagnostic" OR "diagnosis" were used. Various combinations of the above terms were included in the searches across the three databases. All the search results were recorded and summarised in Table 3.1.

#### 3.2 Screening, inclusion and exclusion criteria

To ensure the data retrieved from the literature are relevant to the scope of this review, several screenings were conducted based on the inclusion and exclusion criteria. The inclusion criteria of this review included all original studies that use 2D shear wave elastography (SWE) for clinical diagnosis or research in small animal medicine. Studies with detailed data sufficient to evaluate the diagnostic performance of SWE, i.e. Mean  $\pm$  SD shear-wave velocities (SWVs) (m/s) or Young modulus elasticity measurements (*E*) were also included.

As for the exclusion criteria, conference proceedings, published books, review articles, and case reports regarding SWE were discounted. Exclusion criteria also included studies of other SWE techniques besides 2D-SWE (such as acoustic radiation force impulse SWE), SWE in species other than canine or feline, overview, pathogenesis or treatment for parenchymatous organ injury. Studies that focused on other elastographic techniques were excluded. The study focused on the region of interest besides parenchymatous organs were excluded.

After an appropriate search across databases, the first screening was conducted to remove unrelated studies and duplicates based on citations using EndNote X9. The second screening was conducted manually to remove studies focusing on general ultrasound techniques and scope irrelevant or beyond SWE based on the title. The final screening was performed manually based on the evaluation of the title, abstract and methodology of the publications to finalize the

total number of literature to be reviewed according to the inclusion and exclusion criteria. The process and result of the screening are illustrated in Diagram 4.1.

#### 3.2.1 Result synthesis

All of the literature was systematically reviewed and the result of the literature assessment was tabulated.



Table 3.1: Search strategy across different databases and literature retrieved

Database	Google Scholar	PubMed	<b>Science Direct</b>	
Search	Sonoelastography	Sonoelastograph* OR	Shear wave	
strategy	OR ultrasound	ultrasound elastography*	elastography OR	
	elas <mark>tography O</mark> R	OR quantitative ultrasound	sonoelastography	
	shear elastic	OR shear elastic modulus	AND	
	modulus OR 2-D	OR 2-D shear wave	AND	
	shear wave	elastography OR point	Medicine OR	
	elastography OR	shear wave elastography	feline OR canine	
	elasticity imaging	OR elasticity imaging	AND	
	technique	technique* OR "Elasticity	AND	
	AND	Imaging	Diagnostic	
	AND	Techniques/veterinary"[Me	accuracy OR	
	Veterinary OR	sh]	reliabili <mark>t</mark> y OR	
	sma <mark>ll animal O</mark> R	AND	performance OR	
	com <mark>panion anim</mark> al	AND	assessment	
	OR feline OR	Veterinary OR small		
	canine	animal* OR companion		
	AND	animal* OR pet OR feline		
	AND	OR canine OR cat OR dog		
	Diagnostic	OR "Pets"[Mesh]		
	accuracy OR	AND		
	reliability OR	AND		
	eval <mark>uation OR</mark>	Diagnostic accuracy OR		
	assessment OR	diagnostic reliability OR		
	performance OR	evaluation OR examination		
	reproducibility	OR assessment OR		
		performance OR		
		reproducibility OR "Data		
		Accuracy"[Mesh]		
		AND		

		Medical OR "Med [Mesh]	Medical OR "Medicine" [Mesh]		
Number of literature retrieved	9,634	3,645	2,060		
Total		15,339			

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#### 4.0 RESULTS

The search strategy identified a total of 534 publications that were eligible to be assessed after removing duplications and publications beyond the scope of interest. A total of 17 publications were selected for the systematic review after sequential screenings where the result is depicted in Diagram 4.1. Among the studies included, prospective studies (10 out of 17, 58.8%) and cross-sectional studies (7 out of 17, 41.2%) were analyzed. Table 4.1 summarizes the published studies and the region of interest for SWE diagnosis reported from 2010 to 2022. The raw data retrieved from the selected studies were summarized in Appendix 1. The 10 assessed tissues include the liver, mammary gland, muscle, spleen, kidney, pancreas, prostate, salivary gland, thyroid, and peripheral lymph nodes, whereby the liver was the organ most frequently studied across 16 studies (9 out of 25 examinations, 36.0%), followed by the pancreas (3 out of 25, 12.0%). The mammary gland, spleen, and kidneys were included in this review (2 out of 25 examinations, 8.0%, respectively), while thigh musculature, thoracolumbar multifidus muscle, prostate, salivary glands, and thyroid were the least studied among the publications (1 out of 25 examinations, 4.0%, respectively). Most publications focused on canine subjects (14 out of 17, 82.4%) while three studied feline shear wave elastography (3 out of 17, 17.6%).

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Diagram 4.1: Flowchart illustrating methodology and result of screening for literature review

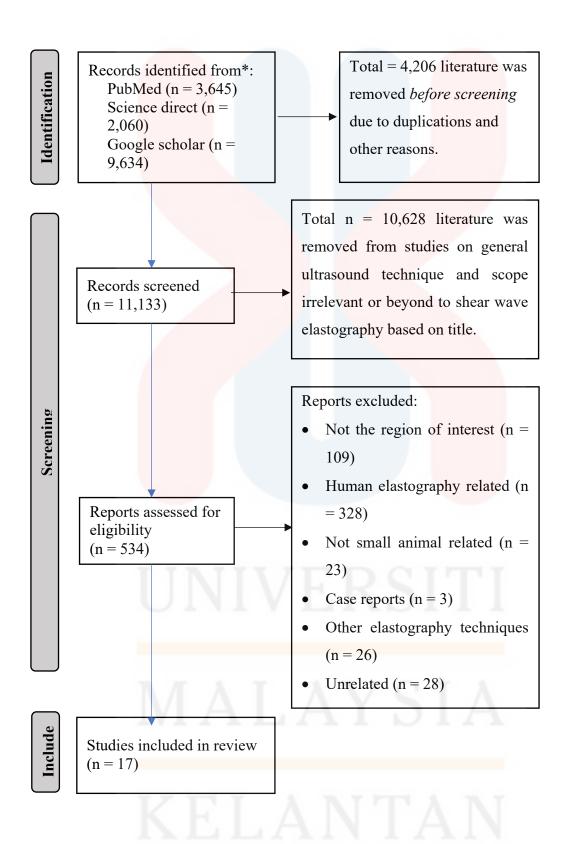


Table 4.1 Studies included for analysis

First author (Year of publications)	Subject	Organ of interest	Correlated diagnostic workup	Operator (experience in diagnostic imaging)
Glińska- Suchocka (2013)	12 canines	Mammary gland	FNA biopsy	NM
Feng (2016)	14 canines	Liver	Histopathology, plasma MEGX liver function test	NM
Shimizu (2019)	12 canines	Thigh muscles	NA	2 veterinarians (>20 y and 1 y)
Tamura (2019)	36 canines	Liver	Serum HA concentration and histopathology	NM
Tamura (2019)	8 canines	Liver and spleen	NA	1 operator (NM)
Thanaboonnipat (2019)	48 felines	Kidney	Serum biochemistry, urinalysis and uPIIINP	NM
Avante (2020)	25 canines	Pancreas	CEUS, ARFI and Doppler ultrasound	1 operatory (9 y)
Jung (2020)	9 canines	Liver, spleen, kidneys, pancreas, prostate, LNs,	NA	2 veterinarians (7 y and 2 y)

		salivary glands,		
Kang (2021)	11 canines	Peripheral LNs	NA	3 trained operators (NM)
Kim (2020)	29 felines	Liver	NA	2 veterinarians (NM)
Park (2021)	18 felines	Liver	NA	1 operator (NM)
Tamura (2021)	20 canines	Liver	NA	3 trained operators (>10 y)
Tokunaga (2021)	12 canines	Muscles	MRI	2 sonographers (NM)
Cho (2022)	41 canines	Pancreas	Spec cPL immunoassay	1 veterinarian (6 y)
Massimini (2022)	22 canines	Mammary gland	STE and histopathology	1 operator (3 y)
Puccinelli (2022)	45 canines	Liver	NA	1 sonographer (NM)
Toom (2022)	21 canines	Liver	NA	NM

 $\overline{CEUS} = contrast\ enhanced\ ultrasound;\ FNA = fine\ needle\ aspiration;\ HA = hyaluronic\ acid;\ LN =$   $lymph\ node;\ NA = not\ available;\ NM = not\ mentioned;\ MRI = magnetic\ resonance\ imaging;\ STE =$   $strain\ elastography;\ uPIIINP = urinary\ procollagen\ type\ III\ amino-terminal\ propeptide$ 

#### 4.1 Canine shear wave elastography

Jung et al. (2020) investigated numerous tissues, including the lymph nodes, pancreas, spleen, kidney, liver, prostate, salivary glands, and thyroid, in a study of canine shear wave elastography (SWE). The author reported that liver has an excellent reproducibility (ICC:

0.864-0.948) and most abdominal organs, with the exception of the right prostate (Intraclass correlation coefficient, ICC: 0.534) and axillary lymph node (ICC: 0.552).

The review showed that the liver remained the most studied organ in canine shear wave elastography, comprising 6 out of 16 studies or 37.5%. The reliability and performance of shear wave elastography on the normal healthy hepatic tissues hepatobiliary parenchymatous changes such as hepatic fibrosis, extrahepatic biliary obstruction, and hepatic vascular anomalies were investigated. A baseline reference range of hepatic stiffness in shear wave values (SWV) and Young's modulus were established by Jung et al. (2020) and Tamura et al. (2019) in healthy Beagles. The study conducted by Feng et al. (2016) and Tamura et al. (2019) revealed increased SWVs in dogs with hepatic fibrosis, as compared to healthy patients. The former discussed a significant positive correlation of liver stiffness between histologic grading and SWVs (p < 0.001), which shows that it was beneficial to incorporate this non-invasive imaging modality into assessing liver disease severity. However, Tamura et al. (2019) concluded that SWE was still insufficient for quantifying different levels of hepatic necroinflammatory activities because there was no significant difference in the SWVs between healthy dogs, dogs without inflammatory activity, and dogs with inflammatory activity (p =0.11). Toom et al. conducted the initial investigation of SWE on canine hepatic vascular anomalies (2022). There were no significant differences between the mean SWVs of dogs with a surgically closed extrahepatic portosystemic shunt (EHPSS) and dogs with multiple acquired portosystemic shunts (MAPSS), indicating that SWE was unable to distinguish between the two groups. Even though liver was commonly assessed in 2D-SWE practices, including in the human medicine field, in another study by Tamura et al. (2021), the occurrence of extrahepatic biliary obstruction (EHBO) in hepatic fibrosis prediction was studied. The author concluded that EHBO could increase the SWVs of dogs without clinically significant alterations in the liver parenchyma, thus interfering with the noninvasive hepatic fibrosis prediction using this elastographic technique. Puccinelli *et al.* (2022) found that the use of anesthesia could be a source of variation in SWE studies.

SWE was also proved feasible for assessing pancreatic stiffness in acute pancreatitis, as concluded by Cho *et al.* (2022). High pancreatic SWVs were demonstrated in the canine patients with acute pancreatitis compared to the normal control group (p < 0.05). The author also revealed a positive correlation between SWVs and Spec cPL concentration (p < 0.05) which was suggested to be closely related to the increase in pancreatic stiffness from neutrophilic inflammation and pancreatic interstitial edema. A preliminary study conducted by Avante *et al.* (2020) demonstrated similar results as to Cho's, where a significant difference (p = 0.014) was observed between the mean SWVs of the pancreas between the healthy control group and the diseased group. Avante also concluded that the cutoff value of a healthy pancreas is at 1.98 m/s with a 78% sensitivity and 69& specificity, any SWV higher than this cutoff could represent pancreatic disease, in which acute inflammatory processes can resulted in lower SWV than in chronic alterations.

A study conducted by Glińska-Suchocka *et al.* (2013) on canine mammary gland neoplasia proved that benign neoplasms of the mammary gland (fibroadenoma and adenoma) had a significantly lower stiffness as compared to the malignant neoplasms (carcinomas). According to the author, it was safe to state that the noninvasive SWE enables the differentiation of benign and malignant neoplastic lesions of the mammary gland in bitches and can be suggested as a screening examination in the future. Another recent study by Massimini *et al.* (2022) discussed the correlations between SWE, STE, and histopathological examination in canine mammary nodular lesions. No significant correlations were found between STE and SWE (p > 0.05) whiel significant Pearson correlation coefficient between fibrosis and SWE-S (p < 0.001) were identified. Among the two elastographic techniques, SWE was found more replicable in

quantifying canine mammary tumors, largely attributed to the changes in mammary tissue stiffness.

A few studies in healthy patients have proven the repeatability of SWE and these results could serve as baseline reference ranges in canine patients. According to Kang *et al.* (2021), the mandibular lymph nodes (LN) were the most superficial, and the medial retropharyngeal LNs were the deepest. Supported by Jung *et al.* (2020), no significant difference was identified from the SWVs of the different lymph nodes. In this study, 3 operators established a significant positive intra- and interobserver interclass correlation, further supporting that SWE is accurate and reproducible in assessing peripheral LNs.

Next, Shimizu & Ito (2019) investigated the relationship between the change in the shear elastic modulus and the change in muscle length, particularly on the thigh muscles, namely the cranial part of the sartorius, vastus lateralis, biceps femoris, and semitendinosus muscles. The results showed an increased shear elastic modulus when all muscles were elongated, which suggested that SWE can be used as an adjunct diagnostic modality in assessing the elastic properties of canine muscle. The intra- and inter-observer correlation coefficients were excellent except in the semitendinosus muscle, which was suggested to be due to different joint angles and acquisition methods. Another SWE study on musculature, particularly on the thoracolumbar multifidus muscles, conducted by Tokunaga & Shimizu (2021) also demonstrated the feasibility of SWE in measuring muscle stiffness. The authors have concluded that the thoracolumbar multifidus muscle stiffness decreased with age.

Studies by Tamura *et al.* (2019) and Jung *et al.* (2020) have demonstrated high repeatability and reproducibility for 2D-SWE of the spleen in canines. When comparing the right lobe of the liver to the spleen, the stiffness of the spleen was found to be significantly greater. For both the spleen and liver, the intra-day and inter-day coefficient of variation was less than 10%,

which is clinically acceptable. It is safe to conclude, based on repeatability and reproducibility, that 2D-SWE is capable of assessing splenic stiffness in healthy dogs. According to Jung, however, the results of splenic elastography may be affected by the use of anesthesia drugs, as higher SWVs and Young's Modulus were observed in the anesthetized patient compared to the pre-anesthesia phase. Thus, it was demonstrated that anesthesia could be a source of variation in splenic SWE examinations.

#### 4.2 Feline shear wave elastography

Three publications were revealed for the clinical applications of SWE in feline patients. A study conducted by Thanaboonnipat *et al.* (2019) showed a higher renal cortical E value in CKD patients than in healthy cat patients. There was a significant positive correlation between the renal cortical E values and three other parameters, which included plasma creatinine, blood urea nitrogen (BUN), and urinary procollagen type III amino-terminal propertide (uPIIINP) (p < 0.001; p < 0.05; p < 0.001, respectively). At the same time, they negatively correlated with urine specific gravity and urine osmolality per plasma ratio (p < 0.001 and p < 0.01, respectively).

Next, supported by Kim *et al.* (2020), Park *et al.* (2021) concluded that a quantitative SWE of the liver in healthy adult cats is repeatable and feasible in clinical settings. Both studies demonstrated no significant correlation between the SWVs and the cat's body weight or between the SWVs and the depth of measurement. Kim further concluded that gabapentin administration was not a source a variability and the feline liver SWE can be reliably performed with or without anesthesia.

#### 5.0 DISCUSSION

### Feasibility and Reproducibility of Shear Wave Elastography in Small Animal Soft Tissue Organs

Several shear wave elastography (SWE) studies in healthy patients have set baseline reference ranges for future studies. A study conducted by Jung et al. (2020) has comprehensively evaluated the feasibility and reproducibility of 2D-SWE in multiple soft tissue organs, including the vital abdominal organs, salivary glands, thyroid, lymph nodes, and prostate gland of canine patients. Excellent reproducibility was demonstrated in the liver which once proven that liver is indeed sensitive toward elastographic assessment. There are no significant differences between studies conducted by Jung and Tamura et al. (2019) on hepatic shear wave values (SWVs) in healthy canines. The former concluded that the mean SWVs of the healthy canine right liver lobe was at  $1.60 \pm 0.11$  m/s while the latter concluded at 1.51 (range, 1.44-1.66) m/s. As for the feline hepatic SWE study, Park et al. (2021) and Kim et al. (2020) demonstrated a reliable mean SWV of 1.46 (1.36-1.55) m/s and  $1.52 \pm 0.13$  m/s respectively, in feline patients. Feng et al. (2016) compared the diagnostic accuracy of SWVs and histologic grading of canine liver stiffness due to induced hepatic fibrosis, ranging from F0 to F4 with increased severity. The median E was found to increase significantly from F0 (5.0  $\pm$  0.4) kPa to F4 (28.3  $\pm$  17.8) kPa, which supported the hypothesis that increasing organ stiffness due to disease severity will have a higher propagation velocity from reduced elasticity and viscosity. According to Feng, the 2D-SWE also had a better performance in assessing liver fibrosis than the conventional transient elastography. This statement was also supported by Massimini et al. (2022) as their study demonstrated the high reliability of SWE in quantifying the stiffness of canine mammary nodular lesions, which will be discussed later. In Feng's study, the 2D-SWE shows precise cutoff values of 8.0 kPa and 13.1 kPa for F2 and F4. The results demonstrated by mammary SWE correlated well with the histologic grading of experimental fibrosis with p

< 0.001. Although hepatic SWE has been proven with high reliability, this technique was still unable to differentiate between a canine patient with a closed extrahepatic portosystemic shunt (EHPSS) and a multiple acquired portosystemic shunt (MAPSS) as demonstrated by Toom et al. (2022) (p = 0.33). The authors suggested that similar results between the two groups could be due to insufficient liver fibrosis and alteration in hepatic stiffness caused by the persistent MAPSS. exThus future research regarding dynamic changes between the pre- and postoperative elastography results should be carried out for further investigation. Another study conducted by Tamura et al. (2021) studied the effects of extrahepatic biliary obstruction (EHBO) and hepatic stiffness assessment by using 2D-SWE in dogs. The study demonstrated that EHBO could reversibly increase the SWVs of dogs without clinically relevant hepatic fibrosis, as previously reported in human studies (Harata et al., 2011; Kubo et al., 2016). The cause of increased SWVs in EHBO still remains unknown – as the histopathological hepatic fibrosis stages were not different between dogs with and without EHBO. Therefore more studies need to be conducted to identify the true cause attributed to changes in elasticity in the case of EHBO, aside from the changes in structural organization and molecular constitution in relation to the peculiar organ's disease status.

The study conducted by Cho *et al.* (2022) has again proven that the increase in SWVs is significantly related to tissue stiffness, represented by the infiltration of inflammatory cells and the edematous parenchyma or expansion of the particular organ interstitium, driven by the chemical mediators and complement cascade. Spec cPL immunoreactivity test is currently recognized as one of the most sensitive method (sensitivity 70.0-90.0%; specificity 74.1-88.0%) to diagnose canine acute pancreatitis, by measuring the level of canine pancreas-specific lipase level (Cridge *et al.*, 2021; McCord *et al.*, 2012; Cridge *et al.*, 2018; Haworth *et al.*, 2014). A moderate positive correlation (r = 0.489; p < 0.05) between the pancreatic SWVs and Spec cPL concentration was demonstrated in the case of acute pancreatitis canine patients. SWE of the

right pancreatic lobe was performed in this study as the right pancreatic stiffness is more sensitive towards injury with a higher reproducibility, supported by Jung et al. (2020). The triangular canine pancreas is anatomically divided into the pancreatic body and two lobes. The study conducted by Jung demonstrated a significant difference in the SWVs between the body and the right lobe of the pancreas, which is not aligned with the findings from human studies using pSWE. Ferraioli et al. (2015) suggested that the difference in SWVs between different pancreatic regions is mostly due to technical factors, including the range of interest (ROI), angle and depth. However, this theory is less practical in the case of canine anatomy as both the body and the right lobe of the pancreas are located just superficially within the abdominal cavity. Jung concluded that the differences in SWE could be caused by probe compression during the investigation of the pancreatic body as it is located below the pylorus. Another study conducted by Avante et al. (2020) demonstrated that chronic pancreatic changes commonly had higher SWVs as compared to acute pancreatic alterations. Similar findings were also discussed in human patients by Goertz et al. (2016) by using ARFI technique. The high SWVs in chronic pancreatitis were suggested to be due to chronic fibrosis from prolonged inflammatory cascade which occurred within the pancreatic parenchyma, in which the increased fibrous content resulted in greater stiffness and decreased elasticity within the organ parenchyma.

A prospective study conducted by Massimini *et al.* (2022) demonstrated a significant correlation between the mean SWVs of mammary tissue and the extent of fibrosis. The SWVs were lower for benign mammary hyperplasia (100.8  $\pm$  15.8 kPa) with a 37.06  $\pm$  15.59% of fibrosis. However, for a benign mammary tumor with a 70.50  $\pm$  0.79% of fibrosis, the SWVs increased to 137.4  $\pm$  4.8 kPa, which again proved the correlation between tissue stiffness and SWVs (p < 0.001). The grade III malignant canine mammary tumor was reported to have a lower mean SWVs at 88.7  $\pm$  56 kPa compared to grade I (114.9  $\pm$  4.9 kPa). This result was

supported by another study conducted by Glińska-Suchocka et al. (2013). The author discussed that the neoplastic changes in most malignant tumors had a lower elasticity and lesser tissue deformation since the malignant neoplastic tumors were growing rapidly. The stromal fibrous tissue infiltration did not take place within a short period of time thus they were accompanied merely by an inflammatory reaction. A similar finding was demonstrated in a study conducted on a group of 52 women with mammary gland lesion, conducted by Evans et al. (2010). However, in the case of *tumor mixtus*, cartilaginous and bone tissue infiltration could produce false positive results as they contributed to the higher tissue stiffness. A tissue biopsy or FNA should be carried out to determine the underlying tumor type because in such cases, the role of elastography is limited (Dobruch-Sobczak & Sudoł-Szopińska, 2011). Many publications in the field of human medicine have demonstrated positive results of the studies on sonoelastographic differentiation of the female mammary gland lesion, in which the performance of this diagnostic modality has been proved (Olgun *et al.*, 2014; Youk *et al.*, 2017; Evans et al., 2010). 2D-SWE is safe to differentiate between the benign and malignant neoplastic lesions of the mammary gland. Yet, it should be remembered that the identification of the exact tumor type requires a further diagnostic workup.

Tamura *et al.* (2019) evaluated the spleen stiffness of healthy dogs by using 2D-SWE in which the results can be served as a baseline reference. Due to the splenic anatomical tissue organization which consists of red and white pulp and also the fibroelastic reticular parenchyma, the mean SWV and mean E was higher as compared to the liver, which was  $2.18 \pm 0.27$  m/s and  $14.66 \pm 3.79$  kPa, respectively, across 8 healthy Beagles. Also supported by Jung *et al.* (2020), the acquisition of splenic elastographic images could be easily induced due to the superficial anatomical location of the spleen. In Tamura's opinion, splenic stiffness measured with 2D-SWE can be served as supporting evidence to assess secondary splenomegaly from

portal hypertension. It can be used as a prediction tool to identify the onset or severity of portal hypertension in small animal patients with chronic hepatitis or cirrhosis.

As for the renal elastographic technique, the anatomical complexity of the kidney parenchyma renders inconsistent SWE values. A study conducted by Thanaboonnipat *et al.* (2019) demonstrated no significant difference across the average Young's modulus values of feline renal cortex and medulla bilaterally in each healthy and chronic kidney disease (CKD) group. However, higher average *E* values of the renal cortex and medulla of CKD patients (left kidney:  $51.89 \pm 11.25 \text{ kPa}$ ;  $39.16 \pm 13.07 \text{ kPa}$ ) were demonstrated in this study as compared to the normal control group (left kidney:  $38.40 \pm 7.12 \text{ kPa}$ ;  $30.16 \pm 5.97 \text{ kPa}$ ), with a p-value of p < 0.001 and p < 0.01, respectively. Similar findings were demonstrated in a human study conducted by Grosu *et al.* (2019), in which the SWV values are significantly lower in the CKD patient group as opposed to the healthy volunteer. According to Jung *et al.* (2020), canine renal medulla elastographic measurements are unreliable due to anatomical anisotropy of the renal pyramids, which can result in heterogenous propagation of the shear wave as depicted in the color map, within the region of interest.

The prior ARFI study conducted by Silva *et al.* (2018) demonstrated that the 2D-SWE approach might also be applied to other organs, such as peripheral lymph nodes. Significantly elevated SWVs were seen in the inguinal and axillary lymph nodes of canines with metastatic tumors. 2D-SWE was superior to B-mode and Doppler in detecting metastatic lymph nodes, with 100% sensitivity and 94% specificity in the axillary lymph node and 95% sensitivity and 87% specificity in the inguinal lymph node, respectively. In contrast, the study conducted by Kang *et al.* (2021) on healthy peripheral lymph nodes revealed no significant difference between the positions (peripheral, central, entire) and scanning planes (transverse, sagittal) of the LNs in relation to their respective SWVs. This is likely due to the less anatomical complexity of LNs

and their relative sizes when compared to other organs, despite their anatomical division into cortex and medulla.

In a study of numerous soft tissue organs conducted by Jung *et al.* (2020), the salivary gland and thyroid exhibited dependable interobserver agreement and a homogenous colour map appearance without transducer compression. Cosgrove *et al.* (2017) demonstrated comparable results in their investigation of humans. In another human investigation, however, pSWE using ARFI imaging shown greater sensitivity and specificity in distinguishing thyroid nodules than 2D-SWE (90% and 79%; 73% and 66%, respectively) (Kyriakidou *et al.*, 2018). The SWE of the salivary gland in humans has only been the subject of a few number of studies, but prior to Jung *et al.* (2020), there was no research had been conducted on canine populations. Additional research is necessary to investigate the technical aspects influencing the 2D-SWE in salivary glands and their relative accuracy in clinically afflicted dogs.

It is difficult to visualize the prostate elastography in the canine population due to its intrapelvic anatomical position. Quantitative elastography can only be performed on the visible portion of the prostate, and according to Jung *et al.* (2020), there was no significant difference between the left and right SWVs, which is validated by Feliciano *et al.* (2015) using the ARFI approach.

Shimizu & Ito (2019) investigated the shear elastic modulus of muscle, specifically on the thigh musculatures including the cranial portion of the sartorius, vastus lateralis, biceps femoris, and semitendinosus muscle. As the first study to investigate the feasibility of ultrasound SWE for muscle stiffness in the canine population, this study demonstrated an increase in the shear elastic modulus of muscle during muscle elongation, proving that changes in muscle stretch are responsible for the increase in muscle stiffness. Maïsetti *et al.* (2012), Koo *et al.* (2015), and Miyamoto *et al.* (2017) demonstrated comparable results in human medical research. Tokunaga & Shimizu (2021) also concluded that in adult Beagles, the thoracolumbar multifidus

muscle stiffness decreased with age. The author's hypothesis regarding the relationship between muscle stiffness and the onset of intervertebral disk diseases was rejected as there was no significant difference demonstrated from the study. Further study is required in order to identify the reason of the segmental difference between the adult and young Beagle's muscle shear modulus.

#### Sources of Variation on SWE Measurement

Even though this innovative imaging technology has been demonstrated to be increasingly beneficial in clinical settings, there are still limitations and sources of variation in its use in small animal medicine. As numerous technological aspects are not standardized, the comparability of data across various system configurations and characteristics will vary. The study conducted by Tamara et al. (2019) regarding hepatic SWVs in healthy beagles demonstrated an SWVs difference between the left and right liver lobes in which the right lobe had significantly higher SWVs than the left lobe. Whereas in the study conducted by Jung et al. (2020), no significant difference were identified between different measurement sites and approaches to the liver. However, when comparing the SWVs between these two studies, Jung's demonstrated a generally higher hepatic SWVs than Tamara's (right lobe 7.57 ± 1.17 kPa and left lobe 7.8  $\pm$  0.06 kPa; right lobe 6.93  $\pm$  0.79 kPa and left lobe 6.02  $\pm$  0.61 kPa, respectively). Yet, a direct comparison of the data across these two studies is difficult, as a different model of the ultrasound machine and probe were used. A multifrequency linear probe was used in the study conducted by Jung, and as supported by human literature by Ferraioli et al. (2018), the linear probe can derive a higher hepatic SWS than the convex probe in the case of liver fibrosis and cirrhosis.

Besides the technological aspects, the examination technique itself such as the application of anesthesia, selection of ROI, number of valid measurements, the plane of acquisition, pressure,

and angle of the probe. The usage of sedatives and anesthesia can help in reduce respiratory motion in animals while making the elastography procedure smooth, especially in uncooperative patients (Holdsworth *et al.*, 2014; Jung *et al.*, 2020). However, a study conducted by Puccinelli *et al.* (2022) demonstrated that the median 2D-SWE was significantly higher in anesthetized dogs, which proved that anesthesia was a source of variability in the SWE values. The study conducted by Jung also described an increment in splenic SWVs in the post-anesthetic phase. Both of the findings could be due to the contribution of the anesthetic drugs in transient cardiovascular modifications and hemodynamics, which results in alterations in liver and splenic perfusion. Similar findings were also demonstrated in human medicine regarding hepatic congestion caused by right-sided congestive heart failure, cardiovascular anomalies, and disease conditions related to the heart valves (Ferraioli *et al.*, 2020).

In addition to the patient's respiration and cardiac motion, the SWE can also be altered by patient-specific variables such as body weight, body condition score, sex, and anatomical geometry (Holsworth *et al*, 2014). According to Kim *et al*. (2020), the patient's age, weight, and body condition score were not confounding factors for feline hepatic SWVs. Similar findings were also discussed by Jung *et al*. (2020) in canine patients. However, a pSWE study by Cosgrove *el al*. (2013) conducted in the canine populations demonstrated that sex and body weight had a significant effect on SWVs in certain organs. Tokunaga & Shimizu also concluded that thoracolumbar multifidus muscle stiffness in dogs was affected by their age. Thus, further studies with larger sample sizes across different breeds with even female to male numbers are required to examine the effect of patient factors to the SWVs.

Concurrent diseased status can also affect the SWV values in a SWE study. A study conducted by Tamara *et al.* (2021) in canine hepatic SWE has demonstrated that a concurrent biliary disease, particularly extrahepatic biliary obstruction can reversibly elevate the hepatic SWVs

in a patient without clinically relevant hepatic fibrosis, as proven by histopathological examination, to such a degree that might cause confusion. The author also concluded that EHBO can interfere with predicting noninvasive hepatic fibrosis using 2D-SWE. A similar finding was also demonstrated in human studies conducted by Harata *et al.* (2011) however in this study, liver biopsies were not conducted as the biliary drainage in all patients was achieved by noninvasive techniques such as endoscopic or percutaneous transhepatic biliary drainage. Thus it is not clear whether the patients with EHBO in this study had accompanying histopathological hepatic fibrosis during measurement of SWV.

#### 6.0 CONCLUSION AND RECOMMENDATION

In this review, the feasibility and sensitivity of shear wave elastography (SWE) in small animal soft tissue injuries were reviewed. It is safe to say that SWE has reliable accuracy and reproducibility in diagnosing small animal soft tissue injuries. Many studies have established a baseline for different organs which can be used as a reference. Up until December 2022, the liver remains the most studied organ in small animal practices. 2D-SWE has effectively proven its sensitivity and feasibility in small animal studies and is supported by many previous literature, in both human and veterinary medicine. However, to further investigate the reliability and reproducibility of 2D-SWE in diagnosing particular organ injury and alteration of tissue stiffness, additional studies must be conducted across species and breeds with other diagnostic modalities as references (e.g., other imaging or elastography techniques, cytological examination, histopathological examination, and blood work). Different sources of variation must be identified to ensure that the data are standardized.

As a recommendation to improve this review, more feline SWE studies should be included as there is a marked imbalance in the proportion of the studies across canine and feline SWE. More studies that correlates the shear wave values to other diagnostic references should also be included to further investigate the accuracy and sensitivity of SWE itself. Other databases can be included to further improvise this review. Lastly, bias assessment and meta-analysis can be performed on all the literature included. This can further evaluate the quality of the data and the degree of reliability of the evidence, presented in this review.

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#### **REFERENCES**

- Avante, L. M., Rossi, F. M. A., Ramirez, U. R. A., Cristina, M. M., Aguila, S. P. D., Ricardo, P., Rodrigues, S. A. P., Priscila, S., Beatriz, G., Letícia, P., Nogueira, A. L. P., & Carlos, C. J. (2020). Pancreatic Evaluation in Dogs using Different Ultrasonographic Techniques Preliminary Results. *Acta Veterinaria*, 70(2), 255-266. https://doi.org/10.2478/acve-2020-0018
- Çebi Olgun, D., Korkmazer, B., Kılıç, F., Dikici, A. S., Velidedeoğlu, M., Aydoğan, F., Kantarcı, F., & Yılmaz, M. H. (2014). Use of shear wave elastography to differentiate benign and malignant breast lesions. *Diagnostic and interventional radiology* (*Ankara*, *Turkey*), 20(3), 239–244. https://doi.org/10.5152/dir.2014.13306
- Cho, H., Yang, S., Suh, G., & Choi, J. (2022, Sep). Correlating two-dimensional shear wave elastography of acute pancreatitis with Spec cPL in dogs. *J Vet Sci*, 23(5), e79. https://doi.org/10.4142/jvs.22055
- Cosgrove, D., Piscaglia, F., Bamber, J., Bojunga, J., Correas, J.-M., Gilja, O. H., et al. (2013). EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: clinical applications. *Eur. J. Ultrasound* 34, 238–253. doi: 10.1055/s-0033-1335375
- Cridge H, MacLeod AG, Pachtinger GE, Mackin AJ, Sullivant AM, Thomason JM, et al. Evaluation of SNAP cPL, spec cPL, VetScan cPL rapid test, and precision PSL assays for the diagnosis of clinical pancreatitis in dogs. J Vet Intern Med. 2018;32(2):658-664.
- Cridge H, Twedt DC, Marolf AJ, Sharkey LC, Steiner JM. Advances in the diagnosis of acute pancreatitis in dogs. J Vet Intern Med. 2021;35(6):2572-2587.
- DeJong, H. M., Abbott, S., Zelesco, M., Kennedy, B. F., Ziman, M. R., & Wood, F. M. (2017). The validity and reliability of using ultrasound elastography to measure cutaneous stiffness, a systematic review. *International journal of burns and trauma*, 7(7), 124–141.
- Dobruch-Sobczak K, Sudoł-Szopińska I (2011) The useful- ness of sonoelastography in the differential diagnosis of solid breast lesions. Ultrasonografia 11: 8-16.

- Evans, A., Whelehan, P., Thomson, K. *et al.* Quantitative shear wave ultrasound elastography: initial experience in solid breast masses. *Breast Cancer Res* **12**, R104 (2010). https://doi.org/10.1186/bcr2787
- Feliciano MA, Maronezi MC, Simões AP, Uscategui RR, Maciel GS, Carvalho CF, Canola JC, Vicente WR. Acoustic radiation force impulse elastography of prostate and testes of healthy dogs: preliminary results. J Small Anim Pract. 2015 May;56(5):320-4. doi: 10.1111/jsap.12323. Epub 2015 Jan 23. PMID: 25615284.
- Feng, Y. H., Hu, X. D., Zhai, L., Liu, J. B., Qiu, L. Y., Zu, Y., Liang, S., Gui, Y., & Qian, L. X. (2016, May 7). Shear wave elastography results correlate with liver fibrosis histology and liver function reserve. World J Gastroenterol, 22(17), 4338-4344. https://doi.org/10.3748/wjg.v22.i17.4338
- Ferraioli G, Barr RG. Ultrasound liver elastography beyond liver fibrosis assessment. World J Gastroenterol. 2020;26(24):3413–3420.
- Ferraioli, G., Filice, C., Castera, L., Choi, B. I., Sporea, I., Wilson, S. R., et al. (2015). WFUMB guidelines and recommendations for clinical use of ultrasound elastography. part 3: liver. *Ultrasound Med. Biol.* 41, 1161–1179. doi: 10.1016/j. ultrasmedbio.2015.03.007
- Figueira, C., Thassila, C. F., & Maria, C. C. (2015). Elastography: Principles and considerations for Clinical Research in Veterinary Medicine cibele. *Journal of Veterinary Medicine and Animal Health*, 7(3), 99–110. https://doi.org/10.5897/jvmah2014.0344
- Glinska-Suchocka, K., Jankowski, M., Kubiak, K., Spuzak, J., Dzimira, S., & Nicpon, J. (2013). Application of shear wave elastography in the diagnosis of mammary gland neoplasm in dogs. *Pol J Vet Sci*, 16(3), 477-482. https://doi.org/10.2478/pjvs-2013-0066
- Goertz, R. S., Schuderer, J., Strobel, D., Pfeifer, L., Neurath, M. F., and Wildner, D. (2016). Acoustic radiation force impulse shear wave elastography (ARFI) of acute and chronic pancreatitis and pancreatic tumor. *Eur. J. Radiol.* 85, 2211–2216. doi: 10.1016/j.ejrad.2016.10.019
- Grosu, I., Bob, F., Sporea, I., Popescu, A., Sirli, R., & Schiller, A. (2019). Two-Dimensional Shear-Wave Elastography for Kidney Stiffness Assessment. *Ultrasound quarterly*, 37(2), 144–148. https://doi.org/10.1097/RUQ.000000000000000461

- Harata M, Hashimoto S, Kawabe N, et al. Liver stiffness in extra- hepatic cholestasis correlates positively with bilirubin and neg- atively with alanine aminotransferase. *Hepatol Res*. 2011;41:423-429.
- Haworth MD, Hosgood G, Swindells KL, Mansfield CS. Diagnostic accuracy of the SNAP and Spec canine pancreatic lipase tests for pancreatitis in dogs presenting with clinical signs of acute abdominal disease. J Vet Emerg Crit Care. 2014;24(2):135-143.
- Holdsworth A, Bradley K, Birch S, et al. Elastography of the normal canine liver, spleen and kidneys. Vet Radiol Ultrasound. 2014;55(6):620–627.
- Jung, J. W., Je, H., Lee, S. K., Jang, Y., & Choi, J. (2020). Two-Dimensional Shear Wave Elastography of Normal Soft Tissue Organs in Adult Beagle Dogs; Interobserver Agreement and Sources of Variability. *Front Bioeng Biotechnol*, 8, 979. https://doi.org/10.3389/fbioe.2020.00979
- Kang, Y. L., S.; Seo, I.; Ko, J.; Kim, J.; Eom, K. (2021). Comparison of shear-wave velocities obtained with shear-wave elastography of various peripheral lymph nodes in healthy Beagles
- Kim, D. W., Suh, C. H., Kim, K. W., Pyo, J., Park, C., & Jung, S. C. (2019). Technical performance of two-dimensional shear wave Elastography for measuring liver stiffness: A systematic review and meta-analysis. *Korean Journal of Radiology*, 20(6), 880. https://doi.org/10.3348/kjr.2018.0812
- Kim, K., Lee, J., So, J., Jang, Y. S., Jung, M., Kang, K., Choi, M., & Yoon, J. (2020). Feasibility and Reliability of Two-Dimensional Shear-Wave Elastography of the Liver of Clinically Healthy Cats. *Front Vet Sci*, 7, 614750. https://doi.org/10.3389/fvets.2020.614750
- Koo TK, Guo JY, Cohen JH, Parker KJ. Relationship between shear elastic modulus and passive muscle force: an ex-vivo study. J Biomech 2013;46(12):2053–2059
- Kubo, K., Kawakami, H., Kuwatani, M., Nishida, M., Kawakubo, K., Kawahata, S., Taya, Y., Kubota, Y., Amano, T., Shirato, H., & Sakamoto, N. (2016). Liver elasticity measurement before and after biliary drainage in patients with obstructive jaundice: A prospective cohort studya prospective cohort study. BMC Gastroenterology, 16(1). https://doi.org/10.1186/s12876-016-0479-3
- Kyriakidou, G., Friedrich-Rust, M., Bon, D., Sircar, I., Schrecker, C., Bogdanou, D., Herrmann, E., & Bojunga, J. (2018). Comparison of strain elastography, point shear

- wave elastography using acoustic radiation force impulse imaging and 2D-shear wave elastography for the differentiation of thyroid nodules. *PloS one*, *13*(9), e0204095. https://doi.org/10.1371/journal.pone.0204095
- Maïsetti O, Hug F, Bouillard K, Nordez A. Characterization of passive elastic properties of the human medial gastrocnemius muscle belly using supersonic shear imaging. J Biomech 2012;45 (06):978–984
- Massimini, M., Gloria, A., Romanucci, M., Della Salda, L., Di Francesco, L., & Contri, A. (2022, Sep 15). Strain and Shear-Wave Elastography and Their Relationship to Histopathological Features of Canine Mammary Nodular Lesions. *Vet Sci*, 9(9). https://doi.org/10.3390/vetsci9090506
- McCord K, Morley PS, Armstrong J, Simpson K, Rishniw M, Forman MA, et al. A multi-institutional study evaluating the diagnostic utility of the spec cPLTM and SNAP® cPLTM in clinical acute pancreatitis in 84 dogs. J Vet Intern Med. 2012;26(4):888-896.
- Miyamoto N, Hirata K, Kanehisa H. Effects of hamstring stretching on passive muscle stiffness vary between hip flexion and knee extension maneuvers. Scand J Med Sci Sports 2017;27(01):99–106
- Park, S. C., J.; Kim, K.; Oh, D.; Yoon, J.; Choi, M. (2021). Point shear wave elastography of the liver in healthy adult cats.
- Puccinelli, C., Pelligra, T., Briganti, A., & Citi, S. (2022). Two-dimensional shear wave elastography of liver in healthy dogs: anaesthesia as a source of variability. *Int J Vet Sci Med*, *10*(1), 46-51. https://doi.org/10.1080/23144599.2022.2073138
- Samani, A., Zubovits, J., & Plewes, D. (2007). Elastic moduli of normal and pathological human breast tissues: An inversion-technique-based investigation of 169 samples. *Physics in Medicine and Biology*, 52(6), 1565–1576. https://doi.org/10.1088/0031-9155/52/6/002
- Shiina, T., Nightingale, K. R., Palmeri, M. L., Hall, T. J., Bamber, J. C., Barr, R. G., Castera, L., Choi, B. I., Chou, Y. H., Cosgrove, D., Dietrich, C. F., Ding, H., Amy, D., Farrokh, A., Ferraioli, G., Filice, C., Friedrich-Rust, M., Nakashima, K., Schafer, F., Sporea, I., ... Kudo, M. (2015). WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 1: basic principles and terminology. *Ultrasound in*

- *medicine* & *biology*, 41(5), 1126–1147. https://doi.org/10.1016/j.ultrasmedbio.2015.03.009
- Shimizu, M., & Ito, Y. (2019, Nov). Change in Shear Elastic Modulus of Thigh Muscle by Changing Muscle Length Using Ultrasound Shear Wave Elastography in Beagle Dogs. *Vet Comp Orthop Traumatol*, 32(6), 454-459. https://doi.org/10.1055/s-0039-1692449
- Sigrist, R. M. S., Liau, J., Kaffas, A. E., Chammas, M. C., & Willmann, J. K. (2017).

  Ultrasound Elastography: Review of Techniques and Clinical Applications.

  Theranostics, 7(5), 1303–1329. https://doi.org/10.7150/thno.18650
- Silva, P., Uscategui, R. A. R., Maronezi, M. C., Gasser, B., Pavan, L., Gatto, I. R. H., et al. (2018). Ultrasonography for lymph nodes metastasis identification in bitches with mammary neoplasms. *Sci. Rep.* 8:17708. doi: 10.1038/s41598-018-34806-9
- Tamura, M. O., H.; Nisa, K.; Osuga, T.; Sasaki, N.; Morishita, K.; Takiguchi, M. (2019). Evaluation of liver and spleen stiffness of healthy dogs by use of two-dimensional shear wave elastography.
- Tamura, M., Ohta, H., Osuga, T., Sasaki, N., Morishita, K., & Takiguchi, M. (2021, Jul). Extrahepatic biliary obstruction can interfere with hepatic fibrosis prediction using two-dimensional shear wave elastography in dogs. *Vet Radiol Ultrasound*, 62(4), 483-489. https://doi.org/10.1111/vru.12969
- Tamura, M., Ohta, H., Shimbo, G., Osuga, T., Sasaki, N., Morishita, K., Kagawa, Y., & Takiguchi, M. (2019, Sep). Usefulness of noninvasive shear wave elastography for the assessment of hepatic fibrosis in dogs with hepatic disease. *J Vet Intern Med*, 33(5), 2067-2074. https://doi.org/10.1111/jvim.15598
- Thanaboonnipat, C., Sutayatram, S., Buranakarl, C., & Choisunirachon, N. (2019, Feb 11).

  Renal shear wave elastography and urinary procollagen type III amino-terminal propeptide (uPIIINP) in feline chronic kidney disease. *BMC Vet Res*, 15(1), 54. https://doi.org/10.1186/s12917-019-1801-4
- Tokunaga, A., & Shimizu, M. (2021). Age-related change in shear elastic modulus of the thoracolumbar multifidus muscle in healthy Beagle dogs using ultrasound shear wave

elastography. *Journal of veterinary science*, 22(1), e3. https://doi.org/10.4142/jvs.2021.22.e3

- Toom, M., Saunders, J. H., Duchateau, L., Serrano, G., De Rooster, H., Devriendt, N., & Stock,
   E. (2022). Shear wave elastography measurements in dogs treated surgically for congenital extrahepatic portosystemic shunts. Front Vet Sci, 9, 991148.
   https://doi.org/10.3389/fvets.2022.991148
- Youk, J. H., Gweon, H. M., & Son, E. J. (2017). Shear-wave elastography in breast ultrasonography: the state of the art. *Ultrasonography (Seoul, Korea)*, *36*(4), 300–309. https://doi.org/10.14366/usg.17024

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Appendix A: Raw data summary from each study included for the review

Author (year)	OOI	Subjects	Ultrasound system	Use of anaesthesia	Results	Conclusion
Type of study	ROI					
Glińka-Suchocka	MG	12 dogs with	Aixplorer, 7.5-15	NM	The benign mammary	SWE effectively
(2013)		MG tumoral	MHz probe		tumor has a lower stiffness	differentiate different MG
n		lesions			as compared to the	lesion particularly
P					malignant tumor, average	between the benign and
					22.42 kPa and 235.44 kPa,	malignant neoplastic
					respectively.	condition.
Feng (2016)	Liver	12	Aixplorer color	Anesthetized,	Positive correlation	SWE LSM has a
CC		experimental	Doppler ultrasound	drugs were not	between SWE LSM and	significant correlation
CS		Beagles with	system, 4-15 MHz	mentioned	histologic hepatic fibrosis	with hepatic fibrosis
		induced	probe		grading (r = 0.835, p <	confirmed with
		hepatic			0.001). Significant increase	histopathological
		fibrosis, 2			of G in the F4 group as	examination and MEGX
		control			compared to F3, F2 and F0.	liver function test.
		animals				

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Shimizu (2019)	Thigh muscles	12 healthy	Aplio i600 with a	Sedated with	Increment in the thigh	Changes in muscle length
P		Beagles	hi <mark>gh-freq</mark> uency	medetomidine 20	musculature elastic	can caused an increment
r			1 <mark>0MHz li</mark> near array	ug/kg, IM	modulus were demonstrated	in shear elastic modulus of
			tr <mark>ansducer</mark> (PLT-		in all thigh muscle groups	the thigh musculatures
			1 <mark>005 BT)</mark>		when it was elongated.	and SWE is feasible in
						assessing the stiffness of
						healthy dog musculature.
Tamura (2019)	Liver	28 dogs with	Aplio 500 with a 3.5-	All dogs were not	High median SWVs were	2D-SWE is feasible in
CS		hepatic	MHz convex probe	anesthetized or	demonstrated in canine	detecting the disease
CS		diseases and 8	(PVT-375 BT)	sedated	patient with significant	condition of liver in
		normal			hepatic fibrosis (2.04 m/s	canine patient particularly
		healthy			with the range of 1.81-2.26	on hepatic fibrosis.
		Beagles			m/s) than in healthy control	
					group (1.51 m/s with the	
					range of 1.37-1.67 m/s).	
					However, SWE cannot	
					significantly differenciate	
					between dogs with	
					necroinflammatory activity	
					and those without the	
					activity.	
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Tamura (2019)	Liver, spleen	8 healthy	3.5-MHz convex	All dogs were not	The hepatic and splenic	SWE showed feasibility in
P		Beagles	transducer	anesthetized or	SWVs as demonstrated in	assessing both hepatic and
P				sedated	this study was $1.51 \pm 0.08$	splenic tissue stiffness in a
					m/s and $2.18 \pm 0.27$ m/s,	healthy canine population.
					respectively. Higher	
					elasticity was identified in	
					the splenic SWVs as	
					compared to the hepatic	
					values.	
Thanaboonnipat	Kidney	23 CKD cats	Resona-7 with a 9-	No, restrained	The E value in the feline	SWE showed feasibility in
•	Kidiley	and 25		,		•
(2019)				manually	renal parenchyma (both	
CS		healthy cats	tr <mark>ansducer</mark>		cortex and medulla) was	•
					significantly higher in the	the uPIIINP/Cr can be use
					CKD group as compared to	as a biomarker in
					the healthy cat group. A	diagnosing early feline
					positive correlation	renal fibrosis or CKD.
					between the cortical E	
					values, plasma creatinine	
					and BUN was identified.	
Avante (2020)	Pancreas	16 healthy	ACUSON S2000 -	NM	The group with suspected	SWE has a good
n		dogs and 9	SIEMENS, with a		pancreatic disease has a	sensitivity and specificity
P		dogs with	linear and convex		higher SWV than the	as compared to CEUS and

		suspected	multifrequency		healthy group $(2.4 \pm 0.5 \text{ m/s})$	Doppler ultrasound in
		pancreatic	transducers (7.5-9.0		and $1.9 \pm 0.3$ m/s,	identifying pancreation
		disease	MHz)		respectively), with a	alteration in canine study.
					sensitivity of 78% and a	
					specificity of 69%.	
Jung (2020)	Liver, spleen,	9 healthy	Aplio i600 with a 5.0-	All dogs were	All abdominal organs	SWE is feasible and
ח	kidney,	Beagles	14.0 MHz linear-	anesthetized with	showed moderate to	reproducible in canine
P	pancreas,		array transducer	0.75mg/kg	excellent reproducibility	practice with anaesthesia
	prostate, LNs,			zolazepam-	except for the left hepatic	and measuring sites as the
	SGs, thyroid			tiletamine, IM and	lobe, while the renal	possible sources of
				0.03mg/kg	medulla could not be	variability.
				medetomidi <mark>ne.</mark>	assessed with SWE	
					effectively. Anaesthesia	
					significantly increase the	
					splenic G. Significant	
					differences in the SWE	
					across different measuring	
					site and scan approach of	
					pancreas and kidneys were	
					observed (p $< 0.001$ ), but	
					not in the liver.	

Kim (2020)	Liver	29	healthy	Aplio i800	with a	Gabapentin	n was	SWVs and stiffness were	Patient's factors (age,
D		cats		12.0-MHz	linear	prescribed	during	lower in the right hepatic	body weight, BCS) and
P				transducer		transport	and	lobe than the left, with 1.52	usage of gabapentin does
						examinatio	n	$\pm$ 0.13 m/s and 1.61 $\pm$ 0.15	not influence the SWVs in
						100mg/cat		m/s respectively ( $p = 0.005$ ,	feline hepatic study. SWE
								p = 0.002). No significant	is reliable in feline study
								result detected from the	and these data can be
								patient's factor and usage of	served as a baseline
								anaesthesia ( $p > 0.05$ ).	reference.
Kang (2021)	PLNs	11	healthy	Aplio 500 a	and Anlie	Some do	os ore	The image acquisition plane	SWV effectively
Kang (2021)	FLINS		•	•	•				•
P		Beagl	les	A with	10-MHz		with	is significant in the LNs	
				linear	array	medetomid	line	SWV, in which all scans	PLNs with good
				transducer		hydrochlor	ride;	examined in sagittal plane is	reproducibility. This data
						maximum	dose of	higher than the transverse	can be served as a
						$40 \mu g/kg$	IM to	plan. The mandibular LN is	reference for other future
						minimize		the most superficial, with	SWE study.
						movement		the highest SWVs while the	
						artifacts.		medial retropharyngeal LN	
								is the deepest.	
Park (2021)	Liver	18	healthy	ARIETTA	830	No sedat	ion or	The right hepatic SWVs	pSWE was feasible in
n		cats		ultrasound	machine	anesthesia	was	were higher as compared to	quantifying the hepatic
P				with a small	4-8 MHz	used in a	ll cats,	the left hepatic lobe, with	stiffness in healthy

			curved-array transducer and 2-12 MHz linear-array transducer.	restrained manually.	1.36-1.55 m/s (1.46 m/s) and 1.26-2.47 m/s (1.36 m/s), respectively.	
Tamura (2021)	Liver	7 dogs with	Aplio 500 with a 3.5-	All dogs were not	A significantly higher	EHBO can reversibly
CS		EHBO and 13	MHz convex	anesthetized or	median SWVs were	increase and interfere the
CS		healthy	transducer (PVT-	sedated	identified in the EHBO	canine hepatic SWVs at
		Beagles	375BT)		group as compared to the	the degree that is similar
					healthy control group, with	to clinically significant
					1.91 (1.8102.54) m/s and	hepatic fibrosis.
					1.57 (1.37-1.64) m/s,	
					respectively, although there	
					was no histopathological	
					relevant hepatic fibrosis in	
					the patient with EHBO,	
					after a FNA biopsy	
					examination.	
Tokunaga (2021)	Thoracolumbar	5 young dogs	Aplio a450 with a 10-	All dogs were	Increment of multifidus	SWE effectively measures
	multifidus	with IVDH	MHz linear array	\ \/ E   /	length and cross-sectional	•
P	muscle	onset < 2yo	transducer (PLT-	medetomidine	area towards the caudal.	2
		and 7 adult	1005 BT)	intramuscularly	The multifidus E of T13 <	thoracolumbar region.
		dogs with	KELA	NTAN	L3 for the young group	Č

		IVDH onset >			while E for L1-L3 in the	
		2yo			adult group is lower as compared to the young group.	age.
Cho (2022)	Pancreas	31 healthy	EPIQ 5 with a 4-18	All dogs were	The acute pancreatitis	SWE showed high
CS		dogs and 10 dogs with	MHz linear array transducer	manually restrained without	patient has a significantly higher SWVs as compared	
		acute pancreatitis		sedation or anaesthesia	to the healthy control group, with $2.67 \pm 0.20$ m/s and $2.30 \pm 0.26$ m/s,	increased as compared to
					respectively (p < 0.05).  Moderate positive	patients. It can be used as
					between the Spec cPL concentration and the acute pancreatitis shear wave values.	
Massimini (2022)	MG	22 female dogs with	Logiq S8 with a 9L-D multi-frequency	NM	Similar mean SWVs for STE and SWE were	SWE showed high reliability and correlation
P		MG lesion	linear probe			with histologic mammary
					benign and malignant mammary lesion.	fibrosis. SWE also demonstrated better

					Significant correlation was revealed between the level of fibrosis, STE and SWE. (p < 0.001 and p < 0.001, respectively).	to other elastography
Puccinelli (2022)	Liver	45 healthy	Aplio a CUS-AA000	IM injection of	Higher SWVs were	Anesthesia can help with
CS		dogs	by one sonographer, with a 3.5 MHz convex probe	dexmetomidine, methadone and ketamine, followed by IV propofol for induction and isoflurane for maintenance.	demonstrated in the patient administrated with anesthetic drugs than other awake dogs.	motions however, it also
Toom (2022)	Liver	15 dogs with	Philips ElastQ	NM	No significant was	SWE is insufficient in
P		closed EHPSS and 6	Imaging and an eL 18-4 ultra-broadband		demonstrated between the median hepatic SWVs in the	EHPSS and those with
		dogs with MAPSS	linear array transducer		canine group with closed EHPSS and those with MAPSS (2.83 $\pm$ 0.11 m/s	MAPSS.
					and $2.71 \pm 0.17$ m/s, respectively).	

CEUS = contrast-enhanced ultrasound; CKD = chronic kidney disease; CS = cross-sectional; EHBO = extrahepatic biliary obstruction; EHPSS = extrahepatic portosystemic shunt; IVDH = intervertebral disk herniation; LSM = liver stiffness modulus; MAPSS = multiple acquired portosystemic shunts; MG = mammary gland; NM = not mentioned; OOI = organ of interest; P = prospective; PLNs = peripheral lymph nodes; ROI = region of interest; SG = salivary gland; STE = strain elastography; SWE = shear wave elastography

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