



ADRIANA CRISTINA DA SILVA

***STRAIN E STRAIN RATE* LONGITUDINAL POR
MEIO DO *SPECKLE TRACKING* BIDIMENSIONAL
EM GATOS DOMÉSTICOS SADIOS E NÃO
SEDADOS**

LAVRAS – MG

2012

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Dissertação apresentada à Universidade Federal de Lavras, como parte das exigências do Programa de Pós-Graduação em Ciências Veterinárias, área de concentração em Clínica, Cirurgia e Patologia Veterinária, para a obtenção do título de Mestre.

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2012

**Ficha Catalográfica Preparada pela Divisão de Processos Técnicos da
Biblioteca da UFLA**

Silva, Adriana Cristina da.

Strain e strain rate longitudinal por meio do *speckle tracking*
bidimensional em gatos domésticos saudáveis e não sedados / Adriana
Cristina da Silva. – Lavras : UFLA, 2012.

58 p. : il.

Dissertação (mestrado) – Universidade Federal de Lavras, 2012.

Orientador: Ruthnéa Aparecida Lázaro Muzzi..

Bibliografia.

1. Felinos. 2. Cardiopatia. 3. Ecocardiografia. 4. Strain. I.
Universidade Federal de Lavras. II. Título.

CDD – 636.08961207543

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APROVADA em 28 de fevereiro de 2012.

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LAVRAS – MG

2012

*Aos meus pais, José e Rosa,
por me ensinarem o valor
das pequenas coisas,*

DEDICO

AGRADECIMENTOS

Agradeço a Deus, por me permitir vencer mais esta etapa e conquistar, durante o caminho, amigos de quem jamais me esquecerei.

A meus irmãos e irmãs, que compartilharam comigo muitas felicidades e dificuldades encontradas.

Ao meu amor, amigo e companheiro, Guilherme, que esteve comigo em todos estes momentos, com muita paciência e carinho, compartilhando cada conquista e temor, me incentivando sempre a buscar meus sonhos. E à sua família, que também considero como minha, pelo apoio e consideração.

À professora Ruthnéa, a quem considero mais do que uma orientadora e sim uma amiga e um exemplo, como pessoa e como profissional, pela confiança, apoio e por compartilhar conosco seu conhecimento.

Aos amigos que sempre estiveram presentes em algum momento e que torceram para que tudo fosse perfeito, em especial meus companheiros de mestrado, Gisele, Rosane e Matheus, por estarem ao meu lado, mesmo nos arranhões e miados, pelos risos e lágrimas que juntos compartilhamos. E aos colegas residentes do HV UFLA e alunos, que se mostraram sempre prontos a nos ajudar.

Aos membros da banca examinadora, professores Gregório, Rodrigo, Leonardo e Lacrete, por aceitarem o convite, pela disponibilidade e por compartilharem seu conhecimento.

Ao Departamento de Medicina Veterinária e ao Programa de Pós-Graduação em Ciências Veterinárias, por propiciarem o desenvolvimento do projeto e pela oportunidade de aprendizado.

À Universidade Federal de Lavras, por sempre acolher seus alunos com braços de mãe.

À Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), pelo suporte financeiro durante a realização do projeto.

Aos proprietários dos gatos, que prontamente se dispuseram a nos ajudar E a todos os gatos que participaram do projeto. Todos foram “gracinhas” para mim.

Aos meus gatos, Pretinha, Batata, Toninho e Neném, por estarem em minha vida e ajudarem a despertar o imenso amor que tenho pelos felinos.

“Um gato vive um pouco nas poltronas, no cimento ao sol, no telhado sob a lua. Vive também sobre a mesa do escritório, e o salto preciso que ele dá para atingi-la é mais do que impulso para a cultura. É o movimento civilizado de um organismo plenamente ajustado às leis físicas, e que não carece de suplemento de informação. Livros e papéis beneficiam-se com a sua presteza austera. Mais do que a coruja, o gato é símbolo e guardião da vida intelectual.”

Carlos Drummond de Andrade

RESUMO

A ecocardiografia tem se tornado um dos métodos diagnósticos mais importantes em cardiologia veterinária. Dessa forma, novas ferramentas incorporadas à ecocardiografia, como o Doppler tecidual e, mais recentemente, o *speckle tracking* bidimensional, têm auxiliado no diagnóstico definitivo assim como na determinação do prognóstico das alterações cardíacas. O *speckle tracking* é uma ferramenta já consolidada e validada em medicina humana, sendo utilizada em diversas cardiopatias. Em medicina veterinária, o uso dessa ferramenta já foi demonstrado em cães e equinos. No entanto, por ser recente, ainda não abrange várias espécies, havendo poucas informações ou, mesmo, ausência delas em felinos domésticos. Diante disso, o presente trabalho foi realizado com o objetivo de demonstrar o uso da ferramenta *speckle tracking* bidimensional em gatos, de forma a estabelecer valores de referência e padronizar a técnica em felinos domésticos saudáveis não sedados. Para isso, foram utilizados 30 gatos clinicamente saudáveis e não sedados, dos quais foram obtidos pressão arterial sistólica, eletrocardiograma (ECG) e ecoDopplercardiografia. Três a cinco ciclos cardíacos consecutivos utilizando ECG contínuo foram armazenados em formato digital para posterior avaliação *off-line*. Os *cine loops* foram obtidos a partir da vista apical quatro câmaras esquerda e seis mensurações, utilizando o *software* do *speckle tracking*, foram obtidas em dois diferentes *cine loops* (três medidas para cada *cine loop*) ao final da sístole para todas as variáveis estudadas e, então, a média foi calculada. A função miocárdica longitudinal foi avaliada e as variáveis *strain* (%), *strain rate* (1/s), velocidade (cm/s) e deslocamento (mm) longitudinais foram obtidas, demonstrando os seguintes valores $-15,65 \pm 5,46$, $-1,80 \pm 0,59$, $1,41 \pm 0,87$, $1,27 \pm 0,80$, respectivamente. Dessa forma, o presente estudo auxilia na melhor compreensão da função miocárdica em felinos domésticos.

Palavras-chave: Cardiopatia. Ecocardiografia. Felinos. *Strain*.

ABSTRACT

Echocardiography has become one of the most important diagnostic methods in veterinary cardiology. Thus, new tools incorporated into echocardiography such as tissue Doppler and, more recently two-dimensional speckle tracking has been assisting in the definitive diagnosis, as well as in determining the prognosis of cardiac diseases. The speckle tracking is a well-established and validated tool in human medicine and is used in several heart diseases. In veterinary medicine its use has been demonstrated in dogs and horses. However, its use is recently applied to veterinary, given that, there is little species being studied with speckle tracking. Regarding felines, there is little or even absence of information about the use of this tool in domestic cats. Thus, the present work aimed to demonstrate the use of the two-dimensional speckle tracking echocardiography, in order to establish preliminary reference range and the technique in healthy non-sedated cats. For this purpose, were used 30 clinically healthy non-sedated cats, which were obtained the systolic blood pressure, electrocardiogram (ECG), and Doppler echocardiography. Three to 5 consecutive heart cycles using a continuous monitoring ECG were stored in digital format on a workstation for off-line analysis. Cine loops were acquired from left apical four chamber view and 6 measurements using speckle tracking software were obtained in two different Cine loops (3 measurements for each Cine loop) at end-systole for all studied variables and then average was calculated. Myocardial longitudinal function was evaluated and the variables longitudinal Strain (%) Strain Rate (1/s), velocity (cm/s) and displacement (mm) were obtained, showing the values -15.65 ± 5.46 , -1.80 ± 0.59 , 1.41 ± 0.87 , 1.27 ± 0.80 , respectively. Thus, the present study helps in the better understanding of myocardial function in cats.

Keywords: Cardiopathy. Echocardiography. Felines. Strain.

LISTA DE FIGURAS

PRIMEIRA PARTE

- Figura 1 Padrão de *speckles* em escala de cinza em imagem bidimensional. Pontos acústicos (*speckles*) são identificados na região de interesse. A posição relativa dos pontos é, então, rastreada quadro a quadro (taxa de frames/s), de acordo com a movimentação do miocárdio. dY : deslocamento dos pontos; dX : tempo de deslocamento. Fonte: Suffoletto e Herszkowicz (2006)..... 18
- Figura 2 Esquema demonstrando a deformação miocárdica longitudinal, radial, circunferencial e cisalhamento (*shear strain*). Fonte: Dell Castilho e Herszkowicz (2008)..... 21

SEGUNDA PARTE

- Fig 1. Figures illustrating myocardial tracking in a cat. (A) 2D Apical Four chamber view in a non-sedated healthy cat, demonstrating myocardial tracking process and velocity vectors by STE; (B) 2D-STE analysis of left ventricular epicardial longitudinal strain in a healthy cat. The myocardium is automatically divided into 6 segments: Basal (Bas Sept), Middle (Mid Sept) and Apical (Apic Sept) segments for the interventricular septum and Basal (Bas Lat), Middle (Mid Lat) and Apical (Apic Lat) lateral segments for the left ventricular posterior wall..... 51

Fig 2. Graphical illustration of segmental differences of 2D STE measurements of LV longitudinal function in non-sedated healthy cats (n=30). The line near the middle of the box indicates the middle half of the observations, the top and the bottom of the box indicates the upper and lower quartile, and the whiskers corresponds to the range of observations (smallest and largest observations, respectively). Boxes marked with different letters are significantly different from each other to Mann-Whitney test ($P < 0.05$).....

LISTA DE TABELAS

SEGUNDA PARTE

Table 1	Demographic data (age, weight, heart rate, gender and breed) and systolic blood pressure in non-sedated healthy cats (n = 30).....	53
Table 2	Data of main conventional echocardiographic variables in non-sedated healthy cats (n = 30).....	54
Table 3	Values of global, endocardial and epicardial regions of longitudinal strain, strain rate, displacement and velocity, displayed as mean \pm standard deviation of healthy cats (n=30).....	55
Table 4	Values of segmental and averaged longitudinal strain, strain rate, displacement and velocity, displayed as mean \pm standard deviation of healthy cats (n=30).....	56
Table 5	Table displays the value of between-day intra-observer variability (%).....	57

LISTA DE ABREVIATURAS

DT	Doppler tecidual
ECG	Eletrocardiograma
ROI	Região de interesse
ST	<i>Speckle tracking</i>
St	<i>Strain</i>
StR	<i>Strain rate</i>
VE	Ventrículo esquerdo
2D	Bidimensional

LISTA DE SÍMBOLOS

%	Porcentagem
1/s	Um dividido por Segundo
cm/s	Centímetros por Segundo
mm	Milímetros
±	Mais ou menos

SUMÁRIO

	PRIMEIRA PARTE	15
1	INTRODUÇÃO.....	15
2	REFERENCIAL TEÓRICO	16
2.1	Ecocardiografia.....	16
2.2	Ecocardiografia <i>speckle tracking</i> bidimensional	18
2.2.1	<i>Strain e strain rate</i> bidimensional	20
3	CONSIDERAÇÕES GERAIS	23
	REFERÊNCIAS.....	24
	SEGUNDA PARTE	30
	ARTIGO - Longitudinal strain and strain rate by two-dimensional speckle tracking in non-sedated healthy cats	31
	ANEXO	58

PRIMEIRA PARTE

1 INTRODUÇÃO

O felino doméstico (*Felis catus*) vem se tornando um dos animais de companhia mais populares no mundo. Este fato leva a uma demanda crescente por atendimento veterinário especializado para a espécie. Além disso, há um aumento na longevidade destes animais e, com isso, o surgimento de doenças até recentemente pouco diagnosticadas na rotina.

As cardiopatias em felinos têm recebido grande interesse, uma vez que estes são modelos experimentais para algumas alterações que ocorrem em humanos. Assim, o entendimento da fisiopatologia dessas afecções nesta espécie corrobora para o desenvolvimento não apenas da cardiologia veterinária, mas também da área cardiológica humana.

Neste contexto, a ecocardiografia tem se tornado um dos métodos diagnósticos mais importantes na cardiologia veterinária. O desenvolvimento de novas ferramentas, como o *speckle tracking* (ST), tem auxiliado tanto no campo clínico quanto experimental, uma vez que pode fornecer o diagnóstico definitivo, de forma não invasiva e muitas vezes precoce, das alterações cardíacas.

Em nosso país, a medicina de felinos ainda é uma área em ascensão e que cada vez mais pesquisas em torno desta espécie têm sido desenvolvidas.

O presente estudo foi realizado com o objetivo de avaliar, por meio da ecocardiografia bidimensional (2D) ST, a deformação miocárdica ventricular esquerda pela mensuração do *strain* (St) e do *strain rate* (StR) longitudinal, obtidos em diversos segmentos miocárdicos em felinos clinicamente saudáveis e não sedados, uma vez que não há dados semelhantes relatados na literatura.

2 REFERENCIAL TEÓRICO

2.1 Ecocardiografia

Durante os últimos anos, a ecocardiografia transtorácica tem se tornado uma das ferramentas de imagem mais importantes para o diagnóstico não invasivo e o manejo clínico adequado das doenças cardiovasculares em pequenos animais. Avanços mais recentes em ultrassonografia como o Doppler tecidual (DT) e o ST, têm acrescentado novos parâmetros para a avaliação da função miocárdica, incluindo velocidade regional e deformação, torção ventricular e sincronia mecânica (CHETBOUL, 2010).

Em relação aos felinos, o exame ecocardiográfico é essencial para a avaliação de doenças cardíacas, especialmente animais com suspeita de doença miocárdica adquirida. Este exame é também indicado em casos suspeitos de doenças cardíacas congênitas ou, mesmo, quando alterações são observadas à auscultação, no eletrocardiograma (ECG) ou em outros exames auxiliares (BONAGURA, 2000).

Várias modalidades ecocardiográficas são utilizadas nas doenças cardíacas em felinos (BONAGURA, 2000), como a ecocardiografia convencional (modo-M, 2D, Doppler clássico espectral e mapeamento de fluxo a cores) e novas modalidades do Doppler (tecidual, St e StR) (ABBOTT; MACLEAN, 2006; BOON, 2011a, 2011b, 2011c; WESS; SARKAR; HARTMANN, 2010).

O modo-M e o 2D são utilizados para se obter o diâmetro das câmaras cardíacas e a espessura do septo interventricular e parede ventricular, além da avaliação qualitativa do movimento e função. Estes métodos, associados ao Doppler, podem fornecer uma mensuração mais detalhada do miocárdio (BONAGURA, 2000).

O DT é uma técnica ecocardiográfica que permite a quantificação da função miocárdica global e regional por meio de medidas de velocidade miocárdica em tempo real (CHETBOUL, 2002, 2010; SIMPSON et al., 2007). As modalidades do DT pulsado e modo-M em cores têm demonstrado serem ferramentas sensíveis para se detectar doença miocárdica em felinos (KOFFAS et al., 2006, 2008; MACDONALD et al., 2006).

Em gatos com cardiomiopatia hipertrófica, em alguns estudos foi demonstrado que o DT foi capaz de fornecer o diagnóstico precoce da doença, mesmo na presença de hipertrofia em grau leve ou ausente (CHETBOUL et al., 2006a, 2006b; SIMPSON et al., 2007). Por sua vez, em cães com doença crônica da valva mitral, Schober et al. (2010) demonstraram que novos índices obtidos a partir do DT foram capazes de prever a ocorrência de insuficiência cardíaca congestiva nos animais estudados.

Segundo Pavlopoulos e Nihoyannopoulos (2008), St e StR miocárdico são definidos como a magnitude de encurtamento ou alongamento das fibras cardíacas (%) e a taxa em que esta deformação ocorre (1/s). Estes são considerados novos índices incorporados à medicina veterinária (CHETBOUL, 2010). St e StR obtidos a partir do DT foram capazes de demonstrar alterações miocárdicas em felinos com cardiomiopatia hipertrófica, mesmo quando os índices ecocardiográficos convencionais estavam dentro da normalidade (WESS et al., 2010). No entanto, entre as limitações desta técnica está a dependência da translação cardíaca e do ângulo de insonação, uma vez que o alinhamento incorreto do feixe ultrassônico com a parede miocárdica pode influenciar os resultados obtidos (CHETBOUL et al., 2007). Além disso, incorporação de ruídos, reverberação de artefatos, limitação relativa à resolução lateral, *aliasing* e inadequada taxa de repetição de quadros (*frame rate*) constituem os principais desafios da técnica (PAVLOPOULOS; NIHOYANNOPOULOS, 2008).

2.2 Ecocardiografia *speckle tracking* bidimensional

A ecocardiografia 2D ST é uma das mais recentes ferramentas de ultrassonografia que permitem o acesso à função miocárdica, utilizadas em medicina veterinária (CHETBOUL, 2010). Esta técnica de imagem é baseada no rastreamento de pontos criados pela interferência entre o feixe ultrassonográfico e o miocárdio em imagens ecocardiográficas 2D em escala de cinza. Estes *speckles* aparecem como elementos (pontos) pequenos e brilhantes dentro do miocárdio e representam marcadores acústicos teciduais naturais que podem ser monitorados (*tracking*) momento a momento, durante todo o ciclo cardíaco (Figura 1) (CHETBOUL, 2010; HOOGE, 2007).

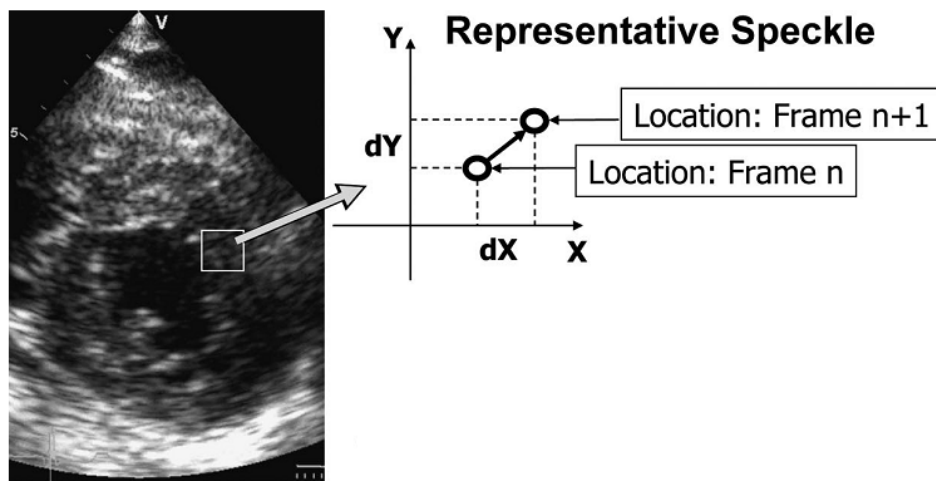


FIGURA 1 Padrão de *speckles* em escala de cinza em imagem bidimensional. Pontos acústicos (*speckles*) são identificados na região de interesse. A posição relativa dos pontos é, então, rastreada quadro a quadro (taxa de frames/s), de acordo com a movimentação do miocárdio. dY : deslocamento dos pontos; dX : tempo de deslocamento. Fonte: Suffoletto e Herszkowicz (2006)

Ao contrário do DT, a ecocardiografia 2D ST permite a mensuração das deformações miocárdicas em sentido longitudinal e circunferencial pelos cortes

apical quatro câmaras e paraesternal eixo curto do ventrículo esquerdo (VE), uma vez que não há restrições quanto ao ângulo de insonação. Além disso, os pontos acústicos rastreados são representados por vetores de velocidade, que permitem observar a direção e a intensidade do movimento (DEL CASTILLO; HERSZKOWICZ, 2008). No entanto, este método ecocardiográfico também possui algumas limitações, como resolução lateral em regiões miocárdicas distantes, pontos fora do plano miocárdico, reverberações e, sobretudo, a qualidade da imagem 2D, que deve ser acima da média (PAVLOPOULOS; NIHOYANNOPOULOS, 2008).

Nos últimos anos, a técnica 2D ST tem sido aplicada intensamente em medicina e seus resultados validados com a ressonância magnética marcada e sonomicrometria, técnicas consideradas padrão para a obtenção da deformação miocárdica. Foi demonstrado que os valores encontrados eram semelhantes aos obtidos através do 2D ST (AMUNDSEN et al., 2006; GOFFINET et al., 2009). Esta ferramenta tem sido empregada na obtenção de valores de referência em humanos saudáveis (HURLBURT et al., 2007) e em portadores de diversas alterações cardíacas, como cardiomiopatia hipertrófica ou dilatada, embolismo pulmonar, torção ventricular, sincronia e avaliação da resposta à terapia de re-sincronização cardíaca (DELGADO et al., 2008; MELUZIN et al., 2011; OPDAHL et al., 2008; SERRI et al., 2006; SUFFOLETTO et al., 2006; TAKAMURA et al., 2011).

Em medicina veterinária, a ecocardiografia 2D ST tem sido utilizada em cães, para se obter o St e StR, assim como a torção e a sincronia miocárdicas, tanto em animais saudáveis para se estabelecer valores de referência e padronizar a técnica (CHETBOUL et al., 2007, 2008; GRIFFITHS; FRANSIOLI; CHIGERWE, 2011; WESS et al., 2011), como em animais cardiopatas (TAKANO et al., 2011). Em equinos, esta ferramenta tem sido aplicada na avaliação miocárdica, obtendo-se valores de referência em repouso e em

exercício (DECLOEDT et al., 2011; SCHEFER et al., 2010). No entanto, há pouca informação na literatura sobre o uso desta ferramenta em gatos domésticos (RIESEN et al., 2011), assim como valores de referência para St, StR longitudinal, radial ou circunferencial, além de torsão ventricular, sincronia e outras aplicações já validadas em outras espécies.

2.2.1 Strain e strain rate bidimensional

Vários trabalhos têm sido desenvolvidos utilizando-se as variáveis St e StR obtidas pela ecocardiografia 2D ST, em humanos (DELGADO et al., 2008; OPDAHL et al., 2008; SERRI et al., 2006; SUFFOLETTO et al., 2006; TAKAMURA et al., 2011) e na área da cardiologia veterinária (CHETBOUL et al., 2007; TAKANO et al., 2011; WESS et al., 2011). Estas variáveis têm grande importância, uma vez que podem ser consideradas novos índices sistólicos que podem, muitas vezes, predizer alterações miocárdicas, mesmo antes de serem observadas na ecocardiografia convencional (ARTIS et al., 2008).

As variáveis de deformação miocárdica St e StR são diretamente dependentes da disposição das fibras miocárdicas e esta deformação ocorre no sentido destas, podendo ser longitudinal, radial, circunferencial ou em cisalhamento (DEL CASTILLO; HERSZKOWICZ, 2008).

O St longitudinal é representado pela deformação que ocorre no miocárdio entre o anel mitral e o ápice cardíaco, ou seja, no eixo longitudinal. Por sua vez, o St radial é aquele que ocorre pelo espessamento da parede ventricular e septal durante a sístole. O St circunferencial ocorre devido à rotação do miocárdio em torno de seu eixo longitudinal. E, por último, o St de cisalhamento é aquele formado pelo deslocamento do endocárdio em relação ao epicárdio (Figura 2) (GEYER et al., 2010).

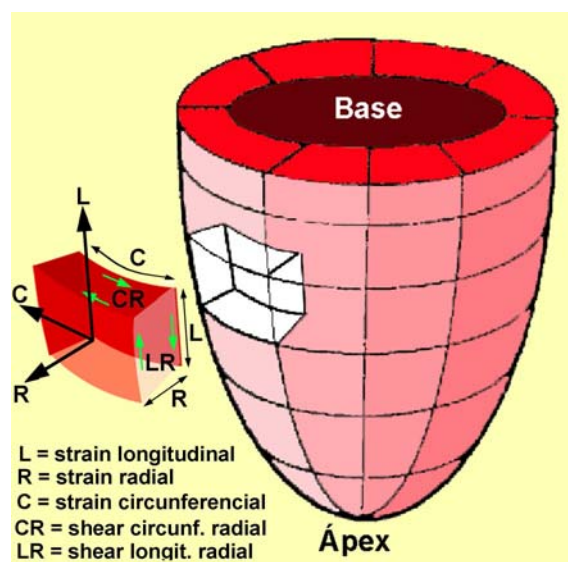


FIGURA 2 Esquema demonstrando a deformação miocárdica longitudinal, radial, circunferencial e cisalhamento (*shear strain*). Fonte: Dell Castilho e Herszkowicz (2008)

Em cães, Wess et al. (2011) demonstraram que os valores St e StR longitudinais, obtidos tanto pela ecocardiografia 2D ST quanto pelo DT, são semelhantes e com pouca variação inter e intraobservador. Dessa forma, os dois métodos podem ser utilizados alternadamente, de acordo com a disponibilidade destas ferramentas na rotina da clínica cardiológica. No entanto, o 2D ST apresenta a vantagem de maior facilidade e rapidez em sua execução, além de menor influência de fatores, como o ângulo de insonação nos resultados.

Em eqüinos, a ecocardiografia 2D ST demonstrou ser uma técnica confiável para se obter o St e o StR longitudinal, além de velocidade e deslocamento (DECLOEDT et al., 2011). Por sua vez, em humanos, o St longitudinal demonstrou ser mais adequado como índice prognóstico em várias alterações como em doenças valvares, além de auxiliar como indicativo de disfunção ventricular esquerda (LANCELLOTTI et al., 2008; MARCINIAK et al., 2009; MIZUGUCHI et al., 2008).

Em cães, a técnica do 2D ST foi padronizada para o corte paraesternal eixo curto por Chetboul et al. (2007), que quantificaram o St e StR radial em cães saudáveis e não sedados, além de comparar os valores obtidos com o DT, tendo sido observada semelhança entre eles. Além disso, em humanos, foi demonstrado, por Delgado et al. (2008), que o St radial é o melhor método para se avaliar a resposta em pacientes submetidos à terapia de ressincronização cardíaca, quando comparado ao St longitudinal e circunferencial.

Quanto às variáveis St e StR circunferenciais, em um estudo em paciente humano tratado para insuficiência cardíaca com marcapasso, foi demonstrado que, apesar de o DT mostrar velocidade radial e longitudinal sincronizada, o St e o StR mostraram uma disparidade persistente, fato que poderia ser justificado como uma possível melhora não sustentada do desempenho sistólico do VE no paciente em questão (VANNAN et al., 2005).

Em outro estudo em humanos, identificou-se significativa correlação entre o St circunferencial e a fração de encurtamento na região média miocárdica, obtida pela ressonância magnética cardíaca ou modo-M, podendo atuar, dessa forma, como um índice prognóstico em casos de doença cardíaca hipertensiva e disfunção sistólica intramural, assim como a fração de ejeção (HURLBURT et al., 2007).

3 CONSIDERAÇÕES GERAIS

Diante do exposto, a ecocardiografia 2D ST tem demonstrado ser de grande utilidade no diagnóstico das cardiomiopatias, tanto em humanos quanto em medicina veterinária. Diversos estudos demonstram a importância de St e StR como novos índices sistólicos para a avaliação da função miocárdica ventricular esquerda. No entanto, sua viabilidade e sensibilidade ainda não foram demonstradas em gatos domésticos. Dessa forma, o presente estudo atua de modo a colaborar para o melhor entendimento desta ferramenta e suas variáveis e seu papel na cardiologia de felinos, além de padronizar a técnica e fornecer valores de referência para o St e o StR obtidos por meio do 2D ST nesta espécie.

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SEGUNDA PARTE

ARTIGO

Longitudinal strain and strain rate by two-dimensional speckle tracking in non-sedated healthy cats

Artigo segue as normas e formato do periódico *Journal of Veterinary Internal Medicine (JVIM)** ao qual foi submetido.

*Este artigo é uma versão preliminar, considerando que o conselho editorial da revista poderá sugerir alterações para adequá-lo ao seu próprio estilo.

1 **Longitudinal Strain and Strain Rate by Two-dimensional Speckle tracking**
2 **in non-sedated healthy cats**

3

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10

11 **Short Title:** Longitudinal Function by 2D-STE in Cats

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13 **Keywords:** Echocardiography, Cardiomyopathy, Felines, Myocardial function.

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23 **Abbreviations:**

24	2D-STE	Two-dimensional speckle tracking echocardiography
25	St	Strain
26	StR	Strain Rate
27	LSt	Longitudinal Strain
28	LStR	Longitudinal Strain Rate
29	Lvel	Longitudinal Velocity
30	Ldisp	Longitudinal Displacement
31	2D	Two-dimensional
32	LVDd	Left ventricular diastolic diameter
33	RVDd	Right ventricular diastolic diameter
34	LVDs	Left ventricular systolic diameter
35	PWd	Posterior wall at diastole
36	PWs	Posterior wall at systole
37	IVSd	Interventricular septum at diastole
38	IVSs	Interventricular septum thickness at systole
39	FS	Fractional shortening

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47

48 *Partial data of this study were accepted to be presented as a research*
49 *report at the American College of Veterinary Internal Medicine Forum*
50 *(ACVIM), New Orleans, Louisiana, USA, May 30-June 2, 2012.*

51

52 **Acknowledgments**

53 The authors wish to thank to Fundação de Amparo a Pesquisa do Estado
54 de Minas Gerais (FAPEMIG), Coordenação de Aperfeiçoamento de Pessoal de
55 Nível Superior (CAPES) and Conselho Nacional de Desenvolvimento Científico
56 e Tecnológico (CNPq), for the financial support.

57

58 **Background:** 2D speckle tracking is a new tool that has been used in
59 humans and veterinary medicine to quantify myocardial longitudinal function.
60 However, there is an absence of information about the use of this tool in healthy
61 non-sedated cats to obtain myocardial longitudinal strain, strain rate, velocity
62 and displacement.

63 **Objectives:** To evaluate myocardial longitudinal strain and strain rate in
64 awake clinically healthy cats, as well as, longitudinal velocity and displacement
65 by means of 2D speckle tracking echocardiography.

66 **Animals:** The study population consisted of 30 clinically healthy no-
67 sedated cats, weighting 4.11 ± 0.94 kg and mean age 36.00 ± 33.43 months.

68 **Methods:** All cats were examined physically, were obtained systolic
69 blood pressure and performed electrocardiography and echocardiography to
70 assess the healthy status. During conventional echocardiography 2D images
71 were obtained and evaluated off line at speckle tracking software.

72 **Results:** Speckle tracking echocardiography demonstrated to be feasible
73 and reliable to obtain left ventricular longitudinal function. The global mean
74 obtained for strain and strain rate were -15.65 ± 5.46 (%), -1.80 ± 0.59 (1/s),
75 respectively. Regarding velocity and displacement were observed 1.41 ± 0.87
76 (cm/s), 1.27 ± 0.80 (mm), respectively.

77 **Conclusions and Clinical Importance:** 2D speckle tracking
78 echocardiography was found to be a reliable technique for measuring LV
79 myocardial LSt, LStR, Lvel and Ldisp. These measurements offer new insights
80 into feline ventricular deformation and motion. In addition, based on our results,
81 preliminary reference values for healthy non-sedated cats could be formulated.

82

83

84 Two-dimensional Speckle Tracking (2D-STE) is a new tool that has
85 been used in veterinary medicine to evaluate myocardial strain (St) and strain
86 rate (StR).¹ St is expressed as a percentage (%) and it is the magnitude of
87 myocardial fibers lengthening or shortening. On the other hand, StR is the rate at
88 which deformation occurs, it describes the velocity of deformation (1/s).²

89 This technique was already validated for dogs, showing to be useful in
90 the diagnosis of cardiomyopathies.³⁻⁶ In humans, several studies demonstrated
91 the efficacy of 2D-STE in the diagnosis of various cardiac diseases and
92 hemodynamic conditions, as myocardial infarctation, hypertrophic
93 cardiomyopathy, coronary disease, ventricular dyssynchrony, among others.⁷⁻

94 ⁹There is some studies in horses, which were obtained some 2D-STE variables,
95 such as St and StR.¹⁰⁻¹³

96 In veterinary medicine longitudinal strain (LSt) and strain rate (LStR)
97 were obtained in dogs⁶ and in horses¹¹ and its reliability and feasibility were
98 demonstrated for these species. Although, there are little information regarding
99 2D-STE variables, such as St and StR in cats,^{14,a} being that its feasibility has not
100 yet clarified for this species. In addition, to our knowledge, there is no data
101 about LSt and LStR obtained by 2D-STE in non-sedated clinically healthy cats,
102 as well as, longitudinal velocity (Lvel) and displacement (Ldisp).

103 Thus, the aim of this study was to evaluate myocardial LSt and LStR in
104 non-sedated clinically healthy cats, as well as, myocardial Lvel and Ldisp by
105 means of 2D-STE.

106

107 **Material and Methods**

108

109 *Study Population*

110

111 The study population consisted of 30 healthy cats of different breeds and
112 origins (companion animals presenting for vaccinations or cardiac screening
113 programs, as well as ,student- or faculty-owned cats). Owner consent was
114 obtained before enrollment into the study. The study protocol was in compliance
115 with the institutional Animal Care and Use Committee under the protocol
116 number 052/11. In this study none of the animals were under any type of
117 treatment. In all cats, clinical examination, electrocardiography,
118 echocardiography, and indirect systolic blood pressure measurements were
119 performed to exclude cardiovascular disease.

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124 ***Conventional Echocardiography***

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126 Echocardiographic studies were performed using an ultrasound unit
127 equipped with a 4-10 MHz phased-array transducer.^b All examinations were
128 performed without sedation in gently restrained cats in lateral recumbency.
129 Standard echocardiographic views were obtained in right and left lateral
130 recumbence.^{17,18} Conventional echocardiographic variables, included ventricular
131 measurements taken from the right parasternal short-axis view by two-
132 dimensional (2D) guided M-mode, such as the left ventricular diastolic diameter
133 (LVDd), right ventricular diastolic diameter (RVDd); left ventricular systolic
134 diameter (LVSd), posterior wall at diastole (PWd) and systole (PWs)
135 interventricular septum at diastole (IVSd) and at systole (IVSs) and fractional
136 shortening (FS %). Were also included measurements of the aorta (Ao) and left
137 atrial (LA) diameter by 2D mode and was calculated the LA/Ao ratio. All valves
138 were examined using color Doppler and velocities over the valves were
139 measured using pulsed wave Doppler examinations. At least 3 measurements
140 were performed for all echocardiographic variables and the mean value of the
141 measurements was calculated for each variable.

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143

144

145 *Speckle Tracking Echocardiography*

146

147 The 2D echocardiographic loops used for STE analysis were acquired
148 and recorded in all cats using the same ultrasound unit as for the standard
149 examinations. Three to five consecutive heart cycles using a continuous
150 monitoring ECG were stored in digital format on a workstation for off-line
151 analysis. Cine loops were acquired from left apical four chamber view with
152 sampling rates from 56.10 ± 23.49 (38 to 159) frames/s and 6 measurements
153 were obtained in two different Cine loops (3 for each Cine loop) at end-systole
154 for all studied variables and then average was obtained. Semi-automatic tissue
155 tracking and analysis for 2D-ST was performed using a commercially software.^c
156 For myocardial tracking, endocardial border was marked manually and then,
157 epicardial border was marked automatically by the software, which performed
158 myocardial wall tracking process and velocity vectors were displayed at the
159 region of interest (Fig 1A). Manual adjustment of the myocardial wall borders
160 was performed when necessary. Graphics and curves of studied variables were
161 automatic displayed and myocardium was divided in six segments by the
162 software (Fig 1B) and the values of peak systolic of LSt, LStR, Lvel and Ldisp
163 were shown for each segment at endocardial and epicardial region.

164

165

166 *Statistical Analysis*

167

168 All data were tested for normality by the Kolmogorov-Smirnov test
169 ($P>0.05$). Statistical and graphical analyses were performed by computer
170 software.^d Summary statistics for the different measurements (mean \pm standard
171 deviation-SD; $n=30$ cats) were calculated using the average measurement of 6
172 consecutive heart cycles per cats obtained of two different cine loops (3
173 consecutive cycles for each cine loop). The data demonstrated not be normally
174 distributed and therefore the Mann-Whitney and Kruskal-Wallis test were
175 applied to compare the cardiac regions (Endocardium and Epicardium) and
176 segments (Bas Sept, Mid Sept, Apic Sept, Bas Lat, Mid Lat and Apic Lat),
177 respectively. These data were displayed as boxplots, and each segment, the
178 median and spread of the peak value or timing were indicated by a
179 boxplot, based on the averaged measurement values for each cat. A value
180 of $P<0.05$ was considered statistically significant.

181 The intra-observer repeatability was obtained from 3 echocardiograms
182 that were randomly selected to be subjected to 6 repeated analyses at 3 different
183 days for the same recorded loops, to determine intra-observer between-day
184 measurement variability for LSt, LStR, Lvel and Ldisp. Each variable was
185 measured 6 times on 6 consecutive cardiac cycles in 2 different cine loops (3
186 consecutive cardiac cycles for each cine loop), and the between-day intra-

187 observer variability was determined based on the analysis of variance results of
188 all measurements.

189

190 **Results**

191

192 Demographic data (Table 1) and conventional echocardiography (Table
193 2) are displayed as mean and standard deviation. In this study were observed a
194 higher number of males than females and the mean age of cats were about 36
195 months. The study population was compounded by mixed breed, Persian and
196 Siamese cats. Regarding to weight a minimal variation was present. The mean of
197 systolic blood pressure was into normal ranges (< 150 mmHg). Regarding
198 conventional echocardiography was observed that all variables were into the
199 normal range described at literature.¹⁹⁻²¹

200 The 2D STE demonstrated to be feasible in cats, using apical four
201 chamber view to obtain longitudinal variables. A total of 8,640 measurements
202 were obtained for all segments of all STE variables analyzed and 77% of
203 measurements could be considered with adequate tracking quality.

204 The values of endocardial and epicardial variables are displayed on
205 Table 3 and global endocardial values were lower than epicardial for LSt, Ldisp
206 and Lvel. Table 4 shows the peak values of global, average and segmental
207 measurements of 2D STE variables of all cats studied and significant differences

208 among regions were observed. Heterogeneity was observed at different
209 myocardial segments analyzed, but LV posterior wall regions demonstrated no
210 significant difference. Apical regions of variables Ldisp and Lvel demonstrated
211 significant lower values than other regions for these same variables. Regarding,
212 other variables were observed lower variability, despite significant differences
213 among segments (Fig 2).

214 The Table 5 displays the between-day intra-observer variability,
215 demonstrating that the variables LSt and LStR had higher values than the
216 others, despite these values were considered with low variability.
217 Endocardial region presented higher variability than epicardial for the
218 variables LSt, Lvel, Ldisp. Regarding the global average Lvel and Ldisp
219 demonstrated to be similar and have lower variability than LSt and LStR.

220

221 **Discussion**

222

223 The present study describes the technique of the 2D STE to obtain LV
224 longitudinal myocardial function and its feasibility in non-sedated healthy cats.
225 The left apical four chamber view demonstrated to be adequate to obtain
226 measurements of LSt, LStR, Lvel and Ldisp in felines.

227 In this study was observed a larger number of males than females, this
228 fact were also observed in a study with cats presenting hypertrophic

229 cardiomyopathy.²² In our study it can be justified by the fact that cats were
230 selected randomly and gender was not controlled.

231 Regarding conventional echocardiography, to be included in this study
232 cats must be in the normal range for all variables, excluding any cardiac
233 alteration.

234 The 2D-STE demonstrated to be feasible to obtain longitudinal function
235 in all cats evaluated, despite some measurements had to be excluded of the
236 analyzes because inadequate tracking. This fact was mentioned before by others
237 studies in dogs^{3,6} and could be justified by the difficulty of obtain an optimal
238 quality image compatible with STE software. In our study another fact that
239 could be added is the higher heart rates that non-sedated cats can present at
240 echocardiographic examination which could to interfere in the adequate
241 tracking. The frame rate presented in our study were in accordance with
242 previous data demonstrated in studies in dogs,^{3,6} humans,^{15,16} horses^{11,13} and
243 sedated cats (radial St and StR).¹⁴

244 In this study, epicardial and endocardial LSt demonstrated to be
245 significantly different, being epicardial values higher than endocardial one. This
246 fact is different of data reported in a previous study with humans, in which
247 endocardial region presented higher strain values.²³ In our study the global mean
248 of LSt were similar to previous data for the same variable obtained in
249 dogs⁶ and in human fetus²⁴ and much lower than data from horses.¹¹ This result

250 could be justified by the species differences, as heart size, which is expected
251 higher values of St, proportionally to the size, and heart rate, that may influence
252 the quality of the image.

253 Heterogeneity was observed at different myocardial segments analyzed,
254 but for the variable LSt there was no significant difference among the segments
255 of the LV posterior wall (Apic Lat, Mid Lat and Bas Lat). In dogs was also
256 demonstrated no significant difference among these segments for LSt.⁶ This fact
257 was also observed in a study with horses¹¹ and in humans.²⁵ In humans was
258 demonstrated that apical values of LSt were higher than in other segments,²⁵ and
259 in the present study we observed that basal segments of septum and posterior
260 wall demonstrated higher values. In a study with cats using tissue Doppler to
261 obtain the variable St,²² were demonstrated values of basal segments of septum
262 and posterior wall a little higher than values of our study. This difference could
263 be justified due to the data of studies were obtained using different techniques,
264 and also was reported at literature the fact that tissue Doppler can be influenced
265 by the insonation angle.¹ Another explanation to these differences is the fact that
266 the cats of the tissue Doppler study were sedated and in the present study the
267 animals were awake, which could influence the results of measurements.

268 Regarding the variables Lvel, Ldisp and LStR, were observed
269 differences among the segments, despite the middle and basal segments of IVS
270 and LV posterior wall demonstrate no significant differences for the LStR. In

271 dogs, were observed no significant differences in the segments for LStR,
272 however, for the variable Lvel were observed that the values were different and
273 increasing from the apex to the base,⁶ as were demonstrated in our study in cats
274 for this same variable.

275 Regarding the between-day intra-observer the values of variability could
276 be considered with low variability due to all values were lower than 15%. It was
277 also observed at a study with dogs, which were found similar values for the
278 variable LStR.⁶ Although, in this same study lower values for LSt were observed
279 than in our study. Lower variability was shown for the variables Ldisp and Lvel
280 in the present data.

281 Limitations of the present study must be clarified. Firstly, it is a
282 noninvasive study design, performed on companion animals without any
283 invasively obtained hemodynamic data to corroborate with the healthy status of
284 the cats. Another limitation is the high dependency of STE of image quality,
285 which is difficult to obtain in non-sedated cats, given that they can present high
286 heart rates at the examination.

287 Another limitation of this study is the fact that data obtained may not be
288 applicable to all clinical situations due to differences in machine settings,
289 software, equipment, observer experience and image quality, which may
290 influence the values and variability of the data.

291 Our study was performed on 30 non-sedated healthy cats and mixed
292 breeds were over represented, being only Persians and Siamese cats presented in
293 small number. Then, a larger study population would be performed in order to
294 determine if there is an influence of breed, gender and age over the 2D-STE
295 variables in cats. Despite the limitations, the study provide preliminary reference
296 values of LSt, LStR, Lvel, Ldisp for non-sedated healthy cats, as well as the
297 feasibility of the technique in this specie.

298 In conclusion, 2D STE can be considered a reliable technique for
299 measuring left ventricular myocardial LSt, LStR, Lvel and Ldisp in cats. These
300 measurements provide new prospects into feline ventricular deformation and
301 motion, allowing a more complete quantification and understanding of
302 longitudinal myocardial function in this specie. However, more studies should
303 be carried out in order to evaluate the role and reliability of this technique in cats
304 with cardiomyopathies.

305

306 **Footnotes**

307 ^aTakano H, Isogai T, Aoki T, Wakao Y, Fujii Y: 2D speckle tracking
308 echocardiography in clinically healthy cats and cats with hypertrophic
309 cardiomyopathy. J Vet Int Med 2011;25:971 (Abstract)

310 ^bEsaote Mylab 40, Italy

311 ^cXstrain software version 10.1, Esaote

312 ^dSPSS Statistics 17.0, Rel. 17.0.1. 2008, SPSS Inc, Chicago, IL

313

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322 two-dimensional speckle tracking echocardiography and the tissue velocity
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325 systolic left ventricular torsion by 2-dimensional speckle tracking imaging in the
326 awake dog: repeatability, reproducibility, and comparison with tissue Doppler
327 imaging variables. *J Vet Int Med* 2008;22:342–350.

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329 regional function in affected and carrier dogs with duchenne muscular dystrophy
330 using speckle tracking echocardiography. *BMC Cardiovasc Disord* 2011;11:2–8.

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333 longitudinal myocardial tissue velocity, strain, and strain rate measured by two-
334 dimensional speckle tracking and by color tissue Doppler imaging in healthy
335 dogs. *J Vet Cardiol* 2011;13:31–43.

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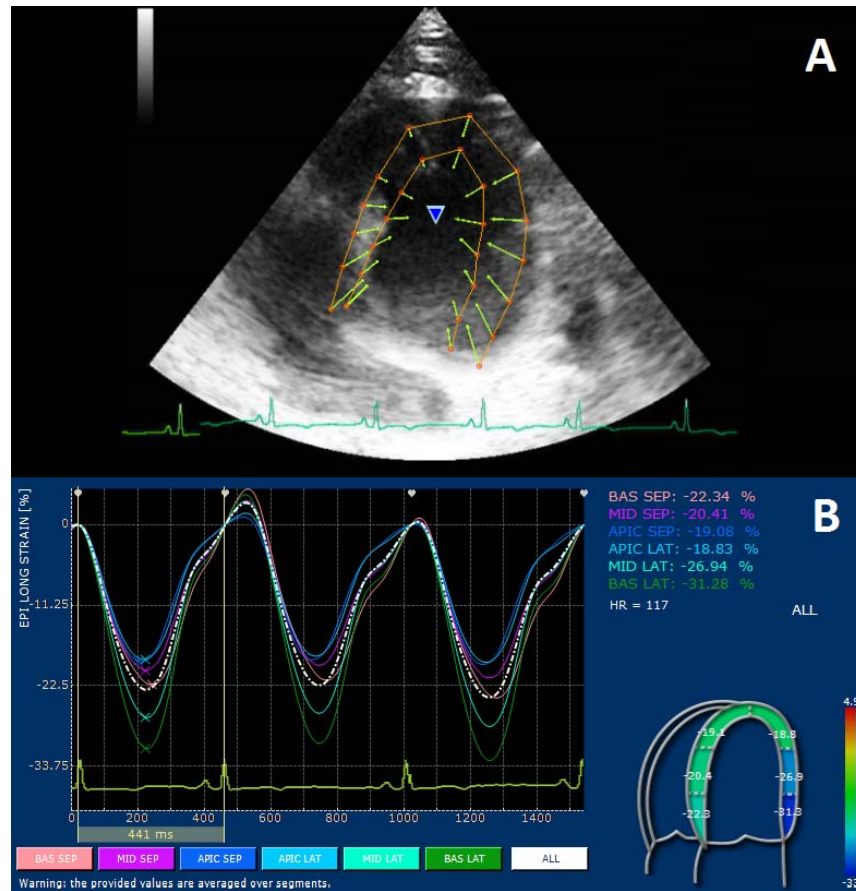
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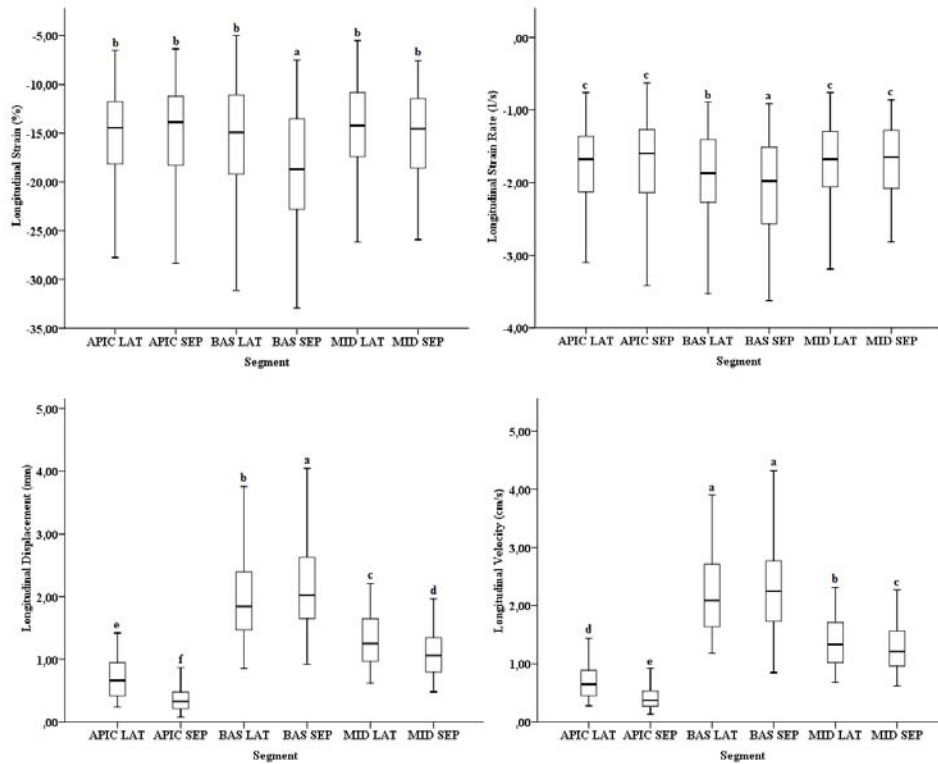
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416 **Fig 1.** Figures illustrating myocardial tracking in a cat. (A) 2D Apical Four
 417 chamber view in a non-sedated healthy cat, demonstrating myocardial tracking
 418 process and velocity vectors by STE; (B) 2D-STE analysis of left ventricular
 419 epicardial longitudinal strain in a healthy cat. The myocardium is automatically
 420 divided into 6 segments: Basal (Bas Sept), Middle (Mid Sept) and Apical (Apic
 421 Sept) segments for the interventricular septum and Basal (Bas Lat), Middle
 422 (Mid Lat) and Apical (Apic Lat) lateral segments for the left ventricular
 423 posterior wall.



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425 **Fig 2.** Graphical illustration of segmental differences of 2D STE
 426 measurements of LV longitudinal function in non-sedated healthy cats
 427 (n=30). The line near the middle of the box indicates the middle half of the
 428 observations, the top and the bottom of the box indicates the upper and lower
 429 quartile, and the whiskers corresponds to the range of observations (smallest and
 430 largest observations, respectively). Boxes marked with different letters are
 431 significantly different from each other to Mann-Whitney test ($P < 0.05$).

432

433 **Table 1.** Demographic data (age, weight, heart rate, gender and breed) and
 434 systolic blood pressure in non-sedated healthy cats (n = 30).

Variables	Mean \pm Standard deviation (SD)
Age (months)	36.00 \pm 33.43
Weight (kg)	4.11 \pm 0.94
Heart rate (beats/min)	161.20 \pm 39.55
Gender	
Male	n = 20 (66.67%)
Female	n = 10 (33.33%)
Breeds	Mixed breed cats (n = 22 – 73.34%)
	Persa (n = 7 – 23.33%)
	Siamês (n = 1 – 3.33%)
Systolic pressure (mmHg)	129.50 \pm 15.03

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447 **Table 2.** Data of main conventional echocardiographic variables in non-sedated
 448 healthy cats (n = 30).

Variables	Mean \pm Standard deviation (SD)
Left atrium (mm) – LA	7.25 \pm 0.96
Aorta (mm) – Ao	7.04 \pm 0.85
Ratio LA/Ao	1.03 \pm 0.11
Pulmonary artery (m/s)	0.88 \pm 0.16
RVDd (mm)	2.75 \pm 0.98
IVSd (mm)	4.10 \pm 1.08
LVDd (mm)	11.07 \pm 2.06
PWd (mm)	4.39 \pm 0.97
IVSs (mm)	5.77 \pm 0.94
LVDs (mm)	6.07 \pm 1.26
PWs (mm)	6.45 \pm 1.07
FS (%)	44.86 \pm 7.82
E mitral (m/s)	0.90 \pm 0.14
A mitral (m/s)	0.65 \pm 0.15
Tric flow (m/s)	0.76 \pm 0.11
Aortic flow (m/s)	0.92 \pm 0.16
Aortic root (mm)	6.41 \pm 0.69

449 RVDd: right ventricular diastolic diameter; IVSd: interventricular septum at
 450 diastole; LVDd: left ventricle diastolic diameter; PWd: posterior wall at diastole;
 451 IVSs: interventricular septum at systole; LVDs: left ventricle systolic diameter;
 452 FS: fractional shortening; E mitral: transmitral peak early diastolic velocity; A
 453 mitral: transmitral peak late diastolic velocity; Tric flow: peak of tricuspid flow
 454 velocity.

455

456 **Table 3.** Values of global, endocardial and epicardial regions of longitudinal
 457 strain, strain rate, displacement and velocity, displayed as mean \pm standard
 458 deviation of healthy cats (n=30).

Variables	Endocardium	Epicardium	Average	P value
LSt (%)	-15.15 \pm 5.25 a	-16.12 \pm 5.61 b	-15.65 \pm 5.46	0.0020*
LStR (1/s)	-1.79 \pm 0.56 a	-1.82 \pm 0.62 a	-1.80 \pm 0.59	0.6720
Ldisp (mm)	1.22 \pm 0.67 a	1.32 \pm 0.91 a	1.27 \pm 0.80	0.6440
Lvel (cm/s)	1.36 \pm 0.74 a	1.46 \pm 0.98 a	1.41 \pm 0.87	0.6280

459 LSt: Longitudinal Strain (%); LStR: Longitudinal Strain Rate (1/s); Ldisp:

460 Longitudinal displacement (mm); Lvel: Longitudinal Velocity (cm/s).

461 *Means followed by different letters in the line differ by the Mann-Whitney test
 462 (P<0.05).

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474 **Table 4.** Values of segmental and averaged longitudinal strain, strain rate,
 475 displacement and velocity, displayed as mean \pm standard deviation of healthy
 476 cats (n=30).

Variable	Segment	N	Mean \pm Standard deviation*
Longitudinal Strain (%)	APIC LAT	278	-15.15 \pm 4.81 b
	MID LAT	279	-14.57 \pm 4.92 b
	BAS LAT	270	-15.57 \pm 6.18 b
	APIC SEP	289	-14.91 \pm 5.14 b
	MID SEP	282	-15.23 \pm 4.54 b
	BAS SEP	265	-18.63 \pm 6.10 a
	Global mean	1663	-15.65 \pm 5.46
Longitudinal Strain Rate (1/s)	APIC LAT	299	-1.74 \pm 0.54 c
	MID LAT	291	-1.73 \pm 0.56 c
	BAS LAT	281	-1.91 \pm 0.61 b
	APIC SEP	313	-1.73 \pm 0.63 c
	MID SEP	298	-1.69 \pm 0.50 c
	BAS SEP	279	-2.04 \pm 0.64 a
	Global mean	1761	-1.80 \pm 0.59
Longitudinal Displacement (mm)	APIC LAT	260	0.70 \pm 0.32 e
	MID LAT	260	1.30 \pm 0.42 c
	BAS LAT	260	1.96 \pm 0.67 b
	APIC SEP	260	0.37 \pm 0.20 f
	MID SEP	260	1.09 \pm 0.37 d
	BAS SEP	289	2.14 \pm 0.68 a
	Global mean	1589	1.27 \pm 0.80
Longitudinal Velocity (cm/s)	APIC LAT	260	0.69 \pm 0.27 d
	MID LAT	263	1.38 \pm 0.42 b
	BAS LAT	274	2.20 \pm 0.67 a
	APIC SEP	260	0.41 \pm 0.20 e
	MID SEP	259	1.28 \pm 0.41 c
	BAS SEP	310	2.31 \pm 0.75 a
	Global mean	1626	1.41 \pm 0.87

477 *Means followed by different letters in the column differ by the Mann-Whitney

478 test (P<0.05).

479

480 **Table 5.** Table displays the value of between-day intra-observer
 481 variability (%).

	Variable	Endocardium	Epicardium	Average
Between-Day	LSt	12.2	10.8	11.7
Intra-observer	LStR	10.8	11.3	11.5
Variability	Ldisp	7.2	1.3	6.0
(CV in %)	Lvel	5.3	2.8	5.8

482 LSt: Longitudinal Strain (%); LStR: Longitudinal Strain Rate (1/s); Ldisp:
 483 Longitudinal displacement (mm); Lvel: Longitudinal Velocity (cm/s).

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496 ANEXO

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498 Certificado fornecido pela Comissão de Ética no Uso de Animais da UFLA.

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CERTIFICADO

Certificamos que o **Protocolo nº 052/11**, relativo ao projeto intitulado **"Avaliação Ecocardiográfica da Função Miocárdica em Felinos Domésticos"**, que tem como responsável **Ruthnéa Aparecida Lázaro Muzzi**, está de acordo com os Princípios Éticos da Experimentação Animal, adotados pela **Comissão de Ética no Uso de Animais (Comissões Permanentes/PRP-Ufla)**, tendo sido aprovado na reunião de 29/09/2011.

CERTIFICATE

We hereby certify that the **Protocol nº 052/11**, related to the project entitled **"Echocardiographic Evaluation of Myocardial Function in Domestic Cats"**, under the supervision of **Ruthnéa Aparecida Lázaro Muzzi**, is in agreement with the Ethics Principles in Animal Experimentation, adopted by the **Bioethic Committee in Utilization of Animals (Comissões Permanentes/PRP-Ufla)**, and was approved in **September 29, 2011**.

Lavras, 29 de setembro de 2011.


 Prof. Gabriela Rodrigues Campes
 Presidente em exercício da Comissão de Ética no Uso de Animais CEUA

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