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Searching for clinically useful parameters in 2-Dimensional speckle tracking

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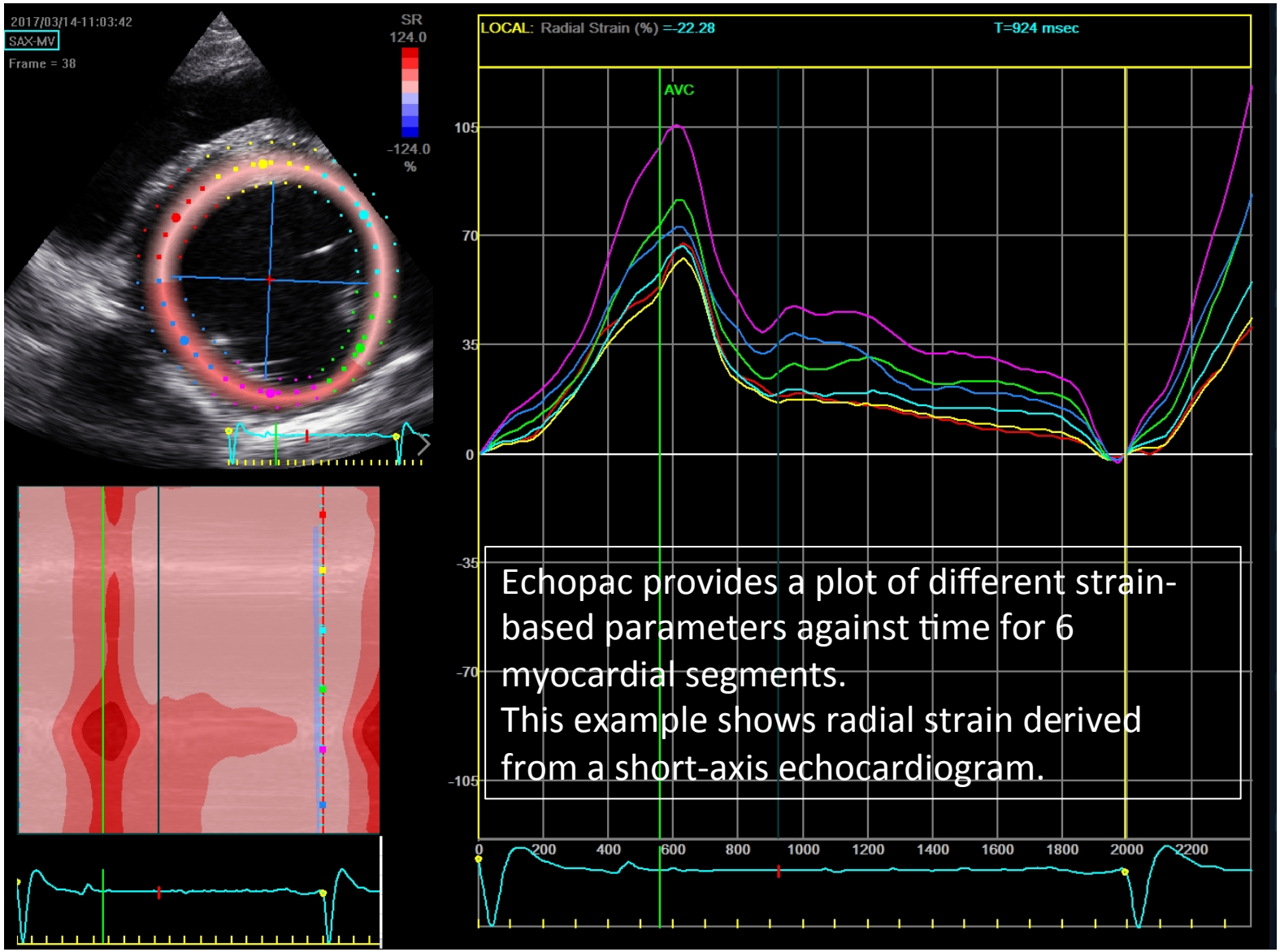
2-Dimensional speckle tracking

- Tracks the movement of 'speckles' on the ultrasound image of the myocardium.
- By comparing the movement of different speckles, can measure deformation
- Deformation can be in radial, circumferential & longitudinal axes

Speckles in the myocardium are like spots on a stressball, by following how individual dots move, deformation of the structure can be estimated

Echopac output



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Dataset

Used CMM's database of archived echocardiography exams

- Many individuals but few repeats
- Images were not produced for current research- not always the optimal view and quality
- Wide range of clinical problems and signalment
- Between 1-3 cardiac cycles were found in for each individual horse at chordal or apical level. Some horses had exams at both levels, some had exams at one.
- "n" refers to the number of cardiac cycles in the analysis unless otherwise stated

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Criteria for potential parameters

- Low variability in healthy population
- Repeatability
- Significant difference between healthy and unhealthy cases
- Measureable from routine image planes.
- Operator-friendly and fast

My problem: very few measurements per individual- I cannot distinguish between inter-horse and intra-horse variation.

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Parameters measured

- Radial strain
- Longitudinal strain
- Rotation
- In all segments, at chordal and apical levels
- Torsion
- Semi-subjective quality scores for the graphs produced for certain parameters
- Time points of certain peaks

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Healthy population

- Established reference values in nine 2-4 year old thoroughbred horses in flat race training.
- 4 male, 5 female
- Separate reference values calculated for chordal and apical levels
- Chordal level- inclusive of mitral valve and beginning of papillary muscle
- Apical level- inclusive of apical part of papillary muscle
- Reference values for every segment as well as a global or average measurement

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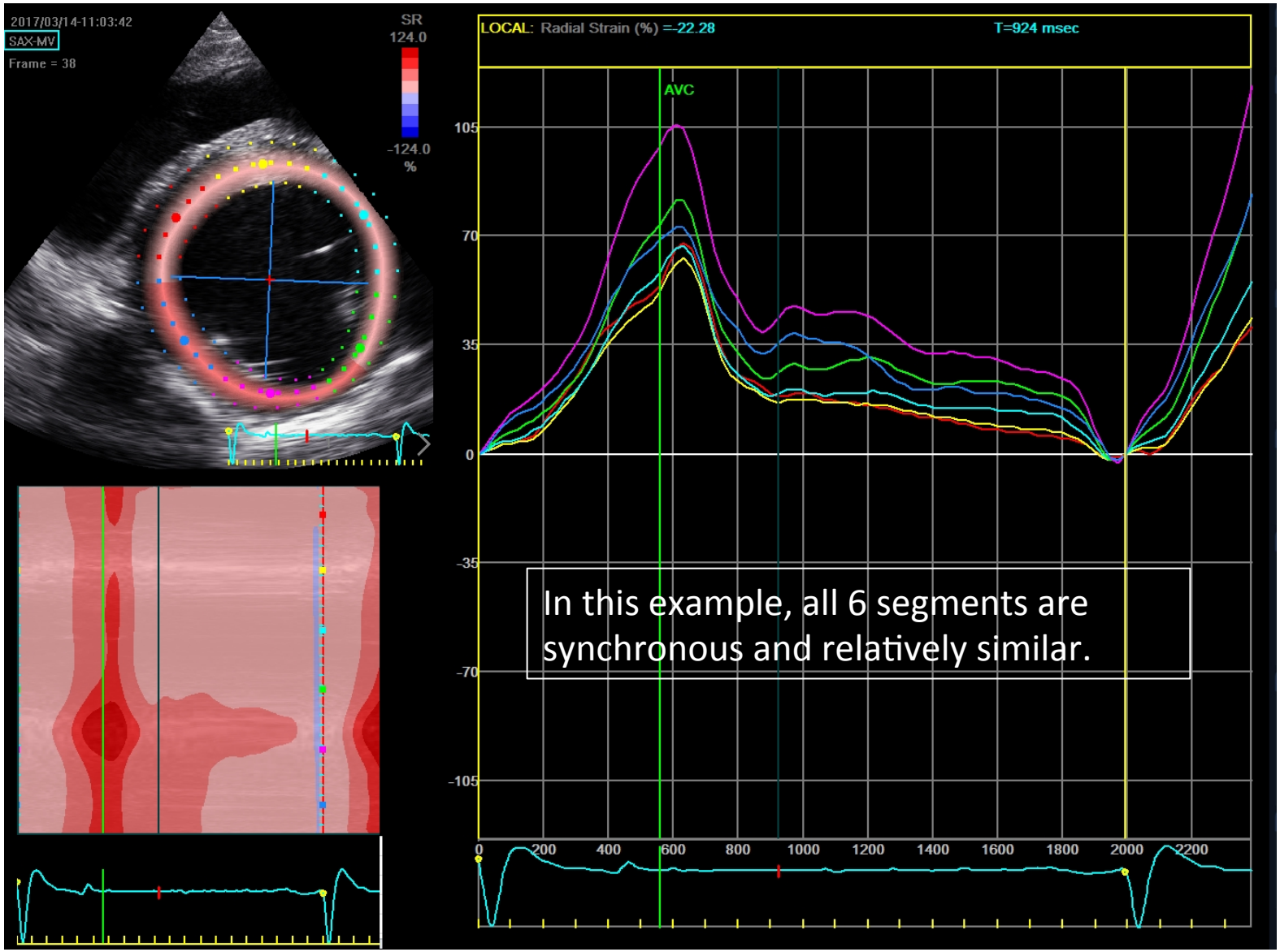
Subjective quality scores

Scored graphs out of three for:

- Synchrony
- Similarity of values of different segments
- ‘Smoothness’

Subjective scores



Time point variables

- Length of trough in overall circumferential strain
- Time of peak rotation
- Other studies have investigated the time difference between peaks of different segments

Verheyen, T., Decloedt, A., De Clercq, D. and van Loon, G. (2012), Cardiac Changes in Horses with Atypical Myopathy. J Vet Intern Med, 26: 1019–1026. doi:10.1111/j.1939-1676.2012.00945.x

Circumferential strain ‘trough length’

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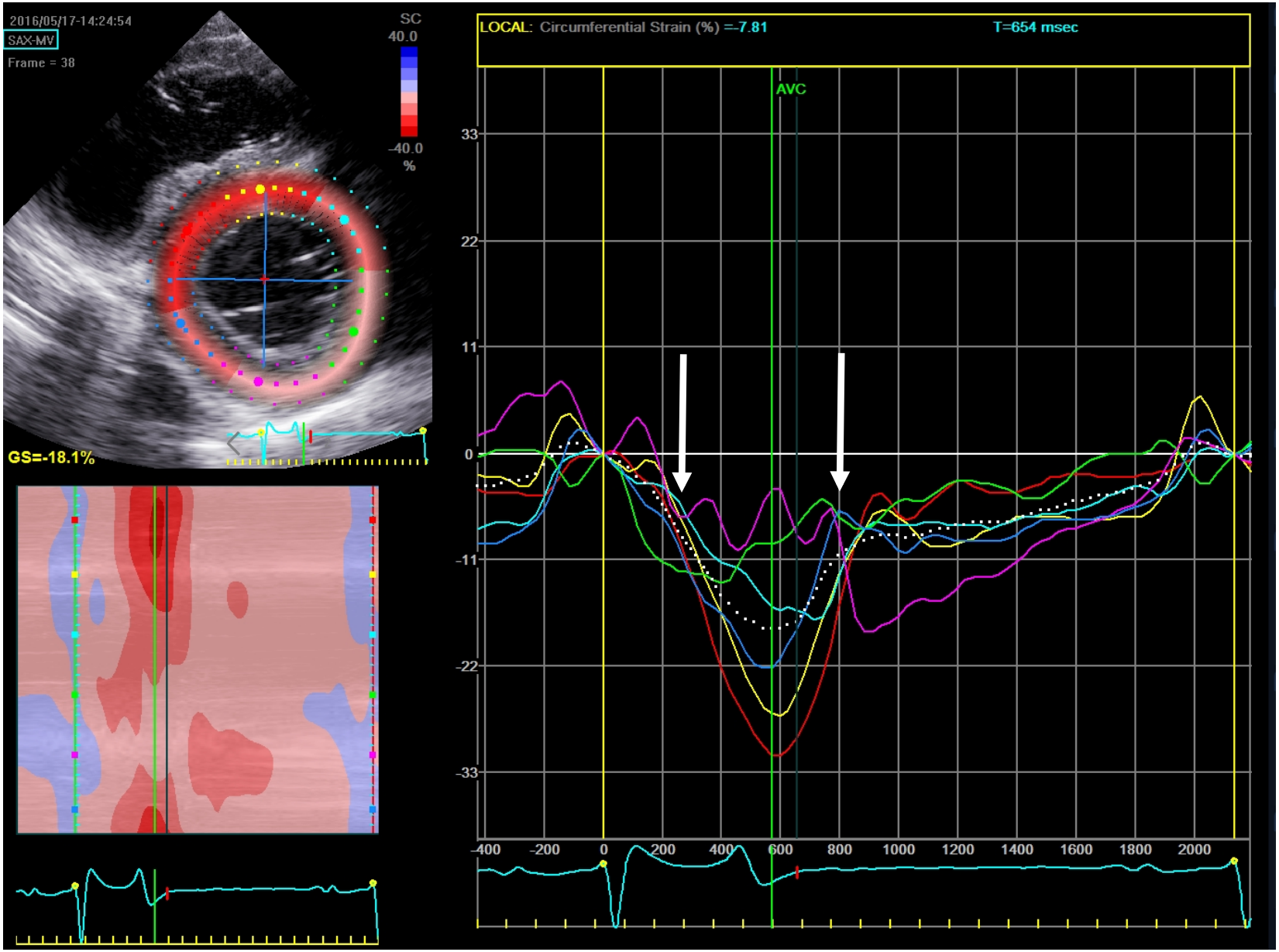

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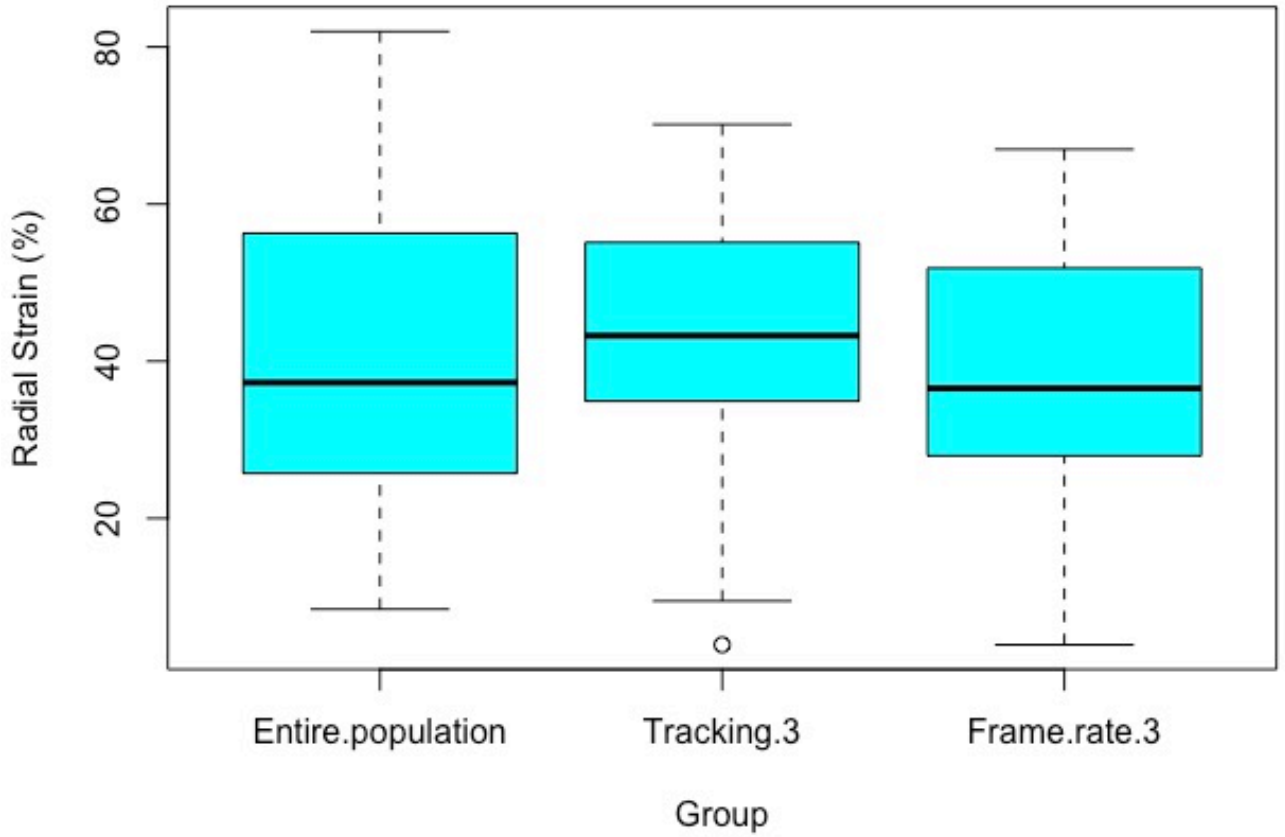
Does the quality of image affect variability?

- Used varied population of 29 normal horses with 46 useable heartbeats in total.
- Subjectively scored aspects of image quality out of 3 within each segment:
  - Frame rate
  - Fraction of endocardial border visible
  - Resolution
  - Shadowing
- Also subjectively scored how closely echopac tracked endo- and epicardial borders out of three for each segment.
- Then recorded radial and circumferential strain and rotation for each heartbeat
- Compared CV for each variation between the whole population and between heartbeats with the top score (3) for each of the subjective quality measures above

No clear difference in mean or in variation was found for radial or circumferential strain nor for rotation between entire population and group with high score in any of the ‘quality’ measurements.

Example: difference in radial strain between entire population and those heartbeats that scored 3 for tracking or for frame rate



Which parameters have low coefficients of variation?

Parameter	CV: 10–20%	CV: 20–30%
Radial strain	none	Chordal average
		Chordal anterior septal
Circumferential strain	Chordal septal	Chordal glogbal
	Apical anterior	Chordal anterior septal
		Chordal anterior
		Chordal average
Rotation	none	none
Radial subjective	none	none
Circumferential subjective	none	Chordal trough length
Rotational subjective	Apical time of peak	Apical synchrony

Which parameters have low coefficients of variation?

- Rotation measurements had extremely high CVs
- Few parameters had 'acceptable' CVs BUT
- Neither did heart rate!- CVs aren't the only important measure. HR had CV>20% for chordal data.
- "Low is a relative term"
- Need to separate variation between individuals and repeatability within individuals- not possible with this dataset. Most similar studies reported low CV for repeatability but still had high variation.
- Chordal level had lower strain CVs. Apical level had lower rotation CVs
- Circumferential measurements had lowest variation, as previously reported.

Schwarzwald, C.C., Schober, K.E., Berli, A.-S.J. and Bonagura, J.D. (2009), Left Ventricular Radial and Circumferential Wall Motion Analysis in Horses Using Strain, Strain Rate, and Displacement by 2D Speckle Tracking. Journal of Veterinary Internal Medicine, 23: 890–900. doi:10.1111/j.1939-1676.2009.0321.x

What parameters are different in disease?

- Identified recordings from eight horses with severe heart disease of mixed pathogenesis (cardiomyopathy N=2, dysplastic valvular disease N=1, acquired valvular disease N=5. (N=number of horses)
- Compared to healthy population
- Hypothesised that radial and circumferential strain and rotation were different in diseased horses as previously reported
- Tested difference between global or average values because they had relatively lower CV values.
- Also tested difference in length of trough in circumferential strain graph and in the time point of peak rotation because time points had been reported as significant in similar study and CVs were relatively low.

Bijnens, Bart; Cikes, Maja; Claus, Piet; Sutherland, George R (2009) Velocity and deformation imaging for the assessment of myocardial dysfunction. European Journal of Echocardiography, 10:216-226. doi 10.1093/ejechocard/jen323

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Which findings are significant?

Bonferroni correction: 10 tests performed- α set at p=0.005

Normally distributed- T test					
Parameter	p value	n normal	n abnormal	mean±SD normal	mean±SD abnormal
Chordal radial average strain	0.062	24	17	48±14	36±21
Apical radial average strain	0.017	9	10	57±19	37±12
Apical average circumferential strain	0.070	9	10	−17±6	−13±4
Chordal average rotation	* 0.0023	24	17	−4.6±2.9	−0.7±4.1
Apical average rotation	0.010	9	10	−7.2±3.9	−2.4±3.3
Chordal circumferential trough length	0.034	24	14	0.26±0.09	0.19±0.09
Apical circumferential trough length	0.89	8	8	0.22±0.09	0.22±0.06
Chordal time of peak rotation	* 0.00071	24	11	0.29±0.11	0.41±0.07
Not normally distributed- Wilcoxon test					
Parameter	p value	n normal	n abnormal	median±IQR normal	median±IQR abnormal
Chordal circumferential strain	0.099	24	17	−17±4	−16±4
Apical time of peak rotation	0.13	9	9	0.27±0.05	0.32±0.28

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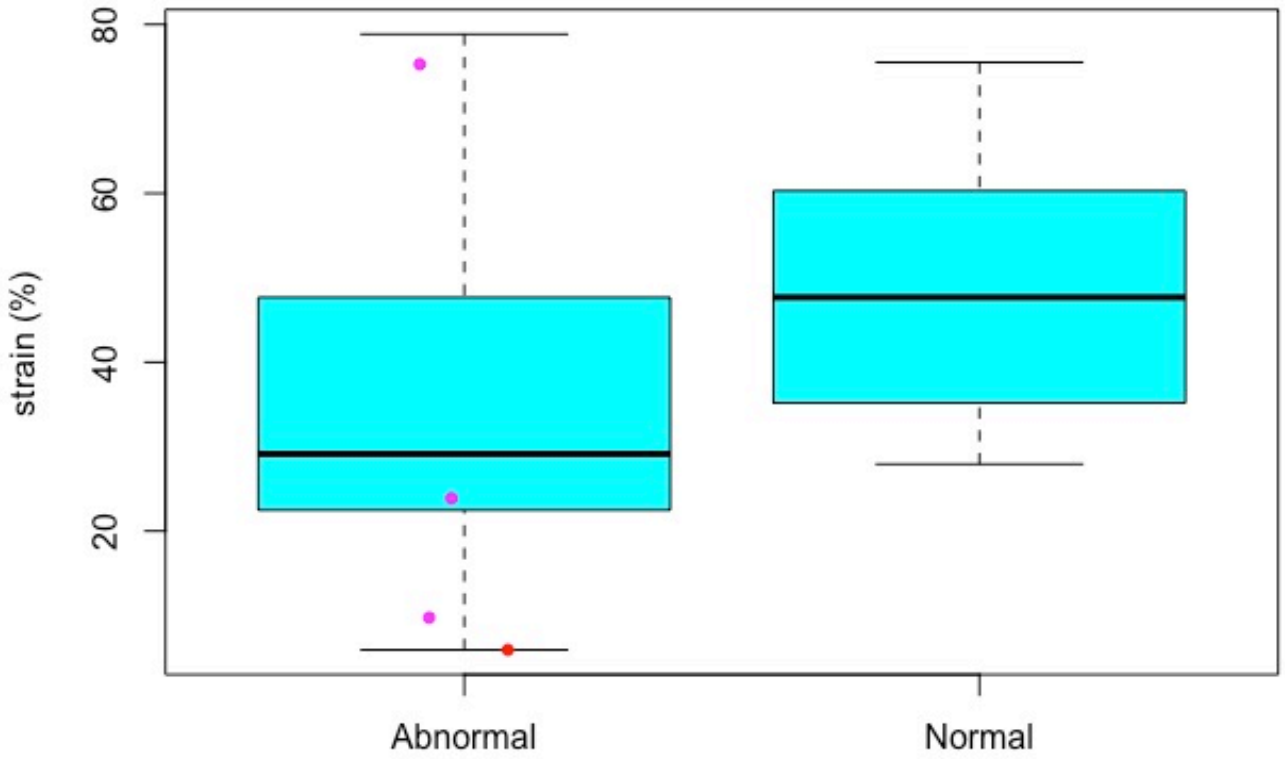
Results

- Despite higher CVs, rotation and time of rotation changes significantly in disease
- This study was weak. A stronger study would likely have found significant p values for more parameters
- Changes were more extreme at chordal level than apical level for everything except strain

Radial average strain- chordal



P=0.062

Central line marks the median, box spans interquartile range and outside lines mark the 10th and 90th percentiles. Red dots and purple dots show data points from two different horses, both of which had severe heart failure. Red = 'L, Purple= 'UO'

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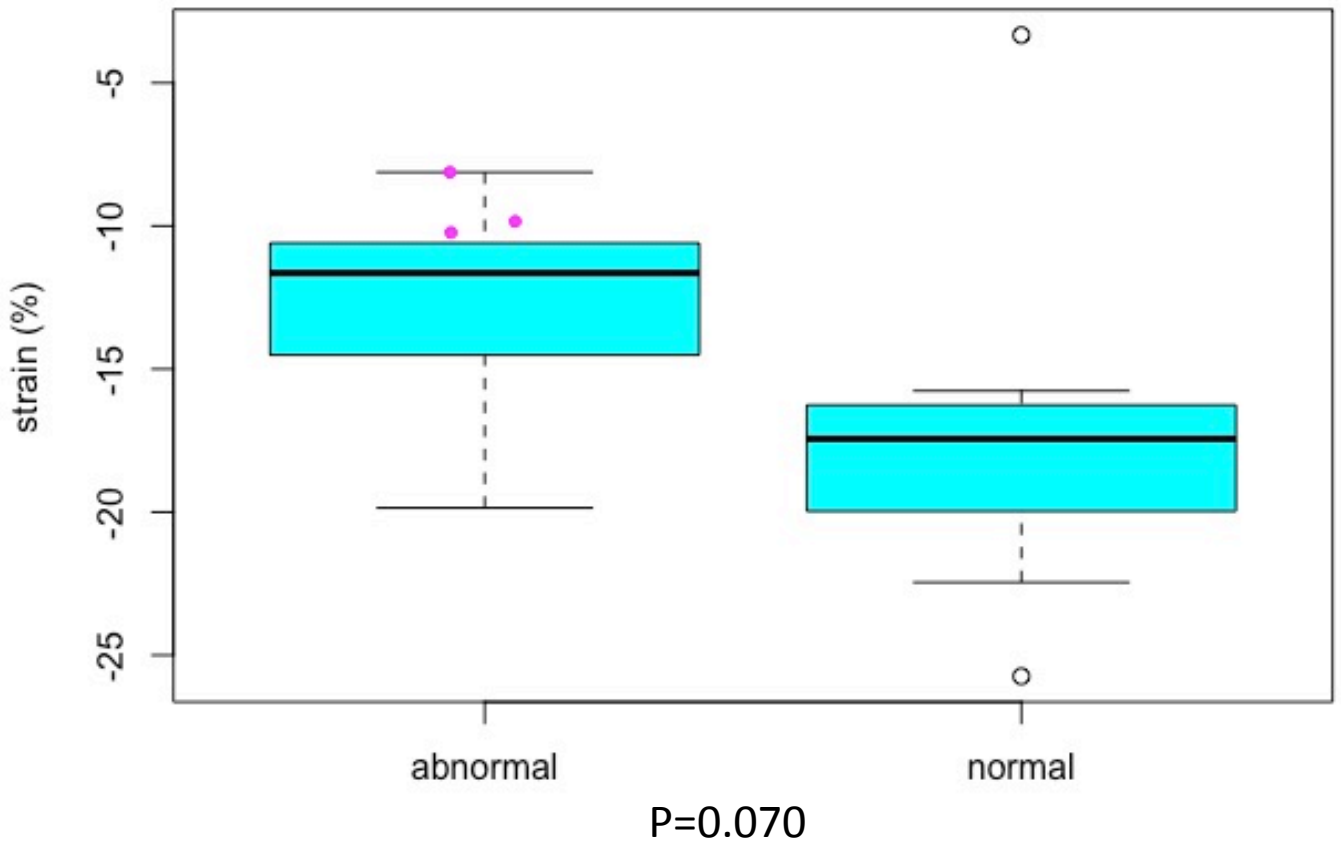
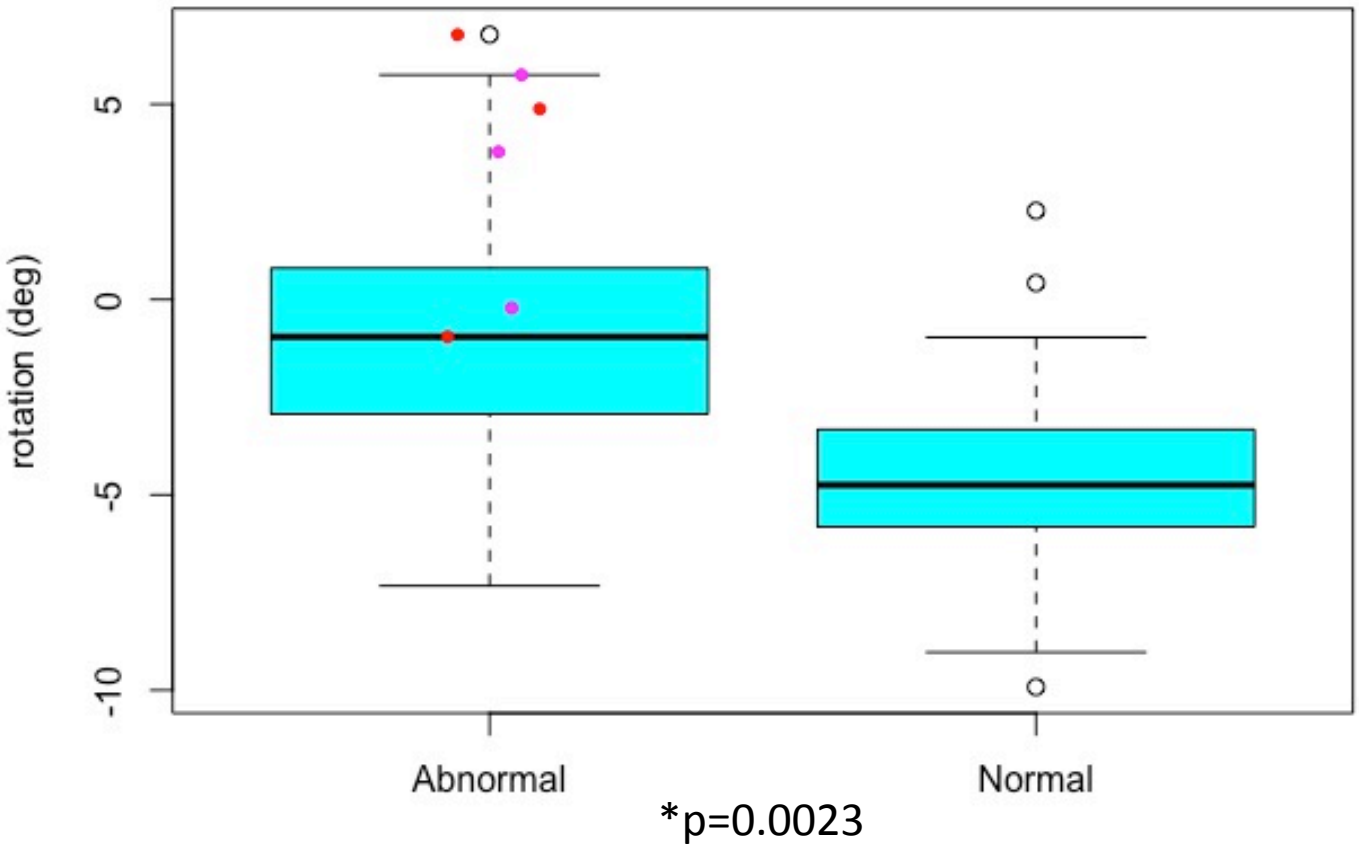
Circumferential average strain- apical



P=0.070

Central line marks the median, box spans interquartile range and outside lines mark the 10th and 90th percentiles. Red dots and purple dots show data points from two different horses, both of which had severe heart failure. Red = 'L, Purple= 'UO'

Average rotation- chordal



Central line marks the median, box spans interquartile range and outside lines mark the 10th and 90th percentilesRed dots and purple dots show data points from two different horses, both of which had severe heart failure. Red = 'L, Purple= 'UO'

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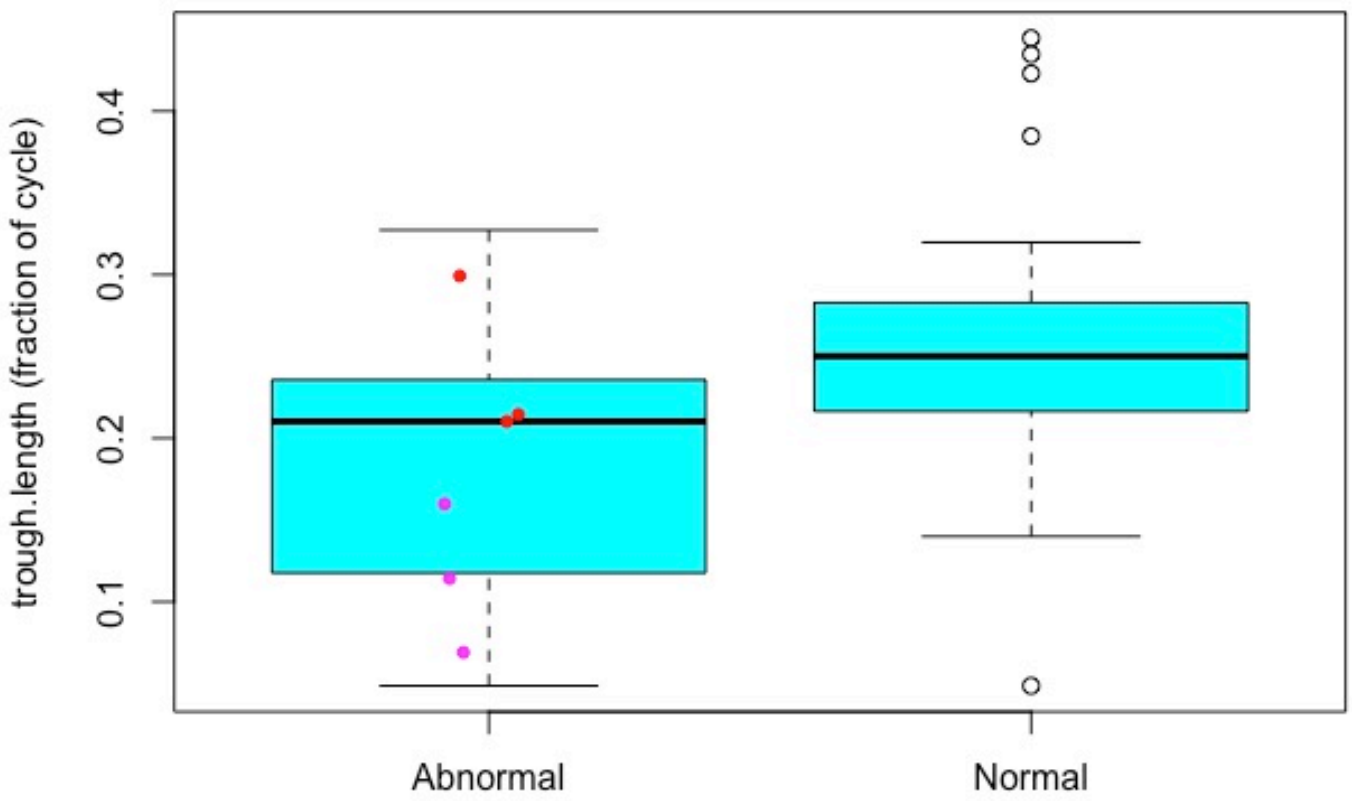
Circumferential 'trough length'- chordal

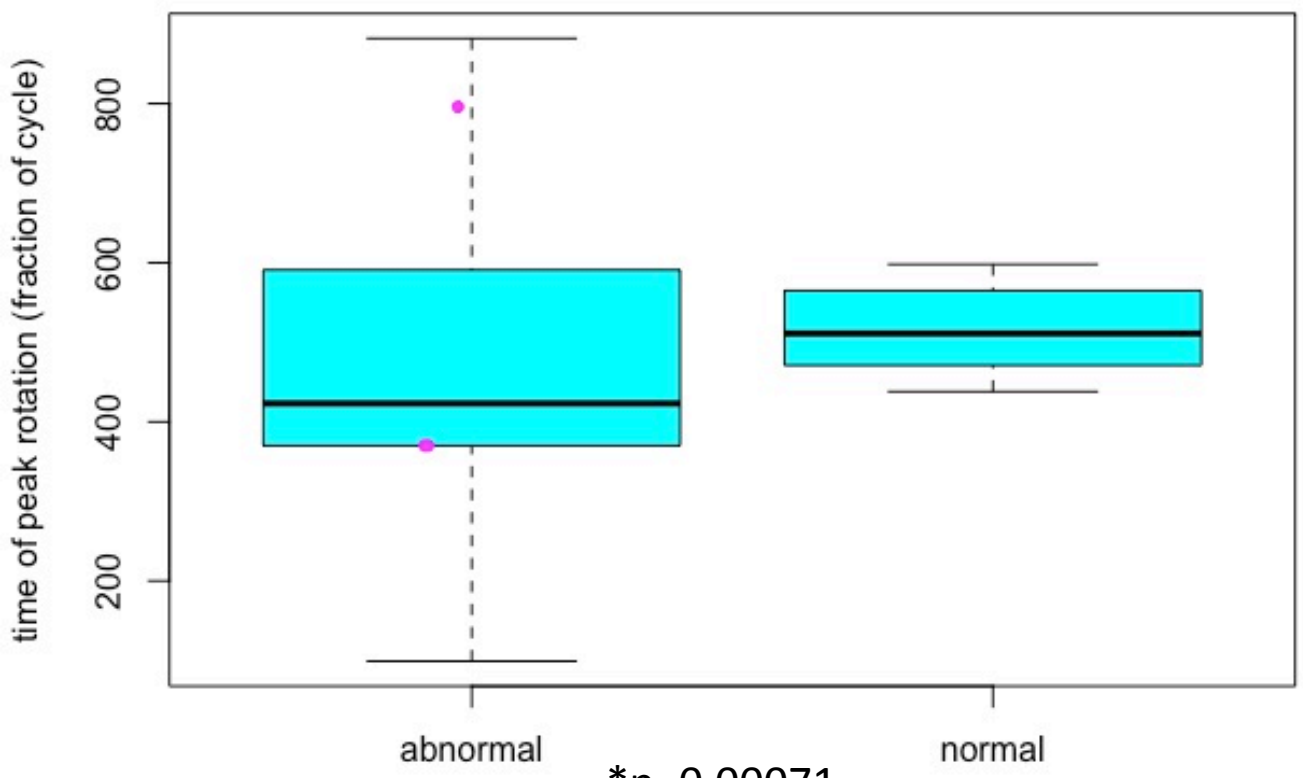


p=0.034

n.b. trough length is the fraction of the cardical cycle (ie Q wave to Q wave) that is occupied by the 'trough' in the overall circumferential strain plot

Central line marks the median, box spans interquartile range and outside lines mark the 10th and 90th percentiles. Red dots and purple dots show data points from two different horses, both of which had severe heart failure. Red = 'L, Purple= 'UO'

Point of peak rotation- chordal



*p=0.00071

n.b. point of peak rotation is the fraction of the cardial cycle (ie Q wave to Q wave) where global rotation peaks.

Central line marks the median, box spans interquartile range and outside lines mark the 10th and 90th percentiles

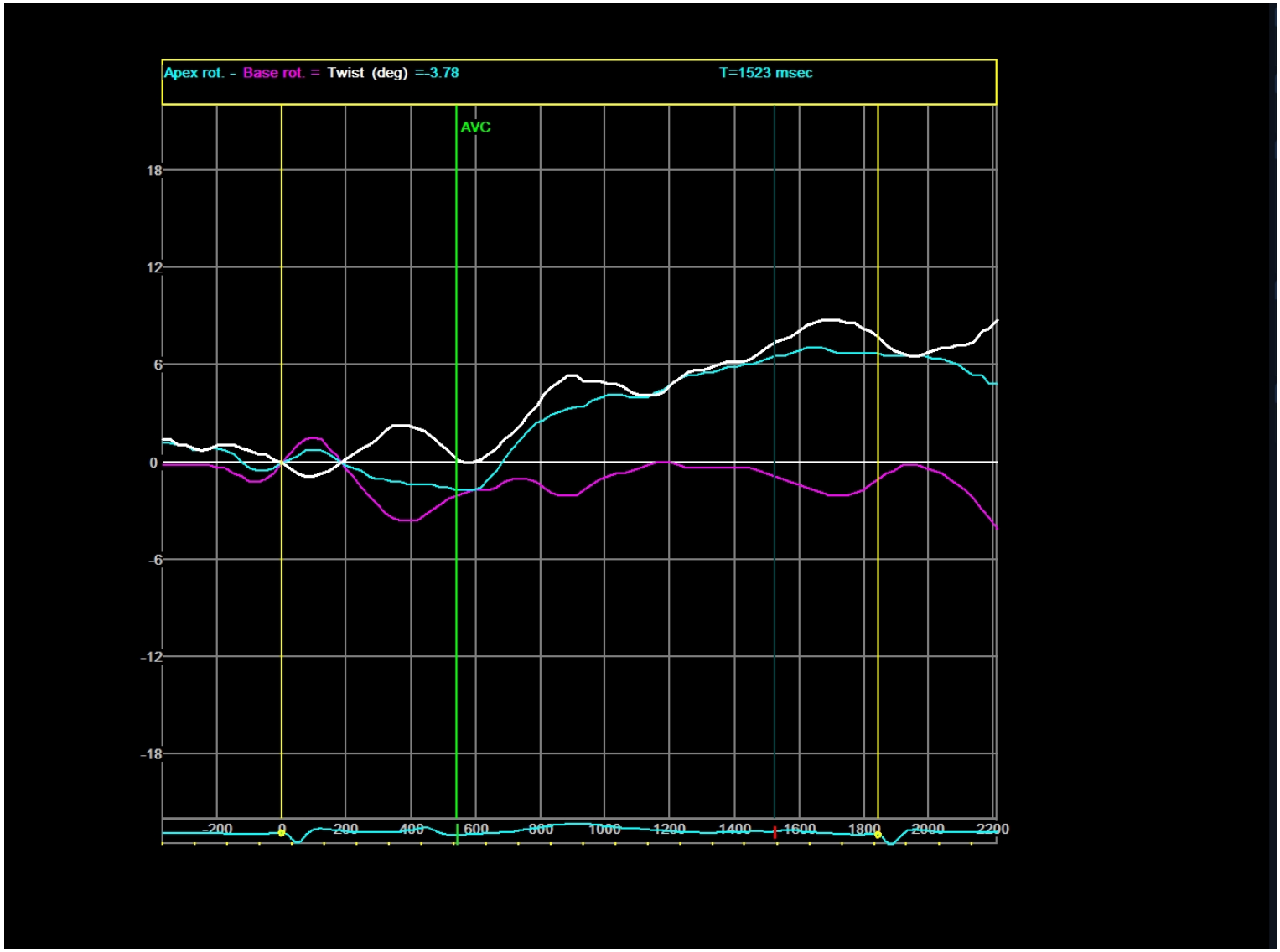
Additional question: Does torsion change with disease?

Apical rotation- basal rotation. Never measured before in horses!

Bonferroni correction: 2 tests performed-α set at p=0.025

	Normally distributed- T-test	p value	n healthy	n unhealthy	mean±SD healthy	mean±SD unhealthy
*	Range (deg)	0.02	7	10	9.3±6.7	5.7±1.3
*	Timespan (ms)	0.01	7	10	588±342	427±211

- Appropriate images were only available for small sample (4 healthy horses, 4 unhealthy horses)
- Highly variable...
- …but clear, significant difference between healthy and unhealthy



Torsion (white line)= Apical rotation (blue line)- base rotation (pink line)

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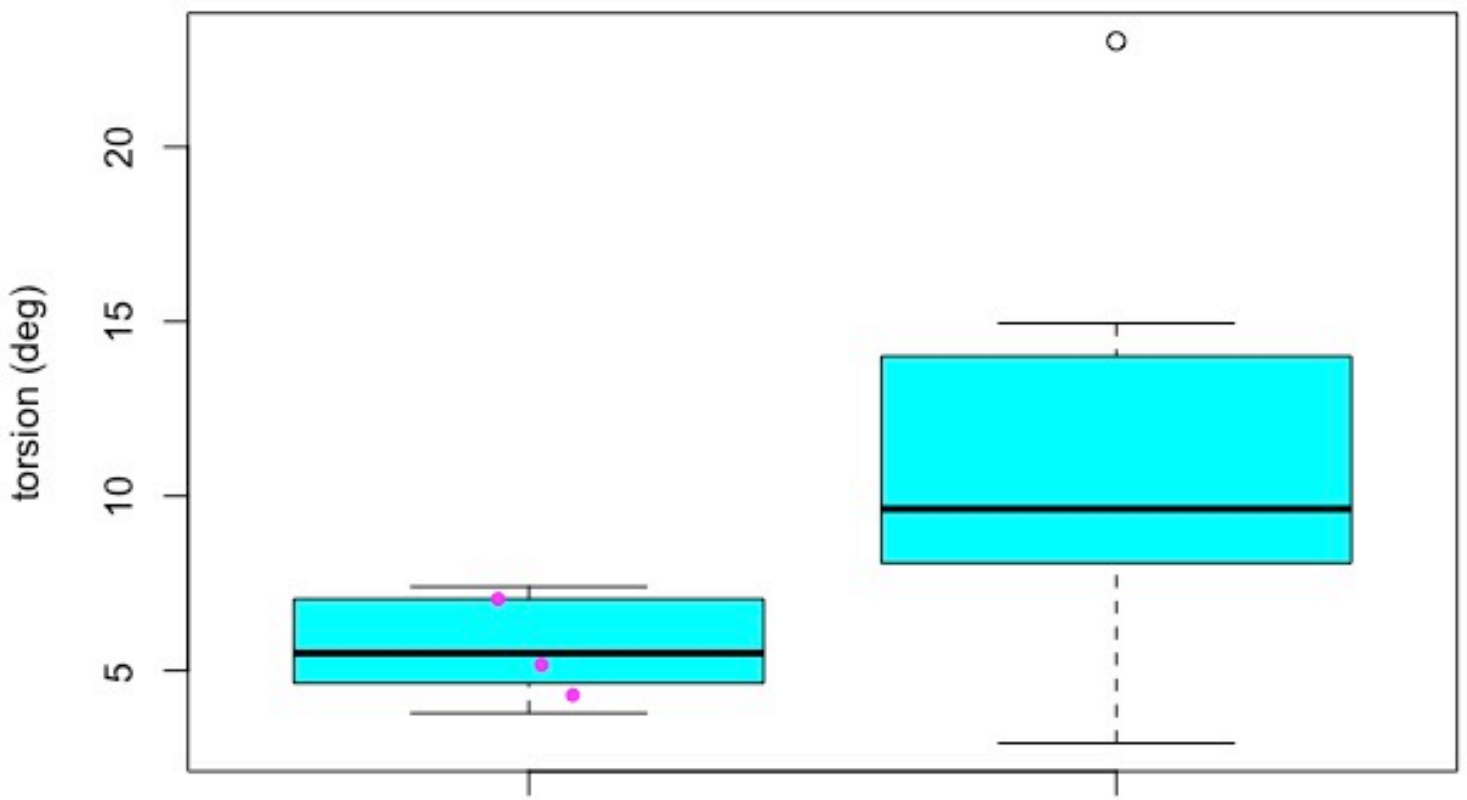
Torsion range



n.b. torsion range is the difference between the maximum and minimum torsion values through the cardiac cycle

Central line marks the median, box spans interquartile range and outside lines mark the 10th and 90th percentiles. Red dots and purple dots show data points from two different horses, both of which had severe heart failure. Red = 'L, Purple= 'UO'

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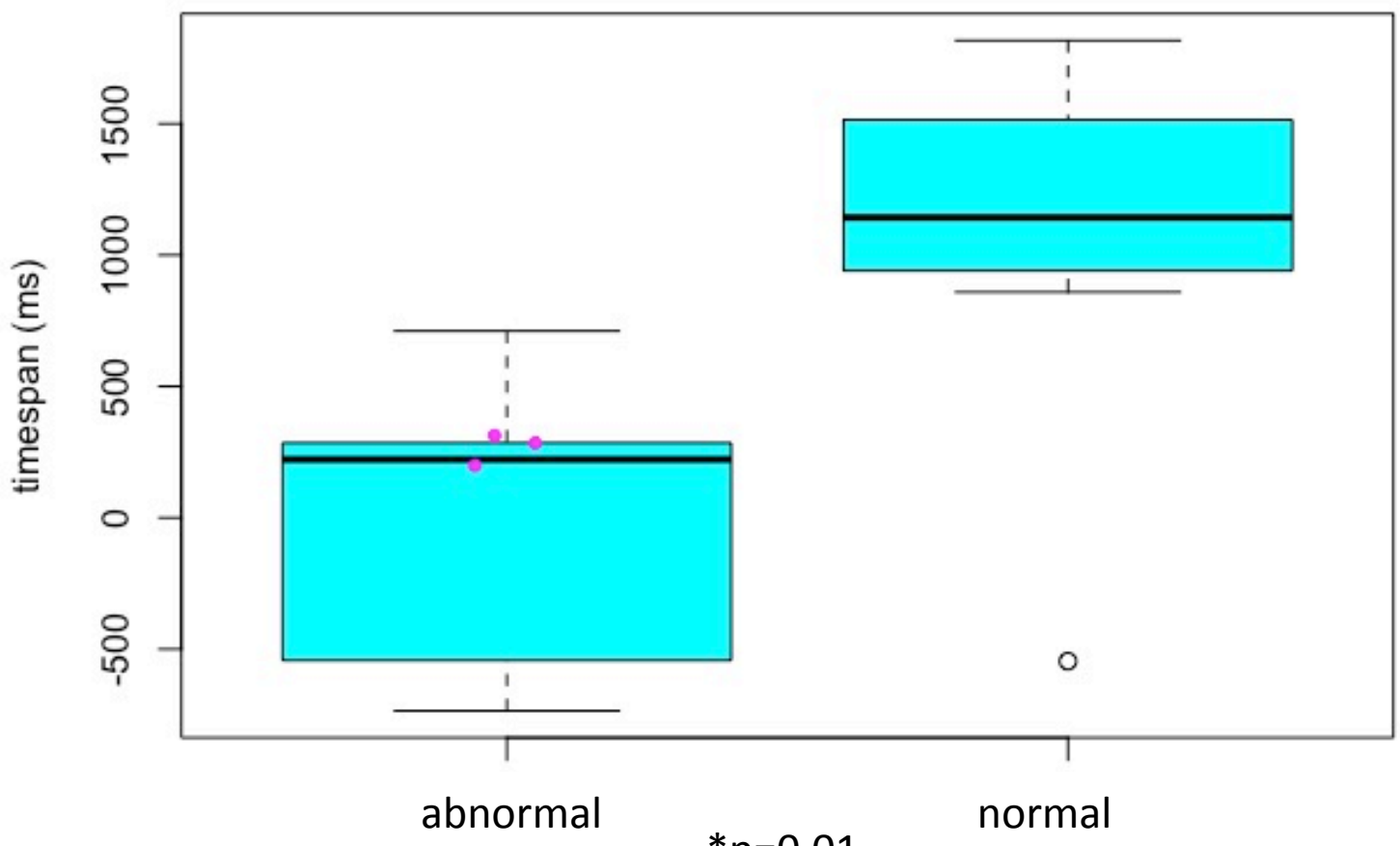
Torsion timespan



*p=0.01

Torsion timespan is the time, in milliseconds, between the peak and trough in the cardiac cycle

Central line marks the median, box spans interquartile range and outside lines mark the 10th and 90th percentiles. Red dots and purple dots show data points from two different horses, both of which had severe heart failure. Red = 'L, Purple= 'UO'

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Should we be looking at variation?

- Healthy horses have more variable strain- this might be an implication of Starling's law and important in keeping a constant cardiac output
- Healthy horses also have more variable torsion are affected by many physiological processes in complex ways and might be a useful overall marker of many problems according to Chetboul et al.
- Further study required

Chetboul, V., Serres, F., Gouni, V., Tissier, R., & Pouchelon, J. L. (2008). Noninvasive assessment of systolic left ventricular torsion by 2-dimensional speckle tracking imaging in the awake dog: Repeatability, reproducibility, and comparison with tissue Doppler imaging variables. *Journal of veterinary internal medicine*, *22*(2), 342-350.

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Future steps

- Study inter/intra-horse variability
- Control population matched for age, sex, breed, exercise level
- Prospective study with standardised imaging protocols
- Compare with standard measurements such as fractional shortening and ejection fraction.

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Conclusions

- Project was limited by low level of repeat measurements- inevitable when using archived data retrospectively. CMM's database useful as contains individuals with wide range of clinical problems and signalment. Can be used to identity potential parameters, but need prospective, high-repeatability trials to test their use.
- High variability, but some parameters show large change in disease
- Rotation and torsion particularly promising
- Few of the quality scores useful, and operator dependent
- Other reports suggest that time difference between peaks may be important

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Thanks to:

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- Dr. John Keen, Royal (Dick) School of Veterinary Science, University of Edinburgh

Appendix: Reference ranges for young Thoroughbreds
Radial strain

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Region	Chordal Mean	Chordal SD	Chordal CV	Apical Mean	Apical SD	Apical CV
Average	48.39	14.46	29.87	56.76	19.22	33.86
Anterior septum	39.69	12.32	28.79	54.60	20.16	36.92
Anterior	39.69	12.08	30.45	51.22	17.25	36.26
Lateral	47.40	17.68	37.30	46.91	17.01	36.26
Posterior	52.12	20.59	39.51	60.25	19.04	31.61
Inferior	49.89	19.43	38.95	63.82	34.69	54.36
Septal	50.82	17.29	34.03	65.53	25.00	38.15

Appendix: Reference ranges for young Thoroughbreds Circumferential strain

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Region	Chordal Mean	Chordal SD	Chordal CV	Apical Mean	Apical SD	Apical CV
Global	−13.34	3.62	27.14	−15.43	5.75	37.29
Anterior septum	−22.73	5.15	22.64	−21.48	5.75	37.29
Anterior	−15.37	3.80	24.73	−15.58	2.90	18.62
Lateral	−12.36	6.27	50.77	−14.72	6.59	44.74
Posterior	−10.42	7.64	73.30	−9.43	16.98	180.04
Inferior	−12.56	6.33	50.40	−14.67	5.32	36.26
Septal	−27.19	3.69	13.58	−22.75	8.14	35.79
Average	−17.77	3.94	22.19	−17.40	6.17	35.46

Appendix: Reference ranges for young Thoroughbreds Rotation

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Region	Chordal Mean	Chordal SD	Chordal CV	Apical Mean	Apical SD	Apical CV
Global	−3.98	2.94	73.93	−7.18	4.19	58.41
Anterior septum	−2.86	2.79	97.46	−7.15	4.43	62.03
Anterior	0.16	3.19	1992.21	−3.83	3.59	93.79
Lateral	−1.06	4.77	447.85	−3.83	4.91	128.34
Posterior	−5.50	4.14	75.34	−7.74	5.22	67.52
Inferior	−8.68	2.82	32.47	−10.86	4.64	42.72
Septal	−6.14	2.72	44.26	−9.39	4.07	43.37
Average	−4.62	2.86	61.85	−7.23	3.93	54.32

Appendix: Reference ranges for young Thoroughbreds
Radial subjective measurements

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Parameter	Chordal Mean	Chordal SD	Chordal CV	Apical Mean	Apical SD	Apical CV
Number of peaks	3.63	1.13	31.31	4.22	1.48	35.08
Synchrony	2.33	0.82	34.99	2.89	0.33	11.54
Segmental similarity	2.08	0.65	31.39	2.22	0.67	30.00
Smoothness	1.92	0.78	40.46	2.00	0.82	40.82

Appendix: Reference ranges for young Thoroughbreds Circumferential subjective measurements

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Parameter	Chordal Mean	Chordal SD	Chordal CV	Apical Mean	Apical SD	Apical CV
Number of misfit segments	1.04	0.91	87.16	1.78	1.92	108.12
Synchrony	2.08	0.72	34.43	1.89	0.93	49.13
Trough length	421.25	118.64	28.16	422.88	140.08	33.13
Trough length % of cycle	0.26	0.09	35.05	0.22	0.09	38.80

Appendix: Reference ranges for young Thoroughbreds

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Parameter	Chordal Mean	Chordal SD	Chordal CV	Apical Mean	Apical SD	Apical CV
Directional similarity	1.46	0.72	49.44	2.22	0.83	37.50
Synchrony	1.67	0.64	38.22	2.11	0.60	28.46
Segmental similarity	1.46	0.72	49.44	2.00	1.00	50.00
Time of peak rotation	463.58	143.48	30.95	517.22	55.20	10.67
Point of peak rotation	−3.98	0.11	39.65	0.28	0.03	11.90
Number of peaks	2.04	0.86	−73.93	2.22	1.30	58.58