AECC University College
Centre for Biomechanics Research

Bournemouth University

Intervertebral motion biomarkers in chronic, nonspecific back pain?

Alan Breen DC, PhD, FRCC, Alexander Breen BSc(hons) MSc, PhD MIPEM

Faculty of Science and Technology, Bournemouth University, UK, Centre for Biomechanics Research, AECC University College Bournemouth, U

Paper presented at the 2022 'Back2Back' meeting, St Anne's College Oxford, 6th April 2

AECC University College
Centre for Biomechanics Research

Bournemouth University

Biomarker

“a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or biological responses to a therapeutic intervention” (FDA)

Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Pharmacol Ther 69:89-95, 2001

Biomarkers in nonspecific back pain

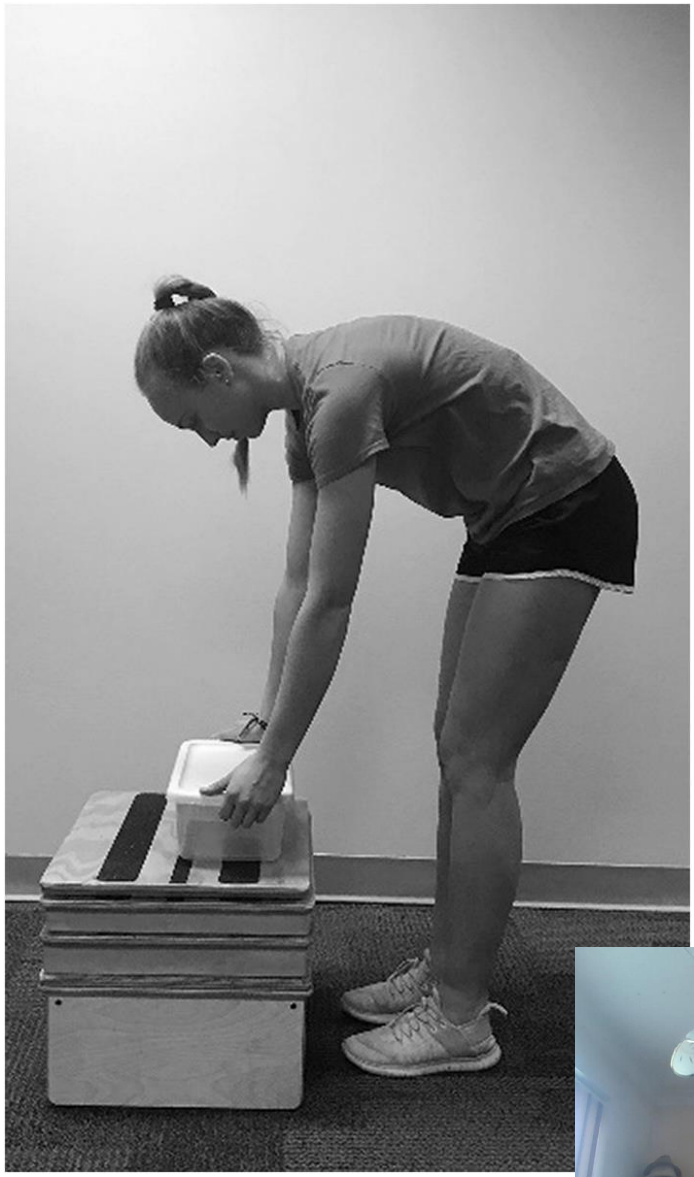
- Intrinsic mechanics (difficult to measure *in vivo)* (Panjabi 2006)
- Chemical markers (low grade inflammation if present) (Li, Liu et al 2016)
- Neuroplastic (once a chronic state established) (Nijs 2010)

Panjabi, M. M. (2006). "A hypothesis of chronic back pain: ligament subfailure injuries lead to muscle control dysfunction." European Spine Journal 15: 668-676.

Li, Y., J. Liu, Z.-Z. Liu and D.-P. Duan (2016). "Inflammation in low back pain may be detected from the peripheral blood: suggestions for biomarker." Bioscience Reports 36.

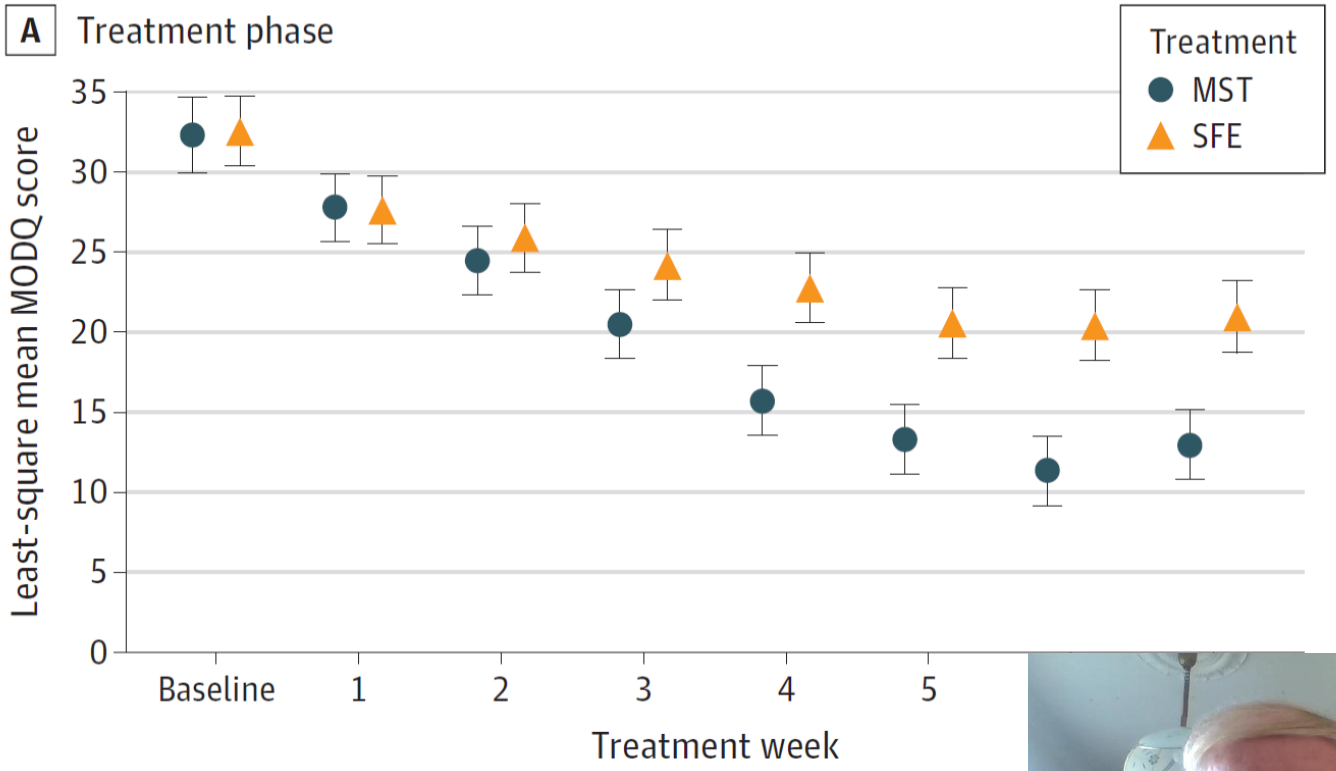
Nijs, J., Van Houdenhove, B., Oostendorp, R.A.B. (2010). "Rec
sensitization in pat
musculoskeletal pa
neurophysiology in
practice." Manual T

Readiness to move



Hooker , Q. L. L., V.M., Roles, K., van Dillen L.R. (2022). "Motor skill training versus strength and flexibility exercise in people with chronic low back pain: Preplanned analysis of effects on kinematics during a functional activity." Clinical Biomechanics 92(105570).

Disability Over Time Comparing MST and SFE



van Dillen, L. R., Lanier, V.M., Steger-May, K., Wallendorf, M., Norton, B.J., Civello, J.M., Czuppon, S.L., Francois, S.J., Roles, K., Lang, C.E. (2020). "Effect of Motor Skill Training in Functional Activities vs Strength and Flexibility Exercise on Function in People With Chronic Low Back Pain A Randomized Clinical Trial." JAMA Neurology 78: 385-395.

AECC University College
Centre for Biomechanics Research

Bournemouth University

Implications

There may be value in investigating spine kinematics as CNSLBP biomarkers.

Contributions to motion may be more promising than raw values for population studies that look for biomarkers.

AECC University College
Centre for Biomechanics Research

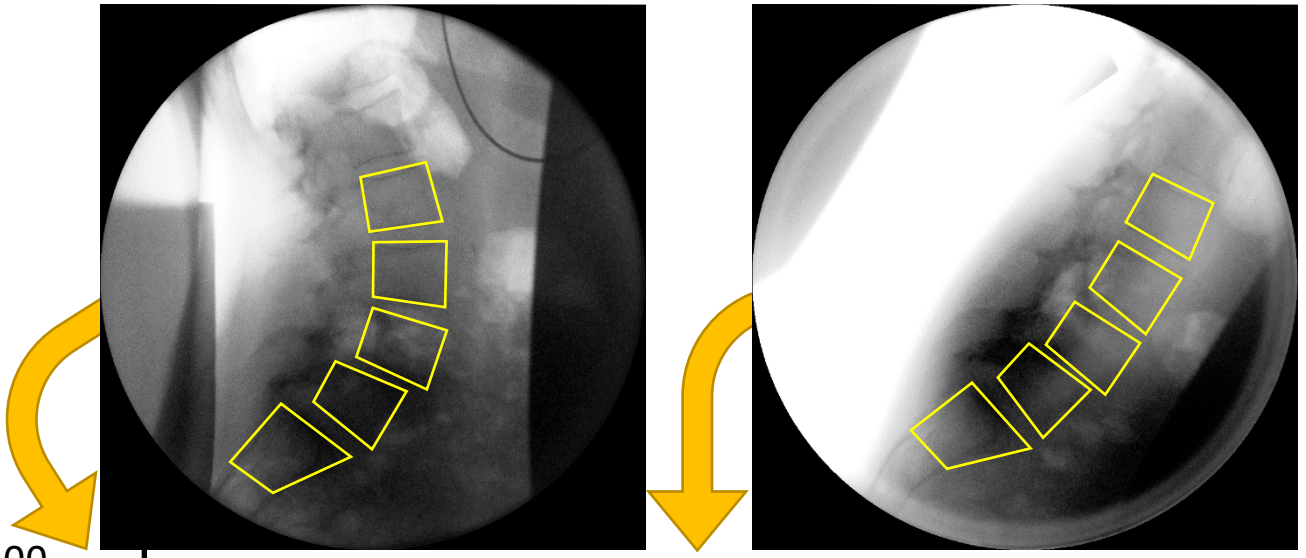
Bournemouth University

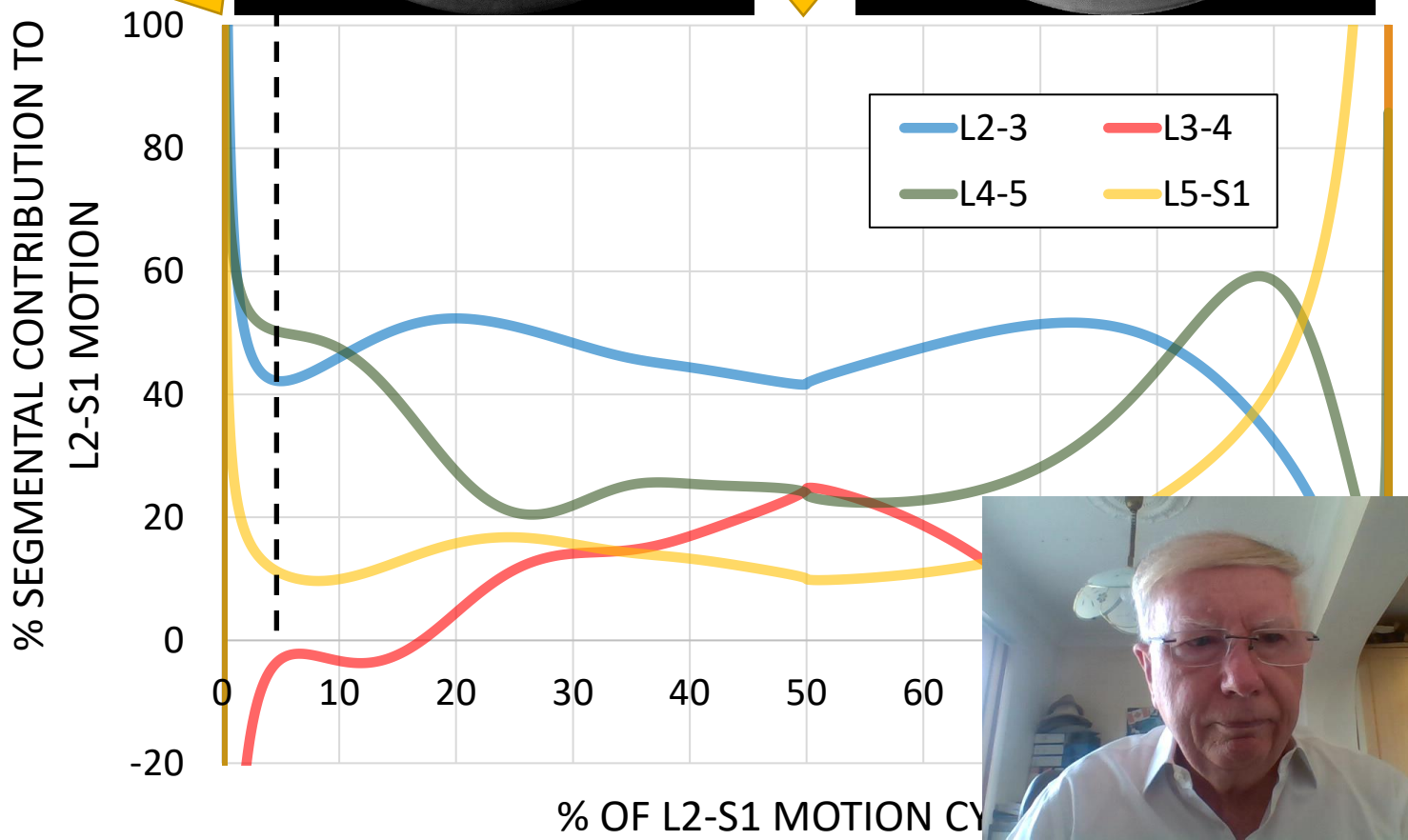
Quantitative Imaging Biomarkers (QIBs)

"..in an era of machine learning and artificial intelligence, it is increasingly desirable that we extract quantitative biomarkers from medical images that inform on disease detection, characterisation, monitoring and assessment of response to treatment."

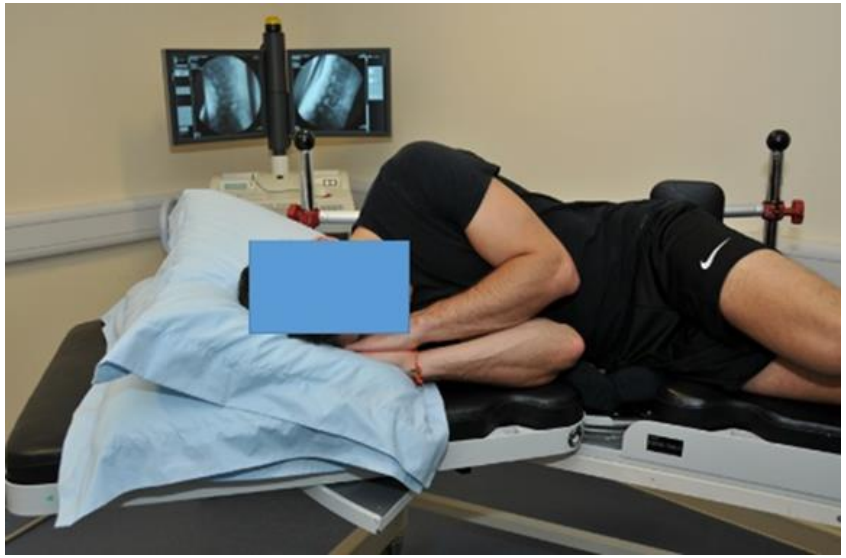
O'Connor JPB, Jackson A, Asselin M-C, Buckley DL, Parker GJM, Jayson GC. Quantitative im
in the clinical development of targeted therapeutics: current and future perspectives. The
2008;9:766–776. doi: 10.1016/S1470-2045(08)70196-7.

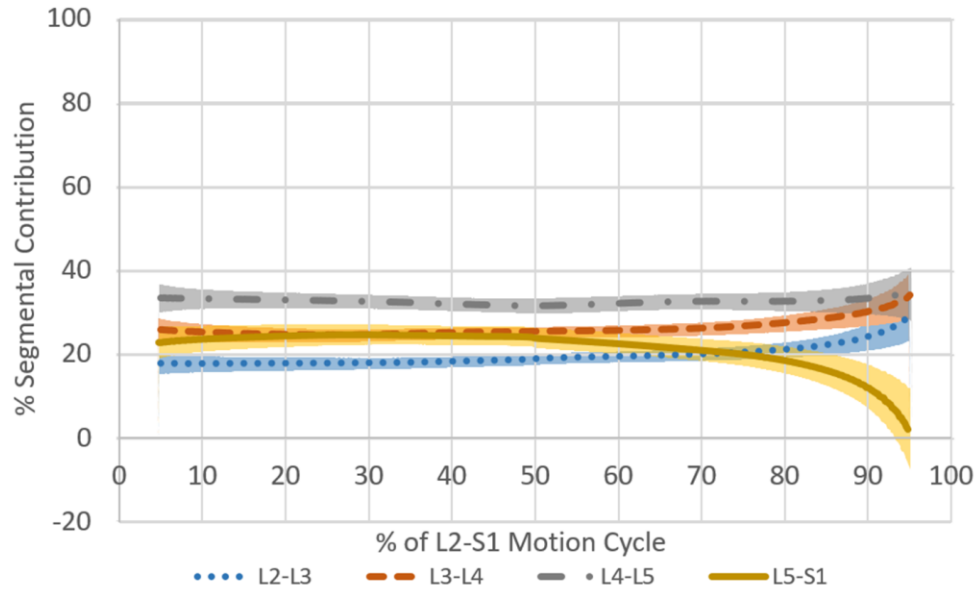
Continuous intervertebral motion contributions in a patient with L4 spondylolisthesis

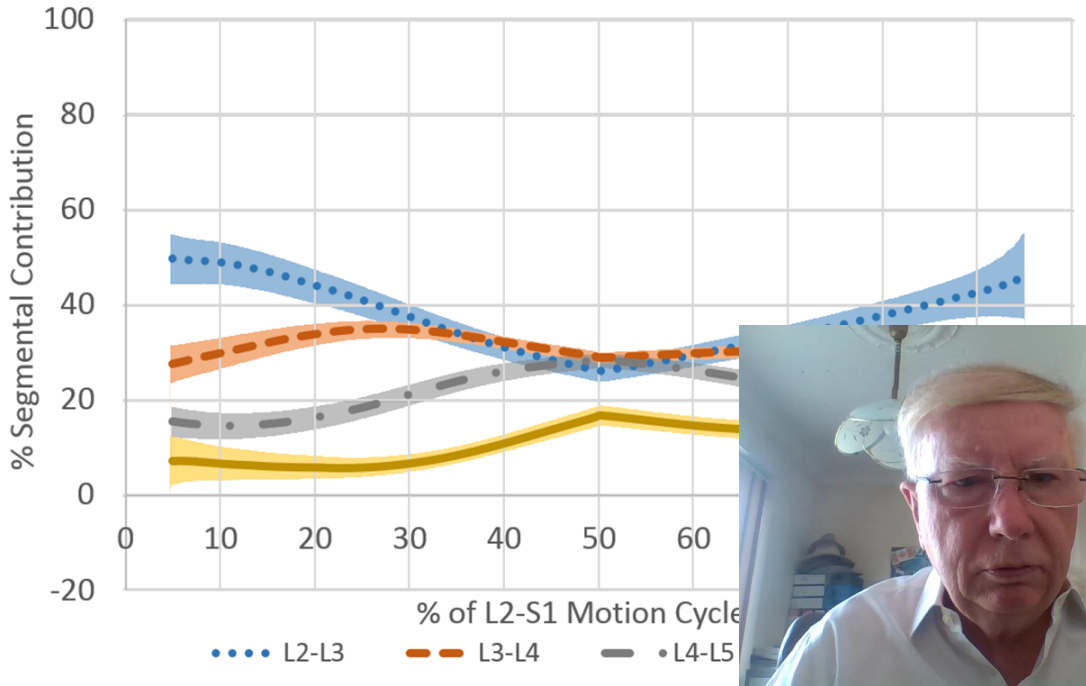




Motion contributions for L2-S1 flexion and return (n=103)

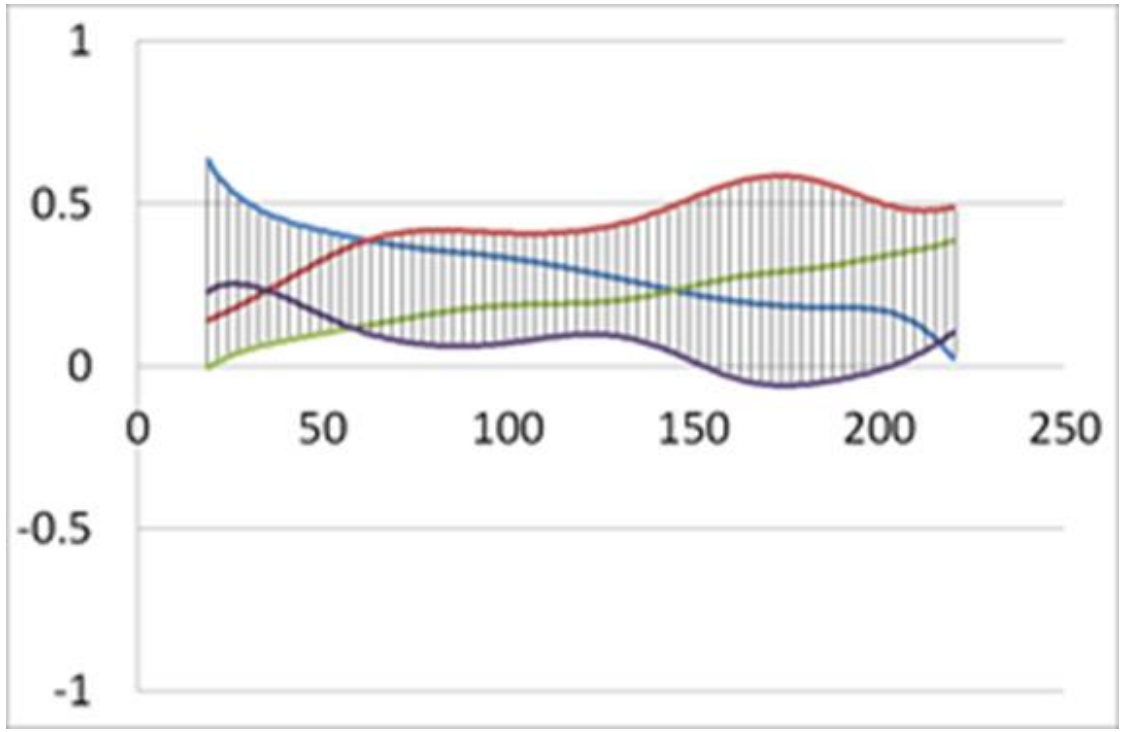






Expressions of the “evenness” of motion sharing

Breen, A. and A. Breen (2018). "Uneven intervertebral motion sharing is related to disc degeneration and is greater in patients with chronic, non-specific low back pain: an in vivo, cross-sectional cohort comparison of intervertebral dynamics using quantitative fluoroscopy." Eur Spine J 27(1): 145-153.

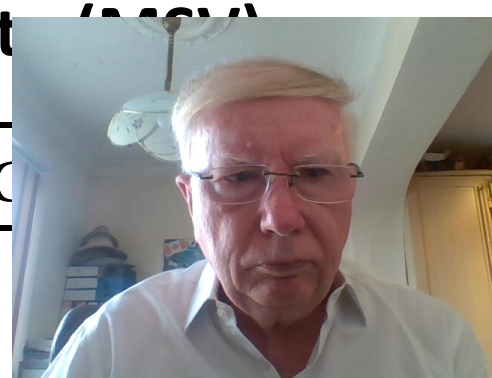


$$MSI = \frac{\sum_{i=1}^{N} fRC_i}{N}$$

Motion sharing inequality (MSI)

Motion sharing variabilit

$$MSV = \sqrt{\frac{\sum_{i=1}^{N} (fRC}{}}$$



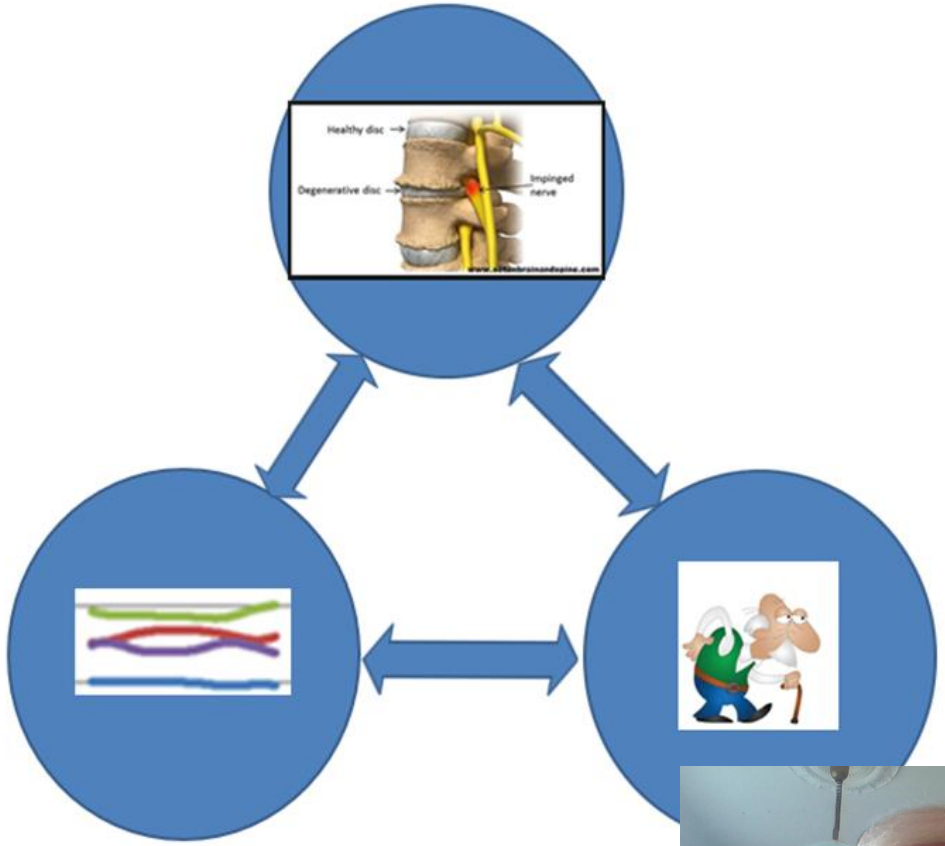
MSI, MSV and Composite DD in CNSLBP patients and matched controls

Recumbent flexion MSI greater in CNSLBP patients (29%) than controls (22%) (n=10, p=0.02)

Correlation of MSI/MSV with DD

	Recumbent	Weight bearing
MSI	**r=0.70, p=0.03**	r=0.43, p=0.23
MSV	r=-0.21, p=0.54	**r=0.77, p=0.01**

Only in patients with CNSLBP!

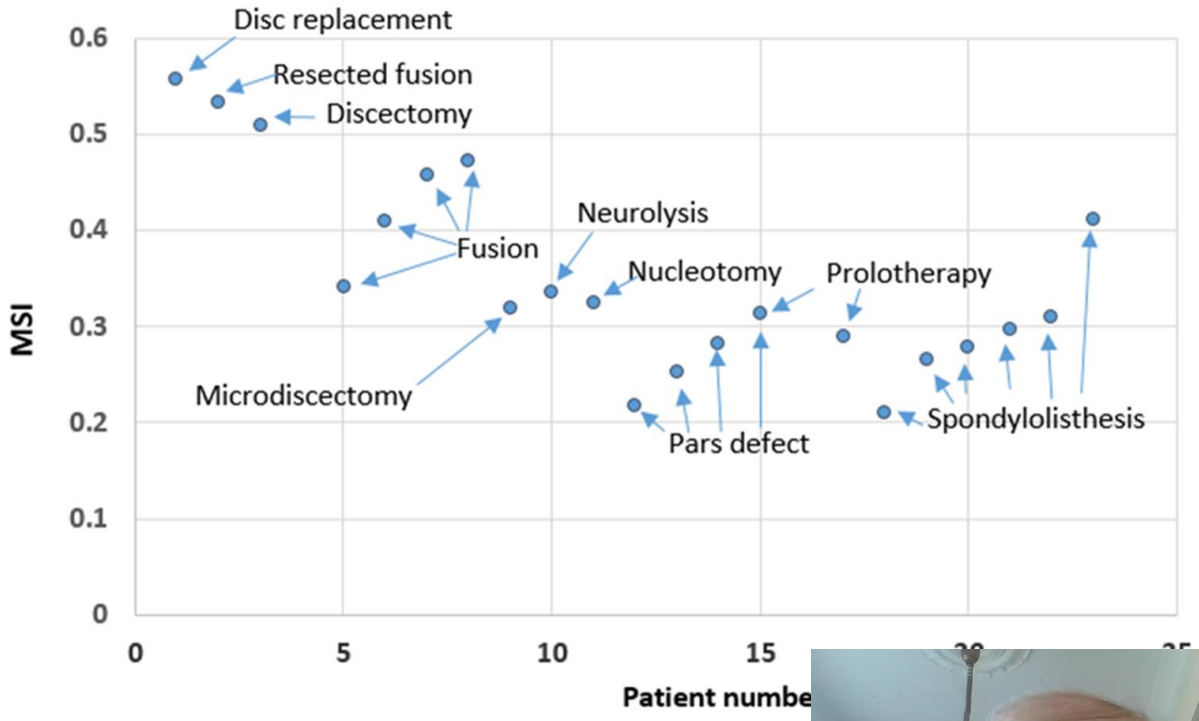


Breen, A. and A. Breen (2018). "Uneven intervertebral motion sharing is related to disc degene
greater in patients with chronic, non-specific low back pain: an in vivo, cross-sectional cohort
intervertebral dynamics using quantitative fluoroscopy." Eur Spine J 27(1): 145-153

Recumbent MSI in a further cohort of 37 matched patients and controls

	MSI (%)		
	Patients	Controls	p
All (n=37)	30	27	0.01
Intact (n=16)	28	27	0.25
Surgery (n=11)	37	28	0.02
Defect (n=10)	30	25	0.12

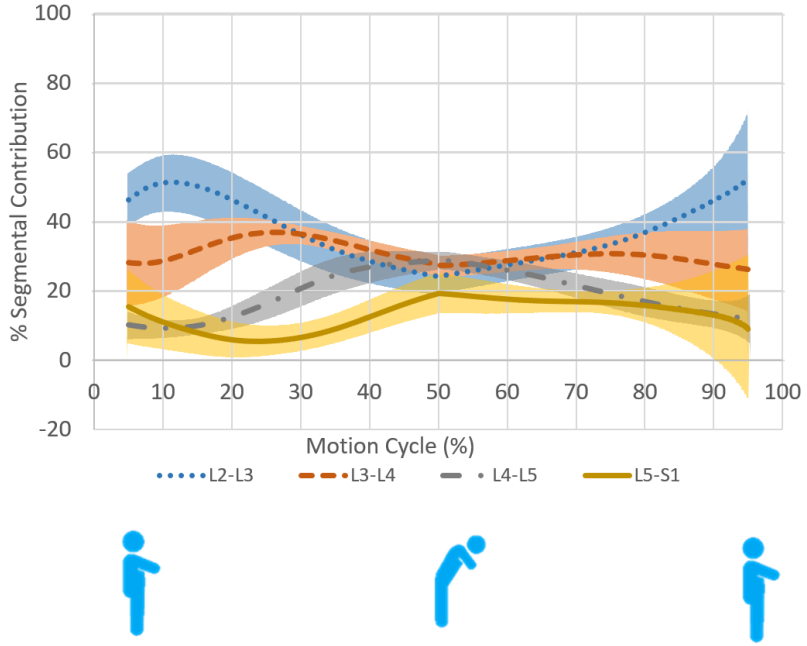
MSI in patients with previous disruption



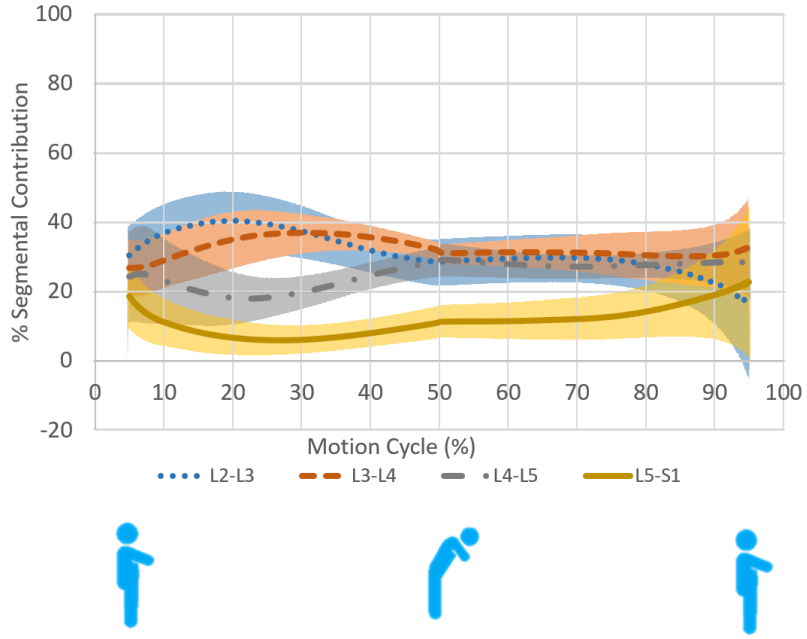
Breen Ax.C., Breen A.C. (2018). "Aberrant intervertebral motion in patients with treatment-resi
low back pain: a retrospective cohort study and control comparison." European Spine Journal 2
2839 http://link.springer.com/article/10.1007/s00586-018-5666-1

Weight bearing motion sharing in a different data set

Controls (n=10)

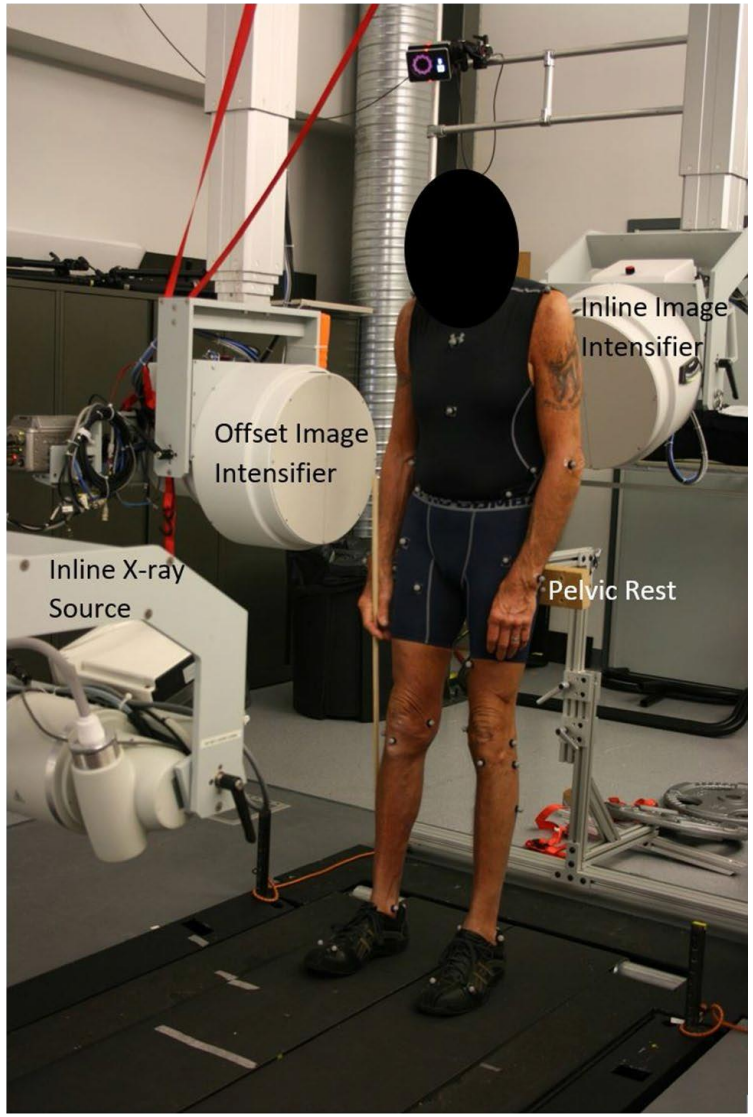


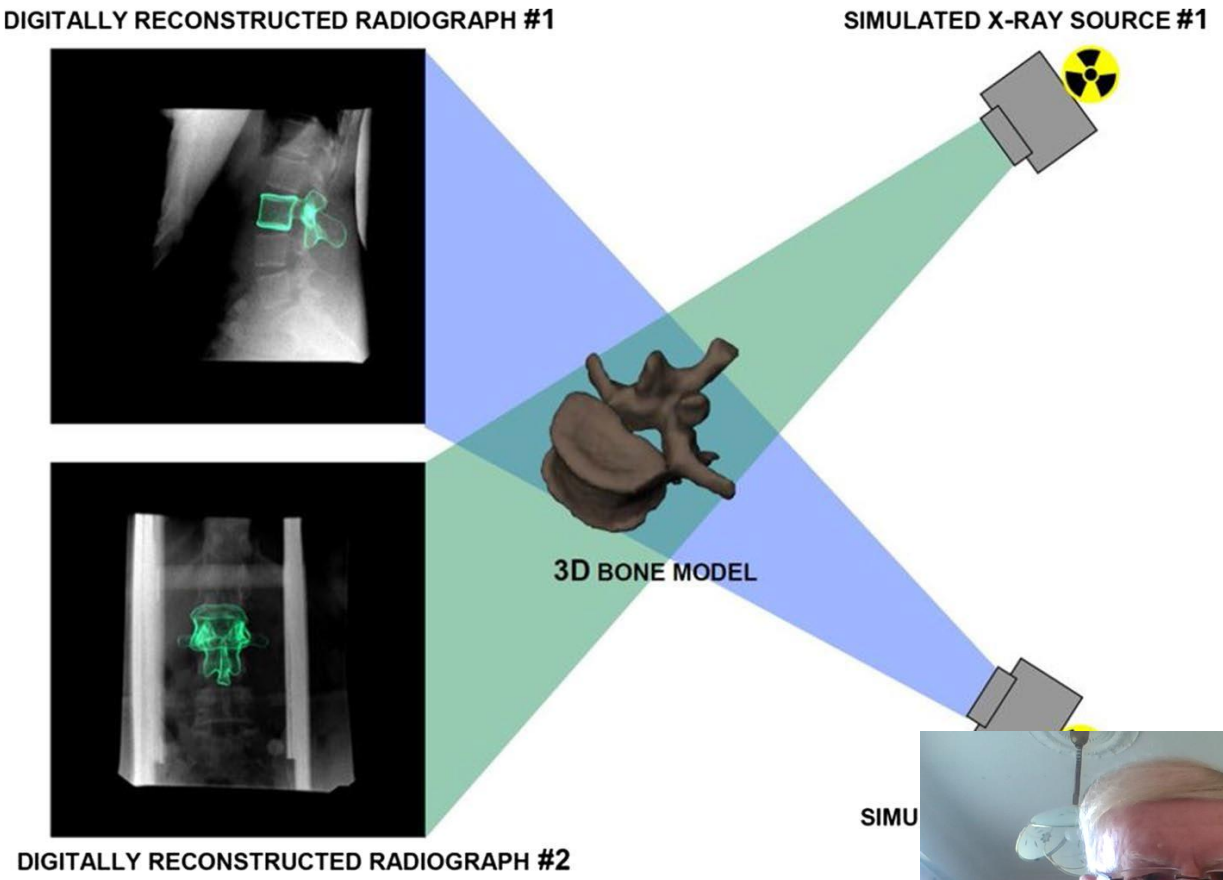
Patients (n=10)



Breen Ax. C., Breen. A. C. (2019). "Dynamic interactions between lumbar interverteb
segments during forward bending." Journal of Biomechanics 102 (109603)
Doi.org/10.1016/jbiomech.2020. (109603).

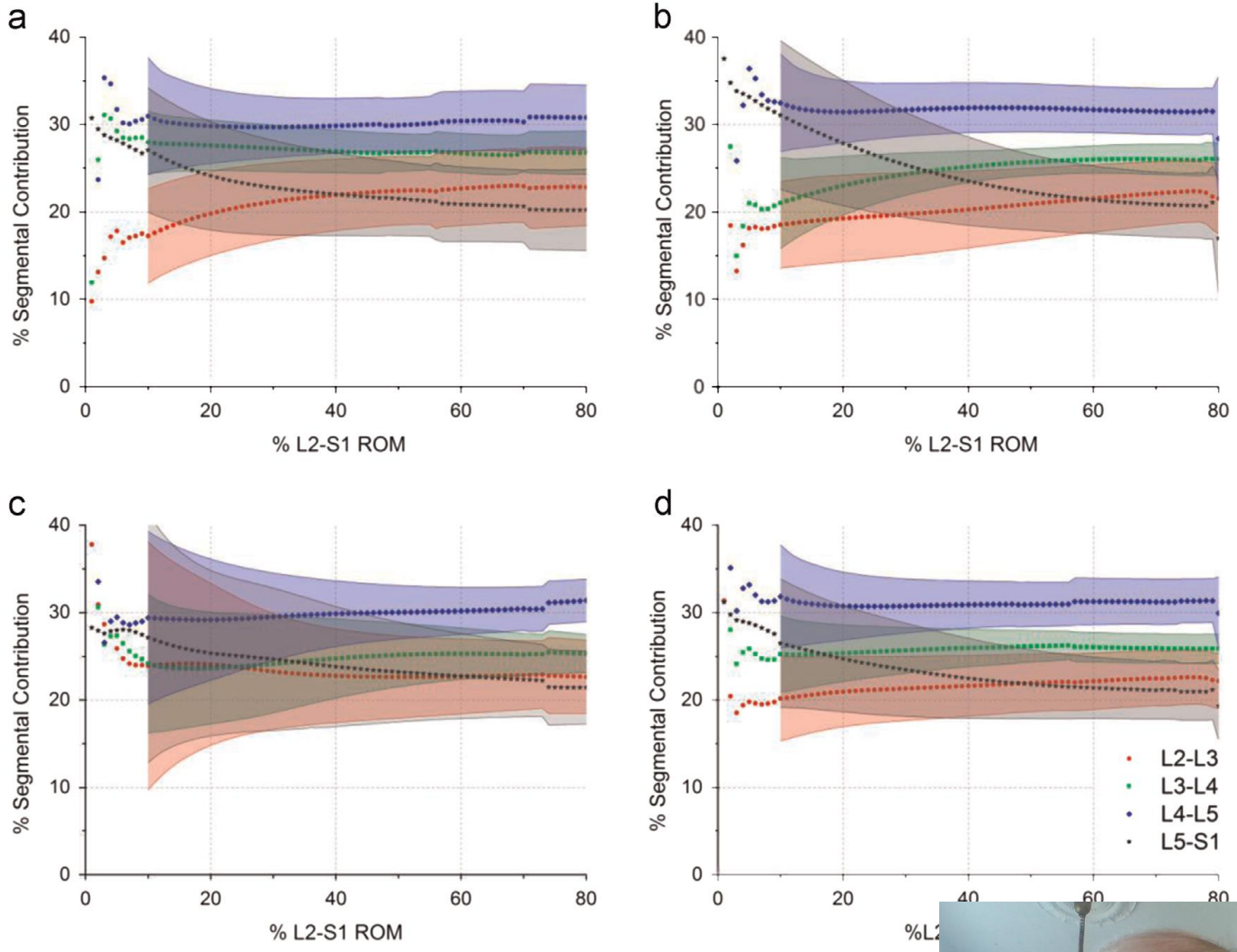
3-D quantitative fluoroscopy (University of Pittsburgh)





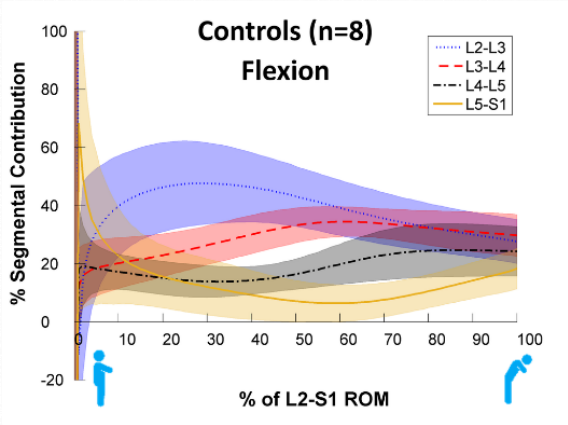
Return phase apportionment of intervertebral motion during lifting (n=6)

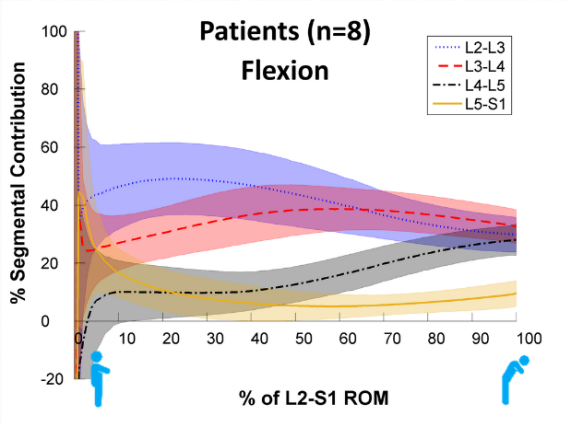
a: 4.5kg,
b: 9.1kg,
c: 13.6kg,
d: mean of a-c

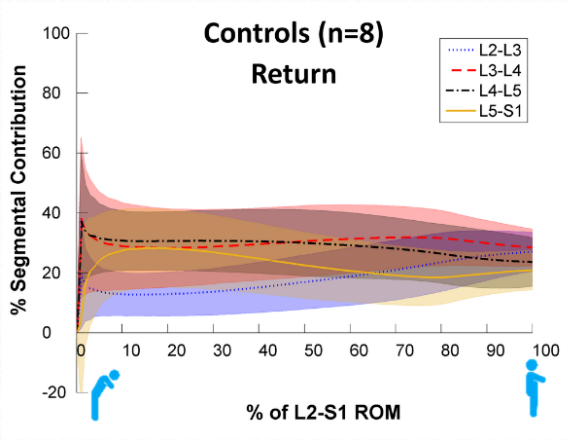


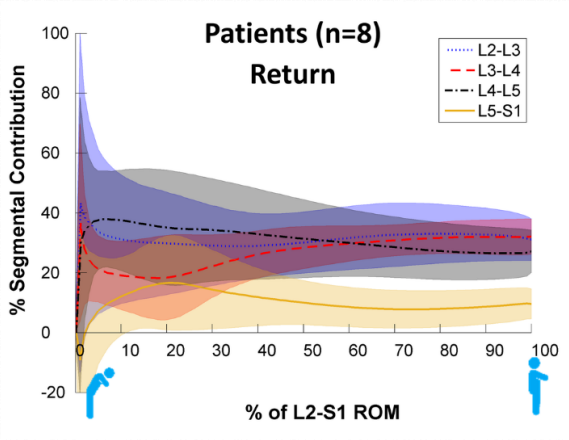
Aiyangar, A., L. Zheng, W. Anderst and X. Zhang (2015). "Apportionment of lumbar L2-S1 rot
individual motion segments during a dynamic lifting task." Journal of Biomechanics 48(13):

Weight bearing motion with outward and return separated



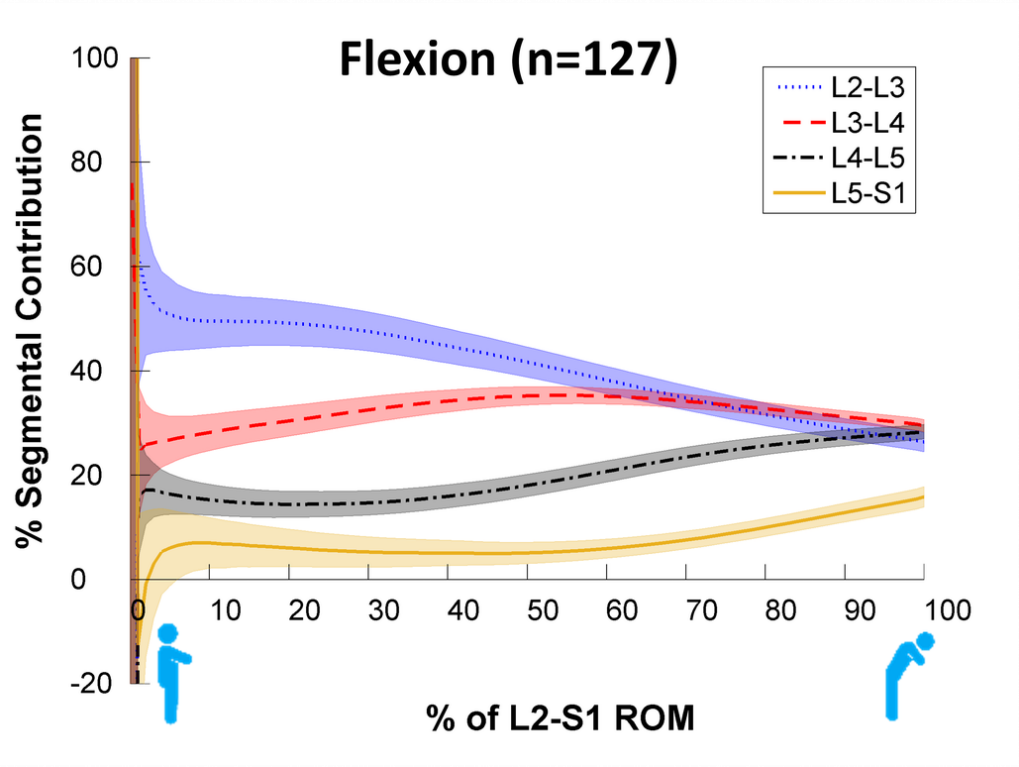


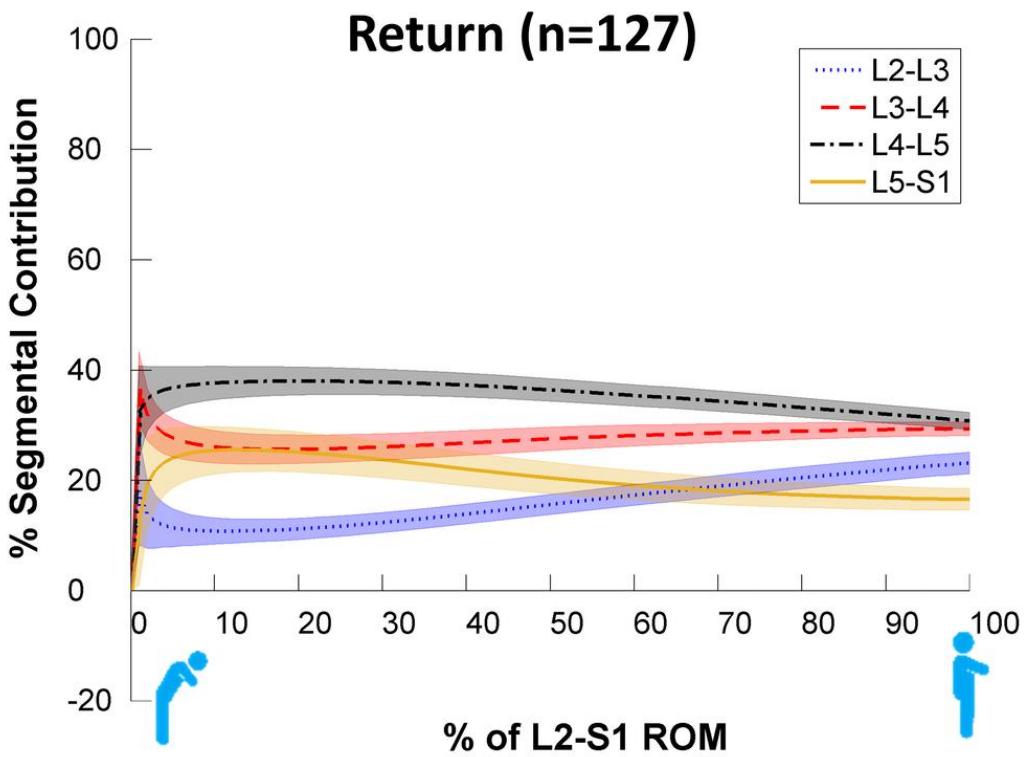




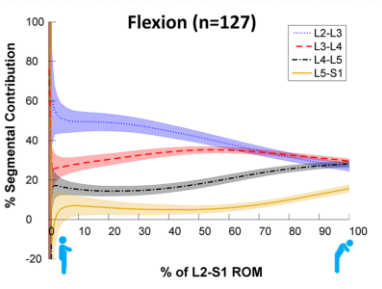
Breen, A., De Carvalho, D, Funabashi, M, Kawchuk, G, Pagé, I, Wong, AYL., Breen, A.C. Reference Database of Standardised Continuous Lumbar Intervertebral Motion Analy Conducting Patient-Specific Comparisons." Front. Bioeng. Biotechnol 9:745837.

Normative database of weight bearing motion contributions

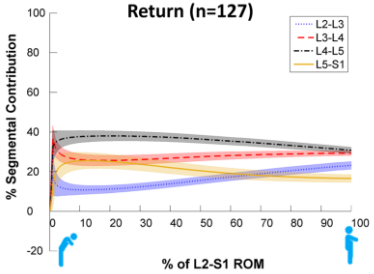




Breen, A., De Carvalho, D,, Funabashi, M,, Kawchuk, G, Pagé, I, Wong, AYL., Breen, A.C
Reference Database of Standardised Continuous Lumbar Intervertebral Motion Analy
Conducting Patient-Specific Comparisons." Front. Bioeng. Biotechnol 9:745837.



Uses of the normative database



1. drive dynamic models of joint and muscular forces

2. reference values against which to make patient-specific comparisons in suspected cases of lumbar spine motion disorders.*

3. Evaluate treatment effects*

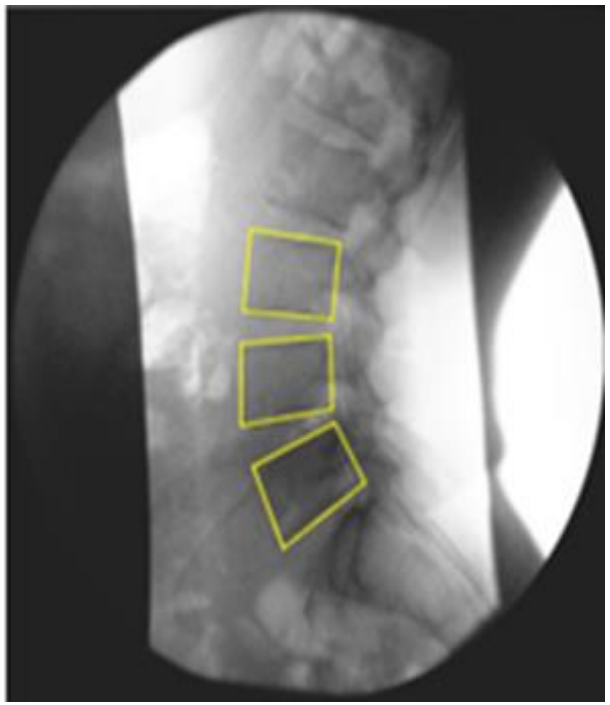
(*requires the patient investigations to be standardised to the same protocol)

Dynamic disc loading models

3-D Volumetric MRI with QF tracking templates

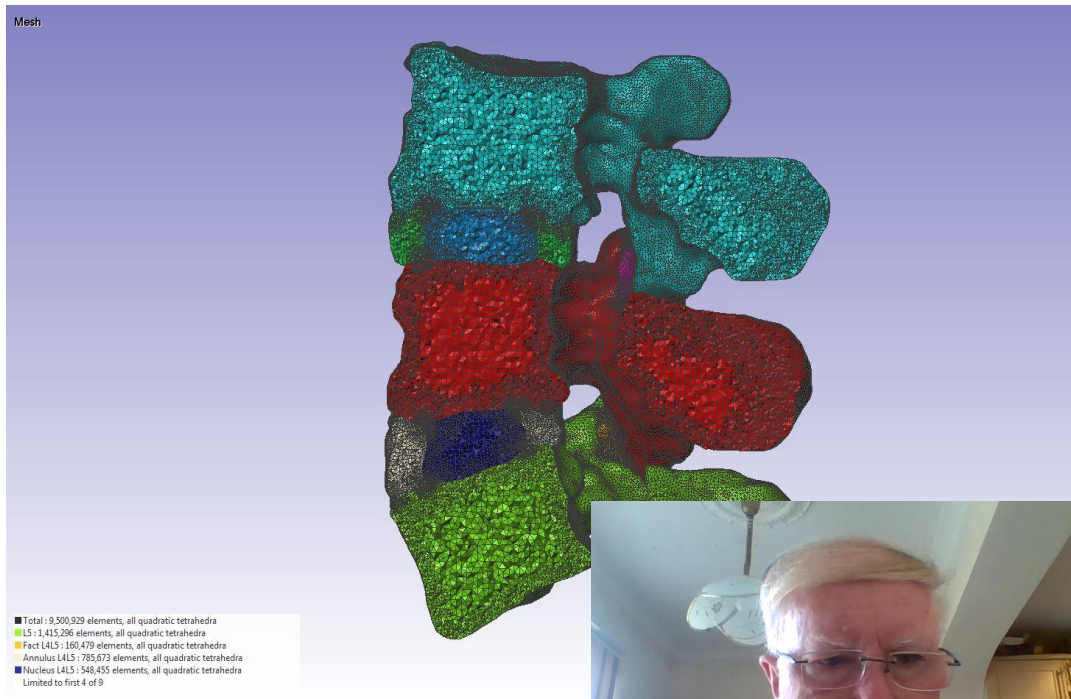
a

QF image with tracking templates



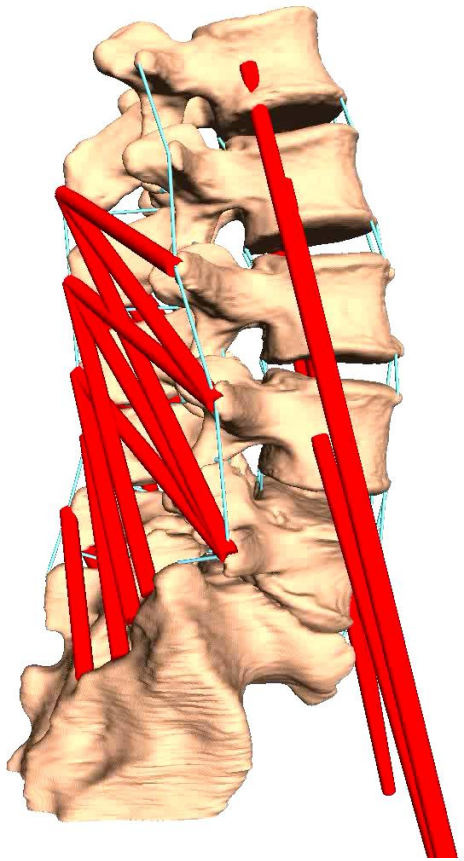
b

Finite element model of spinal levels



Zanjani-Pour, S., Meakin, J,R,, Breen, Ax., Breen A. (2018). "Estimation of in vivo inter-vertebral loading fluoroscopic and magnetic resonance image informed finite element models." Journal of Biomecha

Model of muscle contraction during intervertebral motion in weight bearing flexion



Credit: Dr Ameet Aiyangar (EMPA) & Dr Karin Gruber, University of Koble

Attempted mathematical modelling of ligament torques during weight bearing extension

Neutral

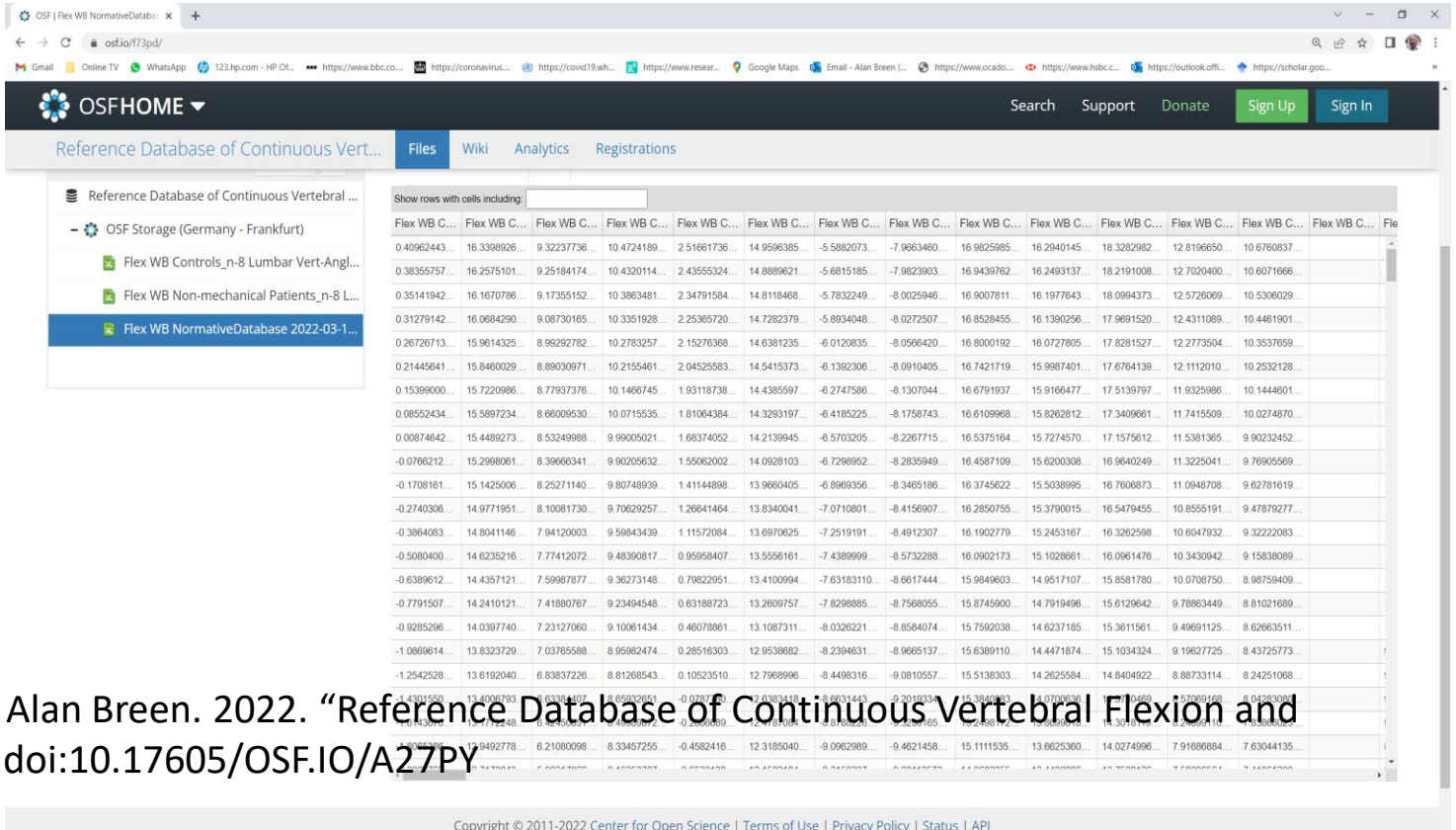
Extension

Extension torques appl

Credit: Dr Karin Gruber, University of Koblenz-Landau

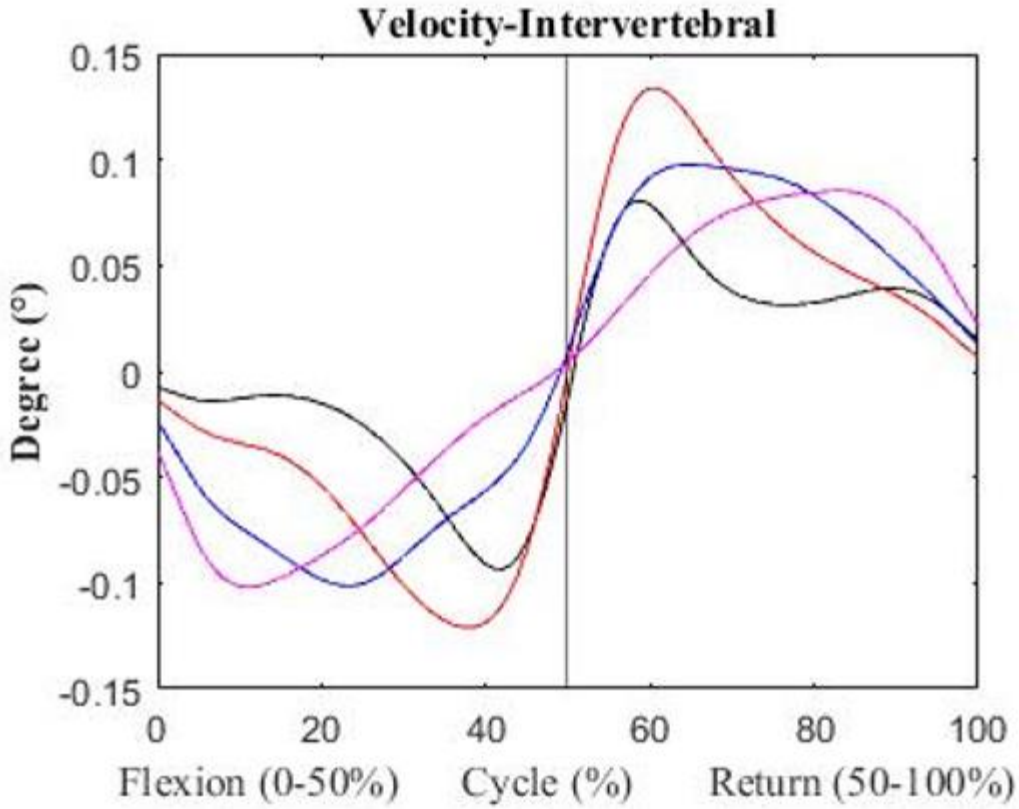
Open Science Framework database

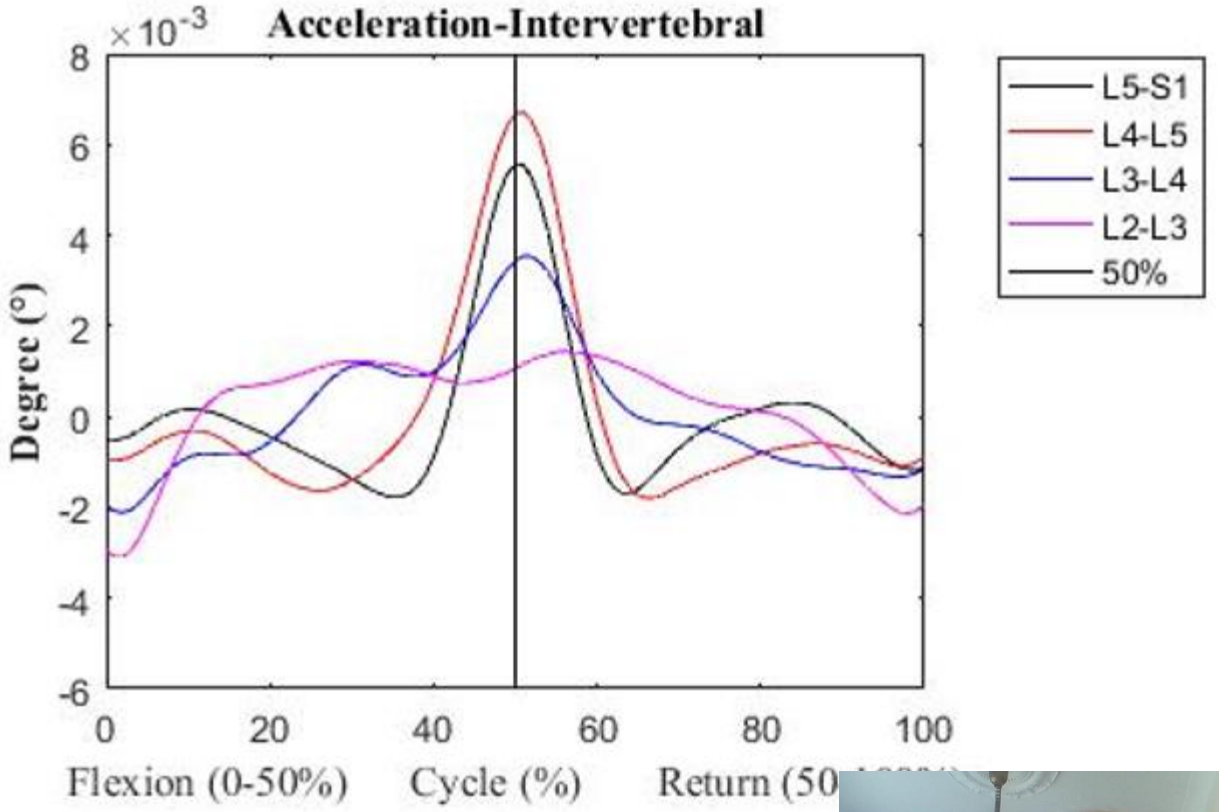
….contains the vertebral angles that formed the basis of the dynamic spinal rhythms published in Breen et al. (2021)



Breen, Alexander C, and Alan Breen. 2022. “Reference Database of Continuous Vertebral Flexion and Return.” OSF. March 20. doi:10.17605/OSF.IO/A27PY

Intervertebral phase lag using velocity and acceleration patterns for weight bearing flexion and return (n=134)

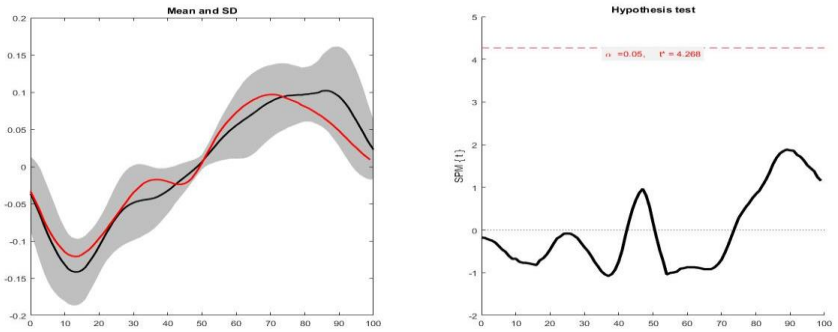




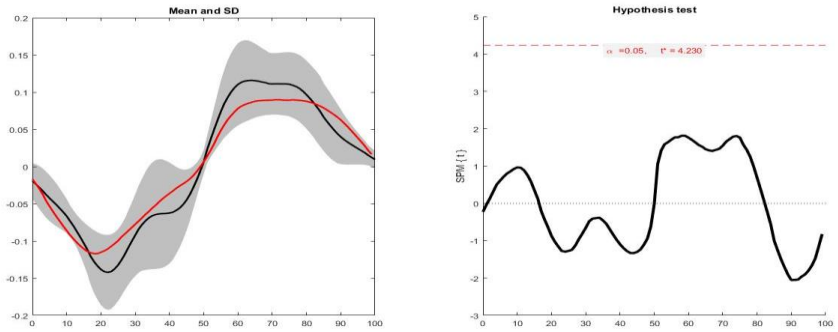
Credit: Dr Mehdi Nematimoez, University of Bojnord

L2-S1 velocities in 8 patients (-) and 8 controls (-)

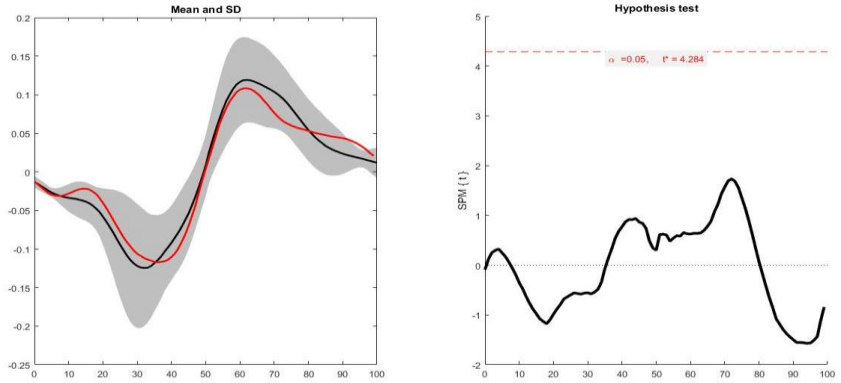
L2-3



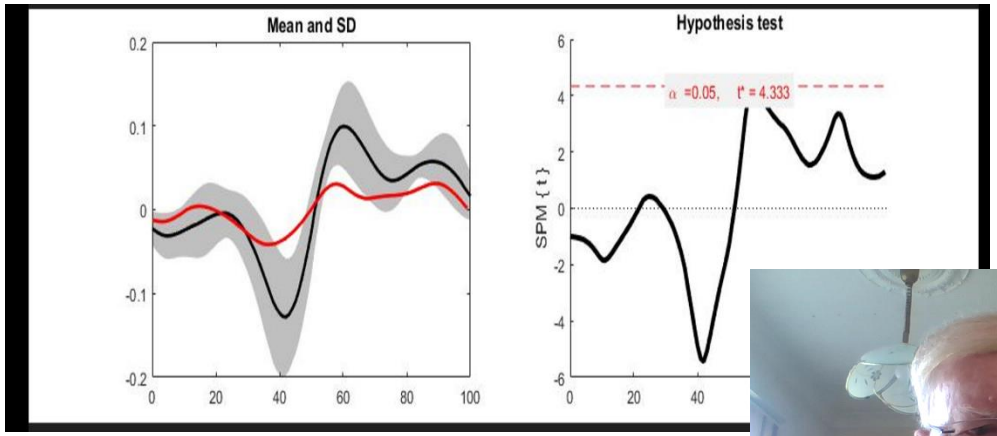
L3-4



L4-5



L5-S1



Credit: Dr Mehdi Nematimoez, University of Bojnord

AECC University College
Centre for Biomechanics Research

Conclusions

Bournemouth University

There is evidence of intervertebral motion biomarkers for CNSLBP.

They do not yet contribute to understanding the mechanism of the condition or to the care pathway.

Exploration of correlations with other biomarkers may reduce this problem.

"Future work should address the variability of measurements, lack of harmonised systems for data acquisition and analysis, and lack of evi on how such quantitation potentially affects clinical decision-making patient outcome." de Souza et al (2019) European Society of Radiolog

Thanks for listening!

abreen4@bournemouth.ac.uk

The authors acknowledge the support of the ECU Research Fund and Paramed ASG for this research.