

**CERVICAL SPINE MENISCOIDS AND THEIR POTENTIAL ROLE  
IN NECK PAIN AND ITS MANAGEMENT**

**Scott Francis Farrell**

**B Physiotherapy (Hons I)**

**Thesis submitted for the degree of  
Doctor of Philosophy (Physiotherapy)  
The University of Newcastle, Australia**

**February 2016**

This is to certify that the thesis entitled *Cervical Spine Meniscoids and their Potential Role in Neck Pain and its Management* submitted in fulfillment of the requirements for the degree of Doctor of Philosophy (Physiotherapy) is in a form ready for examination.

Signed \_\_\_\_\_

Date \_\_\_\_\_

Scott F. Farrell

School of Health Sciences

Faculty of Health and Medicine

The University of Newcastle

## **Declaration**

I, Scott F. Farrell, hereby declare that the work contained within this thesis is my own and has not been submitted to any other university or institution as a part or a whole requirement for any higher degree, and to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I certify that the work embodied in this thesis contains published papers of which I am the lead author. I have included a written statement, endorsed by my supervisor, attesting to my contribution to these joint publications. I have included a written statement from each co-author, endorsed by the Faculty Assistant Dean (Research Training), attesting to my contribution to these joint publications (Appendix A).

In addition, ethical approval from The University of Newcastle Human Research Ethics Committee and/or Hunter New England Research Ethics Committee was granted for the five studies presented in this thesis. Written informed consent was gained prior to data collection and human tissue was bequeathed in accordance with appropriate legislation (see Appendices B and C). Ethical approvals for all studies are included in Appendices D-G.

I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968.

Scott F. Farrell

Signed \_\_\_\_\_

Date \_\_\_\_\_

## Supervisor Statement

I, Professor Darren A. Rivett, attest that Research Higher Degree candidate Scott F. Farrell was the lead author of the following publications:

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2015). Formic acid immersion does not affect the morphometry of cervical zygapophyseal joint meniscoids – a methodological study for anatomical dissection. *Anatomical Science International* 90 pp57-63. DOI: 10.1007/s12565-014-0248-8.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2015). The anatomy and morphometry of cervical zygapophyseal joint meniscoids. *Surgical and Radiologic Anatomy* 37 pp799-807. DOI: 10.1007/s00276-014-1406-3.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2016). Morphology and morphometry of lateral atlantoaxial joint meniscoids. *Anatomical Science International* 91 pp89-96. DOI: 10.1007/s12565-015-0276-z.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2016). Immunohistochemical investigation of nerve fibre presence and morphology in elderly cervical spine meniscoids. *The Spine Journal*. DOI: 10.1016/j.spinee.2016.06.004.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., Lau, P., & Rivett, D.A. (*in press*). Morphology of cervical spine meniscoids in individuals with chronic whiplash

associated disorder: a case-control study. *Journal of Orthopaedic and Sports Physical Therapy*.

## **Acknowledgement of Work Undertaken at the University of Otago**

Studies 1-4 required access to human cadavers, a dissecting room and histology processing facilities. At the time these studies were undertaken, the anatomy facilities of The University of Newcastle were not available as the anatomy department was undergoing building renovations. My Co-supervisor Dr. Jon Cornwall was at the time affiliated with the Department of Anatomy at the University of Otago. Dr. Cornwall negotiated access to University of Otago cadavers, dissection facilities and technical support on my behalf. Dr. Cornwall directly supervised my performance of the dissection and histology components of these studies, in conjunction with my Principal Supervisor Professor Darren A. Rivett and Co-supervisor Dr. Peter G. Osmotherly.

Scott F. Farrell

Signed \_\_\_\_\_

Date        *3/2/16*

\_\_\_\_\_

## Acknowledgements

I would like to begin by expressing my sincere gratitude to my supervisors Prof. Darren Rivett, Dr. Peter Osmotherly and Dr. Jon Cornwall for their patience, guidance, encouragement and support during my PhD candidature and beyond.

I would also like to thank Mrs. Mandy Fisher, Dr. Jonathan Broadbent and A/Prof. Phil Sheard of the University of Otago, as well as Dr. Phil Jobling, A/Prof. Paul Tooney and Prof. Alan Brichta of The University of Newcastle for their expert guidance for the technical aspects of the dissection, histology and immunohistochemistry studies contained in this thesis. I am grateful to Mr. Jameen Arm, Dr. Peter Lau and Conjoint A/Prof. Lindsay Rowe of Hunter New England Imaging and A/Prof. Peter Stanwell of The University of Newcastle for their invaluable input regarding the acquisition and interpretation of magnetic resonance imaging in Chapter 7.

Thank you to my parents Jane and Richard, as well as my brother Peter, for their love and support during my studies. I appreciate you humouring me by patiently sitting through too many conversations about cervical spine meniscoids during the last three years.

Finally I would like to thank my fiancé Daphne for her patience, encouragement, companionship, faith and love. I am humbled by the support you have given me throughout my PhD candidature and I could not have completed this thesis without you by my side.



## **Publications and Presentations Arising from the Work in this Thesis**

### ***Published Papers***

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2015). Formic acid immersion does not affect the morphometry of cervical zygapophyseal joint meniscoids – a methodological study for anatomical dissection. *Anatomical Science International* 90 pp57-63. DOI 10.1007/s12565-014-0248-8.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2015). The anatomy and morphometry of cervical zygapophyseal joint meniscoids. *Surgical and Radiologic Anatomy* 37 pp799-807. DOI: 10.1007/s00276-014-1406-3.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2016). Morphology and morphometry of lateral atlantoaxial joint meniscoids. *Anatomical Science International* 91 pp89-96. DOI: 10.1007/s12565-015-0276-z.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2016). Immunohistochemical investigation of nerve fibre presence and morphology in elderly cervical spine meniscoids. *The Spine Journal*. DOI: 10.1016/j.spinee.2016.06.004.

***Accepted for Publication***

Farrell, S.F., Osmotherly, P.G., Cornwall, J., Lau, P., & Rivett, D.A. (*in press*).

Morphology of cervical spine meniscoids in individuals with chronic whiplash associated disorder: a case-control study. *Journal of Orthopaedic and Sports Physical Therapy*.

***Published Abstracts***

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2014) Does formic acid immersion affect the morphometry of cervical zygapophyseal joint meniscoids? *Clinical Anatomy* 27 p1361.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2014). The anatomy and morphometry of the meniscoids of the lateral atlantoaxial joints. *Annals of Anatomy* 196 (S1) p86. DOI: 10.1016/j.aanat.2014.05.035.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., Lau, P., & Rivett, D.A. (2015). Cervical meniscoid morphology in whiplash associated disorder: a preliminary comparative analysis. *Australian Physiotherapy Association Conference Abstract E-book* p42. URL: <http://www.physiotherapy.asn.au/DocumentsFolder/CONFERENCE2015/APA%202015%20Abstracts%20Final.pdf>.

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2016). Lateral atlantoaxial joint capsules but not meniscoids contain neurofilament heavy reactive axons. For publication in *Clinical Anatomy*.

### ***Conference Oral Presentations***

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2014). The anatomy and morphometry of the meniscoids of the lateral atlantoaxial joints. Presented at the *18th Congress of the International Federation of Associations of Anatomists*, Beijing, August 2014.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., Lau, P., & Rivett, D.A. (2015). Cervical meniscoid morphology in whiplash associated disorder: a preliminary comparative analysis. Presented at *Australian Physiotherapy Association Conference*, Gold Coast, October 2015.

### ***Conference Poster Presentations***

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2013). Does formic acid immersion affect the morphometry of cervical zygapophyseal joint meniscoids? Presented at the *10th Meeting of Australia New Zealand Association of Clinical Anatomists*, Brisbane, December 2013.

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2015). Lateral atlantoaxial joint capsules but not meniscoids contain neurofilament heavy reactive axons. Presented at 12<sup>th</sup> Meeting of Australia New Zealand Association of Clinical Anatomists, Adelaide, December 2015.

### ***Invited Oral Presentations***

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2013). Cervical spine meniscoids and their potential role in neck pain. Invited for presentation at *Physiotherapy Seminar Series*, School of Health Sciences, The University of Newcastle, Australia, December 2013.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2013). The morphology of cervical zygapophyseal meniscoids. Invited for presentation at seminar of *Clinical Anatomy Research Group*, Department of Anatomy, University of Otago, Dunedin, New Zealand, May 2013.

Farrell, S.F., Osmotherly, P.G., Cornwall, J., & Rivett, D.A. (2014). The anatomy and morphometry of the meniscoids of the lateral atlantoaxial joints. Invited for presentation at seminar of *Clinical Anatomy Research Group*, Department of Anatomy, University of Otago, Dunedin, New Zealand, June 2014.

Farrell, S.F., Osmotherly, P.G., Lau, P., Cornwall, J., & Rivett, D.A. (2015). Cervical meniscoid morphology in whiplash associated disorder: a preliminary comparative

analysis. Invited for presentation at *Physiotherapy Seminar Series*, School of Health Sciences, The University of Newcastle, Australia, August 2015.

***Arising from PhD Candidature but not Included in Thesis***

*Published Papers*

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2015). Can E12 sheet plastination be used to examine the presence and incidence of intra-articular spinal meniscoids? *Anatomy* 9 (1) pp13-18. DOI: 10.2399/ana.14.046.

*Published Abstracts*

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2015). Can E-12 sheet plastination be used to visualise intra-articular spinal meniscoids? *Clinical Anatomy* 28 p943. DOI: 10.1002/ca.22520.

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2015). Visualisation of intra-articular spinal meniscoids using E12 sheet plastination – a tool for physiotherapy clinical anatomy education. *Australian Physiotherapy Association Conference Abstract E-book* p42. URL:

<http://www.physiotherapy.asn.au/DocumentsFolder/CONFERENCE2015/APA%202015%20Abstracts%20Final.pdf>.

### *Conference Poster Presentations*

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2014). Can E-12 sheet plastination be used to visualise intra-articular spinal meniscoids? Presented at the *11th Meeting of Australia New Zealand Association of Clinical Anatomists*, Queenstown, New Zealand, December 2014.

Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2015). Visualisation of intra-articular spinal meniscoids using E12 sheet plastination – a tool for physiotherapy clinical anatomy education. Presented at *Australian Physiotherapy Association Conference*, Gold Coast, October 2015.

### *Awards*

Best E-Poster Presentation, Educators' Stream, *Australian Physiotherapy Association Conference*, Gold Coast, October 2015. Awarded for: Farrell, S.F., Osmotherly, P.G., Rivett, D.A., & Cornwall, J. (2015). Visualisation of intra-articular spinal meniscoids using E12 sheet plastination – a tool for physiotherapy clinical anatomy education.

## Table of Contents

DECLARATION.....	III
SUPERVISOR STATEMENT.....	V
ACKNOWLEDGEMENT OF WORK UNDERTAKEN AT THE UNIVERSITY OF OTAGO.....	VII
PUBLICATIONS AND PRESENTATIONS ARISING FROM THE WORK IN THIS THESIS.....	IX
<i>Published Papers</i> .....	<i>ix</i>
<i>Accepted for Publication</i> .....	<i>x</i>
<i>Published Abstracts</i> .....	<i>x</i>
<i>Conference Oral Presentations</i> .....	<i>xi</i>
<i>Conference Poster Presentations</i> .....	<i>xi</i>
<i>Invited Oral Presentations</i> .....	<i>xii</i>
<i>Arising from PhD Candidature but not Included in Thesis</i> .....	<i>xiii</i>
LIST OF FIGURES .....	XXII
LIST OF TABLES .....	XXVIII
LIST OF ABBREVIATIONS.....	XXX
ABSTRACT.....	XXXII
<b>CHAPTER 1: INTRODUCTION.....</b>	<b>1</b>
BACKGROUND TO NECK PAIN .....	1
<i>Burden to Society</i> .....	<i>2</i>
<i>Prognosis</i> .....	<i>3</i>
<i>Aetiology</i> .....	<i>4</i>
CERVICAL SPINE MENISCOIDS .....	5
RATIONALE OF THESIS .....	9
<i>Aims</i> .....	<i>9</i>

<i>Significance</i> .....	9
<i>Outline</i> .....	10
<i>Scope</i> .....	11
<b>LITERATURE REVIEW</b> .....	<b>1</b>
OVERVIEW OF CERVICAL SPINE MENISCOIDS .....	1
<i>Prevalence of Cervical Spine Meniscoids</i> .....	2
<i>Morphology of Cervical Spine Meniscoids</i> .....	3
<i>Imaging and Radiological Identification of Cervical Spine Meniscoids</i> .....	11
<i>Function of Cervical Spine Meniscoids</i> .....	13
CRITICAL EVALUATION OF METHODS USED IN PREVIOUS STUDIES OF CERVICAL SPINE MENISCOIDS.....	14
THEORIES OF CERVICAL SPINE MENISCOID INVOLVEMENT IN NECK PAIN.....	17
<i>Entrapment Theory</i> .....	18
<i>Extrapment Theory</i> .....	21
<i>Fibrous Tissue Proliferation</i> .....	24
<i>Whiplash Associated Disorder</i> .....	24
LITERATURE REVIEW SUMMARY .....	31
<i>Research Aims:</i> .....	32
<b>CHAPTER 3: STUDY 1 – FORMIC ACID DEMINERALISATION IN MENISCOID DISSECTION</b> .....	<b>33</b>
INTRODUCTION .....	34
<i>Background</i> .....	34
<i>Demineralisation</i> .....	35
<i>Formic Acid Demineralisation in Morphological Investigation</i> .....	36
MATERIALS AND METHODS .....	37



<i>Tissue Preparation</i> .....	38
<i>Demineralisation Protocol</i> .....	39
<i>Measurement of Meniscoid Characteristics and Size</i> .....	40
<i>Data Analysis</i> .....	43
RESULTS .....	43
<i>Measures of Size</i> .....	43
<i>Intra-rater Reliability</i> .....	45
<i>Descriptive Changes</i> .....	47
<i>Decalcification Testing</i> .....	49
DISCUSSION .....	49
<i>Limitations</i> .....	51
CONCLUSIONS .....	52

**CHAPTER 4: STUDY 2 – MORPHOLOGY AND MORPHOMETRY OF**

<b>LATERAL ATLANTOAXIAL JOINT MENISCOIDS</b> .....	<b>54</b>
INTRODUCTION .....	56
MATERIALS AND METHODS .....	58
<i>Ethics Statement</i> .....	58
<i>Dissection Procedure</i> .....	59
<i>Histological Processing</i> .....	62
<i>Data Analysis</i> .....	62
RESULTS .....	63
<i>Meniscoid Morphology and Histology</i> .....	63
<i>Size</i> .....	69
<i>Influence of Age</i> .....	69
<i>Influence of Sex</i> .....	72

<i>Influence of Articular Cartilage Degeneration</i> .....	72
DISCUSSION .....	73
<i>Clinical Implications</i> .....	77
<i>Limitations</i> .....	78
CONCLUSIONS .....	78
<i>Summary</i> .....	79
<b>CHAPTER 5: STUDY 3 - MORPHOLOGY AND MORPHOMETRY OF</b>	
<b>CERVICAL ZYGAPOPHYSEAL JOINT MENISCOIDS .....</b>	<b>81</b>
INTRODUCTION .....	84
MATERIALS AND METHODS .....	86
<i>Histological Processing</i> .....	91
<i>Statistical Analysis</i> .....	91
RESULTS .....	92
<i>Morphology and Histology</i> .....	92
<i>Size</i> .....	100
<i>Influence of Spinal Level</i> .....	102
<i>Influence of Gender</i> .....	102
<i>Influence of Articular Cartilage Degeneration</i> .....	103
DISCUSSION .....	105
<i>Clinical Implications</i> .....	107
<i>Limitations</i> .....	109
CONCLUSIONS .....	109
<i>Summary</i> .....	110
<b>CHAPTER 6: THE PRESENCE OF NERVE TISSUE IN CERVICAL SPINE</b>	
<b>MENISCOIDS 112</b>	

INTRODUCTION .....	114
MATERIALS AND METHODS .....	117
<i>Ethics Statement</i> .....	117
<i>Dissection</i> .....	118
<i>Immunohistochemistry and Histology</i> .....	119
RESULTS .....	121
<i>NF-H Immunohistochemistry</i> .....	122
<i>Pan-NF Immunohistochemistry</i> .....	126
<i>Comparison of NF-H and Pan-NF Staining</i> .....	130
<i>Histology</i> .....	130
DISCUSSION .....	131
<i>Limitations and Future Research</i> .....	135
CONCLUSIONS .....	136
<i>Summary</i> .....	137
<b>CHAPTER 7: MORPHOLOGY OF CERVICAL SPINE MENISCOIDS IN</b>	
<b>CHRONIC WHIPLASH ASSOCIATED DISORDER .....</b>	<b>139</b>
INTRODUCTION .....	141
METHODS .....	143
<i>Ethics Statement</i> .....	143
<i>Study Population</i> .....	143
<i>MRI Technique</i> .....	145
<i>Outcome Measures</i> .....	147
<i>Data Analysis</i> .....	154
RESULTS .....	154
<i>Study Participants</i> .....	154

<i>Presence of Meniscoids</i> .....	155
<i>Meniscoid Length</i> .....	157
<i>WAD Duration</i> .....	161
<i>Articular Degeneration</i> .....	161
<i>Intra and Inter-rater Reliability</i> .....	162
DISCUSSION .....	164
<i>Clinical Implications</i> .....	166
<i>Limitations</i> .....	167
CONCLUSIONS .....	169
<i>Summary</i> .....	170
<b>CHAPTER 8: SUMMARY AND CONCLUSIONS .....</b>	<b>171</b>
SUMMARY OF STUDY FINDINGS .....	171
LIMITATIONS OF STUDIES.....	174
IMPLICATIONS OF FINDINGS .....	176
<i>Basic Science Implications</i> .....	176
<i>Clinical Implications</i> .....	177
FUTURE RESEARCH QUESTIONS .....	182
CONCLUSIONS .....	184
<b>APPENDICES .....</b>	<b>186</b>
APPENDIX A – STATEMENTS FROM CO-AUTHORS RELATING TO PAPERS PUBLISHED...	187
APPENDIX B – UNIVERSITY OF OTAGO DEPARTMENT OF ANATOMY BEQUEST FORM	
STUDIES 1-4 .....	194
APPENDIX C – CORRESPONDENCE, UNIVERSITY OF OTAGO STUDIES 1-4.....	196
APPENDIX D – NOTIFICATION OF ETHICS COMMITTEE APPROVAL STUDIES 1-4 .....	197
APPENDIX E – NOTIFICATION OF ETHICS COMMITTEE APPROVAL STUDY 5.....	200

APPENDIX F – NOTIFICATION OF ETHICS COMMITTEE RECIPROCAL APPROVAL STUDY 5 .....	203
APPENDIX G – NOTIFICATION OF ETHICS COMMITTEE APPROVAL AMENDMENT STUDY 5.....	205
APPENDIX H – JOURNAL PUBLICATION STUDY 1 .....	208
APPENDIX I – NOTIFICATION OF SAFETY COMMITTEE APPROVAL STUDIES 1-4 .....	209
APPENDIX J – PERMISSION LETTER, UNIVERSITY OF OTAGO DEPARTMENT OF ANATOMY STUDIES 1-4.....	211
APPENDIX K – CHARACTERISTICS OF CADAVERS INCLUDED IN STUDIES 1-4.....	213
APPENDIX L – UNIVERSITY OF OTAGO DEPARTMENT OF ANATOMY EMBALMING FLUID RECIPE STUDIES 1-4.....	214
APPENDIX M – JOURNAL PUBLICATION STUDY 2.....	215
APPENDIX O – IMMUNOHISTOCHEMISTRY PILOT TESTING STUDY 4 .....	217
APPENDIX P – DETAILED IMMUNOHISTOCHEMISTRY PROCEDURE STUDY 4.....	238
APPENDIX Q – LABORATORY RECIPES STUDY 4 .....	243
APPENDIX R – HUNTER MEDICAL RESEARCH INSTITUTE RESEARCH REGISTER APPROVAL STUDY 5.....	245
APPENDIX S – HUNTER NEW ENGLAND IMAGING SERVICE AGREEMENT STUDY 5 ....	246
APPENDIX T – PARTICIPANT RECRUITMENT FLYER STUDY 5 .....	247
APPENDIX U – PARTICIPANT INFORMATION SHEET STUDY 5 .....	248
APPENDIX V – PARTICIPANT CONSENT FORM STUDY 5 .....	251
APPENDIX W – MRI SAFETY QUESTIONNAIRE STUDY 5 .....	252
APPENDIX X – JOURNAL PUBLICATION STUDY 4 .....	253
<b>REFERENCES.....</b>	<b>254</b>

## List of Figures

- Figure 1** Schematic representation of sagittal section through mid-cervical spine zygapophyseal joint, demonstrating dorsal and ventral meniscoids. Red rectangle indicates location of cross section. Modified from Friedrich *et al.* (2008) and Webb *et al.* (2011a). ..... 7
- Figure 2:** Following page – Schematic representation of cervical spine meniscoid Entrapment Theory. (a) Meniscoid *in situ* between articular surfaces (b) during an abnormal movement, the meniscoid moves further into the joint cavity, and becomes pinched between the joint surfaces. Articular cartilage indentation occurs about the dense connective tissue apex, lodging the meniscoid into an entrapped position (c) manual therapy treatment such as manipulation or mobilisation may gap the joint surfaces, releasing the trapped meniscoid. Modified from Webb, Collins, Rassoulain and Mitchell (2011)..... 19
- Figure 3:** Following page – Schematic representation of cervical spine meniscoid Extrapment Theory. (a) Meniscoid *in situ* between articular surfaces (b) during movement such as cervical rotation, the articular surfaces move apart and reduce the area of contact (c) on return to the neutral position, the meniscoid fails to re-enter the joint cavity (d) the meniscoid is deformed and the joint capsule distends, leading to pain. Modified from Webb, Collins, Rassoulain and Mitchell (2011)...22
- Figure 4:** Following page – Schematic depiction of S-Shaped deformation of cervical spine following rear impact collision, illustrating altered segmental motion of lower cervical vertebrae, leading to impaction of zygapophyseal joints and distraction of anterior structures. C2 to C7 – second to seventh cervical vertebrae;

ZJ – zygapophyseal joint. Modified from Kanoeka *et al.* (1999) and Bogduk (2011). .....26

**Figure 5:** Following page – Motion of lower cervical spine vertebrae about their instantaneous axis of rotation (IAR) under normal conditions and during a whiplash motion in a rear impact collision. Note that under normal conditions, as the superior vertebra undergoes sagittal rotation in a posterior direction, the zygapophyseal articular surfaces glide upon each other in a smooth motion. During the whiplash scenario, the IAR moves superiorly such that the inferior articular facet of the superior vertebra drives downwards into the superior articular facet of the inferior vertebra. AP – articular pillar; IVD – intervertebral disc; VB – vertebral body; ZJ – zygapophyseal joint. Modified from Kanoeka *et al.* (1999) and Bogduk (2011). .....28

**Figure 6:** Measurement of meniscoids. Distance (z) was the measurement of the widest point perpendicular to the baseline (cd) that connected the bilateral ends of the meniscoid. (a) Base of meniscoid connecting to capsule, (b) free border of meniscoid. Adapted from Inami, Kaneoka, Hayashi, and Ochiai (2000). .....42

**Figure 7:** Timeline of meniscoids immersed in 5% formic acid demonstrating consistent morphometry over the period of immersion. (a) Meniscoid edges outlined with red dashed lines in a superior view of a right atlantoaxial joint showing position and orientation. (x) ventral meniscoid, (y) dorsal meniscoid, (z) articular surface. (b) to (e) Timeline of meniscoids (b) 0 days, (c) 4 days, (d)18 days, (e) 32 days. ....48

**Figure 8:** Measurement of meniscoid protrusion length. Superior view of atlantoaxial joint surface, meniscoid illustrated in red. Distance (D) is the measurement of the widest point perpendicular to the baseline (xy) that connects the bilateral ends of

the meniscoid as they intersect the joint margins. (a) Free border of the meniscoid, (b) meniscoid base connecting to joint capsule. Modified from Inami *et al.* (2000).

..... 61

**Figure 9:** Following page - Photographs of meniscoids upon articular surfaces of two disarticulated right atlantoaxial joints. Superior view showing surface of superior articular facet of axis in each specimen. (a) Adipose type meniscoids (black arrows) located at ventral and dorsal aspects of joint. (b) Fibrous type meniscoid (black arrowhead) and fibroadipose type meniscoid (black arrow) located at dorsal and ventral aspects of joint respectively. ac = articular cartilage. .... 64

**Figure 10:** Following page - Sagittal sections of atlantoaxial joint meniscoids photographed through a light microscope, illustrating different histological characteristics: (a) adipose type meniscoid composed primarily of adipocytes; (b) fibrous type meniscoid composed primarily of dense irregular connective tissue; (c) fibroadipose type meniscoid composed of fibrous and adipose tissue. ac = articular cartilage; jc = joint cavity; m = meniscoid. Haematoxylin and eosin, x4 magnification. .... 66

**Figure 11:** Measurement of meniscoids. Distance (L) was the measurement of the widest point perpendicular to the baseline (ab) that connected the bilateral ends of the meniscoid. (x) Base of meniscoid connecting to capsule. (y) Free border of the meniscoid. Adapted from Inami *et al.* (2000). .... 90

**Figure 12:** Following page - Photographs of meniscoids upon articular surfaces of three disarticulated zygapophyseal joints. Superior view showing surface of superior articular facet of inferior vertebra in each specimen. (a) Adipose type meniscoid (black arrow) located at ventral aspect of right C3-4 zygapophyseal joint. (b) Fibrous type meniscoid (arrowhead) located at dorsal aspect of zygapophyseal



joint. (c) Fibroadipose type meniscoid (white arrow) located at dorsal aspect of left C4-5 zygapophyseal joint. ac = articular cartilage..... 95

**Figure 13:** Following page - Sagittal sections of zygapophyseal joint meniscoids photographed through a light microscope, illustrating different histological characteristics. (a) Adipose type meniscoid composed primarily of adipocytes, located at ventral aspect of a right C2-3 zygapophyseal joint. (b) Fibrous type meniscoid composed primarily of dense irregular connective tissue, located at ventral aspect of a right C5-6 zygapophyseal joint. (c) Fibroadipose type meniscoid composed of fibrous and adipose tissue, located at ventral aspect of a right C4-5 zygapophyseal joint. ac = articular cartilage; jc = joint cavity; m = meniscoid. Haematoxylin and eosin, x4 magnification..... 97

**Figure 14:** Schematic representation of sagittal section of cervical spine meniscoid at dorsal aspect of a zygapophyseal joint. Basal, middle and apical regions forming the body of a meniscoid are shown as per Webb *et al.* (2011a). ac = articular cartilage..... 124

**Figure 15:** Nerve fibres immunoreactive to antibody to neurofilament heavy using diaminobenzidine immunohistochemistry located in the dorsal joint capsule of a lateral atlantoaxial joint from a 73-year-old female cadaver. Haematoxylin counterstaining. (a) Positively stained fibres (brown staining); (b) adjacent section processed as negative control..... 125

**Figure 16:** Following page – Nerve fibres immunoreactive to antibody to pan-neurofilament (Pan-NF) using diaminobenzidine immunohistochemistry located in the ventral joint capsule and meniscoid of a lateral atlantoaxial joint from an 83-year-old male cadaver. Haematoxylin counterstaining. (a) Positively stained fibres (brown staining) within joint capsule; (b) section of joint capsule adjacent to a)

processed as negative control demonstrating no staining; (c) sagittal section of meniscoid, red rectangle indicates location of Pan-NF immunoreactive fibres within body of meniscoid viewed at x4 magnification; (d) area of red rectangle from (c) viewed at x40 magnification demonstrating bundle of small nerve fibres.

..... 127

**Figure 17:** Nerve fibres immunoreactive to antibody to pan-neurofilament using diaminobenzidine immunohistochemistry with haematoxylin counterstaining (brown staining). (a) Small bundle of nerve fibres from dorsal aspect of a lateral atlantoaxial joint from an 83-year-old male cadaver; (b) large bundle of nerve fibres from dorsal aspect of a lateral atlantoaxial joint from a 77-year-old female cadaver. .... 129

**Figure 18:** Participant MRI scanning position: a) lateral view of participant in supine lying in the neutral cervical spine position, with the head and neck coil removed to demonstrate the position; b) superior view with the head and neck coil in place, demonstrating foam wedges (FW) used to maintain participant position..... 146

**Figure 19:** Measurement of cervical spine meniscoid protrusion length at (a) lateral atlantoaxial joint and (b) cervical zygapophyseal joint. m = meniscoid, ac = articular cartilage, jc = joint capsule, d = meniscoid protrusion length, c = articular cartilage length. Meniscoid length expressed in mm (distance d) and as a percentage of articular cartilage length ( $d \div c \times 100$ ). Modified from Friedrich *et al.* (2008). .... 149

**Figure 20:** Following page - Assessment of cervical spine meniscoid composition on sagittal images as per Friedrich *et al.* (2008) (a) T1-weighted volumetric interpolated breath-hold examination (T1 VIBE) sequence lateral atlantoaxial joint (b) T2-weighted sampling perfection with amplification-optimised contrast using

different angle evolutions (T2 SPACE) sequence lateral atlantoaxial joint (c) T1 VIBE sequence C3-4 zygapophyseal joint (d) T2 SPACE sequence C3-4 zygapophyseal joint. White arrowhead (a, b) denotes adipose meniscoid: primarily hyperintense on the T1 VIBE and T2 SPACE sequences; white arrow (a, b) denotes mixed fibroadipose meniscoid: partly hyperintense and partly hypointense on the T1 VIBE and T2 SPACE sequences; white arrow (c, d) denotes fibrous meniscoid: primarily hypointense on T1 VIBE and T2 SPACE sequences. .... 152

## List of Tables

<b>Table 1:</b> Means, standard deviations, and results of repeated measures ANOVA for each measure of morphometry throughout the experiment. N = 11 samples for each day that measures were taken.....	44
<b>Table 2:</b> Results of intra-rater reliability testing for each measure of meniscoid size, for experiment days 0, 4, 18 and 32. For all meniscoids, each measure was repeated three times, with one week separating each measurement session.....	46
<b>Table 3:</b> Characteristics of meniscoid classifications.....	70
<b>Table 4:</b> Meniscoid size (surface area and protrusion length) by location, gender and cartilage degeneration.....	71
<b>Table 5:</b> Characteristics of meniscoid classifications on histological examination (n=73).....	94
<b>Table 6:</b> Meniscoid size (surface area and protrusion length) by location, spinal level, gender and cartilage degeneration (n = 76).....	101
<b>Table 7:</b> Distribution of zygapophyseal joint articular cartilage degeneration across the cervical spine levels C2-3 to C6-7 (n = 56). .....	104
<b>Table 8:</b> Positions of identified meniscoids within lateral atlantoaxial (LAA) and cervical zygapophyseal joints (n = 77). .....	121
<b>Table 9:</b> Characteristics of cervical spine meniscoids containing nerve fibres immunoreactive to antibodies to neurofilament heavy and pan-neurofilament, including location and numbers of positively stained nerve fibre bundles.....	123
<b>Table 10:</b> Location of cervical spine meniscoids within lateral atlantoaxial and zygapophyseal joints for chronic whiplash associated disorder (WAD) and control groups.....	156

<b>Table 11:</b> Protrusion lengths of lateral atlantoaxial and cervical zygapophyseal joint meniscoids for chronic whiplash associated disorder (WAD) and control groups, expressed in mm in accordance with the method described by Friedrich <i>et al.</i> (2008), and as a percentage of inferior articular cartilage anterior-posterior length, with accompanying results of Wilcoxon signed-rank tests.....	158
<b>Table 12:</b> Distribution (n [%]) of cervical spine meniscoid composition types between chronic whiplash associated disorder (WAD) and control groups.....	160
<b>Table 13:</b> Intraclass correlation co-efficients (ICCs) for intra and inter-rater reliability of outcome measures.....	163

## List of Abbreviations

<b>ANOVA</b>	Analysis of variance
<b>BMI</b>	Body mass index
<b>CGRP</b>	Calcitonin gene-related peptide
<b>DAB</b>	Diaminobenzidine
<b>DESS</b>	Double echo steady state
<b>ICC</b>	Intraclass correlation co-efficient
<b>IQR</b>	Interquartile range
<b>LRT</b>	Likelihood ratio test
<b>MRI</b>	Magnetic resonance imaging
<b>MVA/MVC</b>	Motor vehicle accident/motor vehicle collision
<b>NF-H</b>	Neurofilament heavy
<b>NSNP</b>	Non-specific neck pain
<b>OR</b>	Odds ratio
<b>Pan-NF</b>	Pan-neurofilament
<b>PGP 9.5</b>	Protein gene product 9.5
<b>R<sup>2</sup></b>	Co-efficient of determination
<b>SD</b>	Standard deviation
<b>SP</b>	Substance P
<b>T1 VIBE</b>	T1-weighted volumetric inter-polated breath-hold examination
<b>T2 SPACE</b>	T2-weighted sampling perfection with amplification-optimised contrast using different angle evolutions
<b>WAD</b>	Whiplash associated disorder

$\beta$	Regression co-efficient
$\eta^2$	Eta-squared

## Abstract

The overall aim of the work presented in this thesis was to explore the clinical significance of cervical spine meniscoids in neck pain. Cervical spine meniscoids are folds of synovial membrane that extend between the articular surfaces of joints throughout the cervical spine. These structures are thought to function to improve joint congruence and to ensure the lubrication of articular surfaces with synovial fluid. However, little is known about the role of cervical spine meniscoids in neck pain, as understanding of their morphology is not comprehensive. This body of work comprising five studies sought to investigate the pathoanatomical capacity of cervical spine meniscoids by exploring their morphology and innervation, as well as by investigating meniscoid morphology *in vivo* in a symptomatic population.

Study 1 tested a novel method of facilitating gross dissection of cervical spine meniscoids from 12 lateral atlantoaxial and cervical zygapophyseal joints excised from four cadavers. This investigation was necessary as the bony congruence and extensive ligamentous attachments of the articular pillar make disarticulation of cervical zygapophyseal joints difficult, requiring considerable force to separate joint surfaces, and potentially damaging the delicate cervical spine meniscoids enclosed within. Such damage may jeopardise the accuracy of morphological assessment of cervical spine meniscoids undertaken using dissection. The study found that formic acid demineralisation of cadaveric cervical spines did not alter the morphometry of cervical spine meniscoids. This validated the use of this technique as a viable means of facilitating disarticulation of the lateral atlantoaxial and cervical zygapophyseal joints, by allowing the softened bone to be cut away with a scalpel, such that the joint surfaces



could be separated with minimal force. This technique was then utilised in Studies 2 and 3.

Study 2 explored the morphology and histology of lateral atlantoaxial joint meniscoids in 12 cadavers using gross dissection and light microscopy. The study resolved points of contention in previous research, including cervical spine meniscoid prevalence and patterns of composition and morphometry. An association was found between articular cartilage degeneration and fibrous meniscoid composition, suggesting a possible link between meniscoid morphology and articular pathology of the lateral atlantoaxial joint.

The morphology and histology of cervical zygapophyseal joint meniscoids were investigated in Study 3 in 12 cadavers using gross dissection and light microscopy. Consistent with Study 2, Study 3 also noted an association of fibrous meniscoid composition with articular cartilage degeneration, providing further evidence of a potential relationship between cervical spine meniscoid morphology and articular pathology. Meniscoid size was not found to vary with spinal level, position in joint, articular degeneration or sex in an elderly population.

The innervation of cervical spine meniscoids was explored in Study 4 to determine the capacity for meniscoids to generate nociceptive input. This was undertaken using immunohistochemistry with antibodies to neurofilament heavy and pan-neurofilament to identify both myelinated and unmyelinated nerve fibres in 77 cervical spine meniscoids excised from 12 cadavers. Unmyelinated nerve fibres were identified within the bodies of two lateral atlantoaxial joint meniscoids composed of adipose tissue. Myelinated and unmyelinated fibres were observed within joint capsules adjacent to 14

cervical spine meniscoids. These latter findings provide evidence of potential sensory innervation of lateral atlantoaxial and cervical zygapophyseal joint capsules. The identification of nerve fibres exclusively within bodies of two adipose meniscoids perhaps suggests that meniscoid composition may influence the innervation status of cervical spine meniscoids.

The fifth and final study investigated cervical spine meniscoid morphology in a living population with known cervical spine pathology. This was undertaken using magnetic resonance imaging to visualise cervical spine meniscoids in 20 people with chronic whiplash associated disorder (WAD) and 20 age and sex-matched pain-free controls. Cervical spine meniscoids were found to be smaller in the lateral atlantoaxial joints and were more frequently fibrous in composition at the dorsal aspect of cervical zygapophyseal joints of the WAD group. It is postulated that such differences may be the result of altered cervical spine kinematics secondary to pain and hypomobility associated with WAD, and could plausibly serve to perpetuate patient symptoms.

The body of work comprising this thesis extends current understanding of the clinical significance of cervical spine meniscoids. The question of the prevalence of these structures has been addressed through convergent findings of dissection and imaging studies, thus refuting previous reports that cervical spine meniscoids are rare in adults. Patterns of cervical spine meniscoid morphological variation have been explored in elderly cadavers, noting an association between composition and evidence of articular pathology. Nerve tissue has been identified within cervical spine meniscoids (albeit uncommon) and adjacent joint capsules that is potentially nociceptive in function. Cervical spine meniscoids have been studied in a living population with cervical spine

pathology, with results illustrating morphological differences between the meniscoids of people with WAD and a pain-free population. Cumulatively, these findings provide preliminary evidence that cervical spine meniscoids may feasibly be of clinical significance in neck pain, possibly by altering segmental biomechanics or through generating nociceptive input.