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

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B Physiotherapy (Hons I)

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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.

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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

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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.

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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

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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.

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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 *12th 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

List of Figures

List of Tables

List of Abbreviations

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

β	Regression co-efficient
η^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.