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DOCTOR OF MEDICINE

Meniscectomy & osteoarthritis

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Ioannis Pengas

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MENISCECTOMY & OSTEOARTHRITIS

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Thesis submitted in fulfilment of the degree of

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CONTENTS

Table of Contents -----	ii
List of Figures -----	vii
List of Tables -----	ix
Abbreviations -----	x
Acknowledgements -----	xi
Declaration -----	xiii
Summary -----	xiv

TABLE OF CONTENTS

CHAPTER 1 – Introduction, Aims & Objectives-----	1
1.1 Introduction -----	2
1.1.1 Study’s relevance to clinical practice -----	3
1.2 Aims & Objectives-----	5
CHAPTER 2 – Background Anatomy & Literature review -----	6
2.1. Osteoarthritis (What is OA?)-----	7
2.2 The Knee -----	10
2.2.1 Gross Anatomy & Function -----	10
2.2.2 Knee Biomechanics-----	10
2.2.3 The Patellofemoral Joint -----	12
2.2.3.a Patellofemoral Joint Forces -----	13
2.2.4 Kinematics of the Tibiofemoral Joint & Alignment -----	14
2.3 Articular Cartilage -----	19
2.3.1 Composition-----	20
2.3.1.a Chondrocytes -----	20
2.3.1.b Extracellular Matrix -----	21
2.3.2 Structure -----	24
2.3.3 Mechanical Properties and Homeostasis -----	25
2.3.4 Subchondral Bone-----	27
2.3.5 Microdamage Protective Mechanisms -----	28
2.3.6 Articular Cartilage Damage-----	28
2.3.7 Chondrocyte Mechanobiology -----	29

2.3.8 Cytokines & Growth Factors -----	31
2.4 Meniscus -----	33
2.4.1 Anatomy -----	33
2.4.2 Biochemistry & Ultrastructure -----	35
2.4.3 Normal Function -----	38
2.4.4 The Effects of Meniscectomy -----	40
2.5 Radiographic Evaluation of Knee Osteoarthritis -----	51
2.6 Joint Pain -----	53
2.7 PROMs -----	55
2.8 Biomarkers -----	57
2.8.1 MMP-3 & GAG -----	59
CHAPTER 3 – Materials & Methods -----	62
3.1 Introduction -----	63
3.1.1 The Technique of Open Total Meniscectomy -----	63
3.2 Cohort selection -----	64
3.3 Methods of Subjective Evaluation & Objective Assessment -----	66
3.3.1 Objective Data Collection -----	66
3.3.1.a BMI -----	66
3.3.1.b Sagittal Laxity -----	66
3.3.1.c Range of Motion -----	67
3.3.1.d Radiographic Evaluation -----	67
3.3.1.e AP Weight Bearing -----	68
3.3.1.f Lateral Knee -----	69
3.3.1.g Weight bearing Knee Skyline -----	69
3.3.1.h Radiographic Scoring Systems Used -----	70
3.3.1.j Assessing Coronal Alignment -----	73
3.3.1.k Sampling, Treatment & Storage of Synovial & serum Fluid -----	75
3.3.1.l Analysis -----	76
3.3.2 Subjective Evaluation (PROMs) -----	77
3.4 Statistical Analysis -----	79
CHAPTER 4 – Results -----	81
4.1 Descriptive Statistics -----	82
4.1.1 The Whole Group -----	82

4.1.2 The Unilateral Group -----	84
4.2 Preliminary Statistical Analysis-----	85
4.2.1 Site of Meniscectomy-----	85
4.2.2 BMI-----	86
4.3 Statistical Analysis & Correlations for Clinical Outcomes -----	87
4.3.1 Sagittal Laxity -----	87
4.3.2 Range of Motion-----	88
4.4 Statistical Analysis & Correlations for Radiographic Outcomes -----	90
4.4.1 Tibiofemoral -----	90
4.4.2 Patellofemoral Joint-----	91
4.4.3 Malalignment -----	93
4.5 Statistical Analysis & Correlations for Patient Reported Outcome Measures-----	97
4.6 Statistical Analysis & Correlations for Biomarkers -----	100
CHAPTER 5 - DISCUSSION -----	104
5.1. Primary Outcome-----	105
5.2 BMI-----	107
5.3 Type of Meniscectomy -----	109
5.4 Sagittal Laxity -----	112
5.5 Range of Motion -----	113
5.6 Radiographic Outcomes-----	114
5.6.1 Tibiofemoral Joint-----	114
5.6.2 Patellofemoral Joint-----	115
5.6.3 Malalignment -----	119
5.7 Patient Reported Outcome Measures -----	121
5.8 Biomarkers -----	123
5.9 Strengths & Limitations-----	127
CHAPTER 6 CONCLUSIONS -----	129
REFERENCES -----	133
APPENDICES	
Appendix 1: Correlations Matrix-----	153
Appendix 2: Guide to Constructing a weight bearing device-----	154

Appendix 3: PROMs: KOOS & IKDC 2000 questionnaires -----	155
Appendix 4: Publications -----	164

LIST OF FIGURES

Figure 2.1 Knee joint 6° of Freedom diagram -----	11
Figure 2.2 Femoral rollback -----	11
Figure 2.3 Patellofemoral Joint Forces -----	13
Figure 2.4 Normal coronal alignment -----	14
Figure 2.5 Effect of sequential meniscal tissue loss on contact area -----	18
Figure 2.6 Constituents of articular cartilage -----	20
Figure 2.7 schematic diagram showing the proteoglycans subunit -----	23
Figure 2.8 Schematic diagram of the adult articular cartilage -----	24
Figure 2.9 Articular cartilage subjected to different loads -----	26
Figure 2.10 Birds eye view of the tibial plateau -----	33
Figure 2.11 Parameniscal capillary plexus -----	34
Figure 2.12 Collagen fibre arrangement in a Meniscus -----	37
Figure 2.13 Biomarkers in Body Fluids -----	58
Figure 3.1 Flow Chart of Total Cohort -----	64
Figure 3.2 Flow Chart of Current Study Cohort -----	65
Figure 3.3 Diagram Demonstrating the Weight Bearing Skyline Device -----	70
Figure 3.4 Measuring the Tibiofemoral Angle -----	74
Figure 4.1 Histogram of Unilateral group BMI -----	84
Figure 4.2 Graphs demonstrating the ROM between Index & Non-Index knees -----	89
Figure 4.3 Correlations between Ahlback and IKDC -----	99
Figure 4.4 Flow chart of positive knee aspirations -----	100
Figure 4.5 Correlation between GAG and Ahlback -----	102
Figure 4.6 Correlation between GAG and IKDC -----	103
Figure 5.1 Rate of TKA with age -----	105

LIST OF TABLES

Table 2.1 Total Meniscectomy Studies -----	43
Table 3.1 Ahlback and Kellgren & Lawrence Grading systems -----	71
Table 3.2 Definitions for the strength of association between variables -----	80
Table 4.1 Demographic data for the Whole Cohort -----	82
Table 4.2 Whole Group PROMs -----	83
Table 4.3 Unilateral Group Values as per Site of Meniscectomy -----	85
Table 4.4 Sagittal laxity-----	87
Table 4.5 ROM table-----	88
Table 4.6 Mode of Grading systems between Index & Non-Index Knees-----	90
Table 4.7 Correlations of PF JSN with other parameters-----	92
Table 4.8 Knee Malalignment -----	94
Table 4.9 Paired index vs. non-index as per site of meniscectomy -----	95
Table 4.10 Cohort's PROMs-----	97
Table 4.11 Symptomatic Knees as per KOOS -----	98
Table 5.1 Scandinavian rate of TKA with age -----	106

ABBREVIATIONS**A****ACL:** Anterior Cruciate Ligament**AL:** Ahlback**AP:** Antero-posterior**AEBSF:** 4-(2-aminoethyl)-benzenesulfonyl fluoride**B****BML:** Bone Marrow Lesions**BMI:** Body mass index**BW:** Body weight**BSA:** Bovine serum albumin**BSA:** benzamidine-HCl**C****CMP:** Cartilage Matrix Protein**CMPG:** Cartilage Oligomeric GlycoProtein**CoCr:** Cobalt chrome**COMP:** Cartilage Oligomeric Protein**D****E****EACA:** 6-aminohexonic acid**ECM:** Extracellular Matrix**ELISA:** Enzyme-linked immunosorbent assay**EDTA:** Ethylenediaminetetraacetic Acid**F****G****GAG:** Glycosaminoglycans**H****H₂O:** Water**H₂O₂:** hydrogen peroxide**I****IGF-I:** Insulin like growth factor -I**IKDC:** International knee documentation committee**J****JSN:** Joint space narrowing**JSW:** Joint space width**K****KL:** Kellgren & Lawrence**KS:** Keratan Sulfate**L****LM:** Lateral meniscus**M****MCL:** Medial collateral ligament**MES:** 2-(N-morpholino) ethanesulfonic acid**MM:** Medial meniscus**MMP-3:** Matrix metalloproteinases**N****NEM:** N-ethylmaleimide**NO:** Nitric Oxide**O****OA:** Osteoarthritis**P****PBS:** Phosphate buffered saline**PBST:** phosphate buffered saline with TWEEN**PFJ:** Patellofemoral Joint**PG:** Proteoglycan**PMSF:** phenylmethylsulfonyl fluoride**PROMs:** Patient reported outcome measures**PT:** Patella tendon**PVDF:** Polyvinylidene difluoride**Q****QT:** Quadriceps Tendon**R****ROM:** Range of Motion**RR:** Relative Risk**S****SEM :** Scanning electron microscopy**SF:** Synovial fluid**Std. Dev:** Standard Deviation**T****TGF-β:** Transforming growth factor-β**TIMP-1:** Tissue inhibitor for matrix metalloproteinases**TNF:** Tumour necrosis factor**TMB:** etramethylbenzidine**U****UHMW:** ultra-high molecular weight**V****W****WB:** Weight bearing**WHO:** World Health Organisation**WOMAC:** Western Ontario & McMaster Universities index of osteoarthritis**Z**

Dedication

To my Parents

Chloe & Panayiotis Pengas

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No man is an Island

J. Donne 1572-1631

DECLARATION

I hereby declare that the content of this submission is my own work and that it contains no material previously written or published by another person nor material which has previously been submitted or accepted for the degree of Doctor of Medicine (MD).

Mr Ioannis Panayiotou Pengas MBChB, MRCS, MPhil

(07/09/2012)

In capacity as supervisor of the candidate's thesis, I certify that the above statements are true to the best of my knowledge.

Mr Carlos Wigderowitz

Summary

Meniscal tears are the commonest knee injury and currently are addressed almost exclusively by arthroscopy.

Ian Smillie the late Professor of orthopaedics in Tayside, popularised open total meniscectomy worldwide during the 1950s believing that this was necessary for a functioning fibrocartilage replica to completely occupy the ensuing space.

The cohort in this study underwent open total meniscectomy under his care prior to their 19th birthday. It was documented in their then records that no other knee pathology was observed during the operation and that the same post operative regime was followed by all. This presents a unique opportunity to evaluate the long term outcomes of open total knee meniscectomy during adolescence and to further investigate biological markers of osteoarthritis 40 years down the line.

Fifty-three patients who underwent radiographic evaluation at the 30 year follow-up were further studied at this 40 year review. All surviving and contactable patients were consented prior to assessment and were evaluated clinically; biochemically, radiologically and subjectively once ethical approval and funding were secured.

Standardisation of all methods used for examination, radiographic evaluation, sampling of serum and synovial fluid and patient reported outcome measures (PROMs) was achieved by the use of recognised, validated and credible systems as well as good communication between all involved parties. Such examples include the construction of a wooden apparatus standardising the weight bearing skyline views and the need for a smooth and efficient transition between sampling, preparing, storing and transferring the synovial and serum samples.

Once all the data were collected, the first striking finding was the proportion of total knee arthroplasties (TKAs) observed as a hard endpoint in this cohort, which suggested a 132 fold increase when compared to their age and geographically matched population data, as per Scottish Arthroplasty Project.

It was important to assess if in this cohort the site of meniscectomy demonstrated a significant difference in terms of tibiofemoral joint (TFJ) osteoarthritis, range of motion (ROM) and PROMs as per our chosen scoring systems. As this proved not to be the case, the operated knee was assessed against the non-operated knee where possible and not as per site of meniscectomy.

Also the assessed sagittal laxity between the knees did not demonstrate any significant difference and as such was excluded as a confounding factor in terms of initiators of osteoarthritis.

A linear correlation was observed between the chosen scoring systems of TFJ osteoarthritis. The calculated relative risk (RR) of developing osteoarthritis (OA) in the operated vs. non-operated knee was calculated for both the KL & Ahlback grading systems with presumed osteoarthritis as ≥ 2 for KL & ≥ 1 for Ahlback. This was found to be 4.5 & 4.25 respectively.

Decreased ROM between the Index and Non-index knees was observed, with the ROM correlating with PROMs and inversely with TFJ OA.

In addition the usually under investigated patellofemoral joint was assessed.

Patellofemoral joint osteoarthritis was noted in the index knees as opposed to the non-index knees with an observed RR of 1.8 as per presence of osteophytes. There was no significant difference in the degree of patellofemoral joint (PFJ) osteoarthritis between lateral and medial meniscectomies. There was however significant correlations between

the joint space narrowing (JSN) and PROMs, TFJ OA and ROM. Worsening results were observed where the PFJ was <5mm.

Malalignment was greater in those knees that underwent medial meniscectomy as opposed to either lateral or medial & lateral meniscectomies. Malalignment demonstrated correlation with ROM and TFJ OA.

Serum and synovial fluid was processed and analysed with regards to biomarkers of OA in the form of MMP-3 and GAG. Neither serum nor synovial MMP-3 demonstrated any significant correlation with other measured parameters. GAG on the other hand demonstrated a significant difference between the index and non-index knee as well as a positive correlation to IKDC and an inverse correlation with TFJ OA. Although this is suggesting that synovial GAG as a biomarker for OA may indicate progression of disease and symptoms, the wider spread of values questions this.

Two different PROMs were utilised to assess this cohort. Interestingly the KOOS demonstrated that in all its 5 parameters the cohort was symptomatic. Correlations were observed between the KOOS ADL & Sport as well as IKDC with TFJ OA.

This is currently the longest follow-up of open total meniscectomy in adolescence worldwide. A >4 fold increased risk of osteoarthritis in the operated knee as compared to the non-operated knee was demonstrated and possibly a 132 fold increase in TKA as compared to their aged matched geographical peers.