

Bachelor of Medical Science (Honours) Abstracts

Outcome Measures for General Surgery

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Introduction: Robust outcome measures are needed to evaluate surgical performance. The choice of measures for low-risk procedures, such as Laparoscopic Cholecystectomy (LC), is contentious. This study aimed to review the current measures used to evaluate the outcomes of LC, and to apply a novel outcome measure, Days Alive and Out of Hospital (DAOH), to a retrospective cohort of surgical patients.

Materials and Methods: Two systematic reviews were conducted, examining the reporting of complications and patient-reported outcomes (PROs) after LC. Prospective studies published between 2013-2016 were studied. A retrospective analysis of adult patients undergoing LC or colonic resection (CR) at Auckland City Hospital between 2010-2015 was conducted. DAOH values for these patients were calculated. DAOH curves were constructed for surgeons and the surgical unit. The relationship between DAOH and complications was studied.

Results: A wide variety of complications were reported after LC ($n = 976$). Definitions for complications were infrequently provided and variable. PRO measurement for LC is focused on short-term outcomes, such as pain and nausea. In the retrospective study, 1228 patients undergoing LC and 635 patients undergoing CR were studied. Patients who experienced complications after LC ($n=65$) had fewer DAOH than patients that did not (median 82 versus 88, $P<0.0001$). Patients who experienced complications after CR ($n=308$) had fewer DAOH than patients that did not (median 69 versus 81, $P<0.0001$).

Conclusion: A variety of measures are used to evaluate LC. DAOH can be calculated from existing data sources and is sensitive to the occurrence of post-operative complications.

Exploring patterns of weight change and the differences between individual and population trajectories

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Introduction: Overweight and obesity affect around 1.9 billion adults worldwide and are a major risk factor for many chronic conditions. Few practical and affordable strategies have been found to combat obesity at either individual or population levels. This study explores possible paths to a healthy weight future and the implications for individual body weights over the life course.

Materials and Methods: Excel was used to plot and model several hypothetical patterns of weight change over the life span and how this may affect a population. STATA was then used to analyse NHANES data and R was used to plot mean weight and BMI for different age groups over time.

Results: Three population scenarios were developed - a weight gain society, a slimming society, and a static society, one that remained low-weight, and one affected by obesity. Individual and population trajectories are not always in the same direction. It is possible for an average individual to gain weight as the population as a whole gets slimmer. From the NHANES data, it appears the United States tracks the weight-gain society model, with some slowing of the epidemic recently to resemble the model of a static society with high obesity rates.

Conclusion: It is not necessary to eliminate age-related weight gain in order to reduce the prevalence of overweight and obesity in the population. This apparently counter-intuitive finding has important

implications for health policy.

A mouse model to investigate the effect of acute Staphylococcal infection on the tight junctions in nasal mucosa

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Introduction: *Staphylococcus aureus* has been previously noted intramucosally in patients with chronic rhinosinusitis (CRS). It may be that a disruption of the integrity of epithelial tight junctions in these patients provides a mechanism for bacterial entry. We aimed to investigate the ability of *S. aureus* to disrupt epithelial tight junctions by introducing it to the sinuses of healthy mice.

Materials and Methods: A total of 21 BALB/c, species-free mice were used. Three mice were sacrificed at baseline to provide a control group for comparison. The remainder were infected intranasally, with either JSNZ ($n=9$) or 26-T1 ($n=9$), strains of *S. aureus*. Three mice from each group were sacrificed at 2, 5 and 14 days post infection. Sinonasal mucosa was then examined histologically for the presence of intramucosal *S. aureus* and the expression of the tight junction protein zonula occludens-1 (ZO-1) was quantified with immunohistochemical staining techniques.

Results: No intramucosal *S. aureus* was observed in any of the infected mice. There was also no significant difference in the expression of ZO-1 between the infected groups of mice and the control group.

Conclusion: Introducing *S. aureus* to the sinonasal cavities of healthy mice does not result in the disruption of epithelial tight junctions and therefore no intramucosal *S. aureus* was noted. Future work could investigate introducing *S. aureus* to the sinonasal cavities of an animal model of CRS.

Sub-cellular structural and molecular changes in experimental heart failure

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Introduction: Despite a burden of disease affecting over 23 million worldwide, cellular mechanisms for heart failure (HF) remain poorly understood. This investigation quantified changes during right-heart failure, focusing on structural disruption in the t-tubular system of cardiac myocytes and changes to regularity and extent of expression for the Ryanodine Receptor 2 (RyR2) protein.

Materials and Methods: Male Wistar rats (300-350g) were injected with monocrotaline (MCT; 60mg/kg) to induce pulmonary capillary damage and acute decompensated HF within 4-6 weeks. 11 MCT-treated animals and their time-matched controls were dissected at onset of acute HF, with tissue samples from left and right-ventricular free walls, trabeculae carneae, and papillary muscles collected for immunohistochemistry. Slides were labelled with RyR2 primary antibodies and wheat germ agglutinin (WGA) for t-tubular membranes, imaged using confocal microscopy, and analysed for structural periodicity and area quantification.

Results: T-tubular structure showed significant disruption in HF animals, with greatest change against control in structural periodicity (measured by t-power) taking place in the right-ventricular free wall (mean ratio 0.58, $P<0.0001$). RyR2 receptor expression also decreased in HF, especially in the right ventricle (RV) wall (mean ratio 0.64, $P<0.001$), with greatest change in RV trabeculae (mean ratio 0.44, $P<0.0001$).

Conclusion: Decline in heart function is correlated with t-tubular ultrastructural disruption and reduced RyR2 receptor expression. More significant reduction of RyR2 expression within RV trabeculae also suggests that conditions for trabecular cardiomyocytes are different to those within free walls, perhaps contributing to receptor down-regulation.

The effect of position on maternal collateral venous circulation in late pregnancy

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Introduction: Maternal supine sleep position is associated with an increased risk of late stillbirth. In this position the gravid uterus compresses the inferior vena cava (IVC). It is speculated that the azygos venous system provides collateral circulation in order to compensate for this phenomenon.

Materials and Methods: Twelve pregnant women between 34–38 weeks gestation underwent scanning in the supine and left lateral decubitus positions using a 3T Skyra (Siemens) MRI system. Phase contrast images were evaluated to measure blood flow through the AA, IVC and azygos vein.

Results: The supine position was associated with a reduction in cardiac output when compared to the left lateral position (4.64 ± 1.41 vs 5.49 ± 1.10 L/min; $P=0.004$). Blood flow through the IVC at its origin decreased in the supine position (0.17 ± 0.18 vs 1.26 ± 0.38 L/min; $P<0.001$) while blood flow through the azygos vein increased (0.81 ± 0.26 vs 0.31 ± 0.21 L/min; $P<0.001$). Blood flow through the aorta at the level of its bifurcation also decreased in the supine position (1.09 ± 0.24 vs 1.69 ± 0.54 L/min; $P<0.001$).

Conclusion: Women in the third trimester of pregnancy experience an increase in collateral venous blood flow in the supine position, likely to compensate for compression of the IVC. However, a significant reduction in arterial blood flow was found which may cause a significant reduction in uteroplacental blood flow and may explain the association between maternal supine sleep position and increased risk of late stillbirth.

Foot deformities in paediatric neuromuscular disorders – factors affecting plantar pressure distribution

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Introduction: Dynamic pedobarography is used to assess plantar pressure distribution across the sole of the foot during gait. This study explored the relationships between radiographic measures of foot deformity, pedobarographic measures of plantar pressure and the effect of lower limb transverse rotation in gait.

Materials and Methods: Prospectively collected clinical, plain film radiography, pedobarography and 3D gait analysis kinematic data of 80 feet from children with cerebral palsy (CP) and other neuromuscular disorders (NMD) was retrospectively analysed. Seven X-ray parameters, coronal (CI) and sagittal indices (SI) of plantar pressure and dynamic rotational profile measures at the pelvis, hip and ankle level were derived.

Results: Two X-ray measures, talocalcaneal ($P=0.02$) and AP talo-1st metatarsal angles ($P<0.01$) combined with dynamic pelvic rotation ($P=0.02$) best correlated with change in modified CI ($R=0.687$, $R^2=0.473$). Forefoot SI best correlated with AP talo-1st metatarsal angle ($P=0.033$), shank-foot angle ($P=0.051$) and tibiotalar angle ($P=0.002$); ($R=0.396$, $R^2=0.157$). Midfoot SI best correlated with calcaneal pitch angle ($P<0.01$) and tibiotalar angle ($P<0.01$); ($R=0.506$, $R^2=0.256$). Hindfoot SI was predicted by calcaneal pitch angle only ($P<0.01$); ($R=0.356$, $R^2=0.127$). Dynamic rotational profile measures were not correlated with sagittal indices.

Conclusions: Weight bearing X-rays are predictive of dynamic plantar

pressures in both coronal and sagittal planes. When planning corrective surgery of foot deformities secondary to CP and other NMD, in particular coronal deformities, rotational profile should be incorporated as part of quantitative assessment. These findings add further evidence supporting single event multi-level surgery over isolated deformity correction.

Clues to the regenerative potential of notochordal cells: development of a model to study the secretome of intervertebral disc cells

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Introduction: Intervertebral disc (IVD) degeneration accounts for 40% of back pain. The central nucleus pulposus consists of notochordal (NC) and mature nucleus pulposus (MNP) cells. NC cells secrete anabolic factors that maintain a healthy disc, whereas a reduction in NC cells with aging strongly correlates with disc degeneration. However, the precise anabolic factors are not fully characterised. This study aimed to examine protein localisation in the NC cell microenvironment and develop a model to examine the secretome (secreted soluble factors) of NC cells in response to static and dynamic loads.

Materials and Methods: NC and MNP cells were isolated from bovine IVDs, fixed or cultured in 3D-alginate beads in 21% or 5% oxygen for 72h, and assessed for cell viability. Protein concentration from conditioned media was measured using the EZQ protein assay. Collagens I, II, IV, aggrecan and TGF- β 1 expression was examined in NC cell clusters using immunohistochemistry. Intact discs were mechanically loaded (0-1000N, 4h), cultured for 24h and assessed for viability.

Results: NC and MNP cells maintained >85% viability in 5% and 21% oxygen over 72h. Sufficient protein was detected in conditioned media for proteomic analysis, although gel electrophoresis showed contamination from culture media-derived serum. The NC cell microenvironment expressed collagen types I, II, VI, aggrecan and TGF- β 1. Loaded IVDs showed viability >90%.

Conclusion: We have established a 3D-culture model that maintains viability over 72h in phenotypic levels of 5% oxygen. Due to high levels of serum albumin, further study is required before embarking on mass spectrometry proteomic analysis.

Business Impact Assessment – Obesity and Population-level Nutrition: An investigation into the nutrition-related commitments of the New Zealand food industry

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Introduction: The BIA-Obesity has been developed as a national-level tool to monitor and benchmark the commitments of the food industry towards improving population nutrition. It consists of a range of indicators within seven domains: corporate population nutrition strategy (STRAT), relationships with external organisations (RELAT), product formulation (FORM), nutrition labelling and health claims (LABEL), promotion to children (PROMO), product pricing (PRICE) and product distribution and availability (AVAIL).

Materials and Methods: 25 companies were selected to cover at least 50% of the market share in the packaged food ($n=15$), beverage ($n=2$), supermarket ($n=2$) and chain restaurant ($n=6$) sectors in New Zealand. Publicly available information was collected through an online search. A relevant representative from each company was asked to review and/or supplement the publicly available information. The collected commitments were scored according to the BIA-Obesity and presented to the companies as absolute and relative scores.

Results: Overall BIA-Obesity scores ranged from 0-68.4% within the packaged food sector; 41.9-54.5% within the beverage sector; 32.6-55.7% within the supermarket sector; and 2.1-31.2% within the chain restaurant

sector. The best-performing domain was STRAT (median = 48.3%) and the worst-performing domains were PRICE and AVAIL (median = 0%). In general, several good practice examples were collected; however, many commitments were vague and non-specific.

Conclusion: In New Zealand, industry performance on nutrition-related commitments is varied and thus the BIA-Obesity is successful at differentiating between companies.

Epigenetics and changing understandings of heredity

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The idea that effects of our environment can be inherited was considered a *non sequitur* impossibility for most of the 20th century. Emerging research suggesting that environmentally-influenced epigenetic changes induced through DNA methylation, histone modification and non-coding RNA may be inherited is challenging the authority of this claim, and with it our assumption of the individual as autonomous and context-free. This thesis explores the evidence for epigenetic inheritance and how this might construct an alternative understanding of the biosocial body - one that cannot be separated from its historical, cultural and socioeconomic environments. The emerging picture may provide a more nuanced framework within which to understand and deal with the challenges in New Zealand of rising health disparities, child abuse and intergenerational poverty. This framework contrasts with the narrative that has influenced social policy over the last three decades which assumes the individual is rational, universal and individually responsible for their own health, a position that is increasingly untenable given the scientific evidence affirming our connection. I argue however that an alternative conceptual framework is not an inevitable consequence of this science. Unless we make deliberate changes to our social policy approach, we will continue down the same path we have been on over the past decade in which little improvements have been made to reduce inequity and poverty. The thesis concludes that Whakapapa - the Māori conception of heredity, which has always recognised the importance of this connection, may be a useful framework in informing an alternative application of epigenetic science.

Exploring the predisposition of Asian Eye to meibomian gland dysfunction

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Introduction: A higher prevalence and severity of dry eye in Asian populations compared to Caucasian populations is repeatedly reported in literature. A previous Auckland study of young adults showed significantly greater meibomian gland drop out in the Asian eyes compared to the Caucasian eyes. It is unknown whether differences exist from birth or arise at a young age.

Materials and Methods: 70 age matched paediatric participants (5-17 year olds) were recruited. Tear film quality, ocular surface characteristics, and dry eye symptomatology were evaluated in a single clinical session. Metrics were compared across different eyelid shapes - Asian single lid (ASL), Asian double lid (ADL), and Caucasian double lid (CDL).

Results: There were no significant intergroup differences in the tear film quality, dry eye symptomatology and meibomian gland drop out. A greater proportion of ASL and ADL participants exhibited incomplete blinking than CDL patients (all $P < 0.05$). Asian eyelids exhibited significantly more shortening of meibomian glands than the Caucasian eyelids ($P = 0.013$) whereas Caucasian eyelids exhibited significantly more tortuous changes ($P < 0.0001$). Lid wiper epitheliopathy (LWE) in the lower lid was significantly greater in the ASL compared to the ADL group ($P = 0.011$).

Conclusion: Ethnic differences in the meibomian glands do not exist from birth but appear to arise with age. Incomplete blinking may predispose the Asian eyes to MGD. Differences in eyelid tension may also contribute to gland morphology.

Corneal remodelling following cataract surgery

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Introduction: Phacoemulsification is the preferred technique of cataract removal, and the structural integrity of corneal wounds is important for wound healing and optimised vision in the postoperative period. The aim of the study was to characterise corneal wound healing and incision architecture with different incision sizes in the three months following cataract surgery.

Materials and Methods: A prospective randomised study of 100 patients undergoing cataract surgery assigned to incision sizes of 2.20mm or 2.85mm was completed. Incision length, angle, leakage and corneal thickness were recorded. Incision imaging using anterior segment optical coherence tomography and an evaluation of corneal biomechanics was completed at one day, one week, one month and three months, postoperatively. Statistical analysis was completed using R.

Results: Wound leakage was noted in one (1%) main incision (angle=35.0°), mean incision angles were 25.1±4.6° (main), 36.6±7.3° (side incision), $P < 0.001$. Descemet's membrane detachments were observed in 62% (2.2mm) and 40% (2.85mm), $P = 0.005$. Endothelial wound gaping improved within the first month ($P < 0.001$) and wound retraction increased from one to three months post-operatively ($P = 0.004$). Decreases were seen in mean corneal wound thickness between 1 day (949µm), 1 week (866µm) and 1 month (737µm), $P < 0.001$.

Conclusions: Corneal wound integrity was related to the angle of incision rather than the nature of construction. Smaller surgical incisions are more vulnerable to corneal damage. Corneal wound healing is a dynamic process, with an early stage of repair up to 1 month, and a later stage of remodelling extending beyond 3 months after cataract surgery.

Declining tear film and anterior ocular surface health with age - a cross-sectional population study in New Zealand

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Introduction: Dry eye disease (DED) is a very common condition seen by eye care practitioners and is a growing population health problem. In the past decade, limited studies in populations below the age of forty and in regions south of the equator have been conducted. This study helps address these two major gaps in the literature by assessing aging effects in NZ.

Materials and Methods: Satisfying institutional ethical requirements, 277 participants, aged 36±23 years, completed standardized dry eye (DE) assessments evaluating DE symptoms and risk factors, as well as tear osmolarity, blink rate/quality, tear meniscus height (TMH), non-invasive break up time (NIBUT), lipid layer grade, bulbar redness, corneal/conjunctival staining and meibography, to determine the effect of age on the tear film and ocular surface.

Results: According to TFOS DEWS II diagnostic criteria, DED prevalence was 60.7% overall - with 51.1% under 40 and 73.1% over 40 years. Subgroup analysis demonstrated increasing prevalence with advancing age. Measures significantly correlated with age were: DEQ-5 scores (increased, $P = 0.02$), TMH (increased, $P < 0.001$), NIBUT (decreased, $P = 0.005$), osmolarity (increased, $P = 0.005$), bulbar redness (increased, $P < 0.001$), superior and inferior meibomian gland dropout (increased, $P = 0.005$) and superior and inferior lid wiper staining (increased, $P < 0.001$ and $P = 0.002$, respectively)

Conclusions: Almost all tear film and ocular surface measures except late signs, corneal/conjunctival staining, showed significant worsening with age. DE prevalence was 1.4 times higher in the older age group. The study results demonstrate the importance of evaluating DE for early therapeutic intervention to improve quality of life with aging.

Morphological evolution in melanoma in situ – a dermoscopic perspective

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Introduction: Melanoma in situ (MIS) have fewer structural features of malignancy visible under dermoscopy than invasive melanoma. As little is known about how these features change over time, we investigated structural changes in melanoma in situ that had undergone dermoscopic follow-up.

Materials and Method: Three dermoscopists retrospectively compared sequential digital dermoscopic images of histologically diagnosed MIS. By consensus, changes in lesion area, colours, presence of *chaos* (asymmetry of structure or colour) and *clues* to malignancy (9 specified local features) were determined.

Results: 124 MIS in 110 patients (41 male), all of European ethnicity, were compared. Mean age was 52.5 years and mean follow-up 41 months (range 3–144 months). Change in lesion area from baseline was significant at each follow-up time point except 12 months ($P < 0.001$). All lesions had brown pigmentation. The mean time for newly observed pigmentation (black, grey, and white) was 39 months. The number of colours was significantly dependent on follow-up time and lesion area ($P < 0.001$ and 0.01 respectively). Most lesions had chaos (75%) and the number of clues was significantly dependent on time and lesion area (both $P < 0.001$). A clinically significant minority of lesions showed no change or loss of structural features.

Conclusion: MIS predominantly increase in morphological complexity over time. Longer follow-up periods allow identification of initially subtle focal morphological features associated with malignancy.

Zebrafish Gene Editing to functionally characterize a novel PDE6B founder mutation causing autosomal recessive rod-cone retinal dystrophy in Maori

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Introduction: *PDE6B* c.2197G>C; p.Ala733Pro is a novel founder mutation causing autosomal recessive rod-cone dystrophy (ARRCD), and is estimated to account for 15% of inherited retinal disease in Māori. Current therapies retard disease progression, and alleviate symptoms but do not cure disease. This project aimed to create, and characterize a transgenic zebrafish model of *PDE6B* c.2197G>C; p.Ala733Pro ARRCD to facilitate the screening of novel therapeutics, in particular those targeting cyclic GMP – a key role player in *PDE6B* retinal disease.

Materials and Methods: Transient morpholino knockdown of *PDE6B* was performed on zebrafish embryos, with validation by RT-PCR. CRISPR/gRNA-Cas9 complexes were injected into zebrafish embryos to create a stable *PDE6B* mutant. Phenotypic characterisation of the morpholino zebrafish model was performed using light microscopy, OCT, cGMP expression by immunohistochemistry, and the optokinetic response.

Results: RT-PCR confirmed transient *PDE6B* knockdown. Decreased ocular pigmentation was observed in day 6 morpholino embryos. In day 4 and 6 morpholino embryos, no structural differences in histology, nor a reduction in the optokinetic response were seen. Permanent knock-out of *PDE6B* exon 1 has been performed and is awaiting confirmation.

Conclusion: The morpholino system temporarily knockdowns *PDE6B* function in a zebrafish model of retinal disease, with no significant impact on the phenotype, consistent with the theory that prolonged cGMP accumulation is toxic to photoreceptors. The creation and characterization of a CRISPR/Cas9 *PDE6B* zebrafish model will permit therapeutic drug screening, and assessment of changes in gross morphology, anatomy, visual function and cGMP levels which may occur during the retinal disease process.

Integrating health interventions into a youth health survey: exploring adolescent perspectives through the co-design of a prototype user interface

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Introduction: Health surveys and health interventions frequently use digital technology. Large digital surveys, like the Youth2000 surveys exploring health and wellbeing of adolescents in New Zealand, generate important data. However, participants with health needs are not provided with support. Integrating evidence-based health interventions into surveys could address this with likely health benefits. This study aimed to explore adolescent perspectives on surveys integrated with interventions.

Materials and Methods: A systematic literature review was conducted to identify features of digital health interventions that affect usability. Adolescent perspectives were explored through the co-design of a prototype user interface. Four co-design sessions were conducted with eight secondary school students using semi-structured interviews and usability testing applying the “think aloud” method. Additionally, two focus groups ($n = 16$) were conducted to evaluate the prototype. The findings were analysed using affinity diagramming (co-design sessions) and general inductive approach (focus groups).

Results: Survey-integrated interventions were perceived to be helpful for students needing support. A prototype was developed demonstrating the basic functionality of a user interface for survey-integrated interventions. Key features that were perceived to enhance usability included: assurance of confidentiality; adequate information about interventions and external support services; a tool for finding a local doctor; opportunity to message a youth health worker and; having freedom over the context of use. Suggestions were provided on how to optimise the presentation.

Conclusions: Adolescents see value in integrating interventions into a large-scale youth health survey. The findings provide an important basis for operationalising the idea of survey-integrated interventions with important implications for population health.

Consistency of Corneal Contours: The Influence of Accommodation and Biomechanics

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Introduction: Ciliary muscle contraction causes lens deformation during accommodation, and concurrent corneal deformation may occur, affecting vision. The current study aimed to quantify corneal refractive changes during accommodation and assess if corneal biomechanical factors predict these changes.

Materials and Methods: Corneal topography and tomography were assessed in sixty-three participants to a peripheral radius (r) of 5 millimetres (mm) with the GALILEI™ G2 Dual Scheimpflug Analyzer in the accommodated and unaccommodated states. Four dioptres of natural accommodation were induced using an electronic monitor transiently displaying near acuity calibrated words viewed through an externally mounted beam-splitter. Corneal biomechanical characteristics, including time, velocity, and amplitude of applanation, were assessed with the CorVis ST. Statistical analysis was completed in R software.

Results: The mean (\pm standard deviation) participant age was 24.2 ± 4.6 years and 35 participants (56%) were female. Anterior chamber depth reduced by 0.10 ± 0.07 mm with accommodation ($P < 0.01$). Mean anterior instantaneous corneal power increased by 0.1D centrally (95% confidence interval (CI) = $0.02 - 0.2D$) and in the superior nasal periphery (95% CI = $0.05 - 0.2D$), while a 0.1D reduction occurred in the inferior temporal periphery (95% CI = $-0.05 - -0.15D$). Mean

central corneal thickness decreased by 0.5µm and approached statistical significance. Corneal stiffness and the deformation amplitude ratio significantly predicted peripheral corneal changes with accommodation ($P < 0.05$), but did not fully account for the observed changes (adjusted R^2 range = 3.5–16.8%).

Conclusion: Measurements using contemporary technology demonstrate no clinically significant corneal refractive changes during accommodation and corneal biomechanical factors are poor predictors of these changes.

Colonic Dysmotility in Acute Surgical Disease

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Introduction: Aberrations in colonic motility are common in surgical patients but are poorly understood. The objectives of this thesis were: i) review the literature investigating aberrant motility and pathophysiology of post-operative ileus and acute colonic pseudo-obstruction; ii) evaluate post-operative distal colonic motor activity; iii) pilot ambulatory high-resolution manometry recordings; and iv) investigate pre-operative changes in colonic motility.

Materials and Methods: Systematic reviews were conducted to critically appraise studies investigating post-operative colonic motility and the pathophysiology of acute colonic pseudo-obstruction. *In vivo* high-resolution manometry was used to investigate pre-, intra-, and post-operative trends in distal colonic motor activity in patients undergoing elective right hemicolectomy. A novel ambulatory fibre-optic acquisition system was evaluated.

Results: Systematic review showed that colonic transit is prolonged post-operatively and may be a rate-limiting factor in recovery. Electromechanical activity does not cease post-operatively but is abnormal. The pathophysiology of acute colonic pseudo-obstruction is multifactorial, though the underlying motility patterns remain unclear. High-resolution manometry studies showed colonic motility becomes abnormally hyperactive following surgery, characterised by cyclic motor patterns occurring at 3 cycles per minute, and an absence of high-amplitude propagating sequences. Recovery of bowel function is delayed until this pattern normalises. Ambulatory high-resolution manometry was feasible post-operatively. The percentage activity and amplitude of colonic cyclic activity increases with proximity to major surgery, possibly due to anxiety.

Conclusions: Hyperactive colonic motility may be central to ileus after colorectal surgery, and returns to normal prior to recovery of bowel function. Future studies should investigate whether similar derangements underlie prolonged ileus and colonic pseudo-obstruction.

Quantification and optimisation of intranasal fluticasone deposition

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Introduction: The corticosteroid fluticasone is used in the post-operative management of chronic rhinosinusitis. Disease recurrence is common, partly due to poor drug penetration into sinus cavities. The delivery device and associated particle characteristics seem to play a key role in deposition.

Materials and Methods: A standard nasal spray (Flixonase) and pressurised metered-dose inhaler (Flixotide) were studied. High-speed imaging was used to measure particle characteristics in the spray plume of each device. Two CRS patient CT scans were used to generate subject-specific three-dimensional computer models of nasal airways. High-speed imaging data was used to simulate particle deposition in models. Three-dimensional printing was used to manufacture plastic casts of nasal airways. High performance liquid chromatography (HPLC) was used to assess deposition in printed models. Computer modelling was used to

optimize deposition factors for maximal sinus deposition.

Results: Measured particle size of Flixonase plume was significantly larger than Flixotide (median 75 vs. 3.5µm). All simulated Flixonase particles deposited in the anterior nose or nasal septum. Most Flixotide particles escaped into the nasopharynx but achieved greater paranasal sinus deposition, primarily in the maxillary sinus or middle meatus. Frontal sinus deposition was not observed. Sphenoid deposition was minimal. Preliminary HPLC findings support minimal sinus deposition observed in computer models. Smaller particles are favoured for optimal sinus deposition.

Conclusion: Smaller particles produce improved sinus deposition but increases pulmonary deposition. Deposition factors can be altered to optimise sinus deposition. This can open new avenues for research and development of devices for more effective drug delivery and post-operative management.