Welcome

Welcome to the September 2014 edition of New Wave. If you have any relevant articles of papers that you would like to be included in future editions, please email them to warren.jackson@hey.nhs.uk

High-Resolution Fibre-Optic Colonic Manometry
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Functional colonic disorders include irritable bowel syndrome, faecal incontinence and constipation. These chronic conditions induce major economic and social burdens because of their prevalence in society and their dramatic impact upon quality of life. Relating patient’s symptoms to actual gastrointestinal abnormalities is difficult, yet improved therapies can only stem from a clearer understanding of the problems that underpin them. Peristalsis is a process by which rhythmic and synchronised contraction of two distinct types of smooth muscle, circular and longitudinal propel content through the gut. For many colonic functional disorders abnormal peristalsis is implicated. Yet despite well over 100 years of research our knowledge of “normal” colonic peristaltic patterns still relatively simplistic.

Recording real-time in-vivo peristaltic motor patterns, over long lengths of the colon has largely been derived from manometric studies. These studies involve flexible catheters with an array of pressure recording sites being introduced into the colon. However, due to technical constraints these manometry catheters have typically contained between 1 – 16 sensors. This limited number of sensors impacts upon our ability to record and interpret the colonic motor patterns. For example the human colon extend for ~1.2m and propagating colonic motor patterns can extend over segments as short as 3cm. Therefore, by using manometry catheters with such a limited number of sensors, we can either record motor patterns in high detail over very short segments of the colon or we can record with increasing loss of information as the spatial resolution between recording sites increases to accommodate the length of the region studied.
Examination of short segments of the colon is problematic; extrapolation of data captured in one short segment to the whole region is not viable because the motor patterns are not distributed evenly throughout the colon. Alternatively widely spaced sensors can cause confusion because they may be too far apart to capture the propagating activity that is occurring.

In other regions of the gut, such as the oesophagus and ano-rectum, high-resolution manometry (1cm spacing between recording sites) has become increasing popular because it enables users to gain a clear picture of normal or abnormal motor patterns. However, until recently these catheters also had a limited number of recording sites (typically ≤36 sensors @ 1cm) and because of their limited recording length (~35cm) they were not suitable for use in the human colon. To overcome the issues of the catheter length and low sensor count, engineers at Australia’s CSIRO developed a high-resolution manometry catheter based on fibre-optic technology (Arkwright et al., Opt Express 2009; 17: 22423-22431). These catheters can incorporate up to 120 pressure sensors spaced at 1cm intervals, while maintaining high flexibility and an outside diameter of just 3mm.

Figure 1 A fibre-optic manometry catheter, colonoscopically placed inside the colon of a healthy adult male. The tip of the catheter is secured to the colonic mucosa by an endoclip. This clip prevent movement of the catheter. In this example Sensor 1 is located at the hepatic flexure, sensor 25 at the splenic flexure and sensor 44 is located at the sigmoid colon.
These catheters produce exquisitely detailed pressure profiles from the colon that are an order of magnitude more informative than the best recordings achieved previously. This can be seen in Figure 2. In this figure the same data is shown with different sensor spacing. At low resolution recording (10cm spacing) motor patterns can clearly be seen but linking pressure events in adjacent channels to determine if the motor patterns are propagating is simply not possible. Halving the sensor spacing to 5cm intervals displays more data, but defining relationships between pressure events in adjacent channels is still not possible. At high-resolution (1cm spacing) patterns of propagation emerge and these patterns can be viewed as a standard line plot or as a spatiotemporal pressure map. Through a series of studies have now shown that doubling the sensor spacing from 1 to 2 cm, halves your ability to detect propagating motor patterns. While moving from 1 to 3cm spacing results in a 30% chance of incorrectly labeling propagating motor patterns. At 10cm spacing (traditional spacing for colonic manometry recordings) ~60% of all identified motor patterns are incorrectly labeled (Dinning et al. Neurogastroenterol Motil 2013; 25: e640–e649).

**Figure 2** Fibre-optic manometry recording from a healthy adult female. The same data is displayed with different spacing between recording sites. A) represent the traditional low-resolution colonic manometry with 10cm spacing between sensors. In B) sensor have been spaced at 5cm intervals and in C) the full complement of data is shown at 1cm intervals. In D) the high-resolution data is C) is displayed as a spatiotemporal pressure map. Note that at 5 and 10cm spacing the propagating motor patterns cannot be seen (see Dinning et al. Neurogastroenterol Motil 2013; 25: e640–e649; for more details).
To date, the fibre-optic catheters are only being used in two hospitals in Australia (Flinders Medical Centre, South Australia & St. George Hospital, New South Wales) and one hospital in New Zealand (Auckland Hospital). They have been used to quantify colonic motor patterns in healthy controls (Dinning et al, Neurogastroenterol Motil. 2014. (In Press; doi: 10.1111/nmo.12408) and to determine the effects of treatments upon colonic function in patients with constipation (Dinning et al, Br J Surg 2012; 99: 1002-1010) and faecal incontinence (Patton et al, Br J Surg 2013; 100: 959-968).

The potential role of high-resolution manometry in diagnostics of colonic disorders is still to be determined, however with the increased recording resolution we are ideally placed to be able to identify manometric signatures of colonic functional disorders. Ultimately it is hoped that these data will enable quantification of treatment outcomes, which is the primary goal of all manometric investigation.

Masterclass on lower GI Function, Barts and the London School of Medicine and Dentistry, Whitechapel, London, July 10-11th 2014
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Introduction

Ardmore Healthcare, MMS and Queen Mary University of London hosted a Masterclass on Lower GI Function Testing at Barts and The London School of Medicine and Dentistry on July 10-11th, 2014. The two day masterclass, organised by Dr. Mark Scott, Ms. Emma Carrington and Prof. Charles Knowles, was well attended by healthcare professionals spanning across diagnosis and treatment of functional bowel disorders. The topics covered by international speakers, including Prof. James Jones (Ireland), Dr Phil Dinning (Australia), and Prof Klaus Krogh (Denmark) and those by local experts reflected perfectly the multidisciplinary nature of the audience, the disease, and the diagnostic approach we should all be aiming for.

Setting the scene

A prominent theme of the meeting was the need for standardisation of practice so that current methods can be validated leading to consistent and transferable information. Access to comparable information will help us collectively determine the most effective treatments depending on symptom aetiology bringing, as desired by Prof Knowles, better service recognition.

So when can diagnostic testing provide useful information about a patient’s condition? According to Miss Sophie Pilkington, at the heart of an appropriate referral is a good history. Using haemorrhoids as an example, she noted that treating what you can see may not resolve the underlying issues. Questionnaires are frequently used to define symptom severity and impact on quality of life, but can lack sensitivity as they are perceived differently. For a more personal patient perspective it may be useful to simply ask “what is the worst aspect for you?” Alternatively, a patient can be asked to list his/her three worst symptoms scoring each between 0 and 10. A relatively simple task, it can be a useful tool for monitoring improvement in symptoms following treatment satisfying the need for personalised care. However, Miss Pilkington stressed that symptom severity does not always reflect impact on quality of life.

Tests of anorectal function become indicated when quality of life becomes affected - usually when the patient requests help. Dissatisfaction drives investigation, but consideration should be given to conservative measures and exclusion of organic disease first. Nevertheless, early investigation may prove its worth since often the power of a positive diagnosis can be an effective therapeutic tool in itself.
High-resolution manometry

Following an overview of the features and global appreciation of the anal canal gained from HRAM compared to conventional manometry, the audience were treated to a video demonstration of the technique. It was an opportunity to see someone else do what you do on a daily basis, to identify what is done differently and to acknowledge the variability in practice which had been the focus of earlier discussions. The demonstration led into consideration of normality, clinical cases and discussion of technical glitches identified in routine practice. For example:

1. **Familiarisation period:** Following intubation, the catheter should be left in place for at least three minutes prior to recording of resting pressure. In healthy volunteers, a progressive drop in pressure was observed suggesting that immediate measurement could over-estimate resting tone.

2. **The 'heavy-buttock effect':** When placing the high-resolution catheter, acknowledge the number of sensors outside the anus when setting anal canal borders. A heavy buttock lying on top of the sensors outside the anal canal can introduce artefact on the observed pressure trace.

3. **Be aware of catheter movement:** this may occur especially during squeeze or push manoeuvres and may necessitate repositioning. Remember to allow a period of re-familiarisation before continuing with the study.

4. **Ultra slow waves and slow waves:** oscillation in the continuous pressure measurement may be observed as regular increases in tone (identified as warmer colour contour plot).

Pelvic floor imaging

Professor James Jones’ keynote speech focused on new insights into the pathophysiology of faecal incontinence (FI) and improvement of symptoms using sacral nerve root stimulation (SNS). Through research based on an animal model of FI induced by obstetric injury, the group demonstrated the importance of sensory fibres in the mechanism of action of SNS.

To begin with, acute stimulation (of the lumbosacral nerve roots) was shown to have no motor effects on the anal sphincters. However, a potentiation of sensory response to anal canal stimulation was observed. Following induction of obstetric injury, somatosensory function was impaired. However acute SNS resulted in restoration of sensory function and the optimal frequency for this effect was found to be 2Hz. This potential mechanism of action of SNS may be applicable to patients with FI.

Moving from animals to humans, Mr Andy Williams provided an animated demonstration of endo-anal ultrasound both in 2D and 3D form. His comical and entertaining manner left no question of his desire to showcase the lessons that could be learned through ultrasound imaging of “god’s wonderful organ: the anus”. On a basic level, interpretation requires differentiation between ultrasound appearance of muscle layers and an understanding of the anatomical and ultrasonographic differences between males and females. This is particularly with regard to length, appearance and echogenicity of the external anal sphincter (EAS). Whilst 2D endo-anal ultrasound is sufficient to view such differences in real time, 3D acquisition has the advantage of being able to ‘perform’ the procedure over and over again without the patient present! Alternative views not possible using 2D allow for assessment of length, symmetry and insertion within the pelvic floor. In addition, 3D can allow further categorisation of pathology and have given insight into the role of puboanalis tears in defaecatory disorders following delivery. Regardless of the method used, three key questions should be considered:

1. Has there been damage: yes or no?
2. Are the ends separated or does the sphincter have a patchy appearance with some ‘intactness’?
3. Can a new repair be any better?
An informative insight into transperineal and endovaginal ultrasound delivered by Miss Charlotte Chaliha followed. An unknown method to some, this emerging technique provides a whole pelvic floor perspective for urogynaecology and colorectal surgery. Unlike other methods it can give a global view of anterior and posterior compartments, but interpretation requires expertise. The technique has proved particularly useful for the assessment of pelvic organ prolapse, but also allows identification of distortion and division of urethral and anal structures. Much of the work in the area was pioneered by Dietz and colleagues (2004), with emphasis on determining novel symptom aetiology; the technique has now been used to determine the role of levator convulsion injury in relation to risk of prolapse.

A look at colonic motility from Phil Dinning from Adelaide described the use of high resolution colonic manometry to investigate contraction patterns in the colon. Further details about the work are presented in this issue of NewWave.

**Anorectal sensation**

Normal bowel function requires intact and integrated sensory processes, which can be tested in a number of ways. Anorectal sensation and the clinical significance of sensory dysfunction were discussed by Mark Scott. Stimulating the sensory arm of the pudendal nerve can be used to demonstrate sensory impairment in some individuals. Impaired sensation suggests neuropathic damage, which can explain symptoms in the absence of any mechanistic defects. Mucosal electrosensitivity is often blunted in FI, constipation and in patients with haemorrhoids. However, sensory dysfunction may be related to hypo and/or hypersensitivity. For example, patients with FI have been shown to have reduced perception of transient relaxations in the anal canal using HRAM, as might occur during reflex sampling of rectal contents. Conversely, balloon distension can often result in reduced capacity due to heightened sensory awareness of rectal filling.

Balloon distension is an established technique for evaluating rectal capacity, but is inhibited by its lack of ability to assess compliance of the rectum. Henrietta Heinrich introduced the Short Barostat technique currently being used in Zurich, which provides a cheaper and more user friendly means of assessing stiffness of the rectal wall.

**Colonic transit studies and assessment of evacuatory dysfunction**

Current methods for evaluating gastrointestinal transit and evacuation dysfunction tend to rely on radiological imaging, but as with manometric techniques, the protocols used are hospital-dependent. The number and type of radio-opaque markers, x-ray exposure and time of referral vary, making it difficult to assess validity of research and compare diagnostic data between hospitals. Dr Natalia Zarate stressed that we should be wary of the protocol used when interpreting colonic transit time, since study may not actually provide what it says on the tin. The simplest techniques rely on a single abdominal x-ray to determine transit, but in reality these images should only be used to discriminate between health and disease, not to assess segmental delays. In addition, research has shown that particularly in women, complete evacuation of markers may take up to four days in normal controls. Interpretation is made more difficult if imaging is not co-ordinated with natural desire to open bowels, which can lead to a mass movement of rectal and sigmoid contents in some individuals.

Once again, standardised normative data is sparse and as Dr Zarate pointed out, the traditional segmentation of transit using the 5th vertebra and ileac crest as anatomical markers may not be physiological, since this bears no relation to contractions beginning at the splenic flexure. Finally, whilst the presence of markers in the rectum is often assumed to be the result of an evacuatory problem, it could indicate slow-transit in some individuals. Despite room for improvement, there are few alternatives to currently favoured imaging assessment of colonic transit. It is relatively cheap, simple and if used to answer a well-defined question, can provide the distinction from abnormality required to guide treatment or indicate further physiological investigation.
The use of a wireless motility capsule called SmartPill, which has been discussed in previous editions of NewWave, was demonstrated by Dr Anthony Hobson. This ingestible telemetric device capable of measuring pressure, temperature and pH has had an impact on transit assessment in the private sector. It collects information on the gastric and colonic environments, which can be of particular use in the investigation of IBS. As discussed previously, abnormalities in pH at the level of the caecum can act as a marker of SCFAs due to increased bacterial fermentation. The presence of SCFA in turn has been linked to the number of contractions in the colon, evidence of which is provided by pressure data collected by the capsule. The SmartPill is proposed as an alternative to invasive and radiological transit studies. The advantage of the method is its ability to link upper and lower GI procedures to provide panenteric evaluation of patient symptoms. For example, research using the technique suggests that 18% of patients with slow transit constipation may (also) have gastroparesis.

On disadvantage of the SmartPill is that location of the capsule is dependent on environmental changes associated with specific segments of the GI tract. The Magnetic Pill (Motilis, Lausanne) being developed by Professor Klaus Krogh provides a partial answer to this problem. The fully ambulatory method measures rotation, vertical, and forward and backward motion and allows precise tracking and calculation of transit.

**Tests of evacuation**

Presented by Dr Antón Emmanuel, were the different types of dyssynergia evident using HRAM (Rao et al 2004). Attention was drawn to the ability of manometry to define defaecation using the rectoanal gradient as a marker. Interestingly, the presence of an observer in the room during manoeuvres made the gradient smaller, suggesting that dyssynergia was less likely to be demonstrated in a private setting. Balloon expulsion can be used to screen for obstructed defaecation, but in fact 30% of controls are unable to pass the balloon. Although no single measure seems to provide the optimum answer, Dr Emmanuel suggested that investigation should be multimodal- the more tests there are, the more sensitive the result.

Finally, barium and MR proctography were discussed (Dr Michele Marshall and Professor Stuart Taylor) and debated with a reminder that proctography is the voluntary evacuation of contrast; it is not a true reflection of defaecation. However for the most useful information to be obtained, the diagnostic question and referral criteria should be made clear. Attractively, MRI provides a global view of the pelvic floor and involves no radiation. By contrast, barium proctography is cheap, accessible and ‘established’. Nevertheless, certain pitfalls exist and are common to both methods:

1. Incontinent patients: consider location and logistics within the clinic room to preserve patient dignity and comfort
2. Painful intubation and puborectal spasm can make inserting contrast difficult; a bladder syringe was recommended.
3. Lack of clarity: be clear when instructing the patient, but keep instructions short. For example, “empty out as quickly as you can.”
Patients on PPI’s who continue to experience symptoms such as cough, heartburn, regurgitation and chest pain often are difficult to diagnose using traditional acid (pH) monitoring approaches. In fact, a recent study states that physicians using only acid (pH) monitoring for diagnostics, lack the capability of accurately diagnosing GORD in 35% of their patients.*

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Treatment Conclusions
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- Clinical trials have established that non-acid reflux can be associated with GORD symptoms. In addition, ZepHr® provides a true negative study by identifying patients with no reflux association.
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* An Analysis of Persistent Symptoms in Acid-Suppressed Patients Undergoing Impedance-pH Monitoring; Sharma, Agrawal, Freeman, Vela & Castell; Clinical Gastroenterology and Hepatology 2008;6:xxxx
Forthcoming Events:

We hope to publicise forthcoming meetings and educational events. We would like to invite interested parties to contact the NewWave editor (warren.jackson@hey.nhs.uk) to have the details included in future issues.

Sept - Dec 2014  Medical Measurement Systems (MMS) web seminar schedule for 2014: [All webinars are 3.00-4.30pm CE(S)T - Amsterdam time]:

Urodynamics:  Impedance-pH:

Tuesday 16th September  Tuesday 7th October
Wednesday 17th December  Wednesday 29th October

Advanced HRM Case Interpretation:  High Resolution Anorectal Manometry (HRAM):

Tuesday 9th September  Thursday 6th November
Thursday 13th November  
Thursday 11th December

High Resolution Oesophageal Manometry (HRM):

Thursday 16th October
Wednesday 19th November (Paediatric)

Each session is FREE of charge:

30th Sept - 2nd Oct 2014  Sandhill Scientific Clinical Training Seminar

Day 1: Introduction to Impedance/pH Reflux Testing
Day 2: High Resolution Impedance Manometry (HRiM)
Day 3: Introduction to Impedance/pH Reflux Testing (Paediatrics)
Charing Cross Hotel (Canterbury Room), The Strand, London,

Email for further information: sales@synmed.co.uk

18th - 22nd Oct 2014  United European Gastroenterology (UEG) Week Vienna, Austria
www.ueg.eu/week

1st Oct 2014  HRM & Impedance/pH Masterclass Queen Elizabeth Hospital, Birmingham
Email rachel@ardmorehealthcare.com for further information

13th - 14th Nov 2014  Capsule Endoscopy in Clinical Practice (Autumn Course) (Pillcam system) Lumley Castle Hotel, County Durham
http://www.diagmed.co.uk/documents/LumleyCapsuleCourseRegistartionForm2014.pdf

22nd - 25th June 2015  The Digestive Disorders Federation (DDF) Meeting Excel Centre, London

20th - 23rd June 2016  BSG Annual Meeting 2016 Liverpool ACC