Chapter 20
Recording In Vivo Human Colonic Motility: What Have We Learnt Over the Past 100 Years?

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Introduction

The human colon is one of the least understood organs of the human body. The conspicuous lack of understanding about its day-to-day functioning is particularly evident in our relatively simplistic understanding of how it fills and empties its content. Many disorders arise from suspected abnormalities in colonic contractions yet, due largely to technical constraints, investigation of human colonic motor function still remains relatively primitive. A look through the majority of the current literature will reveal that studies of colonic motility show (1) anally propagating high amplitude propagating sequences/contractions; (2) low amplitude propagating sequences; (3) a large amount of non-propagating contractions; (4) period rectal and/or colonic complexes; and (5) the occasional episodes of orally (retrograde) propagating pressure waves. These descriptions are based largely upon colonic manometry recordings, with recording sites spaced at least 7 cm apart (the majority >12 cm; (Dinning and Di Lorenzo 2011; Dinning et al. 2010a; Scott 2003)). With the recent developed of high-resolution manometry catheters with sensors spaced between 1 and 2.5 cm the classification colonic motility patterns has been re-investigated and these new studies are highlighting the inaccuracies of low-resolution recording (Dinning et al. 2015). By examining studies of the past as well the current literature this paper will provide a summary of our current understanding of human colonic motility.

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Measurement of Colonic Motility

Themotor activity of the human colon stores, mixes and propels content. These motor patterns arise from interactions between; (1) spontaneous myogenic activity driven by pacemaker cells; and (2) enteric neural circuits, which are modulated by the chemical and physical composition of colonic contents. Enteric neuronal activity is also influenced byextrinsic parasympathetic and sympathetic pathways driven from the central nervous system. The measurement of colonic motility that arise from these interactions is achieved via two primary means; measurement of transit or measurement of the colonic contractility.

Measurement of Transit

After Wilhelm Conrad Röntgen discovery ofX-radiation in 1895 (Röntgen Ray or X-rays) (Underwood 1946), researchers were provided with a tool that allowed them to directly view radio-opaque solutions moving through the gut. With continued real-time X-ray recording, a swallowed bismuth meal could be tracked through the esophagus, stomach, small bowel and colon. One of the first proponents of this technique, Arthur Hertz published a paper in 1907 in which detailed the timing and movements of content through the entire digestive tract (Hertz 1907). This paper included one of the first descriptions of the movement of colonic content during defecation; with all content below thesplenic flexure evacuated and at the same time the contents of the ascending colon would move into the transverse colon.Retropulsion was also documented with Hertz observing that bismuth injected into the rectum later being seen in the transverse colon or caecum (Hertz 1907). A few years later Guido Holzknechtg provided a detailed description of the colonic mass movement on the basis of direct observation under fluoroscopy "*the haustral segmentation evident in the ascending and transverse colon, disappeared as the colonic content shifted to the descending colon. Once the movement was complete the haustral indentations soon reappeared*" (Holzknechtg 1909). In 1913 Hertz published another paper of observations in which he noted that a chief stimulus for the mass movements of colonic content appeared to be the ingestion of food, a process he coined the "gastrocolic reflex" (Hertz and Newton 1913).

With the exception of these "large" observed events, the early studies of colonic transit concluded that the colon was inactive for most of the day and then in response to certain stimuli a series of coordinated contractions would occur that moved the stool towards the rectum. In patients with constipation similarX-ray images of a barium meal or barium enema indicated that this normal degree of coordination of colonic movements was diminished or absent with "incoordination of muscular motor function" being proposed as the basis of non-obstructive constipation (Kruse 1933). This observation was in stark contrast to the prevailing view at the time (and still today) that the colon in constipated patients is lazy or static.

As the dangers of radiation exposure become known prolonged, continuous X-ray recording of colonic motility ceased and were replaced by a series of static images taken at regular intervals. Using such techniques, in addition to description of the previously described mass movements, Ritchie et al. published details of "peristaltic ripples" (Ritchie et al. 1971). These were defined as a series of progressive contractions following one another along the bowel. Unlike the mass peristaltic events, that always travelled towards the rectum, the peristaltic ripples could moved in either an anal or oral direction at speeds of around ~1 cm/min. The studies by Ritchie also demonstrated retrograde movement of content from the sigmoid to descending colon (Ritchie et al. 1971) and an increase indistal colonic retrograde propulsion after a meal (Ritchie 1968). Additional studies utilizing radio-opaque disks or scintigraphy confirmed earlier findings that 50–100 % of colonic contents can be emptied during defecation (Halls 1965; Lubowski et al. 1995), while also showing that if defecation was withheld the contents in the rectosigmoid could undergo retropropulsion back to the transverse colon (Halls 1965). Other observational studies report abarium enema traveling from the rectum to the stomach in as little as 15 min (Alvarez 1967). More recently the real-time monitoring of an ingested magnet with the Magnet Tracking System (Hiroz et al. 2009) indicated "*retrograde displacement was clearly demonstrated as part of the colonic motility pattern in every colonic segment*".

On the basis of these transit studies while "mass movements" where associated with defecation and the movement of large quantities of content along the colon, retrograde or oral propulsion is also an important component of colonic motility.

Measurement of Colonic Contractility

While the studies above described the movement of content, they provided limited information on the real time contractility of the bowel wall. Such measurements have primarily been recorded through colonic manometry; techniques that measure intraluminal force/pressure. The initial manometry studies utilized water or air filled balloons attached to pressure transducers. These recording provided a single pressure trace, usually from the sigmoid colon, that indicated the colon was rarely inactive, as suggested by the earlier fluoroscopic studies, but actually consisted of almost continual pressure waves, that could increase in amplitude and frequency in response to a meal (Welch and Plant 1926). With recording largely confined to the sigmoid or distal colon, many studies in the 1940s and 1950s concentrated on sigmoid motor activity in relation to defecation. Kern et al. administered Acetyl-Beta-Methylcholine Chloride subcutaneously in healthy human subjects and demonstrated that the induced diarrhea was associated with diminished or inhibited motility in the sigmoid colon (Kern et al. 1949). In another patient with a transverse colectomy, the authors were able to record motility from the caecum, transverse colon and sigmoid colon. Using the same drug they demonstrated an in increase in proximal colonic motility and a completed inhibition of sigmoid motility, in association with stool expulsion (Kern et al. 1949).

This study supported earlier studies in dogs that suggested the "wave like" activity in the sigmoid colon played a role in preventing stool from reaching the rectum and that such activity was inhibited when defecation occurred (Galapeaun and Templeton 1938). Further studies in humans showed that sigmoid hypomotility was associated with patients with an "irritable colon" and diarrhea (Almy et al. 1950) and in patients with colitis the number of stool passed was inversely proportional to the amount of activity in the sigmoid colon; the less the activity the greater the stool frequency (Kern et al. 1951).

This sigmoid activity was shown to increase rapidly after a high calorie meal and could be inhibited by the anticholinergic drug, clidinium bromide, suggesting that the previously described "gastro-colonic reflect" was neurally mediated (Snape et al. 1979). More recent manometry studies using multiple channel manometry catheters recorded similar distal colonic motor patterns, that became know rectal motor complexes (Kumar et al. 1989; Rao et al. 2001). These motor patterns were thought to originate in response to the arrival of stool or gas, and thus act as a brake to untimely retard the flow of colonic contents and so keep the rectum empty (Rao and Welcher 1996).

In other regions of the colon balloon manometry catheters, introduced through colostomies were used to capture peristaltic events induced by laxatives or balloon distension (Hardcastle and Mann 1968; Ritchie et al. 1962; Torsoli et al. 1971). Through such stimulation these studies induced "colonic peristalsis", a likely equivalent of the mass movements described in the earlier radiological work (see above) and importantly showed that these peristaltic events were likely to be neurally mediated because their initiation could be blocked by pre-mucosal application of Lidocaine (Hardcastle and Mann 1968).

In the late 1980s the first of the prolonged recordings of spontaneous colonic activity were reported. Using water perfused manometry catheters colonoscopically placed into the transverse or ascending colon, motor patterns were recorded over a 24 h period (Narducci et al. 1987; Bassotti and Gaburri 1988). One of the most readily apparent motor patterns recorded in the healthy controls consisted of an array of large amplitude pressure waves recorded in adjacent channels. This motor pattern became known as the high amplitude propagating contraction (Narducci et al. 1987) and was believed to be the manometric equivalent of the previously described mass movement. These events were infrequent, occurring between 6 and 20 times per 24 h and were more prevalent after morning waking and in response to a high calorie meal. These motor patterns have been associated with spontaneous (Bampton et al. 2000) and stimulated (Kamm et al. 1992) defecation and while their initiation is incompletely understood, distension is likely to play a role (Bharucha 2012) as is intraluminal chemical stimulation (including chenodeoxycholic acid and short-chain fatty acids) (Torsoli et al. 1971; Kamm et al. 1992; Cook et al. 2000; Bampton et al. 2001). In patients with low transit constipation the frequency of these motor patterns is reduced or absent, suggesting that a potential neuropathy may exist (Bharucha 2012; Singh et al. 2013).

While the high amplitude events, became the primary focus of most colonic manometry studies, in reality they made up only a small percentage of the total colonic motility patterns. The majority of the colonic motility consisted of lower amplitude pressure events, described as segmental activity, consisting of single pressure events or bursts of rhythmic/arrhythmic pressure events, most of which has been classified as non propagating (Bassotti et al. 2005). In health this activity increases throughout the colon (not just the rectosigmoid, as described earlier) after a meal or morning waking (Bassotti and Gaburri 1988; Bampton et al. 2001; Dinning et al. 2010b; Rao et al. 2004), whilst in constipation the colonic response to these stimuli is diminished or absent (Bassotti and Gaburri 1988; Bampton et al. 2001; Dinning et al. 2010b; Rao et al. 2004).

Associating Luminal Transit with Pressure Events

In 1971, using two to four microballoons and combined cinefluroscopy Torsoli et al., temporally associated laxative induced high amplitude propagating events with the movement of content in the transverse colon (Torsoli et al. 1971). Correlating scintigraphic images (one frame per minute) of spontaneous movements of content in the transverse, descending and sigmoid colon with manometry recorded from three recording port separated by 15 cm, Moreno-Osset et al. indicated a degree of association between pressure events and flow (Moreno-Osset et al. 1989). Whilst the manometry traces in that study were relatively simplistic there appeared to be an association between the direction of movement and the levels of motor activity in adjacent sites; content always moving from regions of high activity to low activity (Moreno-Osset et al. 1989). That same paper also suggested that up to 80 % of antegrade movements of content in the descending colon refluxed back into the transverse colon.

In patients with functional diarrhea a combined scintigraphic and manometry study indicated, in comparison to healthy controls, that a lack of distal colonic non-propagating pressure waves appeared to be associated with rapid transport of a radio-opaque tracer into the rectosigmoid after a meal (Bazzocchi et al. 1991). This study supported the finding from the manometric studies described above, which suggested that contractile activity in the sigmoid colon plays a role in preventing rectal filling.

By combining scintigraphic recordings (one frame per 15 s) with colonic manometry incorporating 12 sensors spaced at 10 cm intervals, Cook et al. found a temporal association between spontaneous high amplitude propagating sequences and luminal propulsion (Cook et al. 2000). However, only a third of antegradely propagating events were associated with bolus flow and the effectiveness of the bolus transport was dependent upon site of origin amplitude and velocity of the propagation (Cook et al. 2000). That study also found that a third of isotope movements were associated with apparent non-propagating motor patterns and a further third of movements were associated with no discernible motor pattern. Subsequent studies utilizing a higher scintigraphic frame rate (1 per 10 s) and a manometry catheter with 16 recording sites spaced at 7.5 cm intervals showed that 93 % of all identified propagating motor patterns were associated with flow, however ~50 % of antegrade flow episodes still occurred with no apparent propagating activity and only 10 % of retrograde flow was associated with retrograde propagating motor patterns (Dinning et al. 2008). Indeed despite the fact that studies of colonic transit all report retrograde flow, very few studies report retrogradely propagating motor patterns, a fact that is likely to reflect the technical limitations of the manometric techniques used.

Future Direction

While the expect ion of some minor changes, for the most part colonic manometry has remained unchanged for the past 20 years. In contrast, during this period, esophageal manometry has seen some major technical advances, the most critical of which is the application of high-resolution manometry (Clouse et al. 1998; Williams et al. 2001). High resolution manometry catheters can contain up to 36 sensors, spaced at 1 cm intervals, providing a detailed profile of pressures along the entire studied region. On the basis of the spatiotemporal topographic maps produced from these data an entire diagnostic classification system, has been devised which aids in the treatment of esophageal and motility disorders (Bredenoord et al. 2012).

Until recently high resolution catheters of sufficient length to record pressures throughout the entire colon simply had not existed. However, over the past few years a few new catheter designs have begun to emerge. By using an area-under the curve analysis of data, high-resolution water perfused catheters (20 sensors at 2.5 cm spacing) have been used to help predict potential neuromuscular pathological phenotypes in children with slow transit constipation (Giorgio et al. 2013). While conversion of data recorded by a 36 sensor catheter (spacing between 4 and 2 cm) into a color topographical map, has been used to more clearly identify motor patterns that have been described previously, such as high amplitude propagating events (El-Chammas et al. 2014).

In both of these papers the data acquired through the higher resolution recording, failed to report any new motor patterns and it is notable that while the colonic motility was recorded with more sensors than had previously been used, the catheters failed to match the spatial resolution of catheters used in the esophagus. To achieve 1 cm spacing over length of the colon, an entirely new form of manometry catheter was developed. Utilizing fiber-optic sensor technology manometry catheters were developed with unto 144 sensors paced at 1 cm intervals (Arkwright et al. 2009). Utilizing these catheters, studies have shown that number of propagating events detected is very much dependent upon the sensor spacing used (Fig. 20.1). Doubling the sensor spacing from 1 to 2 cm nearly halves the number of propagating motor patterns detected, while moving from 1 to 3 cm spacing results in a 30 % chance of mislabeling propagating events (Dinning et al. 2013b). At 10 cm spacing ~60 % of all propagating events identified could be incorrectly labeled.

Of particular interest from the high-resolution recordings in healthy controls was the dramatic increase in the identification of retrogradely propagating motor patterns.

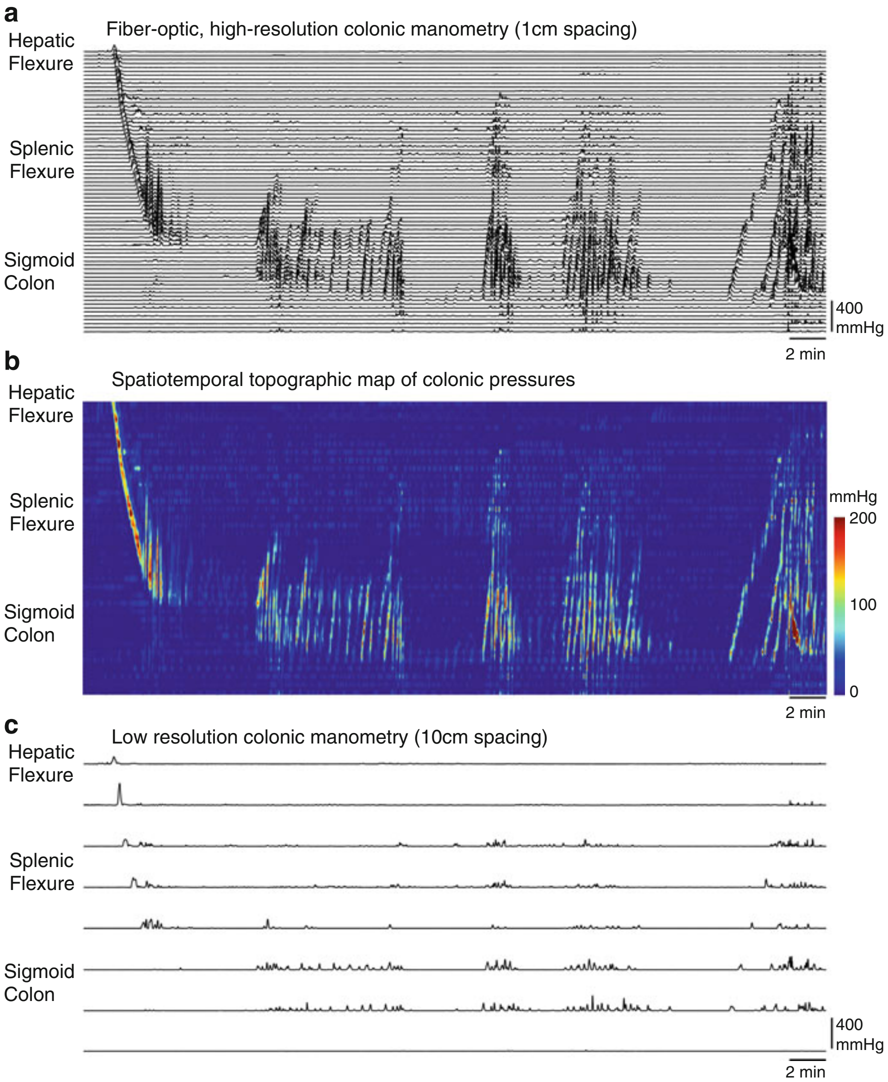

Fig. 20.1 Fiber-optic high resolution manometry trace record from a health adult colon. In (**a**) the entire colonic trace is shown. The same data in displayed as a spatiotemporal topographic map in (**b**). In (**c**) the same data is shown from every tenth sensor, essentially replicating a low-resolution colonic recording. Note that in (**a**) and (**b**) a series of retrograde propagating pressure events can be seen originating in the sigmoid colon. In the low resolution recording these motor patterns can not be identified

As in the previous section, in most studies of colonic manometry retrograde motor patterns were either not identified or were identified in small such small numbers that they hardly rated a mention. At one 1 cm spacing the retrograde motor patterns are by far the most prominent motor pattern identified (Dinning et al. 2013b, 2014).

These motor patterns were most commonly identified in the sigmoid and descending colon occurred in clusters of between 2 and 6 per minute (Fig. 20.1). It is likely that such motor patterns would impede anally directed flow and as such these data support the hypothesis proposed by previous studies that the sigmoid motor activity prevents contents from reaching the rectum until defecation is due to occur (see section "Measurement of Colonic Contractility").

Quantification of motor patterns recorded with these catheters in the healthy colon is only just beginning, however applying discriminant, logistic and cluster analysis of the shapes (gradient, duration, amplitude) of pressure events belonging to different motor patterns suggests that the motor appear to be generated by two independent sources, potentially indicating their neurogenic or myogenic origin (Dinning et al. 2014). The clinical worth and the potential diagnostic value of such recordings in patient groups is still to be determined.

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