Novel Approaches to the Measurement of Gastrointestinal Motor Physiology

DAVID MONRO SMITH
M.B., Ch.B., F.R.C.S.(Ed)

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To my family

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DECLARATION

I declare that I am the author of this thesis, that the work contained in this thesis is my own, and that this thesis has not been accepted previously for a higher degree.

Signed

David M. Smith

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ABSTRACT

Advances in gastrointestinal motility are hampered by current methodology. This thesis sought to evaluate novel methods for measurement of gastrointestinal motor physiology, including *a*) computerised analysis of gastric and small bowel motility and *b*) a non-invasive method of detection of gastrointestinal motor activity, termed Surface Vibration Analysis (SVA). SVA detects vibrational energy emanating from gastrointestinal contractions, using a transducer placed on the abdominal surface. The main objectives of this thesis were as follows:

1. **The development of computerised analysis of gastric and small bowel motility.**
2. **Comparison of SVA against intraluminal manometry.**
3. **Effects of intraluminal content on motility measurements.**
4. **Evaluation of SVA in chronic intestinal obstruction.**

1. Computerised analysis of gastrointestinal motility.

Algorithms for peak detection, measurement of peak amplitude and duration, exclusion of artefact, identification of the individual phases of the Migrating Motor Complex (MMC) were constructed and validated against conventional manual analysis. This development was essential for the assessment of **objective** 2.

2. Comparison of SVA against intraluminal manometry.

The SVA response was decreased during periods of motor quiescence (phase I of the MMC) as compared to motor activity (phases II & III of the MMC). This SVA response was increased by instillation of both gas and fluid in the upper gastrointestinal tract as compared to gas and fluid evacuation (*GFE*). There was no correlation between individual manometric contraction parameters and the SVA response.

3. Effects of intraluminal content on motility measurements.

GFE reduced the duration and contraction amplitude of phase II of the MMC and increased the duration of phase I. Instillation of both gas and fluid had the converse effect. The parameters of phase III were unaffected.

4. Evaluation of SVA in chronic intestinal obstruction.

SVA was applied to the detection of subacute intestinal obstruction in 46 patients and compared to 18 volunteers. On the basis of visual analysis of the SVA tracing, a positive diagnosis of subacute intestinal obstruction was made in 12 out of 14 patients subsequently proven to have adhesions at laparotomy. None of the volunteers had a positive diagnosis of intestinal obstruction. Small bowel transit time, as assessed by the hydrogen breath test, was similar between the two groups. The sensitivity of SVA was 0.86 with a specificity of 0.79.

This thesis has shown that the parameters of fasting gastrointestinal motility are dependent on the intraluminal content and that SVA is able to discriminate between the motor activity and quiescence. Furthermore, SVA may be useful in a clinical setting in the diagnosis of subacute intestinal obstruction. Finally, the developed software for the analysis of fasting motility should provide a rapid and consistent method for further research of fasting motility.

Chapter 1

Introduction

GASTROINTESTINAL MOTILITY

Synchrony of Gastrointestinal Physiology

Synchronization of the processes of digestion and absorption is important for homeostasis. These processes involve the breakdown of highly organised food structures, containing complex macromolecules, and their transfer to the general circulation. Factors including temperature, pH, secretion and contractions of the smooth muscle of the gastrointestinal tract or gastrointestinal motility, are all involved in this complex interaction. In particular, gastrointestinal motility is responsible for mechanical breakdown, grinding, mixing and movement of food to specific regions of the gastrointestinal tract, where selective digestion, secretion and absorption occur, as well as for disposal of waste to the exterior.

Clinical Relevance of Gastrointestinal Motility

The interaction between gastrointestinal motility and digestion is demonstrated by consideration of the process of nutrient absorption. In severe cases of a generalised motility disorder, such as chronic idiopathic pseudo-obstruction or secondary to scleroderma, nutrient absorption is poor and parenteral nutrition may be required. In less extreme circumstances, abnormalities of motility may be related to a variety of conditions including gastroesophageal reflux (Vantrappen G, 1990), gastritis (Moore SC, 1986), small bowel bacterial overgrowth (Vantrappen G, 1977) and functional bowel disturbances (Waldron B, 1991).

The contribution of motility disorders to many gastrointestinal organic disorders, and their effect on non-gastrointestinal conditions are unknown. For example, the effects of disordered motility resulting from diabetic autonomic neuropathy, on glucose homeostasis and diabetic control is unknown. Greater understanding in this area could lead to improvement of the management of many chronic conditions.

Physiology of gastric and small bowel motility

The contractile activity of the gastrointestinal tract has been the subject of scientific study since the distinctive work carried out by Cannon in 1902 in which he examined the peristaltic activity of cats using fluoroscopy and described the pattern of movements within the intestine of conscious animals (Cannon WB, 1902), and receptive relaxation of the stomach in response to the ingestion of food (Cannon WB, 1911). In the same year, William Boldyreff observed 4 periods of gastric activity synchronous with pancreatic exocrine secretion in a dog in the fasting state (Boldyreff W, 1902). This observation was contrary to the views of William Beaumont, a founding figure of digestive physiology and prominent authority of the time, who maintained that the digestive tract was an inert system which responded only to external stimuli (Beaumont W, 1833).

Boldyreff's experiment was the first to demonstrate gastrointestinal activity during the fasting state. In 1925, Ivy and Vloedman confirmed fasting activity and showed that contractions ("hunger contractions") spread from the stomach to both the oesophagus and the duodenum (Ivy AC, 1925). Little progress was made however till 1952, when Code, Hightower and Morlock developed a classification of

fasting motor activity, based on a system developed by Adler and colleagues (Adler HF, 1941). They categorised fasting contractions in three types (I - III). Type I contractions were of low amplitude and relatively short duration. Type II contractions were of greater amplitude and duration and type III were more complex and usually involved a tonic elevation of the baseline (Code CF, 1952). This classification was however crude, non-functional and unable to discriminate disorders of motility. In 1969, Szurszewski described the Myoelectric (or Migrating) Motor Complex (MMC) in a canine model. He was able to demonstrate a myoelectric complex that originated in the duodenum and migrated distally down the length of the small bowel and that on reaching the ileum, the complex was replaced by another complex initiated again in the duodenum (Szurszewski JH, 1969). This notable discovery heralded a new wave of interest in the study of the motor physiology of the fasting gastrointestinal tract. Szurszewski's finding was confirmed by Carlson, Bedi and Code (Carlson GM, 1972) and by Grivel and Ruckebusch (Grivel M-L, 1972).

All early work on migrating fasting activity involved the measurement of electrical activity of the gastrointestinal tract, which comprises of two components; slow wave activity, which is a periodic fluctuation of the membrane potentials of the smooth muscle cells - this slow wave activity is also known as the Basic Electric Rhythm (BER) (Bass P, 1961), pacesetter potential (Code CF, 1970) or electrical control activity (ECA) (Sarna SK, 1985). If the membrane potential depolarises beyond a certain threshold level, then the other component of the electrical activity of the gut - the spike potentials or electrical response activity (ERA) are initiated and result in depolarisation and contraction of gastrointestinal muscle. Only one

spike potential can occur for any given slow wave fluctuation. The rate of the slow wave fluctuation, which differs along the length of the gastrointestinal tract, controls the maximum rate of contraction for specific sites. Various neurohormonal mechanisms control the excitation threshold of the slow wave so that a spike potential is not activated with every slow wave. By examining the electrical activity in greater detail, Code and Marlett apportioned the migrating motor complex into 4 phases (Code CF, 1975); phase I which contained a relative absence of spike potentials, phase II contained persistent but random spike potentials and phase III (the so called activity front) which was characterised by a burst of continuous spike potentials occurring with every slow wave. This phase was then followed by a shorter period of phase IV, characterised by a rapid decrease in the incidence and amplitude of the spike potentials. Nowadays, phase IV is generally disregarded, leaving Code's original first three phases. Code further ascribed a role to the MMC, calling it the "intestinal housekeeper", whose action was to sweep the bowel clean of any residual chyme and food debris (Code CF, Schlegel JF, 1975). Indeed if the normal periodic activity is disrupted pharmacologically in rats, bacterial overgrowth has resulted (Scott LD, 1982) and in the first study carried out on the MMC in humans, small bowel bacterial overgrowth was found in patients with abnormalities or absence of the MMC (Vantrappen G, 1977).

Control of the Migrating Motor Complex

Thus far, the existence of the MMC had been shown. Further work was then carried out to elucidate the control mechanisms involved in the initiation of the MMC, both neural and hormonal.

(i) Neural Control of the MMC

Current concepts of the neuronal control of the MMC have derived largely from animal studies in which the integrity of the intrinsic or extrinsic nerves, or both, have been interrupted. Although initial work demonstrated that the extrinsic neural connections provided the pathway for the initiation and coordination of the MMC (Carlson GM, 1972), it is now known that the MMC continues to cycle following section of the vagus (Weisbrodt NW, 1975) or coeliac and superior mesenteric ganglionectomy (Marlett JA, 1979). Functional disturbances following vagotomy such as rapid gastric emptying do occur, but are probably due to a disorder of the vagally mediated receptive relaxation of the fundus (Thompson DG, 1982). Elegant work by Itoh *et al*, using a Thiery-Vella loop, showed that the MMC cycling in the loop was independent of the rest of the small intestine and that the extrinsic nerves were not a prerequisite for the initiation of the MMC (Itoh Z, 1981). Thus it would appear that the extrinsic nerves are not essential for continuation of the MMC.

The enteric nervous system (ENS) is complex and is the only part of the peripheral nervous system that is able to demonstrate reflex activity in the absence of the central nervous system (Kosterlitz HW, 1964). The ENS is thought to contain inhibitory fibres that suppress the contractions of the circular muscle. Tetrodotoxin, which blocks action potentials in nerves but not smooth muscle, causes the bowel to contract vigorously at the frequency of the slow wave

(Bortoff A, 1975). Further studies of extrinsically denervated bowel have shown cyclical activity similar to the characteristics of the MMC which switch to the more regular pattern of fed activity when infused with nutrients (Sarr MG, 1981, Sarr MG, Kelly KA, Gladen HE, 1981). Concluding from these studies, it would appear that the inherent patterns of motility, such as the MMC, are regulated by the intrinsic ENS and that changes in the basic pattern may be caused by the interaction of the ENS with external factors, such as the extrinsic nerves and hormones. In addition, recent evidence has shown that the interstitial cells of Cajal may play a vital role in the control of gastrointestinal motility (Barajas-Lopez C, 1989). These cells form a network in the myenteric plexus and the circular muscle and are thought to function as the pacemakers of the slow wave. They may also have a role in the neurotransmission of non-adrenergic, non-cholinergic activity. Further studies of the structure and function of the interstitial cells of Cajal are required before fully evaluating their role in the control of the slow wave.

(ii) Hormonal Control of the MMC

The hormone most commonly linked to the control of the MMC is motilin. This 22 amino acid residue hormone is present for the greater part in both the stomach and upper small intestine. It is felt to play a role in the initiation of the MMC as the infusion of motilin, immediately after a period of phase III activity, induces premature phase III activity within 20 minutes in dogs (Itoh Z, 1976). Similar findings were found in man, with the premature phase III activity occurring within 46 minutes (Vantrappen G, 1979). Lee *et al* showed dose dependent disruption of the MMC in dogs following the administration of anti-motilin serum (Lee KY, 1983). The complexes were effectively

abolished in the stomach and duodenum but the distal small bowel still showed some cyclical activity, suggesting that MMCs can occur distally independent of motilin, where the motilin receptors are proportionately less.

Further evidence for the role of motilin in the initiation of the MMC comes from studies in which the plasma levels of motilin have been monitored synchronously with the measurement of contractile activity in both dogs (Lee KY, 1978, Itoh Z, 1978, Thomas PA, 1979) and humans (Vantrappen G, 1979). Cyclical changes in the motilin level were found in association with the MMC, with the peak concentrations found just before or during the phase III activity of the stomach and upper duodenum and trough levels occurring during phase I. However although there does appear to be a connection between motilin and the MMC, the finding that the peak plasma levels of motilin do not occur until during the phase III activity has lead some investigators to suggest that the peak of motilin is caused by the contractions of the phase III (Sarna SK, 1983). Thus the cause and effect action between the MMC and motilin as yet requires to be resolved. Erythromycin has an action similar to that of motilin (Itoh Z, 1984) and a group of erythromycin derived drugs - the motilides - have been developed which have motilin agonist activity without antibacterial activity (Sunazuka T, 1989).

Other hormones, including cholecystokinin, somatostatin and secretin have also been implicated in the control of gastrointestinal tract motility. The normal fasting pattern of motility in human volunteers disappeared during infusions of CCK-octapeptide and was replaced by continuous irregular activity similar to that seen postprandially and is hence thought to participate in the conversion into fed motility pattern postprandially (Kellow JE, 1987).

Somatostatin (Hostein J, 1984) and its analogue Sandostatin (SMS 201-995) (Peeters TL, 1988) have both been shown to induce ectopic activity fronts in dogs. An association between pancreatico-biliary secretion, the release of pancreatic polypeptide hormone and phase III of the MMC has also been shown (Owyang C, 1983). However, the full effect of these hormones and their relationship to the MMC still require to be fully elucidated.

Further to the above neurohormonal control, relationships of the MMC have now been found with pancreatic and biliary secretion (Keane FB, 1980), intraluminal pH (Lewis TD, 1979, Bueno L, 1981, Houghton LA, 1990) and blood sugar concentrations (Fioramonti J, 1982).

Conversion of fasting to fed state motility

It is known that the cyclical fasting activity of the migrating motor complex in non-ruminant animals is interrupted by the ingestion of food and replaced by *fed activity*. This fed activity was seen initially in the dog and consisted of a pattern of varying amplitude, ungrouped contractions often superimposed on low-amplitude tone changes (Carlson GM, 1970). This finding was confirmed in humans (Vantrappen G, 1977). The cause of this change of motility required further evaluation. One mechanism may involve the presence of enteric chyme and intraluminal nutrients as a prerequisite for the conversion to fed activity (Heppell J, 1983). A further control mechanism implicates changes in the postprandial hormonal milieu as certain hormones, such as cholecystokinin (Mukhopadhyay SK, 1977) and pentagastrin (Weisbrodt NW, 1974), inhibit the MMC and induce a fed pattern. Similarly, hormonal factors were implicated by Hakim *et al* by studying autotransplanted loops of jejunum and ileum, which lacked

neural integrity and showed that infusion of nutrients into the autotransplanted loops led to disruption of the MMC in the stomach and duodenum (Hakim NS, 1989).

The effects of specific food components were studied by Schang by the perfusion of nutrients into a duodenal cannula in dogs (Schang JC, 1979). Their results demonstrated that the inhibition of the MMC depended on both the constituents of the food and the caloric content. Lipids caused the longest period of fed activity, followed by glucose, with peptides causing the shortest fed period. Increasing the caloric content of the meal resulted in a longer period of fed activity. Similar findings were shown by De Wever *et al*, who were able to demonstrate a linear relationship between the amount of calories of the test meal and the duration of the fed pattern and disruption of the MMC (De Wever I, 1978).

Effects of intraluminal content on fed motility

The volume of the ingested food may also play a part in the conversion of the motility pattern into fed activity. The initial experiment in this respect was by Code and Marlett, who were able to suppress the MMC in the stomach and duodenum of dogs by inflating a balloon in the stomach (Code CF, 1975). In pigs receiving one meal a day, the fed pattern lasted for about 6 hours. If the same quantity of food was given in two meals, the fed activity lasted for 2-3 hours and if fed *ad libitum* there was no disruption of the fasting motility (Ruckebusch Y, 1976), indicating that the volume of the food may have an effect. This finding may however be explained by De Wever's study demonstrating the linear relationship between the caloric content of a meal and the duration of the fed activity.

The jejunal response to gastric distension in dogs was studied by Bull and his colleagues in Sheffield (Bull JS, 1987). They showed that the latency for the conversion of the jejunal activity from a fasting to fed pattern was (mean ± sd) 7.1 ± 1.2 minutes when giving the dog a meal and 21.5 ± 2.7 minutes in response to distension by a gastric balloon. Although the latency periods were different, the patterns of jejunal motility under the two conditions were the same. A rapid response to feeding and distension would be easy to explain on the basis of a neural reflex, with tension receptors in the corpus detecting the degree of distension and reflexly increasing the vagal afferent discharge to the gastrointestinal tract (Andrews PLR, 1980). Indeed the importance of the vagus in the establishment of fed activity has been shown by Diamant, as vagal blockade, by cooling of the exteriorised vagal trunks, caused a return to fasting activity (Diamant NI, 1980). However the prolonged latencies obtained by Bull following gastric distension with a balloon would be difficult to explain on a neural basis alone.

The viscosity of the intraluminal content also plays a role in the contraction parameters of the gastrointestinal wall. Kelly showed that inert isotonic liquids are evacuated rapidly from the stomach (Kelly KA, 1980). This rapid evacuation was related to their low viscosity and low streaming resistance, causing only a small increase of wall tension during contractions of the proximal stomach. Prove and Ehrlein subsequently established that an increase in viscosity of the intragastric content diminishes the rate of gastric emptying (Prove J, 1982). Owing to the larger streaming resistance of the viscous contents the contractions of the proximal stomach produce an activation of the in-series tension receptors. By increasing the

viscosity of the content, the antral contractions are reduced, probably due to a reflex elicited by the tension receptors of the antral wall. The consequence of a larger orifice of the antral constricting ring is a reduction of forward flow and an increase in the retropulsion, resulting in delayed gastric emptying.

Hence it can be seen from the above experiments that further to the neurohormonal control of gastrointestinal motility, the volume and viscosity of the intraluminal content may affect the conversion to fed pattern and the duration of the subsequent fed activity. Fasting motility, with its benchmark events of the phases, cycle frequency and migration velocity of the migrating motor complex provides a measurable phenomenon for the evaluation of clinical motility disorders. However, there is less information relating to the role of intraluminal content on fasting motility. In humans, Rees was able to alter the intragastric volume by instilling up to 400 mls of saline into the stomach without disrupting the fasting cycle (Rees WD, 1982), but the effects on MMC variables, such as cycle frequency and phase duration, are unknown.

Measurement of Gastrointestinal Motor Function

Abnormalities of motility may contribute to the development of clinical disorders, including gastro-oesophageal reflux (Vantrappen G, 1990), small bowel bacterial overgrowth (Vantrappen G, 1977) and functional dyspepsia (Waldron B, 1991). Scientific advances in the management of these conditions requires comprehension of the process involved and an adequate means of measurement. Several methods address measurement of gastrointestinal motor function and are considered below.

Manometry

Manometry, as the name suggests, measure intraluminal pressure changes within the gastrointestinal tract, resulting from smooth muscle contractions. This method remains the gold standard for human studies and provides very detailed information. It has the advantages of measurement of response to a specific stimulus, eg in the oesophagus, demonstration of contraction propagation after a wet or dry swallow is useful, while in the rectum the demonstration of the anal reflex, ie a fall in anal sphincter pressure in response to rectal distension, is of value in the investigation of neuromuscular integrity. Hence, manometry provides the basis of a reproducible stimulus response test, in certain circumstances.

The facility of measurement of detailed contraction characteristics allow assessment of the migrating motor complex and demonstration of specific pattern abnormalities. The cluster contractions of chronic or subacute small bowel intestinal obstruction (Summers R, 1983) is a notable example.

Although manometry provides detailed information of physiological and diagnostic importance, there are disadvantages.

Firstly, the method is invasive. Essentially, a tube or probe bearing pressure sensitive devices, spaced at fixed intervals, is passed per nasally, per orally or per anally and left in position. The standard technique utilises a multilumen low compliance perfused tube, with pressure ports at spaced intervals. The water column in each lumen of the tube is linked to a separate pressure sensor, which is connected to a chart recorder for accurate demonstration of pressure variation. Recent advances have utilised finer bore solid state devices, linked externally to battery powered data memory packs, which have enabled ambulatory studies. However, the invasive nature of the test has limited its application. It is noteworthy that few manometry studies of clinical subacute obstruction have been carried out despite the diagnostic difficulty of this condition.

The detail of the information provided by manometry can be a disadvantage in terms of the large quantity of data which is generated for subsequent analysis. Physiological events in motility occur slowly and in the stomach and small bowel prolonged recording is preferable (Thompson D, 1980). In a 24 hour recording of 3 sensors, many thousands of contractions may be detected on which important contraction patterns and different artefact events are superimposed. Although some simple computer techniques for peak detection did exist, these lacked sophistication. None had facilities for pattern recognition, detection of the MMC, nor artefact removal. Hence, reliance was placed on manual interpretation by a skilled observer, until the advent of the work contained in this thesis. The great variation of fasting manometry results (Vantrappen G, 1977, Thompson D, 1980) in normal volunteers represents a further limitation of manometry as a benchmark test.

Non-invasive measurement of gastro-intestinal motor function

Scintigraphy

Radionucleide scintigraphy is a convenient method, by which isotopes may be bound to physiological foods, and movement of ingested material may be imaged using a gamma camera. The technique is well appraised by Horowitz (Horowitz M, 1985). This method is more appropriate for fed state motility and provides useful information on transit in several areas of the gastrointestinal tract, for example in the detection of oesophageal motility disorders, such as achalasia, diffuse oesophageal spasm and scleroderma (De Caestecker J, 1986), gastroparesis and abnormalities of gastric emptying following gastric surgery (Smout A, 1987) and small bowel and colonic transit (Read N, 1986). However, scintigraphy only examines the transit of the intraluminal content, which may be a crude reflection of gastrointestinal motor activity, eg there has been shown to be only a weak correlation between transit and the contraction frequency of the upper jejunum (Read N, 1984).

Radiology

Contrast radiology provides an excellent outline of the structure of the gastrointestinal tract and gives some information as to transit, but is generally considered to be an unphysiological approach in the assessment of motility. The contrast agents may be stimulatory and prolonged radiation makes this method unsuitable.

Gastric Impedance

Gastric impedance can be used as a measure of gastric emptying (McClelland GR, 1985). The technique of impedance epigastrography relies on changes in impedance to the passage of an alternating current (4 mA at 100 kHz) between electrodes placed on the anterior and posterior abdominal wall. Conductance of the electric current depends on the medium between the electrodes : a fluid filled stomach conducts better than an empty stomach. A reasonable correlation has been demonstrated between impedance and scintigraphy (Sutton JA, 1985). Impedance Epigastrography can also be used to measure conducting test meals (Mangnall YF, 1988), providing that acid secretion is inhibited by cimetidine, as acid secretion affects conductance. It is a useful research tool, but as yet has not found a clinical application. Its major limitation is that it is unsuitable for the evaluation of solid gastric emptying.

Applied Potential Tomography

Applied Potential Tomography displays sequential measurements of the resistivity of gastric contents after a subject has ingested a liquid or semi-solid meal. It utilises 16 electrodes placed around the abdomen. A current of 5 mA at 50kHz is passed between pairs of adjacent (drive) electrodes, and the potential differences between the 13 remaining electrode pairs are measured. Each pair of electrodes then act cyclically as the drive electrodes, and the resultant data is summated. Applied potential tomography can be used to follow emptying of conducting meals although acid secretion has to be inhibited as well. In patients after gastric surgery, however, it was not possible to image the stomach on 6/54 occasions (Avill R, 1987).

Ultrasonography

High resolution ultrasonography can provide images of the gastric antrum with a variety of test meals, which has the advantage of being both non-invasive and radiation-free. Gastric volumes can be calculated using a technique of summating the values of serial cross-sectional areas (Bateman DM, 1982). Antral emptying curves can be evaluated by measuring a sagittal slice of the antrum with respect to time, using the aorta as a reference point. The curves obtained show a 50% reduction of the antral area over 60 minutes, dropping to 60-65% at 90 minutes. However it is difficult to detect the fundus accurately due to the presence of gas, and total gastric volumes obtained are often unreliable. Furthermore, visualisation is poor in both obese patients and patients who have had previous gastric surgery.

Hydrogen Breath Test

The hydrogen breath test enables measurement of the orocaecal transit time. It relies on the rapid fermentation of nondigestible carbohydrate, on entering the caecum, by colonic bacteria generating hydrogen gas. This hydrogen gas diffuses into the capillaries and 10% of the total hydrogen generated is excreted in expired air (Levitt MD, 1969). Using an interval sampling procedure, the time of a rise in the breath hydrogen can be evaluated. There are however limitations to its measurement of the orocaecal transit time. It may be difficult to distinguish between rapid transit and a hydrogen rise caused by fermentation of the substrate due to small bowel bacterial overgrowth. Furthermore, antibiotics may eradicate the colonic bacteria making the test unsuitable in patients receiving antibiotics (Murphy EL, 1972). Despite these limitations and with appropriate precautions, it provides a useful evaluation of small bowel

transit.

In addition to studying the movement of the intraluminal content within the gastrointestinal tract, techniques have been developed to assess the electrical activity of the stomach, since the pioneering work by Alvarez in 1922 (Alvarez WE, 1922). In much the same way as the electrocardiogram (ECG) is a recording of the depolarisation potentials of the cardiac muscle, the electrogastrogram (EGG) is able to record the slow wave depolarisation potential of the stomach. Using this technique, abnormalities in the gastric slow wave activity have been demonstrated in motion sickness (Stern RM, 1987, Rague BW, 1987), gastroparesis (Abell TL, 1985, Pfister CJ, 1988) and the nausea of pregnancy (Koch KL, 1987). However this technique is limited, as the previous techniques also were, in that it is only able to look at the activity of the stomach without any evaluation of the gastrointestinal tract distal to the stomach. In addition there is a large amount of artefact, caused by the increased gain required to record the low amplitude of the gastric slow wave and from the superimposition of signals arising from multiple sites in the gastrointestinal tract (Familoni BO, 1991). This problem makes the reading of large portions of the EGG undecipherable. Furthermore, the clinical relevance of tachygastria, which is the commonest abnormality recorded by EGG, has previously been questioned (Familoni BO, 1991).

Assessment of motor function by measurement of bowel sounds

The monitoring of bowel sounds as a parameter for evaluating gastrointestinal motility was first proposed by Cannon, who wrote the first systematic account of auscultation of the abdomen in relation to the function of the stomach and intestine (Cannon WB, 1905). In 1954, Du Plessis developed a method of recording bowel sounds using a phonocardiogram placed on the abdomen, which was linked to a pen recorder (Du Plessis DJ, 1954). Chart recordings of bowel sounds were thus obtained and were divided into first-degree bowel sounds, caused by propulsive contractions, and second-degree bowel sounds, caused by segmentation. His studies however were observational and it proved difficult to confirm that the bowel sounds generated were either propulsive or segmenting in character.

Farrar and Inglefinger believed that bowel sounds were generated by the movement of gas within the gastrointestinal tract and developed a quantitative analysis of sound as an index of gastrointestinal motor activity (Farrar JT, 1955). However they found a poor correlation between balloon kymograph recordings and abdominal sounds unless potent motility drugs were administered to control motility namely prostigmine and mepiperphenidol bromide. They felt that the poor correlation was explained by local motor phenomena caused by the balloon itself which could only be abolished by the potent drugs administered. Although subjective in nature, this was the first experiment to compare quantitative sound recordings with intraluminal manometry.

Horn and Mynors reported the technical problems of interpreting bowel sounds (Horn GE, 1966). The amplification required for the low intensity of the majority of bowel sounds resulted in high

hiss or noise levels and microphones at that time had poor signal to noise ratios, compounding the problem. Watson and Knox utilized an automatic sweep frequency analyser which filtered selected sounds at a constantly rising frequency, to produce a record of the relative intensity and rising frequency of the bowel sounds (Watson WC, 1967). They were able to demonstrate that bowel sounds are a mixture of tones and that they have a frequency range of 150-5000 Hz.

More recently, multiple microphones placed on the abdomen have been incorporated to a multichannel analyser to yield a topographical registration of intestinal activity (Garner CG, 1989). They used a low pass and high pass filter to exclude artefactual noise and low frequency heart beats. In addition they utilised an "artefact detector" microphone placed on the side of the bed, to demonstrate room noise artefact. Although problems were encountered with poor signal registration from a multi channel pen recorder, they concurred with Watson and Knox that the frequency range of bowel sounds was 100-5000 Hz. None of the techniques for the measurement of bowel sounds have as yet developed into a clinically useful test.

SUMMARY

Gastrointestinal motility is an important physiological process, which contributes to gastrointestinal synchrony, digestion, absorption and excretion of waste. Despite many years of research, our comprehension of the role of disordered motility in common clinical problems remains poor. Objective data is lacking, hampered by the limitations of current methodology for motility measurement. The current gold standard is not ideal, for reasons previously discussed.

An ideal method would be:

(*i*) **non-invasive**: this confers obvious advantages to the patient and does not disturb the normal gastrointestinal milieu.

(*ii*) **reproducible**: the results should be reproducible and have little inter and intra subject variation.

(*iv*) **adequate detail**: there must be enough relevant detail, from which clinical information may be elicited.

(*v*) **response to stimulus**: the method should be able to respond accurately to various stimuli on the gastrointestinal tract.

Accordingly, in a collaborative project between the departments of Surgery and Physics, we have developed a non-invasive method for the evaluation of gastrointestinal motility, called Surface Vibration Analysis (SVA).

Chapter 2

Surface Vibration Analysis

Background to Project

SURFACE VIBRATION ANALYSIS

Surface Vibration Analysis (SVA) is a non-invasive method of detecting vibrational energy emanating from gastrointestinal activity and has been developed as a collaborative project between the Departments of Surgery and Physics, University of Dundee. The SVA system has been described previously (Cullen PT, 1989). It is based on a piezoelectric electromechanical transducer (accelerometer) which is placed on the abdominal surface (Figure 2.1). This generates an electrical signal in response to vibrational energy, which is amplified, passed through a high pass frequency filter (vide infra) and then fed to a digital integrator (vide infra) before display and analysis by microcomputer (Figure 2.2). The accelerometer has several advantages over a surface microphone, viz.:

i) Direct Coupling

An accelerometer is directly coupled with a vibrating surface and avoids the inefficiency of an air interface. In addition, because of their rigid construction, pressure variations in the air have little effect on the piezoelectric element, giving *low acoustic sensitivity.*

ii) Charge Sensitivity

The charge sensitivity is a measure of the efficiency of a transducer and is defined as the ratio of the electrical output to the mechanical input. Accelerometers have a greater charge sensitivity than microphones, thus reducing the need for high amplification of the input signal, with resultant less distortion.

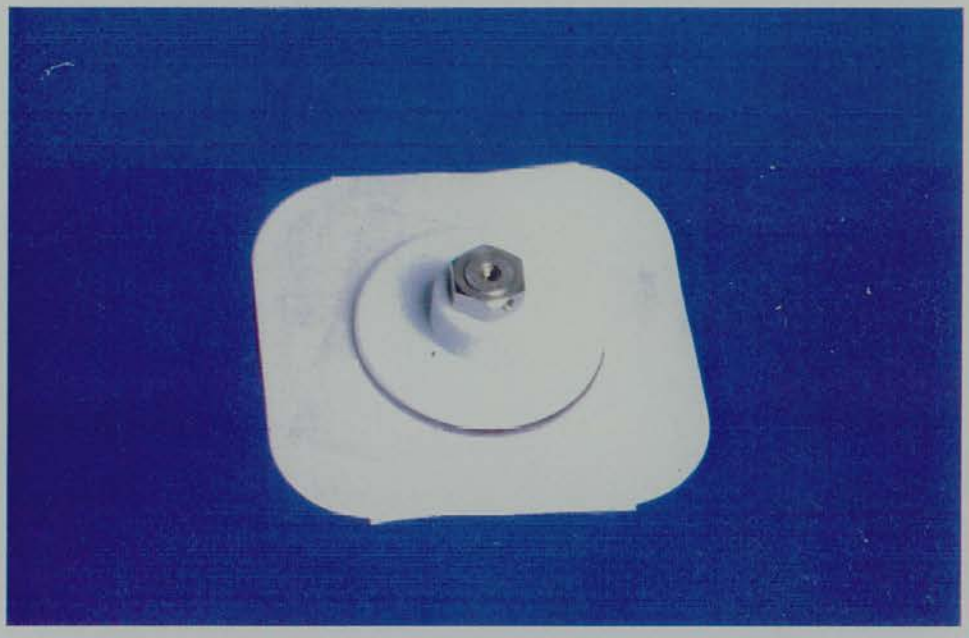

Figure 2.1. The SVA accelerometer, mounted on a teflon cuff. The accelerometer converts the vibrational energy at the abdominal surface into an electrical signal.

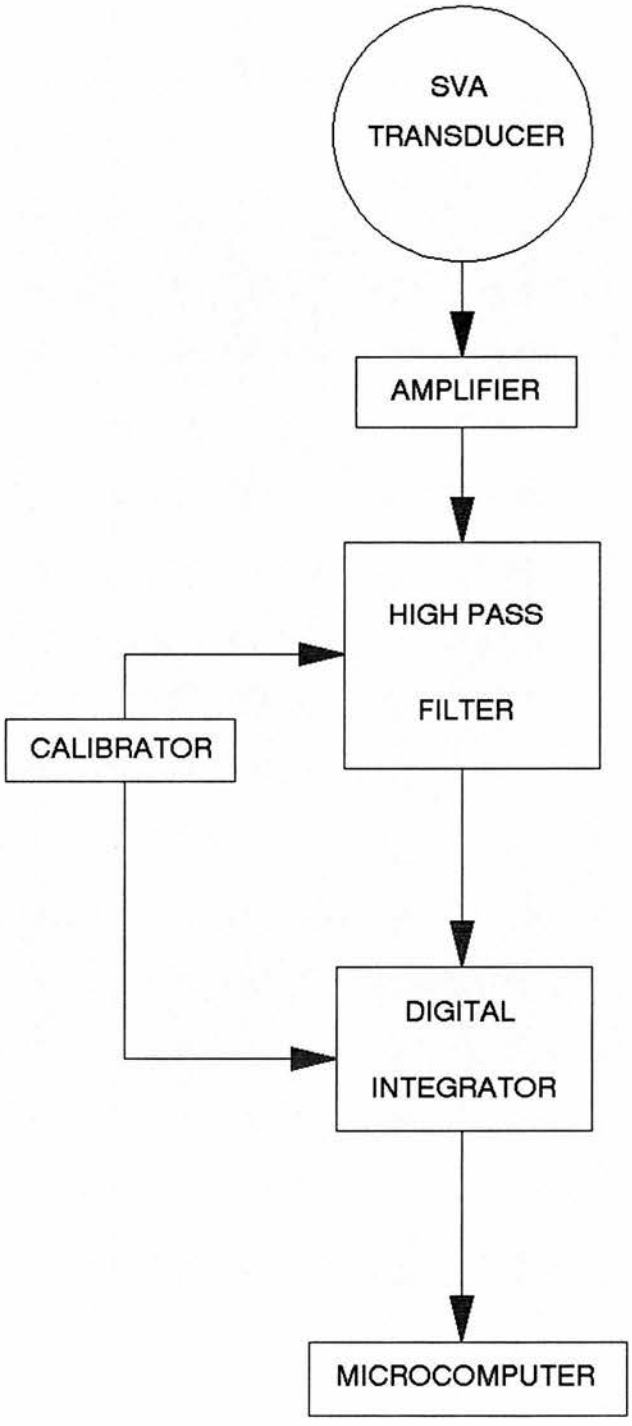

Figure 2.2. Schematic diagram of the SVA system. The calibrator is used to calibrate the SVA signal at the onset of each study.

iii) Resonant Frequency

If the natural resonant frequency of a system is in the same frequency range of the input signals, then natural resonance and distortion will occur. The undamped natural resonant frequency of the accelerometer was 19000 Hz, which is well outwith the frequency range of bowel sounds as shown by Watson and Knox (Watson WC, 1967).

Preliminary observations using this system showed that there appeared to be a regular, repetitive energy signal which was considered to be due to the aortic pulsation. Frequency analysis of this signal, by Fast Fourier Transform using ILS software[1], showed it to occupy a narrow frequency range outwith the acoustic spectrum at 40 Hz, with two consistent peaks at 14 Hz and 21 Hz. At frequencies above 40 Hz, signal strength fell to background levels. In view of this, a 4 pole high pass filter was constructed which gave a flat response to signals above 80 Hz, but with progressive attenuation below that level, to effectively block signals at 40 Hz. In addition, a high frequency filter was utilized to block frequencies above 10,000 Hz, to exclude high frequency electronic noise. This bandpass filter gave a flat response between 80 Hz and 10,000 Hz. The input signal from the accelerometer was amplified by a Bruel and Kjaer type 2626 amplifier[2].

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[1]Interactive Laboratory Systems, Signal Technology Inc., Goletta, California.

[2]Bruel and Kjaer Instruments, Copenhagen, Denmark.

In order to digitise any bipolar signal, the sampling rate must be at least twice the frequency of the input signal frequency, so that there is a minimum of one sample for the peak, and one sample for the trough. This would mean a sampling rate of 10,000 Hz as the upper range of bowel sound frequencies is 5000 Hz. Over a typical recording time of 4 hours this would generate 288 Megabytes of data, which grossly exceeds the RAM capacity of conventional microcomputers. To overcome this problem, a means of averaging or integrating the signal without any quantitative loss was developed. Input signals were sinusoidal waves comprising positive peaks and negative troughs of approximately equal intensity. Hence, the sum of the amplitudes would approximate to zero. This problem was overcome using the principle of rectification, which is a standard in measurement of alternating signals. This technique removes negative excursions, leaving only positive deflections. A rectifier circuit was therefore incorporated.

The method of integration of the signal employed a purpose built circuit which integrated the signal over a fixed time interval. To set this time interval, it was felt that the simplest discrete gastrointestinal motor event (a contraction) should be represented. The highest contraction frequency is in the duodenum and jejunum at 9-12/min (Fleckenstein P, 1978) or approximately one every 5 seconds. An integration signal of 5 seconds was chosen so that a single contraction could be accommodated within at least one interval, giving a reasonable compromise between simplification and resolution.

The signal was further smoothed by a sample and hold circuit which measured the amplitude of a pulse and retained this value until the next spike occurred, when the process was repeated. Thus, only the

peaks of the amplitude were recorded, giving a smoother output. Thus far we were able to monitor the profile of the SVA response, but in order to compute the integrated SVA signal during any desired period, a "Digital Integrator" unit was developed. This unit passed the signal through a voltage to frequency (v-f) converter, passing the generated signal into a digital counter with a seven segment LED display. The number registered on the digital display was proportional to the frequency and hence to the voltage as a function of time. Thus, the reading was proportional to the area under the signal vs time curve.

Finally, the signal was fed into a microcomputer, to allow the total data from a 4 hour recording interval to be displayed on a single monitor screen. For this purpose a BBC microcomputer[3] with an inbuilt analogue to digital converter, with a sampling rate of 20 Hz was chosen. The total SVA system is shown in Figure 2.3.

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[3]Acorn Computers Ltd., Cambridge, England.

Figure 2.3. The total SVA system, linked to a BBC microcomputer.

Quantitative Measurement by Surface Vibration Analysis

Further development of this novel technique was initially hampered by the lack of any standard quantitative unit for vibration energy measurement. Vibration energy within the acoustic range is measured using the decibel scale which is a logarithmic ratio of 2 acoustic values. These had been chosen for their relationship to an arbitrarily defined human hearing threshold. There are no standard measurement units relating to vibration outwith the acoustic range. Despite the lack of any standard quantitative unit, measurement of vibration outside of the acoustic spectrum is widely used in clinical measurement, eg ultrasound scanning and the Doppler assessment of blood flow. In the application of the SVA method described within this thesis, quantification is important. Thus, it was necessary to define a *linear* standard measurement scale which would embrace vibration energy both within and outwith the acoustic spectrum. Within the SVA system, the surface transducer converts vibration energy at the abdominal surface into an electrical signal. This voltage is proportionately converted by the analogue to digital converter (ADC) to a digital number. The ADC within the SVA system is a 12 bit converter, ie its digital output can take up any one of 2^{12} values. Thus the output of the ADC lies between a minimum of zero and a maximum of 4096 (2^{12}), thereby defining a linear scale which was directly proportional to the voltage responses of the sensor. The term *vibration energy units* was applied to this linear scale and was standard for all studies in this thesis.

Previous studies with the Surface Vibration Analysis (SVA) system

1. Effects of clinical mounting of the accelerometer on the signal response.

The accelerometer, in its normal industrial use, is mounted rigidly to minimise any vibration interference. This was obviously not possible in the clinical context and therefore the attenuation of the signal, caused by the clinical mounting of the accelerometer, was assessed. The accelerometer was secured by adhesive tape to a vibrating table, which vibrated at various selected frequencies to allow analysis of the degree of signal attenuation at preselected frequencies. A gradual signal attenuation above 4000 Hz, with a 20 dB reduction in amplitude at frequencies above 6000 Hz was observed. As the upper limit of bowel sound frequencies is around 5000 Hz, it was felt that electronic boosting of the upper frequency signals was not required.

2. Effects of abdominal wall on signal response.

The degree of signal attenuation by varying abdominal wall thickness (from 1.5 cm - 3 cm) using animal muscle and fat, alone and in combination was also assessed using the vibration table. These experiments showed that muscle was associated with greater attenuation of signals over 640 Hz than adipose tissue, but that this attenuation was not proportionately related to wall thickness. This work showed that variation in signal attenuation due to biological variation in muscle and fat thickness was likely to be small.

3. Relationship of quantitative SVA measurement to gastrointestinal transit

Quantitative measurements by the SVA system have been shown to relate to gastrointestinal motor function, as a significant correlation between SVA energy values and oral to caecal transit time of solids has been demonstrated (Campbell FC, 1989).

4. Detection of Intestinal Contraction Patterns

(a) Cluster contractions. SVA has been shown to be able to detect the high amplitude "cluster contractions" in both volunteers with experimentally induced small bowel obstruction and patients with partial intestinal obstruction (Cullen PT, 1989).

(b) Gastric phase III. The SVA response has been shown to correlate with phase III of the gastric migrating motor complex (MMC) (Cullen PT, 1990).

In conclusion, therefore, evidence has been provided that the SVA system provides an objective measurement which relates to gastrointestinal motor activity and that high amplitude energy contractions may be detected. Data showing high SVA readings in the fed state, which considerably exceed those of the fasting state, suggest that intraluminal content may be important. However, despite the success of SVA in these areas, many essential points concerning signal generation remain unproven, and require further elucidation. The basic principle of SVA is the exploitation of the vibrational energy that emanates from the gastrointestinal tract. It thus addresses both the movement of the gut wall and the intraluminal contents, but the relative contribution of these two factors remains obscure. In particular, there are no data to indicate whether movement of the gut

wall alone, in the absence of intraluminal content, is sufficient to produce vibrational energy to generate a SVA signal.

Previous work showed an encouraging correlation between SVA and the gastric MMC, but no such correlation with the small bowel MMC was demonstrated. Most of the variables which affect the SVA response to small bowel contractions are beyond our influence, ie the contraction amplitude within the small bowel cannot be increased, the abdominal wall cannot be altered and the sensitivity of SVA detection cannot be increased, without increasing background pickup. However, fasting intraluminal content could potentially be altered if this proved to be an important variable, in the improvement of the detection rate.

AIMS

This thesis will seek to develop the SVA system further, as a clinical measurement tool. Primary objectives include:

1. **Evaluation of factors which may influence detection of gastrointestinal contractions by SVA, including:**
   (a) Intraluminal Content
   (b) Accelerometer Position
2. **Evaluation of SVA against the current gold standard of manometry, in the measurement of gastrointestinal motility**
3. **To assess SVA in the evaluation of some clinical disorders**

Certain preliminary work and development were necessary to enable us to pursue the above aims to a satisfactory conclusion. Firstly, it was necessary to ascertain the contribution of any motility variation, resulting from variation in intraluminal content, to variation of SVA signals. Secondly, in any comparison of SVA against manometry, the weaknesses of conventional manometry assessment require to be addressed. Thirdly, a more objective means of evaluation of SVA vs manometry than visual assessment is required. Therefore, the secondary aims of this thesis are:

1. **The evaluation of intraluminal content on normal fasting manometry**
2. **The development of automated analysis of gastric and small bowel manometry**

Chapter 3

Fasting Gastrointestinal Motility: Effect of Variation in Intraluminal Content

INTRODUCTION

The SVA system was constructed to measure vibrational energy at the abdominal surface. This energy varies with applied force, but is also is dependent on the density of the medium to which it is applied (Bishop RED, 1979). The ripples from a stone thrown into a pond of water reach further than those of a pond of mud. In the context of the gastrointestinal tract, force is applied by the contractions, which have relatively constant maximal values in given regions of the gastrointestinal tract (Kellow JE, 1986). However, the volume and density of intraluminal content may be variable. Thus, it is desirable to ascertain the influence of intraluminal content on vibration energy and SVA signals, *for a given contraction amplitude.* Herein lies the difficulty. It is possible that variable content could also affect contraction frequency and amplitude in the fasting state, but data are lacking.

The work described in this chapter was intended to test the hypothesis that the fasting gastrointestinal tract may be responsive to volume changes of intraluminal gas or acaloric liquid, with effects on the contractile characteristics. Subsequent chapters will assess the effect of these factors on the SVA response.

MATERIALS AND METHODS

Volunteers

Twenty volunteers, 6 women and 14 men, aged 20-31 (median age 24 years) participated in the study. All were healthy with no gastrointestinal symptoms or previous surgery. In view of the requirement for fluoroscopy a detailed menstrual and contraceptive history was taken from all female volunteers and the likelihood of pregnancy was judged to be remote. All volunteers gave their informed consent to the protocol, which had been approved by the Tayside Health Board Medical Ethical Committee.

Study Design

The perfusion catheter was constructed using two triple lumen pressure monitoring tubes[4] (Internal Diameter [ID] : 0.78 mm, Outer Diameter [OD] : 2mm, Length 3 m) and a single 3 metre radio-opaque tube[5] (ID : 1.0 mm, OD : 2mm) bonded by tetrahydrofuran glue[6]. This allowed 5 channels for manometry, one for inflation of a distal balloon to aid positioning in the caecum and the radio-opaque tube which was perforated throughout its distal 230 cm, provided one channel for evacuation of both gas and intestinal secretion by aspiration. Manometry ports were each marked by a radio-opaque metal marker. The first 2 ports were spaced 5 cms apart (for antral

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[4]Dural Plastics, New South Wales, Australia

[5]Portex Ltd, Hythe, England

[6]BDH Chemicals Ltd., Poole, England

recording) and the distal 3 ports 12 cm apart (for duodenal and jejunal recording). The total diameter of this composite tube was 5.5 mm and total length 3 meters.

In addition to this composite orocaecal tube, a paediatric nasogastric tube (French Gauge 10 - ID : 2 mm, OD : 3.0 mm), which was perforated over its distal 20 cms, was also utilized for both evacuation and instillation of gas and fluid to the stomach.

After an overnight fast, the volunteers swallowed the perfusion catheter and the nasogastric tube. The tubes were positioned under fluoroscopic control, using a GEC Cardiovision image intensifier[7] with the minimum field size as appropriate for the procedure. The maximum exposure time was 20 seconds at 79 kV and 0.05 milliamps, giving a skin entrance radiation dose of 3 mGy. Gonadal shielding was provided by placing a lead apron over the pelvis. Once the distal tip of the orocaecal tube was beyond the pylorus, the balloon was inflated and peristalsis carried it to its required location in the caecum. Once in position, the balloon of the orocaecal tube was deflated and both orocaecal and nasogastric tubes were taped to the side of the volunteer's cheek. In this position, the perforated segment of the radio-opaque tubing lay between the first part of the duodenum and the caecum. The paediatric nasogastric tube was then aspirated and tested for pH. The use of 2 perforated tubes allowed separate aspiration from the stomach and the small bowel.

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[7]GEC Medical, Suffolk, England

After 15 minutes of acclimatization, a total of 5 studies were carried out in the following sequence in all subjects, over 3 hour intervals each, viz:

(i) in the **Baseline** fasting state (*BL*)

(ii) after **Gas and Fluid Evacuation** (*GFE*) from the upper GI tract, through the perforated orocaecal and nasogastric tubes. Both the orocaecal tube and the nasogastric tube were aspirated at 15 minute intervals throughout this study, and gas and fluid volumes from stomach and small bowel were each recorded separately.

(iii) after **Intragastric Instillation of Gas** (*IIG*) [350 mls air]

(iv) after **Intragastric Instillation of Fluid** (*IIF*) of low viscosity [350 mls 0.5% methylcellulose solution - viscosity - 2.95 Centipoise]

(v) after **Intragastric Instillation of Fluid** (*IIF*) of high viscosity [350 mls of 5% methylcellulose solution - viscosity - 325.6 Centipoise]

After each study there was an interval of one hour to allow the bowel to return to its original state as far as possible. The nasogastric tube was aspirated to remove excess perfusate or gas from the stomach. The position of the catheter was confirmed by fluoroscopy at the beginning of each study in all subjects and at the beginning and end in 3 subjects. No evidence of migration was observed. To minimize radiation exposure, the examination at the end of each study was omitted for the remaining 17 subjects and reliance was placed on observation of real time motility recordings for any change of the contraction characteristics, which might have indicated tube migration. For example, if significant movement occurred, then the antral channel would move to the duodenum, with a corresponding change in the contraction characteristics.

At the end of the whole study, both the nasogastric tube and the perfusion catheter were withdrawn by gentle traction.

Study Comparisons

a) *Between Study Comparisons*

The characteristics of the migrating motor complexes (MMC) during the evacuation and instillation studies were all evaluated against the baseline study. In instillation studies, the characteristics of the first occurring migrating motor complex (MMC) after gas and fluid instillation were used in assessment against baseline. In addition, the effects of isovolumetric gas and fluid instillates of variable viscosity on motor activity were also compared with each other.

b) *Within Study Comparisons*

Within study comparisons were possible where two MMC cycles occurred during the same study interval. Observations were confined to phase II during these studies. In the baseline and instillation studies the contraction amplitude of phase II of the first MMC was compared with the subsequent phase II. In 4 volunteers in the *GFE* study, 350 mls of air was reintroduced into the stomach during phase II of a duodenal MMC and then reaspirated after a 30 minute period. This allowed comparison of effects of content evacuation and instillation on contraction amplitude *within* a single phase II.

Motility Recording

Perfusion of the manometry channels of the multilumen catheter was carried out at 0.2 ml/min, using a low compliance, pneumohydraulic pump[8]. Before commencement, the sensitivity of the apparatus was calibrated, using a modified sphygmomanometer applied to each manometry port, to give an identical vertical deflection of 20 mm for each amplitude rise of 10 mmHg. The manometry perfusion catheter was then connected to external pressure transducers with one for each port[9]. Manometry signals recorded by this method were then digitized at 5 hertz by an Amplicon Model PC-30 analog to digital converter[10] then processed and displayed in five channels on an Opus V microcomputer running our own purpose-designed software ("PC-Motil") for acquisition and display of motility data (Waldron B, 1991).

The Arndorfer system was checked for variation in baseline recording by placing the manometric catheter in an enclosed water tube and recording the data for 30 minutes. This revealed a uniformly flat baseline without any significant drift or artefactual contractions, indicating that there was no significant problems with, for example, air bubbles in the water perfused system.

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[8]Arndorfer Medical Specialties, Greendale, Wisconsin

[9]Bell & Howell Ltd., Basingstoke, England

[10]Amplicon Liveline, Brighton, England

During the recording periods, the online manometry recordings were checked visually to ensure that the antral ports had not migrated into the duodenum. Hard copies of motility tracings were provided by a linked digital plotter[11] at a scale of 20 mm/10 mmHg amplitude.

Motility Analysis

The phases of the Migrating Motor Complex (MMC) were defined by recognized criteria (Sarna SK, 1985, Szurszewski JH, 1969). Phase I was defined as the interval of quiescence which separates the end of phase III and onset of phase II. Phase II comprised irregular contractions which followed the quiescence of phase I and terminated in the regular contractile activity of phase III. Phase III comprised frequent regular contractions which terminated in a return to the quiescence of phase I or were followed by a few intermittent contractions of phase IV. Only phases I-III were considered in these studies and analysis of phase III was confined to the sequence of regular activity only. The amplitude of each contraction within phase II and phase III of each migrating motor complex (MMC) was measured against the calibration scale in the vertical axis and expressed in millimeters of mercury (mmHg). Amplitude measurements were taken from the recording baseline. Contraction frequency was calculated as the quotient of the total number of contractions and the total time in minutes. The migration velocity of the MMC was measured in the small bowel and was taken as the quotient of the inter-port distance and the time difference in minutes between the first contraction of phase III

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[11]Advanced Bryans Instruments, Mitcham, Surrey, England

in the proximal channel and the first contraction of phase III in the subsequent channel.

Statistical Analysis

The duration of the individual phases of the MMC, the contraction frequency of phases II and III and the volumes of gas and fluid aspirated during the *GFE* study had a skewed distribution and were expressed as the median and inter-quartile range of the pooled data. The values for the contraction amplitude were normally distributed and were expressed as the mean and standard error of the pooled data for each study. The Mann Whitney U test was used for comparison of contraction amplitude and frequency between studies. The Wilcoxon rank test was used for comparison of within study contraction amplitude, as appropriate for paired data. Differences were considered significant at the $p < 0.05$ level. Bonferroni's correction to the significance level was applied to repeat 2-sample tests.

RESULTS

All subjects showed fasting motility data without conversion to fed activity following instillation or withdrawal of gas or acaloric liquid. The intubation time (time taken for the distal tip to reach the caecum) was 3-8 hours (median 5.3 hours). In no subject did antral tracings change in either port to those of a small bowel pattern. The total number of Migrating Motor Complexes in each study is shown in Table 3.1.

Between study comparisons - MMC phases I and II

(a) Gas and Fluid Evacuation vs Baseline

Aspirated Volumes

A total of (median [inter-quartile range]) 220 [139 - 482] mls gas (stomach : 185 [68 - 460] mls, small bowel : 35 [19 - 49] mls) and 270 [192 - 425] mls of fluid (stomach : 250 [80 - 412] mls, small bowel : 20 [17 - 30] mls) were aspirated during the course of the *GFE* study. The median interval volumes obtained for gas and fluid aspiration are shown in Figure 3.1.

Phase Duration

In 3 volunteers, *GFE* effectively abolished phase II in the duodenum and jejunum (Figure 3.2). The duration of phase I was increased and the duration of phase II decreased in the duodenum and jejunum (Figures 3.3 & 3.4) after aspiration of intraluminal content. There was no change in the duration of phases I & II in the antrum.

Contraction Characteristics

Phase II contraction amplitude decreased following *GFE* in the antrum and duodenum but remained unchanged in the jejunum (Table 3.2). The contraction frequency of phase II was unchanged (Table 3.3).

Table 3.1.

Total Number of MMCs within each study

	Antrum	Duodenum	Jejunum
BL	17	18	17
GFE	18	24	26
IIG	24	27	25
IIF (low viscosity)	18	20	22
IIF (high viscosity)	19	26	23

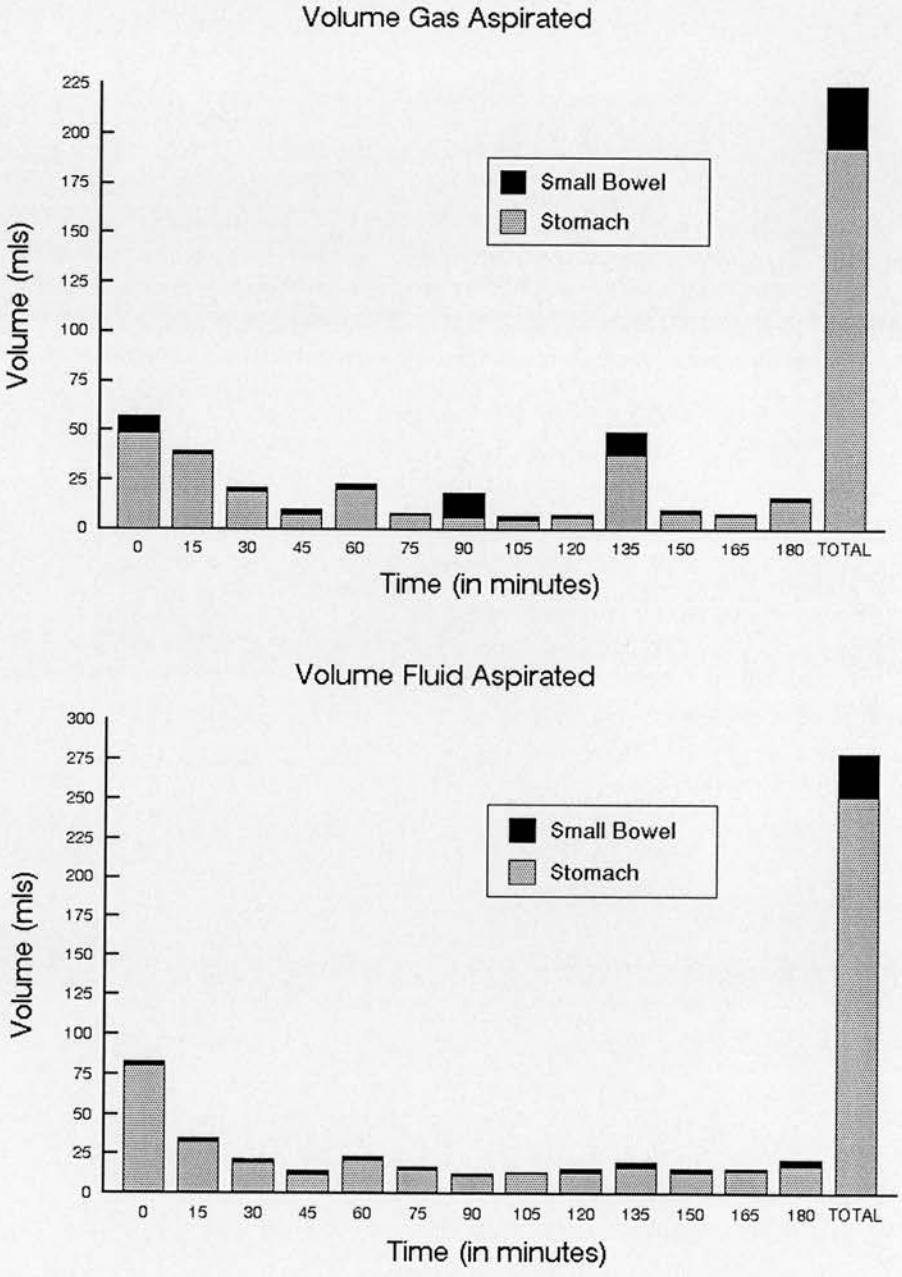

Figure 3.1. The volumes of gas and fluid aspirated from the stomach and small bowel during the *GFE* study

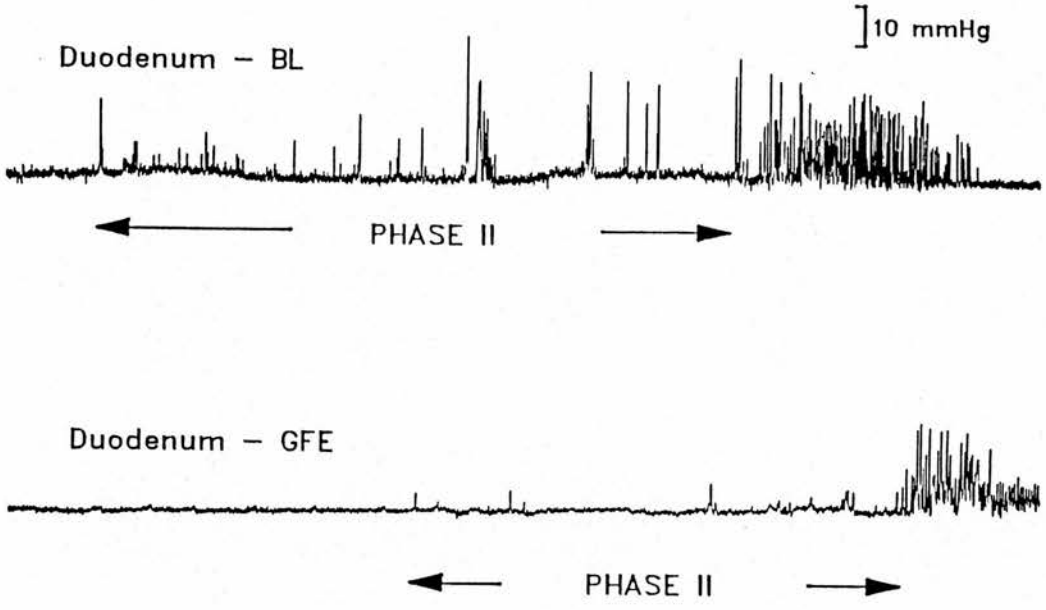

Figure 3.2. Example of the decrease in the contraction amplitude and duration of phase II during the gas and fluid evacuation study (*GFE*) as compared to the baseline study (*BL*).

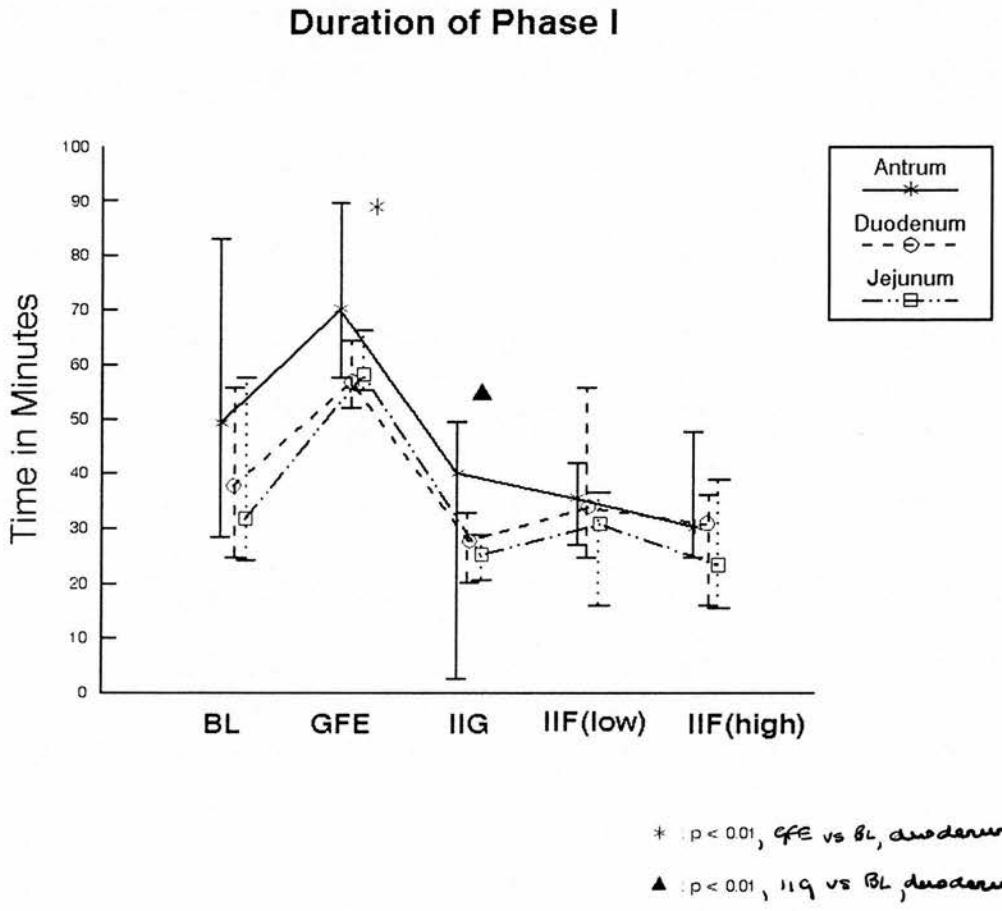

Figure 3.3. Duration of Phase I. Bar lines represent the median [IQR]

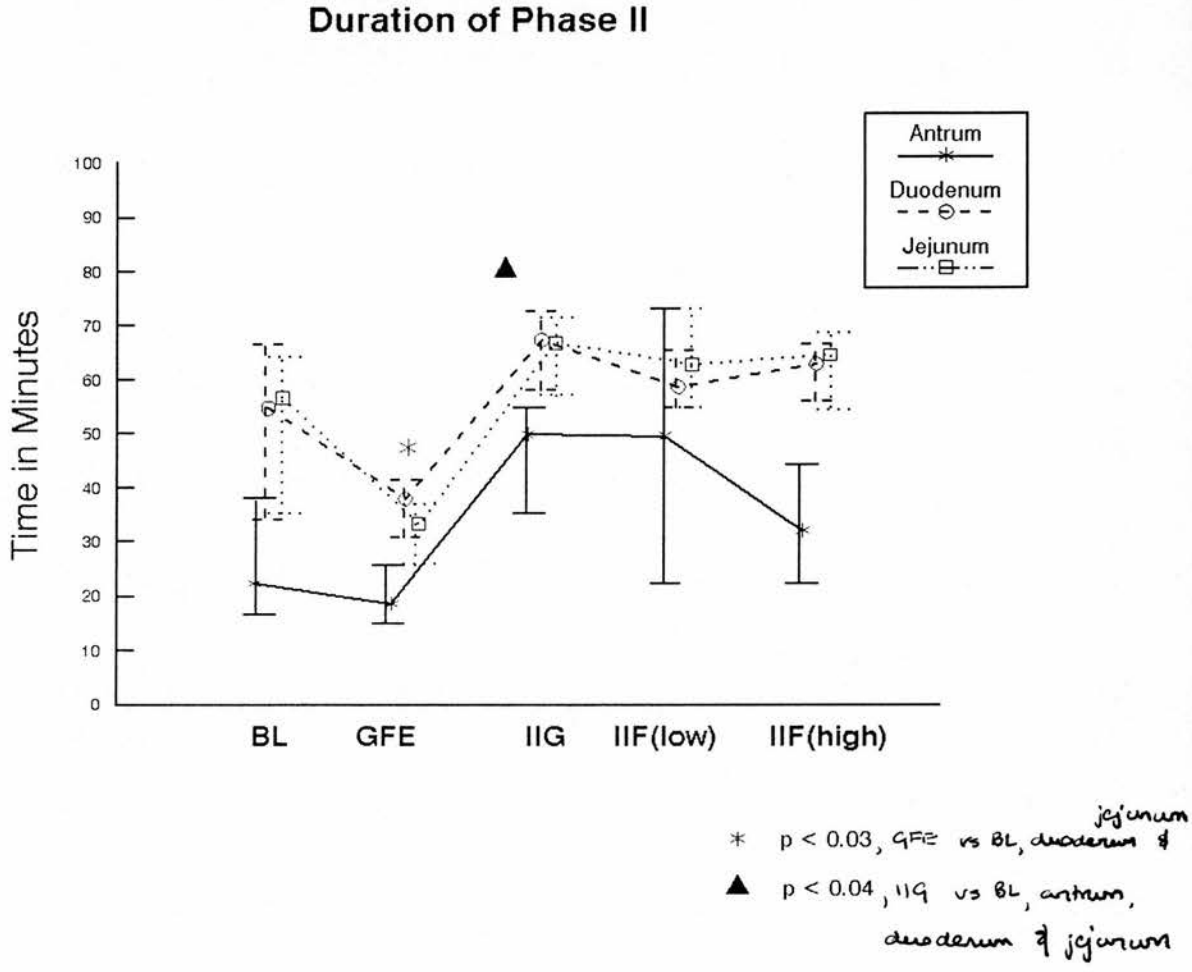

Figure 3.4. Duration of Phase II. Bar lines represent the median [IQR].

Table 3.2.

CONTRACTION AMPLITUDE OF PHASE II (mean ± sem, mmHg)

	ANTRUM		DUODENUM		JEJUNUM	
	Amplitude	*p value	Amplitude	*p value	Amplitude	*p value
BL	27.6 ± 2.7		18.8 ± 0.6		17.3 ± 0.4	
GFE	20.7 ± 0.8	<0.002	16.6 ± 0.7	<0.001	16.9 ± 0.3	0.38
IIG	29.8 ± 0.9	0.003	20.8 ± 0.7	<0.001	20.3 ± 0.4	<0.001
IIF (low)	31.2 ± 1.2	<0.001	21.0 ± 0.2	<0.001	20.6 ± 0.4	<0.001
IIF (high)	27.9 ± 0.8	0.45	19.3 ± 0.6	0.24	17.7 ± 0.5	0.52

*p value indicates statistical difference from baseline value

CONTRACTION FREQUENCY OF PHASE II (median [inter-quartile range])
(contractions/minute)

	ANTRUM*	DUODENUM*	JEJUNUM*
BL	0.43 [0.18 - 0.6]	1.02 [0.46 - 1.4]	1.4 [1.0 - 1.7]
GFE	0.4 [0.07 - 0.56]	0.92 [0.14 - 1.12]	1.04 [0.7 - 1.4]
IIG	0.6 [0.41 - 0.92]	1.04 [0.8 - 1.6]	1.6 [0.73 - 2.61]
IIF (low)	0.8 [0.5 - 0.92	1.2 [0.8 - 1.6]	1.6 [1.16 - 2.05]
IIF (high)	0.56 [0.47 - 0.8]	1.25 [0.72 - 1.65]	1.75 [1.2 - 2.4]

* : No significant difference between studies in the antrum, duodenum or jejunum

(b) Instillation of Intragastric Gas vs Baseline

Phase Duration

The duration of phase II was increased by *IIG* in the antrum, duodenum and jejunum whilst phase I was decreased in the duodenum and jejunum (Figures 3.3 & 3.4).

Contraction Characteristics

Phase II contraction amplitude increased following *IIG* in the antrum, duodenum and the jejunum (Table 3.2) while contraction frequencies remained unchanged (Table 3.3).

(c) Instillation of Intragastric Fluid vs Baseline

Phase Duration

There was no change in the duration of phases I & II in the antrum, duodenum and jejunum in either the *IIF (low viscosity)* or *IIF (high viscosity)* study (Figs 3.3 & 3.4).

Contraction Characteristics

Phase II contraction amplitude was increased in all 3 regions following *IIF (low viscosity)* and in the duodenum following *IIF (high viscosity)* (Table 3.2) but the contraction frequency remained unaffected in both studies (Table 3.3).

Between study comparisons - phase III of the MMC

Phase III contraction frequency was decreased in the duodenum by *GFE* ($p < 0.005$) (Table 3.4). The duration of phase III was unchanged throughout the 5 studies (Figure 3.5), as was the contraction amplitude (Table 3.5) and migration velocity (Table 3.6).

Table 3.4.

CONTRACTION FREQUENCY OF PHASE III (median [inter-quartile range])
(contractions/minute)

	ANTRUM*	DUODENUM*	JEJUNUM*
BL	1.93 [1.72 - 2.34]	10.07 [9.66 - 10.96]	9.3 [8.18 - 9.72]
GFE	2.26 [1.79 -4.12]	7.72 [6.99 - 9.3]	8.3 [7.47 - 8.8]
IIG	1.98 [1.55 - 2.69]	9.7 [7.93 -11.25]	9.88 [9.16 - 10.67]
IIF (low)	2.7 [2.33 - 3.62]	9.3 [8.4 - 10.0]	9.64 [8.83 - 9.93]
IIF (high)	2.8 [2.36- 3.5]	9.4 [8.4 - 10.52]	9.3 [9.04 - 9.46]

* : No significant difference between studies in the antrum, duodenum or jejunum

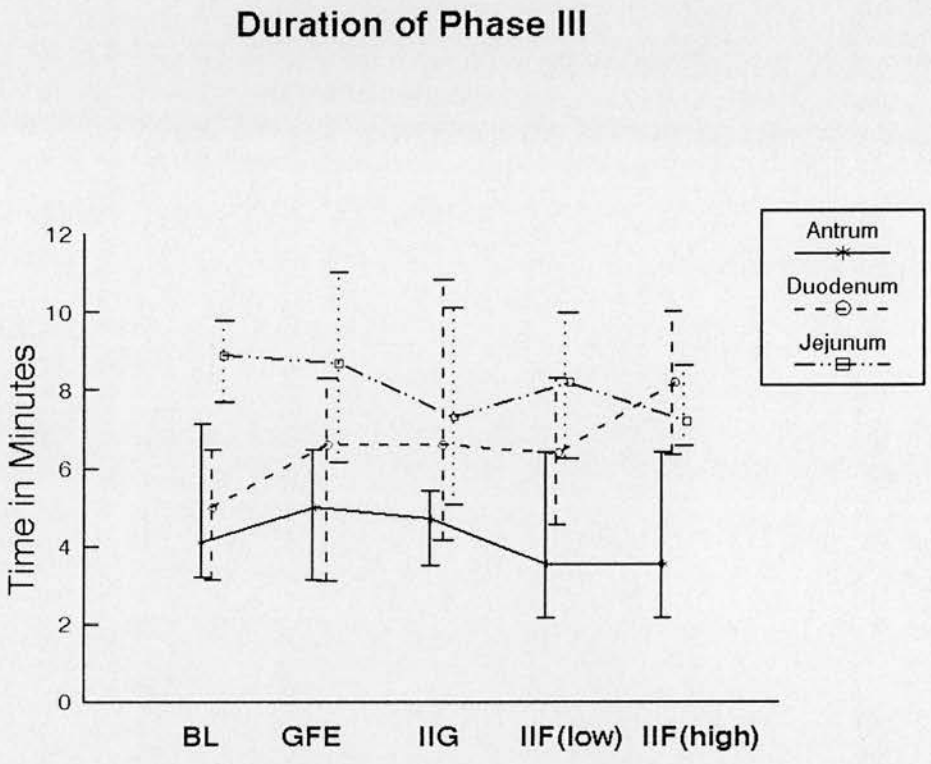

Figure 3.5. Duration of Phase III. Bar lines represent the median [IQR].

Table 3.5.

CONTRACTION AMPLITUDE OF PHASE III (mean ± sem, mmHg)

	ANTRUM		DUODENUM		JEJUNUM	
	Amplitude	*p value	Amplitude	*p value	Amplitude	*p value
BL	27.4 ± 3.8		18.6 ± 1.9		19.2 ± 1.2	
GFE	32.1 ± 5.9	0.27	20.9 ± 1.6	0.19	16.3 ± 0.6	0.09
IIG	28.7 ± 3.4	0.14	20.2 ± 1.8	0.38	19.3 ± 1.2	0.52
IIF (low)	26.1 ± 2.1	0.37	18.2 ± 1.7	0.18	19.1 ± 1.4	0.44
IIF (high)	30.2 ± 2.7	0.17	18.8 ± 1.3	0.35	20.0 ± 1.4	0.59

*p value indicates statistical difference from baseline value

Table 3.6.

PHASE III MIGRATION VELOCITY (cms/min)

(median [inter-quartile range])

BL	5.1 [2.45 - 9.3]
GFE	4.1 [3.74 - 5.47]
IIG	6.88 [3.75 - 12.46]
IIF (low)	6.38 [3.93 - 9.68]
IIF (high)	4.1 [2.83 - 8.22]

Within study Phase II comparisons

The number of volunteers who had ≥ two phase II's of the MMC within a study is shown in Table 3.7. The contraction amplitudes of the phase II of each MMC are shown in Table 3.8.

There were no differences found in contraction amplitude within each phase II in the duodenum or jejunum during the *baseline* study and no subject had more than 1 antral MMC for the comparison of phase II parameters. The contraction amplitude was increased in the antrum, duodenum and jejunum by the instillation of both *intragastric gas* and *low viscosity fluid.* Instillation of *high viscosity fluid* increased the contraction amplitude in the duodenum and jejunum but did not affect the antrum.

In the 4 volunteers in the *GFE* study, 350 mls of air was reintroduced into the stomach during a phase II. This increased contraction amplitude in the duodenum and jejunum.

Table 3.7.

Number of Studies for within study comparison of

Phase II motility parameters

	Antrum	Duodenum	Jejunum
Baseline	-	7	7
IIG	5	9	12
IIF (low viscosity)	6	9	9
IIF (high viscosity)	6	8	10

Table 3.8.

WITHIN STUDY PHASE II CONTRACTION AMPLITUDE (mean ± sem, mmHg)

	ANTRUM			DUODENUM			JEJUNUM		
	Phase II no.1	Phase II no.2	p^*	Phase II no.1	Phase II no.2	p^*	Phase II no.1	Phase II no.2	p^*
BL	-	-		19.7 ± 0.8	18.2 ± 0.7	0.25	14.7 ± 0.4	15.2 ± 0.6	0.12
GFE	-	-		19.4 ± 1.2	16.1 ± 0.9	<0.01	18.9 ± 1.1	14.8 ± 0.7	<0.001
IIG	28.9 ± 1.1	20.9 ± 1.5	<0.001	21.2 ± 0.8	17.6 ± 0.7	<0.001	17.4 ± 0.5	15.3 ± 0.4	<0.01
IIF (low)	31.5 ± 1.7	21.5 ± 1.2	<0.001	22.4 ± 0.6	17.7 ± 0.4	<0.001	20.6 ± 0.5	16.3 ± 0.4	<0.001
IIF (high)	26.2 ± 1.3	22.0 ± 0.5	0.19	20.9 ± 0.7	17.1 ± 0.3	<0.001	18.1 ± 0.5	15.3 ± 0.5	<0.001

* *p* value indicates statistical difference from baseline value

DISCUSSION

This chapter was designed to assess the effect of volume, physical state and viscosity of intraluminal content on the contractile response during normal fasting motility. Hence, the influences of 2 volume extremes of intraluminal gas and acaloric fluid of variable viscosity, on a range of characteristics of the migrating motor complex, including contraction characteristics, phase duration and migration velocity were assessed.

The first experiments addressed the *minimum* volume state following gas and fluid evacuation from the stomach to the caecum. These studies showed that both gas and liquid accumulated, predominantly within the stomach, on a continual basis (Figure 3.1). The volume of gas aspirated from the upper gastrointestinal tract over the 3 hour interval is in accord with the range of 30 - 200 mls as reported by Levitt (Levitt MD, 1971). Fasting gastric fluid volumes in the present study were aspirated repeatedly over 3 hours and hence the total was greater than that reported by other studies, where aspiration was carried out on one occasion (mean volume 31.1 mls, range 0 - 110 mls) (Hardy JF, 1987). Removal of this basal intraluminal content by repeated aspiration caused a general decrease of motor activity, including (i) reduced antral and duodenal phase II contraction amplitude, (ii) reduced duodenal and jejunal phase II duration and (iii) reduced duodenal phase III contraction frequency. Indeed in 3 subjects, no recognizable small bowel phase II was observed after evacuation of content. Previous work has shown a decrease in the phase II duration overnight during sleep (Kumar D, 1990). However, the intraluminal secretions are reduced overnight, with no stimulus to

pancreatic secretion, a decrease in swallowed air (vide infra) and a negligible salivary flow rate (Schneyer LH, 1956). The findings of this chapter suggest that changes in the intraluminal gastrointestinal content may play a part in the observed overnight change in the parameters of the MMC.

In the fasting state, swallowed air, which may initially accumulate in the stomach, is the main source of gastrointestinal gas (Danhof IE, 1968). Our data shows that the stomach is the main reservoir for upper gastrointestinal secretion. Thus, the present study which sought to simulate normal physiology, utilized the stomach as a receptacle for instillation of gas and fluid. The *maximum* volume of 350 mls gas or acaloric fluid was chosen on the basis of our own observations and the experience of others (Rees WDW, 1982), that acaloric fluid volumes of up to 400 mls may be introduced into the stomach without disruption of periodic fasting activity. A further factor of viscosity was considered, by evaluation of isovolumetric samples of fluid of low and high viscosity. In this context, methylcellulose solutions were chosen because of their advantages of being acaloric, that their viscosity is easily changed by concentration alteration and that their volume remains relatively undiminished by absorption (Schemann M, 1982).

Alteration of the intragastric milieu by instillation of *maximum* volumes of both fluid and gas generally increased motor activity. There was an increase in phase II contraction amplitude, though phase III parameters remained unaffected. No difference of phase II parameters was observed between the 3 instillation studies, indicating that the volume, rather than the physical properties, of the

acaloric intragastric content had the major influence on the phase II parameters.

The changes of small bowel contraction amplitude and frequency usually occurred within 15 minutes of either gas or fluid instillation. This observation suggested that the small bowel motility response could be modulated via a gastro-enteric reflex, rather than a local distension effect on the small bowel. Similar observations during the within study assessments, where characteristics of the first small bowel phase II changed rapidly following the change in the intragastric milieu, support this view. Prove and Ehrlein found that increasing the viscosity of a meal tended to decrease the antral motor activity, which they postulated was to inhibit the expulsion of the meal from the antrum and to enable further mixing of the meal (Prove J, 1982). The findings of this chapter, which showed that antral contraction amplitude was inversely related to fluid viscosity, are similar.

This chapter has shown that periodic fasting activity of the human digestive tract is responsive to volume changes of acaloric content. Phase II is most susceptible, with alterations of both duration and contraction amplitude. Although phase III was less responsive, contraction frequency changes were observed. We have therefore demonstrated that the contractile response of the gastrointestinal tract is responsive to changes in the intraluminal milieu. However, further evaluation was required to assess the effects of these changes in contractile response on the SVA signal. Analysis of this correlation required the assessment of a large number of gastrointestinal contractions, a task which was considered too arduous for manual analysis. This problem is considered in the next chapter.

Chapter 4

Development and Validation of a Computerised Method for Analysis of Fasting Gastrointestinal Motility

INTRODUCTION

The thrust of this thesis is aimed at the development of novel methods for assessment of gastrointestinal motility. In particular, we aim to seek any association between SVA signals and intraluminal contractions, as measured by intraluminal manometry. These aims raise a number of problems. Firstly, with conventional methods, the magnitude of the task is considerable. Manometry signals, at the time of the studies of this thesis, were conventionally displayed on a continuous multichannel analogue chart recorder. SVA, with the developed system, was displayed on a separate microcomputer monitor screen and then printed out on a standard form. These limitations raised numerous difficulties, eg how could any correlation between continuous signals from individual or multiple manometric channels and the voltage versus time graph of the SVA system be investigated? How could any association between individual contractions and the SVA response be investigated? How could the effect of specific contraction patterns, such as the different phases of the MMC on SVA characteristics be ascertained? How could we evaluate artefact effects? Given that many contractions occur, within a 3 hour interval of assessment, how could we ascertain the effects of contraction characteristics, such as amplitude, duration propagation and frequency on SVA signals?

At the time of the studies in this thesis, such assessments were carried out by skilled observers using manual measurement. As shown in Figure 4.1, this is a laborious task for even a small number of contractions. Clearly, conventional methods by manual interpretation were inappropriate for our purpose.

The advent of microcomputers has enabled many daunting tasks

in clinical medicine. In the context of motility we had previously devised a simple microcomputer program for the display of motility data on a monitor screen and storage on a floppy disk (Waldron B, 1991). Our first development for the current purpose, therefore, was to enable one channel of our microcomputer system to accommodate data from the SVA system. This small step gave great convenience and allowed both motility and SVA data to be visualised synchronously on the monitor screen. Thus, we could visualise simultaneous events on manometry with SVA but we had no facilities for signal analysis or correlation. At the time of the studies contained in this thesis, some simple peak detection systems were available, but none were suitable for our purposes. None had facilities for pattern recognition of the migrating motor complex, nor artefact exclusion, nor signal correlation. In order to progress with our total project, we considered that the development of a sophisticated objective technique was necessary. This chapter describes our work which led to the development of the first available microcomputer system for the analysis of gastric and small bowel motility data. Furthermore, this chapter describes the validation of the developed system against skilled observer interpretation.

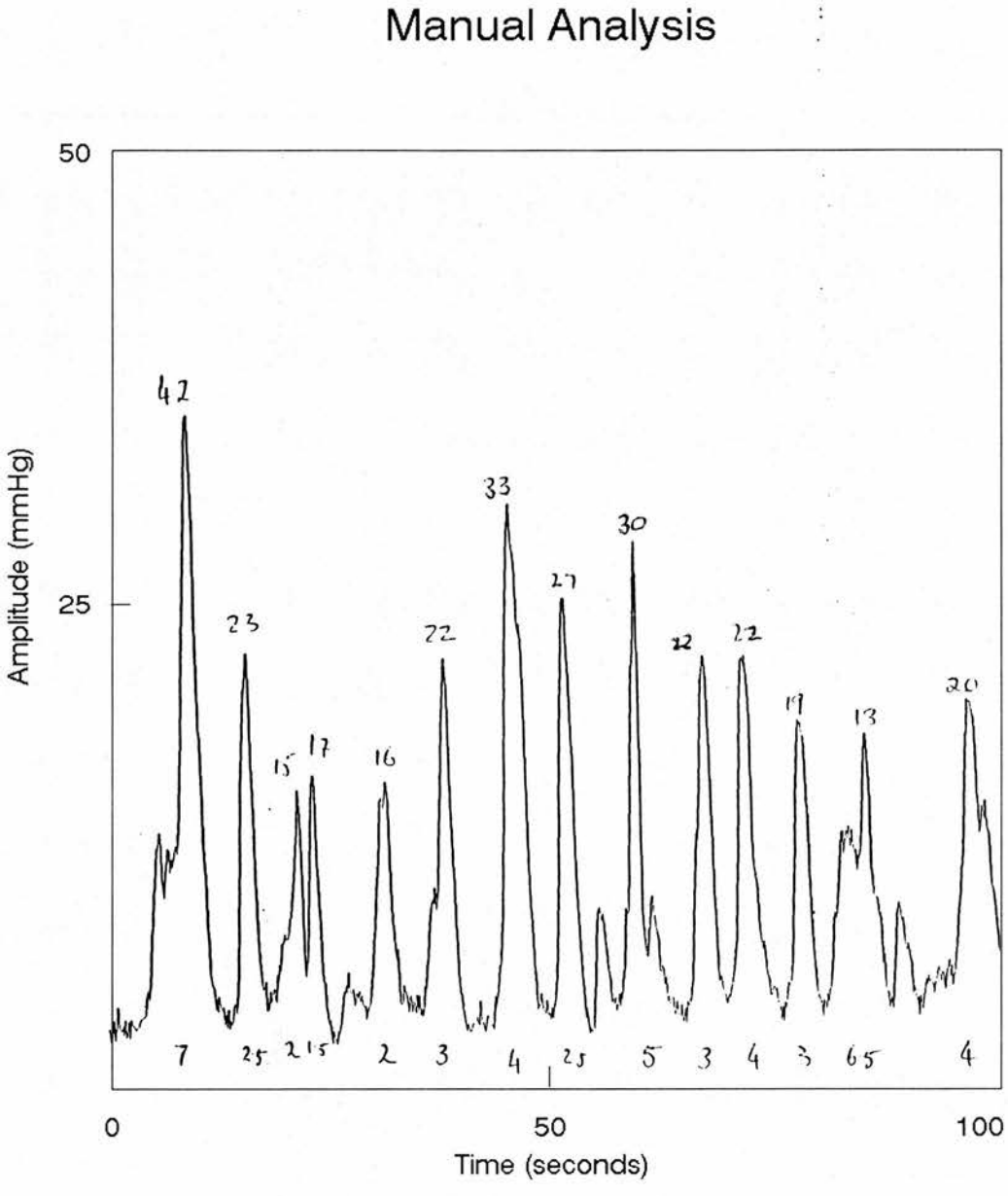

Figure 4.1. Example of manual analysis of a manometric tracing, for detection of peak amplitude and duration. The upper values represent the contraction amplitude (mmHg), the lower values the contraction duration (seconds).

DESIGN OF THE MICROCOMPUTER PROGRAM

Computer Analysis of Gastrointestinal Motility

Two separate systems were employed for the recording of gastrointestinal manometry in our motility laboratory. The first system was the low compliance water perfused Arndorfer stationary system as utilised in this thesis. The majority of these studies were carried out in the fasting state, with up to 5 manometric channels of data being recorded. The second system utilised in our motility laboratory is that of a 3 channel ambulatory manometry system using electronic strain gauge transducers connected to a portable data logger. This system is suitable for studies up to 24 hours in duration. Our intention was that the computer program would be able to analyse data from both systems and the objectives were therefore as follows:

i) Analysis of gastric and small bowel fasting motility data.

ii) Analysis of up to 5 channels of manometric data.

iii) Analysis of the propagation of contractions in the gastrointestinal tract.

iv) Provision of a summary of results or more detailed results as required.

With these objectives as the basis for the development of the program, the program was then divided into separate modules as described overleaf:

As stated, we have previously described our simple software program (PC-Motil) for the **DISPLAY** of motility data (Waldron B, 1991). This allowed simultaneous display of both SVA and manometric signals in real time, but lacked any facility for analysis. The objective of the work described in this chapter, was the development of a sophisticated analysis facility.

Development of the analysis program

The analysis program was designed as a series of linked modules for:

1. **Peak definition**
2. **Artefact exclusion**
3. **Interchannel peak propagation**
4. **Recognition of the Migrating Motor Complex (MMC)**

1. Peak definition

This module was designed initially to recognise a peak and subsequently to measure the peak amplitude, duration, and Motility Index (area under the curve of the given peak).

Peak recognition

In digitised data, a peak is identified if the derivative of the signal changes from uniform to positive, then to negative (Parker R, 1987). Gastrointestinal peak characteristics vary considerably in terms of frequency and duration, within a given range. Furthermore, the signals themselves are not perfect smooth waves but they exhibit points of inflection on the upstroke which could possibly be interpreted as "peaks". Any peak recognition program therefore, should address the variation in peak characteristics within their known range and distinguish points of inflection on the wave upstroke, from true peak apices. At the time of our initial studies, programs are available commercially for simple peak detection, but these were inappropriate for gastrointestinal contractions. It was important that our own algorithm be developed for peak detection with the ability to deal with the complexity of gastrointestinal contractions.

The problems of peak detection are addressed within the software by an algorithm which defines the peak apex relative to the maximal positive and negative slopes of the wave. After detection of the first point of inflection on the upstroke, on the basis of a change of signal value from positive to negative, the signal is then scanned during the preceding 2 seconds and succeeding 5 seconds to evaluate the maximum positive and negative algebraic differences respectively, between successive points during the rise and fall of the wave

(Figure 4.2). These values represent the maximum positive and negative slope respectively (Trahanias P, 1989).The true peak apex is then defined as the highest algebraic value lying between the maximum positive and negative slopes. This approach is appropriate both for simple peaks, characterised by a single upstroke, apex and downstroke and composite peaks, characterised by a single contraction containing more than one apex, without a return to baseline. The upstroke and downstroke of the detected peak must equal or exceed a certain amplitude threshold in order for it to be read as a true manometric peak. This excludes small changes in the baseline and respiratory artefact - this proviso is explained in more detail in the **Artefact Exclusion module** (vide infra).

The intervals for definition of maximum slope (2 seconds for the upstroke and 5 seconds for the downstroke) are important for accurate detection of peak number and duration and have been selected on the basis of observed contraction frequencies, peak duration and interpeak intervals. In the baseline study (Chapter 3) maximum frequency of contractions occurred during phase III of the small bowel migrating motor complex (range 8.7 - 12.2 contractions/minute). During this event, the median [Inter-Quartile Range] interpeak interval was 5.2 [4.7 - 5.7] seconds and the median [Inter-Quartile Range] peak duration was 2.9 [2.2 - 4] seconds. On the assumption that the upstroke of most contractions accounts for ≤ 50% of total contraction duration (median : 2.9 seconds), the interval for definition of maximum positive slope was set at 2 seconds in order to accommodate the entire upstroke yet avoid encroachment on the upstroke of the previous contraction.

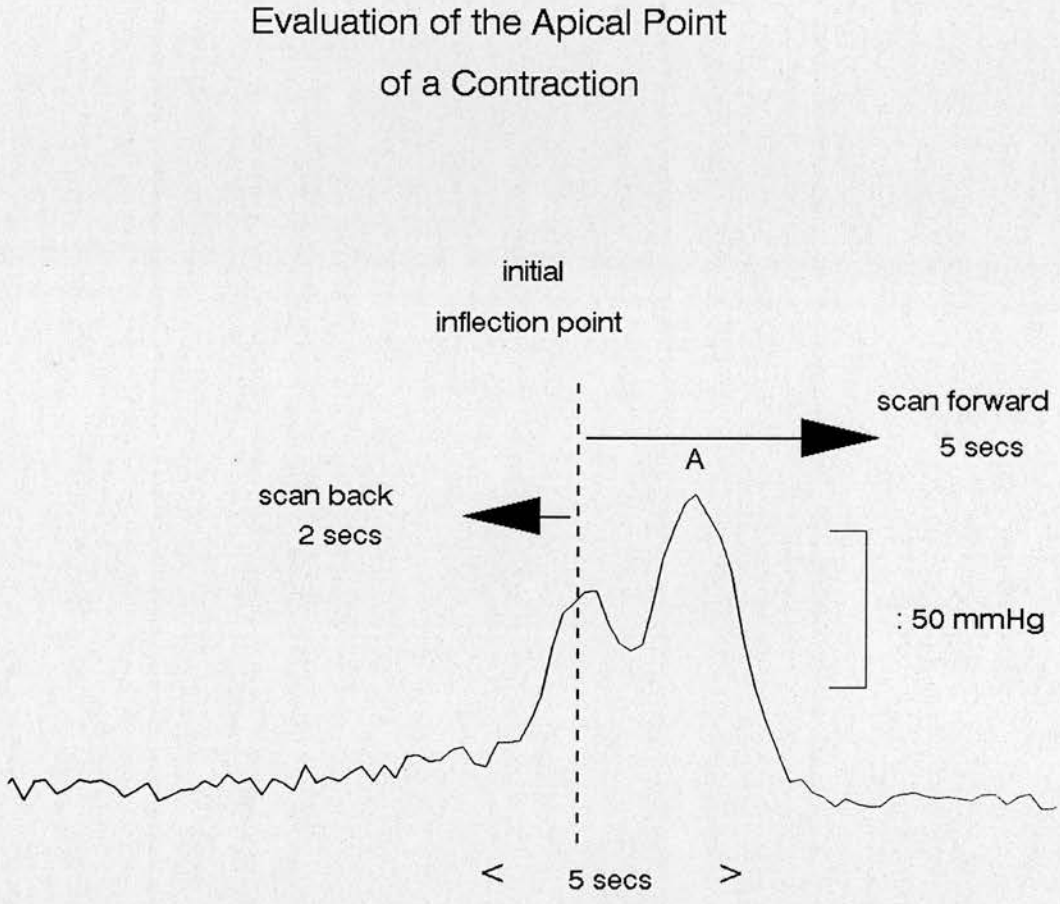

Figure 4.2. The developed system detects the first change in signal polarity from positive to negative (interrupted line). In order to identify the TRUE PEAK, the program scans the signal backwards 2 seconds and forward 5 seconds in order to find the highest algebraic point within that area. This point (A) is then designated as the apex of the contraction. Many gastrointestinal contractions have such inflections on the upstroke during the course of the rise in intraluminal pressure.

Since the minimum interval between contractions in our volunteer studies was 5 seconds, the interval for definition of maximum negative slope was set at 5 seconds. This allowed sufficient time for the signal to reach its apex, then turn in a negative direction and yet avoid encroachment on the downstroke of the following contraction.

These intervals avoid underestimation of peak number by ensuring distinct recognition of closely spaced peaks and avoids overestimation by recognition of only one peak apex, in composite peaks. In addition, the algorithm also includes a mandatory interval of 2 seconds from definition of the peak apex, before the peak recognition sequence is repeated, which allows peak definition up to a maximum frequency of 30 peaks/minute. This frequency is higher than that which is normally sustained in the small bowel, but it is necessary to address this relatively high frequency range in order to accommodate the very short interpeak intervals which sometimes occur between a few contractions, during a small bowel phase II or phase III.

In the baseline study (*BL*) the median duration of gastric contractions was similar to that in the small bowel eg, the median [Inter-Quartile Range] for gastric contraction duration was 3.3 [2 - 5.7] seconds and therefore an identical algorithm was used for gastric peak definition. The intervals chosen for peak recognition were based on observations by skilled observers on gastric and small bowel manometry tracings taken from healthy volunteers. The use of an identical algorithm for peak detection in all channels facilitated synchronous detection of pressure events on all channels, for recognition and exclusion of cough artefact (vide infra). A further advantage of the facility for measurement of relatively high

frequencies in the gastric sensor, is that recognition of sensor movement artefact is possible, on the basis of a sustained increase in contraction frequency from gastric to small bowel range.

The peak apex is utilised as the reference point for peak recognition within this program. The contraction frequency is computed simply as the number of contractions per unit time.

Peak amplitude

Having recognised the peak and its apex, the peak amplitude is calculated from the difference between peak apex and baseline. Baseline value is determined from the average values of 2 x 5 second segments of sub-threshold quiescence, before and after peaks (Figure 4.3). Baseline for closely spaced contractions is determined from quiescent segments on each side of that cluster. If significant downward drift develops during a cluster, the program re-calculates the baseline value by taking the average of the minimum values of the upstroke and downstroke of each contraction.

Peak duration

Baseline is an unsuitable reference for calculation of contraction duration, since the definition of true peak onset and end is not possible from *sub-threshold* data. Thus a value of 6 mmHg above baseline, which provides a useful fixed point above threshold, is used for this purpose. Peak duration is the interval between peak onset and end, as defined above. Area under the curve, which is useful for motility index calculations, is calculated as the sum of the integrated values between baseline and positive and negative slope, from onset to end of each contraction.

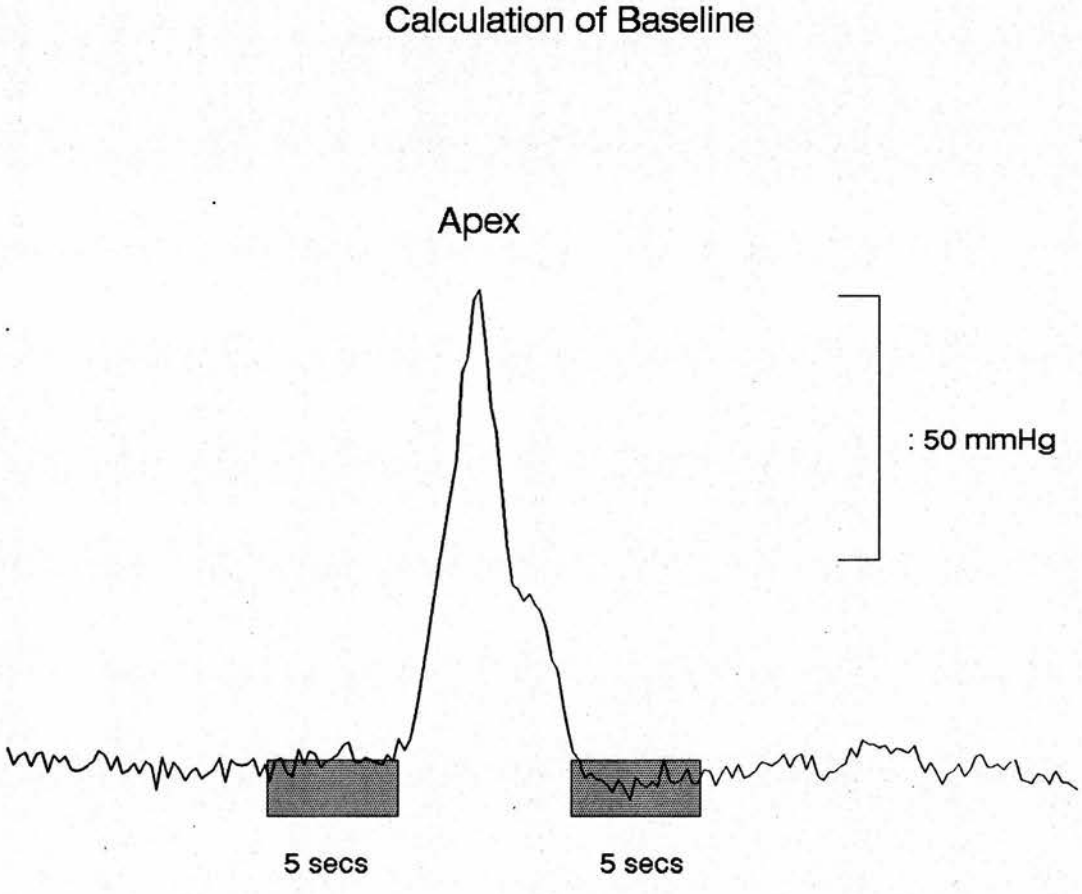

Figure 4.3. Calculation of the baseline. The baseline value is taken as the mean signal amplitude from the 2 five second intervals, before and after the contraction. Contraction amplitude is then taken as the (contraction apex - contraction baseline).

2. Artefact exclusion

Motility signals from the water perfused Arndorfer system may be affected by artefact from a number of sources, which should be excluded prior to analysis. These include:

(i) Respiration artefact

(ii) Cough/Sneeze/Movement artefact

(iii) Sensor movement artefact

(i) Respiratory artefact

In health, the respiratory rate varies between 10 - 16 breaths per minute. Consequently, respiratory artefact may have a similar frequency to small bowel contractions, particularly during phase III. This artefact was identified by its coincident occurrence with respiration and by its continuous appearance during intestinal quiescence. The amplitude of this artefact appeared to depend on the hardware recording the signal. For the water perfused Arndorfer stationary system as utilised in this thesis, the amplitude of the respiratory artefact varied between 2 - 8 mmHg. Therefore an amplitude threshold was set at 9 mmHg above the *minimum detected value* of the incoming signal for definition of true contractions. This approach allowed the exclusion of respiratory artefact before peak definition.

(ii) Cough/sneeze/movement artefact

Coughs, sneezes and vigorous movements produce a generalized rise in intra-abdominal pressure. This increase pressure tends to cause a *simultaneous deflection* on at least 3 of the 5 intraluminal sensors. The synchronous occurrence of contractions at 3 sites separated by wide distances, is uncommon (Kellow JE, 1986). Visual inspection of the

screen display during episodes of cough/ sneeze/ movement artefact showed that all the sensors would pick up an artefact signal but that the signal on some of the sensors were below the amplitude threshold of 9 mmHg (Figure 4.4). Thus, we have included an algorithm within the program for recognition and exclusion of simultaneous pressure events at least 3 sensors, on the grounds that these are more likely to be due to cough/ sneeze/ movement artefact. These sensors do not require to be adjacent to each other for the exclusion of the artefact. This facility was evaluated against the skilled observers' definition of such artefact.

(iii) Sensor movement artefact

During motility recording, a gastric sensor may be propelled by the activity front into the duodenum, with a resulting change in signal characteristics and interpretation difficulties. The maximum gastric contraction frequency of 3/minute ensures that all gastric interpeak intervals exceed 15 seconds, while duodenal interpeak intervals have a shorter duration. Hence an algorithm has been developed which recognizes sensor movement on the basis of a change in interpeak interval from ≥ 15 to < 15 seconds, which is sustained for ≥ 12 contractions. Movement of the gastric sensor into the duodenum, is denoted by the term "Small bowel pull through", which is printed as a warning on the monitor screen.

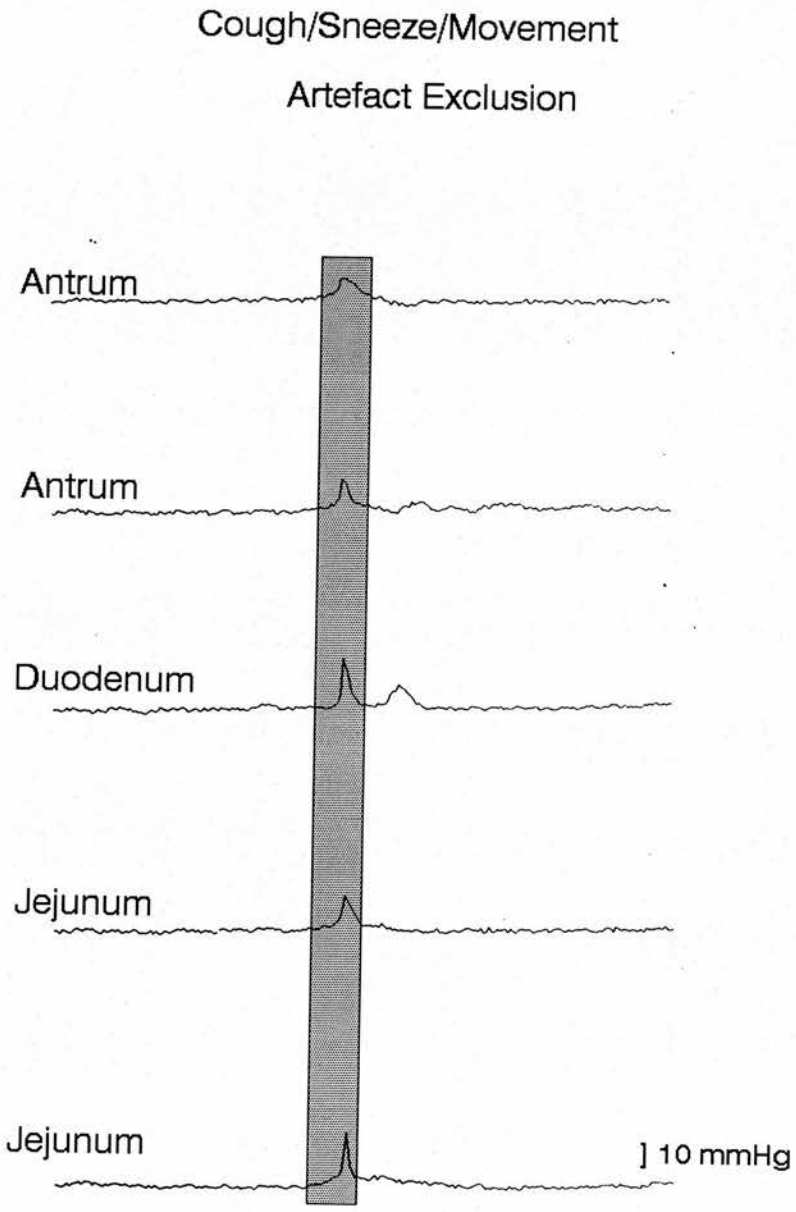

Figure 4.4. Exclusion of Artefact. A simultaneous contraction is seen on all the five channels.

3. Interchannel peak propagation

If both the propagation velocity of contractions and the inter-manometric channel distance is known, then a propagated contraction detected in one channel will appear in the subsequent distal channel within a given time window. Contractions detected at a sequential channel within a calculated "time window", defined by the quotient of the distance between sensors and the mean and one standard deviation of the known velocity of contraction spread may be considered to be propagated (Johnson AG, 1990). An algorithm was therefore developed for recognition of contraction propagation, on the basis of detection of contraction apices at sequential channels within a time window. In this algorithm, aborally propagated contractions are initially evaluated. These aborally propagated contractions are then eliminated from the computer memory and a similar algorithm is run to detect oral (retrograde) propagation. A similar time window is used for both oral and aboral propagation, as the pacesetter potential propagates orally and aborally with the same velocity (Sarr MG, 1981).

In order for propagation to be assessed, the time taken for a contraction to be propagated to the subsequent channel should be less than the intercontractile interval (Ehrlein H-J, 1989). Based on the small bowel propagation velocity of (mean ± SD) 2.3 ± 0.93 cms/sec and a minimum inter-contractile interval of 5 seconds (Fleckenstein P, 1978), this would require that the channels should be ≤ 6 cms apart. In this thesis, the small bowel inter-manometric channel distance was 12 cms and therefore contraction propagation has not been validated against the skilled observers assessment.

4. Recognition of the Migrating Motor Complex (MMC)

This module has been designed to address the migrating motor complex (MMC) and its characteristics, in the small bowel and stomach. Facilities have been developed for:

(i) Recognition of the Migrating motor complex (MMC).

(ii) Recognition of phase anomalies.

(iii) Measurement of phase duration.

(iv) Measurement of phase III migration velocity.

(v) Assessment of contraction characteristics within phases.

(i) Recognition of the Migrating motor complex

The specific contraction frequency of phase III forms the primary reference parameter for MMC recognition and other phases are defined in relation.

In the upper small bowel, phase III has a contraction frequency of approximately 9-12/minute and a duration of 2-16 minutes (Fleckenstein P, 1978, Code CF, 1975). Thus, an algorithm was developed which defined a duodenal or jejunal phase III on the basis of recognition of a burst of $\geq$ 18 contractions over an interval of $\leq$ 2 minutes. The program then scans the regular contractions in the center of the burst, i.e after the first 12 of the 18 contractions have passed. The interpeak interval of this regular activity is defined from the next 6 contractions and taken as representative for the whole phase III. The duration of phase III is defined from the regular activity only, which is determined from the time of onset of the first to the time of completion of the last contraction whose interpeak interval with 5 of its successors and predecessors respectively, was 1 - 1.5 x the mean interpeak interval of regular activity, as defined

above. A return to quiescence (vide infra) within an interval of ≤ 2 minutes of the cessation of the regular activity and which lasts a minimum interval of 2 minutes, is also mandatory for the definition of the end of phase III. This requirement prevents incorrect definition of a phase III due to closely spaced contractions within phase II and premature definition of completion of a genuine phase III due to the occurrence of "lost peaks", within that phase.

Gastric phase III's have a contraction frequency of 1-3/minute, a duration of 2-3 minutes and are temporally related to phase III activity in the small bowel (Richter HM[1988]). These characteristics were addressed by an algorithm which defined gastric phase III by recognition of ≥ 4 sequential regular contractions over an interval of 3 minutes, accompanied by a mandatory temporally related small bowel phase III, in either small bowel channel, within an interval of -5 to +10 minutes. A return of gastric quiescence within ≤ 2 minutes of cessation of regular gastric contractions is also mandatory for definition of gastric phase III. The mean interpeak interval of this phase is calculated from the 4 sequential regular contractions, as defined above. The beginning and end of gastric phase III is defined from the time of onset of the first to the time of completion of the last contraction whose interpeak interval with its successor or predecessor respectively, is 1 - 1.5 x the mean for the regular activity.

In both small bowel and stomach, phase I is defined as the interval of quiescence which follows phase III until the onset of irregular contractile activity of phase II. Contractions may occur within phase I provided that they are followed by quiescence lasting ≥

15 minutes (vide infra). Recognition of phase II is based on irregular timing of contractions, which follow quiescence and lead up to the regular contractile activity of phase III. A maximum of 15 minutes quiescence between contractions, is allowed within phase II.

(ii) Recognition of phase anomalies

The characteristics of the migrating motor complex may differ from standard descriptions. In the present study, the most common of these variations were irregular contractions within phase I and absent gastric phase III, which we have termed "phase anomalies". If unrecognised, these "phase anomalies" could complicate microcomputer definition of phase characteristics and hence algorithms have been included for their recognition.

Contractions may occur within phase I, but are generally sparse. The microcomputer program distinguishes contractions within phase I, from early phase II by the requirement that contractions of the former be followed by ≥ 15 minutes quiescence. Widely spaced contractions and/or < 4 closely spaced contractions are ignored but the program assigns the printed term "Irregular Contractile Activity within phase I" to ≥ 4 closely spaced irregular contractions, which is followed by ≥ 15 minutes quiescence. Thus, this activity is distinguished from phase II.

Gastric phase III may be absent throughout some MMC cycles. The program segregates such signals into areas of quiescence ≥ 15 minutes, followed by areas of irregular contractile activity, followed by return to quiescence ≥ 15 minutes. A temporally occurring small bowel MMC is sought by the program, within -5 to +10 minutes of the irregular gastric contractile activity. If present, then the categories of phase I and II for quiescence and irregular activity respectively,

are assigned. The absence of gastric phase III, in any MMC cycle, is denoted by the program by the printed term "Gastric phase III absent". Irregular contractile activity which is preceded and followed by quiescence ≥ 15 minutes, which bears no temporal relationship to a small bowel MMC, is denoted by the printed term "Irregular contractile activity".

(iii) Measurement of Phase Duration

Having defined each of the MMC phases, the program calculates the duration from the interval between onset and end. In gastric and small bowel phase III, measurements relate only to the regular contractile activity. The duration of phase I is calculated from the start of quiescence following phase III, until the onset of irregular contractile activity of phase II, while the duration of phase II is calculated from the onset of irregular contractions which continues without quiescence lasting ≥ 15 minutes, until the onset of the regular activity of phase III.

(iv) Migration velocity of phase III

The migration velocity of the MMC is defined as the quotient of the distance between sensors (centimetres) and the interval (minutes) from the time of onset of phase III on one channel to the time of onset of phase III on the subsequent channel.

(v) Contraction characteristics within the MMC

Having defined the onset, end and duration of each of the phases of the MMC, the program calculates the contraction frequency and mean contraction amplitude of phases II and III and, if propagation is analysed, the proportion of contractions which are propagated during phase II.

Computer Program - description of the software

The software itself was written using Turbo Basic[12] and will work on any 100% IBM compatible PC with a hard disk and either EGA or VGA display. Machines with 286, 386 or 486 processors are recommended. The program was divided into two parts - a **peak analysis module** and a **pattern analysis module.**

Peak Analysis Module

This module analyses each channel in turn and detects contractions, based on a minimum amplitude threshold (9 mmHg). This threshold must be greater than baseline fluctuations caused by artifact and the value may be adjusted by the user. On the detection of a contraction, its characteristics are then defined in terms of:

Position in time related to peak apex

Amplitude in mmHg

Duration of contraction in seconds

Area under the curve (integrated amplitude values)

This information is then stored in a new file created by the program and is named by the study initials and post-fix notation DTA (ie filename.DTA). The postfix .DTA is an abbreviation for data.

This module may analyse up to 6 channels of motility data, up to a maximum of 10,000 contractions. This limit is unlikely to be breached during the course of a standard study. The length of the source code is 29519 bytes.

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[12] © Borland Inc.

Pattern Analysis Module

This module then reads the .DTA file created by the Peak Detection Module and carries out further analysis. The length of the source code for the pattern analysis is 54371 bytes. Analysis includes:

a) Fasting phase motor activity:

- Recognition of the Migrating Motor Complex - Duration of phases I, II and III
- migration velocity of the MMC
- contraction characteristics of phases II and III

b) Interchannel Peak Propagation

The run-time for the peak detection module is about 5 minutes using a PC-AT 386 with 80387 maths coprocessor for analysis of 5 channels of a 3 hour manometry study. The pattern analysis module then takes 45 seconds. The two modules may be run separately or in conjunction, as a batch file.

Figure 4.5. Computer screen showing options available for combination of SVA and manometry analysis.

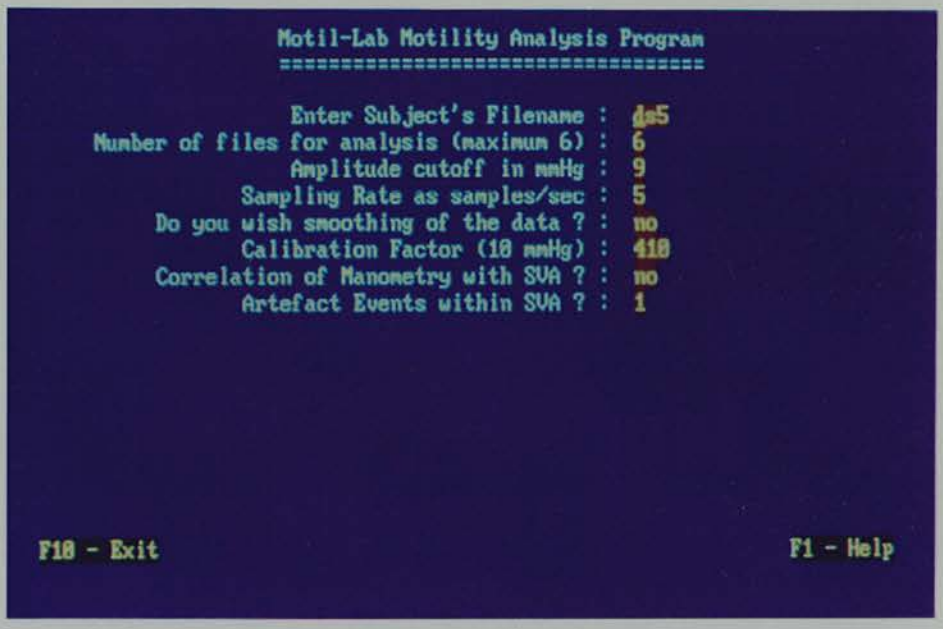

Figure 4.6. On selecting the analysis module, the user is then asked to input parameters as shown above.

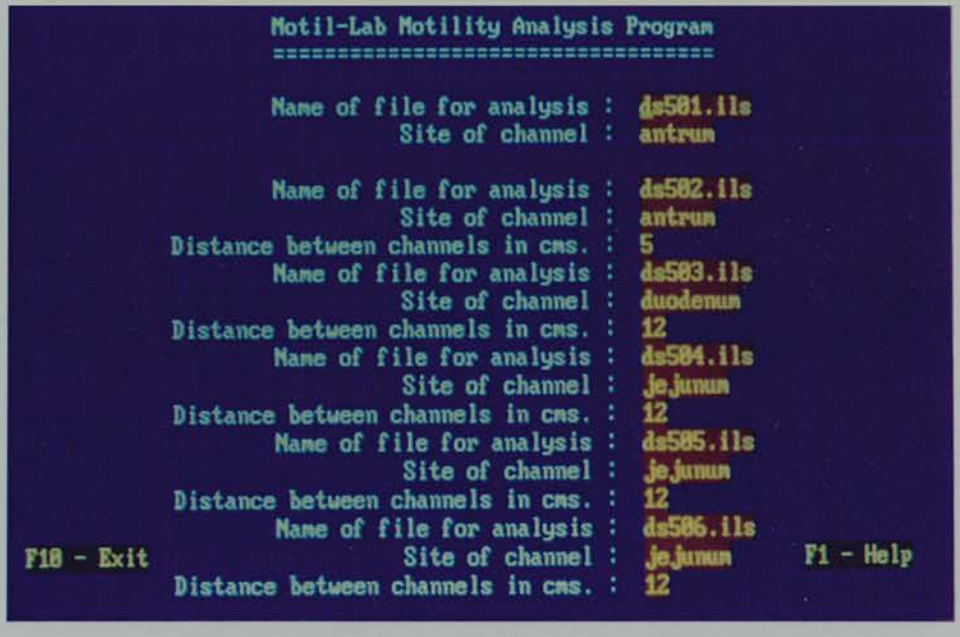

Figure 4.7. The data filenames, sites and distances of the manometric channels are then selected.

Figure 4.8. During the analysis period, there is an on-screen display of which channel is currently being analysed.

Figure 4.9. An example of the on-screen display of the results of analysis. A hard-copy can be obtained by downloading to the printer (see Appendix III).

VALIDATION OF THE MICROCOMPUTER PROGRAM

Observer Analysis

Eight 3 hour volunteer studies were chosen for subsequent motility analysis. Manual analysis was carried out by 2 skilled observers (Mr Brian Waldron and myself). Analysis by each observer was blind of the other's findings and of the microcomputer results, until the study termination. All observer assessments were carried out on 2 separate occasions with at least 2 weeks between them, in order to allow assessment of inter and intra observer reproducibility. Three random 30 minute segments were taken from the above studies for the detailed analysis of the contraction characteristics of contraction amplitude and duration.

Observer criteria for definition of motility parameters

1. Peak characteristics

The microcomputer used *minimum detected value* for reference in peak definition but this was unsuitable for observers because of it's continuous variation. Observers used a baseline value, which was estimated visually and marked by a line drawn through each channel. Contraction amplitude was measured between *baseline* and peak apex. Contraction duration was assessed at a point 6 mmHg above *baseline*, as in the microcomputer program. The microcomputer was programmed to give a printout of the number of contractions and their individual contraction amplitude and duration for the three 30 minute segments of motility data selected for detailed observer analysis.

2. Artefact Recognition

Cough/sneeze/movement artefact was recognised on the basis of simultaneous deflections on at least 3 channels. Respiratory artefact was recognised by subthreshold fluctuations, < 9 mmHg above baseline.

The observers used standard criteria for definition of motility parameters and artefact which approximated those employed by the microcomputer program, as closely as possible.

3. Definition of migrating motor complex characteristics

Assessment of migrating motor complexes and their characteristics were by recognised criteria (Sarna SK, 1985). Specifically, phase I was defined as the interval of quiescence which separates the end of phase III and onset of phase II. Phase II comprised irregular contractions which followed the quiescence of phase I and terminated in the regular contractile activity of phase III. Phase III comprised frequent regular contractions which terminated in a return to the quiescence of phase I. Phase III migration velocity was based on time of onset of regular activity in adjacent channels, as in the microcomputer program.

Signal resolution used in observer assessments

The observers assessed manometry recordings at high resolution in order to ensure optimum accuracy. Measurements of contraction amplitude and duration required greatest precision and were assessed at a scale of 1 minute of manometry recording in one channel, to a single A4 page (295 x 210 mm). A scale of 3 minutes of motility data in five channels, to an A4 page was sufficient for optimum peak

definition, assessment of propagation and definition of cough/sneeze/movement artefact. In assessment of MMC migration velocity, a scale of 4 minutes of motility data was used, while in assessment of phase duration, 4 - 12 minutes of data were printed to these dimensions. For MMC recognition, a resolution of 120 minutes of data, printed to a single A4 page, was sufficient.

Statistical Analysis

Peak characteristics were normally distributed in this study and therefore the descriptive statistics used were the mean and standard error of the mean. The MMC characteristics had a skewed distribution and thus the median and inter-quartile range were used. Microcomputer results were assessed against the mean of both observers, although inter and intra observer differences were also evaluated. Differences between the observer and microcomputer methods were sought by analysis of variance (2 way ANOVA) whereas the measure of the agreement between the 2 methods was calculated as the bias (mean difference) and one standard deviation of the bias (Bland JM, 1986). Measurements of both difference and agreement were used where the number of results for comparison was large, eg, peak detection, amplitude, duration and MMC phase duration. Analysis of variance only was utilised for parameters where the number of comparable results was relatively small, eg MMC detection and migration velocity, peak propagation and detection of cough/sneeze/movement artefact. Probability values (p) have been shown for all analyses to emphasise any differences which approached significance.

RESULTS

Peak Characteristics

(i) Peak Detection

The number of contractions detected by the computer and the two observers is shown in Tables 4.1 & 4.2. These results showed no significant inter-observer differences in peak detection, although in one observer (*Observer I*) the intra-observer difference between the two assessments approached statistical significance. There was no difference between the microcomputer assessment and the mean of both observers (Table 4.2).

In comparison of contraction amplitude and duration defined by microcomputer and observers, only those contractions recognised by microcomputer and both observers in both assessments (n = 140) were considered. Amplitude and duration measurements for antral, duodenal and jejunal contractions were summated and expressed in mean values.

(ii) Peak Amplitude

The peak amplitude values obtained by both observers and the microcomputer are shown in Table 4.3. A significant intra observer difference was found between assessments of peak amplitude by *Observer I*. In addition the inter-observer difference was highly significant (mean of 2 assessments *Observer I* vs mean of 2 assessments *Observer II*, $p < 0.001$).

Table 4.1.

Number of Peaks Detected - Observer Variation

	OBSERVER I		*OBSERVER II*	
	First Assessment	Second Assessment	First Assessment	Second Assessment
Study A				
Antrum	8	8	7	7
Duodenum	22	22	17	16
Jejunum	27	26	20	23
Study B				
Antrum	9	8	10	9
Duodenum	21	19	17	19
Jejunum	21	24	23	20
Study C				
Antrum	11	9	12	12
Duodenum	21	16	17	17
Jejunum	16	16	26	22

Statistics		†*p* value
Intra-Observer:	*Observer I*	0.06
	Observer II	0.56
Inter-Observer:		0.67

†2 way ANOVA

Table 4.2.

Number of Peaks Detected - Observers vs Computer

	‡Mean of *Observer I*	‡Mean of *Observer II*	Mean of 2 Observers	Computer Assessment
Study A				
Antrum	8	7	7	10
Duodenum	22	16	19	18
Jejunum	26	21	23	22
Study B				
Antrum	8	9	8	7
Duodenum	20	18	19	20
Jejunum	22	21	21	23
Study C				
Antrum	10	12	11	12
Duodenum	18	17	17	18
Jejunum	17	24	20	21

Statistics	†*p* value
Computer vs. mean of 2 Observers :	0.19

‡mean of two assessments

†2 way ANOVA

Table 4.3.

Contraction Amplitude

	1st Assessment	2nd Assessment	†Intra-observer difference (*p* value)	Intra-observer Mean Bias	Mean of 2 Assessments
Observer I (mmHg)	29.8 ± 1.47	29.7 ± 1.46	0.02	0.19 ± 0.8	29.7 ± 1.47
Observer II (mmHg)	29.1 ± 1.4	29.1 ± 1.46	0.63	-0.07 ± 0.93	29.1 ± 1.45

†Inter *Observer I / Observer II* difference (*p* value) : <0.001

Overall Observer Mean Assessment : 29.4 ± 1.46 mmHg

Computer Assessment : 29.7 ± 1.37 mmHg

Mean Bias : 0.31 ± 3.5 mmHg

†Inter Observer/Computer difference (*p* value) : 0.68

Values for mean bias expressed as mean ± s.d.

Values for assessments expressed as mean ± s.e.m.

†2 way ANOVA

No significant differences however were found between the microcomputer and the mean of both observers in assessment of contraction amplitude and the difference of agreement between the microcomputer and the mean of both observers was very small (mean bias ± sd : 0.31 ± 3.5 mmHg).

(iii) Peak duration

The peak duration values obtained by both observers and the microcomputer are shown in Table 4.4. A significant intra observer difference was found between assessments of peak duration by *Observer II*. In addition the inter-observer difference was highly significant (mean of 2 assessments *Observer I* vs mean of 2 assessments *Observer II*, $p < 0.001$).

No significant differences however were found between the microcomputer and the mean of both observers in assessment of contraction duration, and the difference of agreement between the microcomputer and the mean of both observers was also very small (mean bias ± sd : 0.18 ± 2.37 secs).

Artefact Removal

Extraction of cough/sneeze/movement artefact

The number of such artefacts obtained by both the microcomputer and the two observers are shown in Tables 4.5 & 4.6. No significant inter or intra observer differences were found in definition of simultaneous pressure events consistent with cough artefact (Table 4.5). The microcomputer detected fewer of these events than observers, although differences were not significant (Table 4.6).

Table 4.4.

Contraction Duration

	1st Assessment	2nd Assessment	†Intra-observer difference (*p* value)	Intra-observer Mean Bias	Mean of 2 Assessments
Observer I (seconds)	5.19 ± 0.23	4.85 ± 0.25	0.55	0.33 ± 0.7	5.01 ± 0.24
Observer II (seconds)	5.45 ± 0.25	5.29 ± 0.25	0.002	0.17 ± 0.65	5.36 ± 0.25

†Inter *Observer I / Observer II* difference (*p* value) : <0.001

Overall Observer Mean Assessment : 5.19 ± 0.24 seconds

Computer Assessment : 5.37 ± 0.25 seconds

Mean Bias : 0.18 ± 2.37 seconds

†Inter Observer/Computer difference (*p* value) : 0.62

Values for mean bias expressed as mean ± s.d.

Values for assessments expressed as mean ± s.e.m.

†2 way ANOVA

Table 4.5.

Detection of Cough/Sneeze/Movement Artefact: Observer Variation

		STUDY A	STUDY B	STUDY C
OBSERVER I	first	9	15	16
	second	9	13	16
OBSERVER II	first	12	13	17
	second	12	12	15

Statistics		*p* value †
Intra-Observer:	*Observer I*	0.42
	Observer II	0.23
Inter-Observer:		0.63

†2 way ANOVA

Table 4.6.

Detection of Cough/Sneeze/Movement Artefact

	STUDY A	STUDY B	STUDY C
COMPUTER	10	12	14
OBSERVER 1*	9	14	16
OBSERVER 2*	12	13	16

Statistics	*p* value†
Computer vs Observers:	0.3

*Mean of two assessments

†2 way ANOVA

Recognition of the migrating motor complex

(a) Migrating motor complex detection

The total number of MMC's detected by the observers in each assessment and by microcomputer is shown in Table 4.7. The microcomputer correctly identified each of the MMC's detected by both the observers.

(b) Migrating motor complex phase duration

Significant differences were found in intra-observer (*Observer II*) and inter-observer assessment of jejunal phase I (Table 4.10) and inter-observer assessment of duodenal phase I (Table 4.9). There was no significant intra and inter observer differences in assessment of the duration of all phases of the gastric MMC or of phase II and phase III in the duodenum and jejunum (Tables 4.8-4.10). Differences between the microcomputer and mean of both observers in assessment of duodenal and jejunal phase I duration, were significant (Table 4.11). The difference of agreement in assessment of phase I duration in the duodenum was 1.83 ± 2.08 mins [mean bias ± sd], and in jejunum was 0.48 ± 0.69 mins [mean bias ± sd], (Table 4.11). No significant differences were found in assessment of duration of any other phase of the MMC and differences of agreement were small.

(c) Migration velocity of the migrating motor complex

A comparison of microcomputer *vs* observer assessment of migration velocity of the MMC in the small bowel is shown in Table 4.12. No significant differences were found between microcomputer results for this parameter and the mean of both observers (Table 4.12), and the difference of agreement small (mean bias ± sd : -0.004 ± 0.26 cms/min).

Table 4.7.

Total Number of Migrating Motor Complexes Detected

	ANTRUM	DUODENUM	JEJUNUM
Observer I	8	14	15
Observer II	8	14	15
Computer	8	14	15

Table 4.8.

Duration of the Phases of the MMC - Antrum

	OBSERVER I			*OBSERVER II*			
	First Assessment (minutes)	Second Assessment (minutes)	†Intra-Obs. *p* value	First Assessment (minutes)	Second Assessment (minutes)	†Intra-Obs. *p* value	†Inter-Obs. *p* value
Phase I	16.6 [11-50.9]	14.2 [11.6-46.1]	0.89	25.6 [13-56.4]	25.7 [13.3-55.7]	0.52	0.28
Phase II	37.3 [20.6-54.9]	29.8 [9.6-52.3]	0.91	40.7 [9-54.3]	32.5 [9.2-54.5]	0.5	0.36
Phase III	3.85 [2.85-4.7]	4.2 [2.8-5.6]	0.27	3.8 [2.9-5]	3.95 [3.3-4.6]	0.9	0.9

Values for the Observer Assessments expressed as median [inter-quartile range]

†2 way ANOVA

Table 4.9.

Duration of the Phases of the MMC - Duodenum

	OBSERVER I			*OBSERVER II*			
	First Assessment (minutes)	Second Assessment (minutes)	†Intra-Obs. *p* value	First Assessment (minutes)	Second Assessment (minutes)	†Intra-Obs. *p* value	†Inter-Obs. *p* value
Phase I	19.2 [16.4-40]	26.2 [16.6-40.4]	0.6	20.0 [17.3-46]	19.4 [16.7-46.6]	0.84	0.04
Phase II	45.9 [31-58.5]	49.8 [31.1-58.4]	0.23	41.2 [31-53.9]	43 [31.5-55]	0.63	0.2
Phase III	4.55 [3.5-6.6]	4.3 [3.6-5.9]	0.31	4.15 [3-6.5]	5.1 [3.2-6.7]	0.09	0.87

Values for the Observer Assessments expressed as median [inter-quartile range]

†2 way ANOVA

Table 4.10.

Duration of the Phases of the MMC - Jejunum

	OBSERVER I			*OBSERVER II*			
	First Assessment (minutes)	Second Assessment (minutes)	†Intra-Obs. *p* value	First Assessment (minutes)	Second Assessment (minutes)	†Intra-Obs. *p* value	†Inter-Obs. *p* value
Phase I	20.9 [13.8-24.5]	20.8 [13.8-24.3]	0.71	22.1 [13.1-25.2]	21.9 [12.8-24.9]	0.12	0.05
Phase II	43.4 [35.8-52.5]	43.5 [35.3-52.6]	0.09	43.5 [35.9-52.5]	43.6 [35.2-52.8]	0.64	0.64
Phase III	6.2 [5.2-8.4]	5.6 [5.1-8]	0.3	5.9 [5-8]	5.9 [5-8.1]	0.79	0.72

Values for the Observer Assessments expressed as median [inter-quartile range]

†2 way ANOVA

Table 4.11.

Duration of the Phases of the MMC - Observer vs Computer

		Mean of 2 Observers (minutes)	Computer Assessment (minutes)	Computer/Observer difference (p value)	Mean Bias (minutes)
ANTRUM	Phase I	20.7 [12.3-52]	15.1 [10.4-54.4]	0.6	-1.27 ± 6.35
	Phase II	39.9 [11.7-54]	40.8 [23.8-49]	0.64	4.1 ± 6.69
	Phase III	4.2 [3-5]	3.8 [2.3-5.5]	0.2	-0.07 ± 0.8
DUODENUM	Phase I	19.7 [16.8-43.2]	22 [18-45]	0.25	1.83 ± 2.08
	Phase II	44.9 [31.2-55.3]	44.8 [30.9-54.6]	0.14	-0.56 ± 1.54
	Phase III	4.4 [3.3-6.6]	5.2 [2.9-6.4]	0.63	0.09 ± 0.64
JEJUNUM	Phase I	22 [13.4-24.7]	22.2 [13-25]	0.03	0.48 ± 0.69
	Phase II	43.5 [35.6-52.6]	41.5 [33-50]	0.65	-2.47 ± 8.29
	Phase III	5.8 [5.1-8]	6 [5-7.9]	0.82	-0.01 ± 0.26

Values for the Assessments expressed as median [inter-quartile range]

Values for the Mean Bias expressed as mean ± s.e.m.

†2 way ANOVA

Table 4.12.

Migration Velocity of the MMC (Small Bowel)

	1st Assessment	2nd Assessment	†Intra-observer difference (*p* value)	Mean of 2 Assessments
Observer I (cms/min)	8.85 [5.2-11.2]	8.55 [5.3-10.8]	0.88	8.7 [5.25-11]
Observer II (cms/min)	9 [4.9-11.4]	8.8 [5.1-11.9]	0.56	8.9 [5-11.7]

†Inter *Observer I / Observer II* difference (*p* value) : 0.21

Overall Observer Mean Assessment : 8.71 [5.12-11.35] cms/min

Computer Assessment : 8.85 [5.1-11.3] cms/min

Mean Bias : -0.004 ± 0.26 cms/min

†Inter Observer/Computer difference (*p* value) : 0.36

Values for assessments expressed as median [inter-quartile-range]

Values for mean bias expressed as mean ± s.d.

†2 way ANOVA

DISCUSSION

The aim of the work described in this chapter was to develop a microcomputerised method of analysing the contractile response of the gastrointestinal tract, prior to correlating this response with the SVA signal. Useful programs for measurement of contractions, including contraction amplitude, duration and propagation have been developed in previous studies (Parker R, 1987, Farrar T, 1960) but none had facilities for pattern recognition for the migrating motor complex (MMC), nor measurement of MMC characteristics in stomach and small bowel. None have undergone a comprehensive evaluation against skilled observers for the above complex parameters. Standards were set for peak recognition, peak propagation, pattern recognition for the gastric and small bowel migrating motor complex and definitions of signal artefact characteristics, on the basis of manometry studies from our own laboratory. Appropriate algorithms were developed, as described.

Difficulties associated with observer validation were addressed as far as possible in the design of this study. A number of steps were taken to reduce observer bias. Firstly, a large number of parameters were provided for analysis. Eight 3 hour fasting studies were analyzed for MMC characteristics and 3 x 30 minute segments of fasting data were analysed in detail for contraction characteristics and cough/sneeze/movement artefact. Secondly, measures were taken to optimise observer accuracy. Observers were given fixed criteria and high scale resolution of recordings for definition and precise measurement of motility events. Thirdly, observer reproducibility was addressed by the requirement in this study for two independent assessments of all motility parameters. Finally, in circumstances where a new method is compared against an established, though inexact,

technique, measurements of agreement between the methods as well as of significant differences of results are necessary in order to ascertain whether agreement is sufficient for the new method to replace the old (Bland JM, 1986). In this study therefore, measurements of agreement as well as significant differences were sought where possible, between the microcomputer and observer methods.

Assessment of microcomputer results was considered with reference to observer bias, which was variable in this study. No significant intra or inter observer differences were found in definition of cough/sneeze/movement artefact, MMC occurrence or MMC migration velocity, which may be because these events have readily recognisable characteristics (Tables 4.5,4.7,4.12). Whilst no significant inter and intra observer differences were found for assessment of peak number, differences were found in the assessment of contraction amplitude and duration. Significant intra-observer differences were manifest by *observer I* in the assessment of contraction amplitude and *observer II* in assessment of contraction duration (Tables 4.3,4.4). In addition the inter-observer differences were highly significant in the assessment of these two parameters. These differences highlight the subjective nature of manual analysis in that not only did the two observers differ markedly in their assessment of these two parameters, but that the individuals' assessment differed over the period of two weeks between the two assessments. Although the inter-observer differences in contraction amplitude were small (Table 4.3), the differences were highly significant ($p < 0.001$) because *Observer I* was *consistently* higher in the assessment of amplitude than *Observer II*. Similar findings occurred with the assessment of contraction duration (Table 4.4). These findings would

imply that a standardised approach to the interpretation of the contraction characteristics, such as the microcomputer analysis, is required for consistency in the analysis of motility recordings.

Excellent correlation between the microcomputer analysis and the two observers was found in the evaluation of the duration of the phases of the MMC in the antrum, duodenum and jejunum. The only significant differences were seen in the duration of phase I in the small bowel; the inter-observer difference for duodenal phase I was significant (p = 0.04) and that for the jejunal phase I approached significance. In addition the difference between the mean of the 2 observers and the microcomputer was significant (p = 0.03) for the assessment of duodenal phase I duration. Reproducibility, however, is relevant to method comparison and is related to the difficultly in discriminating the end of phase I and the onset of phase II. Poor reproducibility of an old established method may lead to consistent differences between old and new, even if the new method represents an improvement. In these circumstances standard statistical tests may be misleading and measurements of agreement are often more relevant (Bland JM, 1986). In this study, differences between the microcomputer definition of the duodenal phase I and the mean of both observers reached statistical significance yet the magnitude of those differences were relatively small. For example, the difference of agreement for duodenal phase I duration, between the microcomputer and mean of both observers, was approximately 30 seconds for an event which lasted approximately 22 minutes (mean of both observers for duodenal phase I duration). This difference may be explicable on the basis of repeatability error and is sufficiently small to be unlikely to affect clinical management. Good agreement between the microcomputer and mean

of both observers was found for all other gastric and small bowel MMC phases.

During the development of this program, many alterations to the algorithms were tried and evaluated, in advance of the formal assessment described in this chapter. We believe that the current algorithms are optimal for this program and that the overall similarity of results between the microcomputer technique and observer findings is encouraging. This microcomputer technique has the advantages of convenience and total reproducibility relating to any specific motility recording. Total analysis of 5 channels of a 3 hour motility recording takes only 5 minutes per subject, using a 80387 coprocessor. This study has shown that the new (microcomputer) technique agrees well with the established (observer) technique. Differences relating to any of the measured parameters, were sufficiently small for us to be confident in the use of the microcomputer method. Further algorithms, however, for the correlation of the deflections of the Surface Vibration Analysis recording and the contractions recorded by intraluminal manometry, were required.

Chapter 5

Evaluation of Surface Vibration Analysis against intraluminal manometry, in detection of fasting gastrointestinal motor activity

INTRODUCTION

This thesis seeks to develop, then validate, the Surface Vibration Analysis (SVA) system against the gold standard of intraluminal manometry, in detection of fasting gastrointestinal motor activity. Some of the problems which would impede the achievement of this objective have been addressed in previous chapters and satisfactory solutions have been obtained. For example, the development of the microcomputer system has enabled reproducible objective assessment of gastrointestinal manometry, for both contraction characteristics as well as contraction patterns. However, further problems require consideration.

A number of considerations are paramount in any comparison of a new method for measurement with an old one, viz:

i) Firstly, it is desirable to reduce measurable events to common factors appropriate for both methods, so that like may be compared with like.

ii) Secondly, in an ideal comparison, simultaneous recording of the same events should be carried out, by both old and new methods.

iii) Thirdly, the study design should address any known differences of specificity or sensitivity of the methods being evaluated.

iv) Finally, an objective correlation is required, of events detected by both old and new methods, in order to eliminate observer bias.

These considerations will be addressed in the present chapter.

MATERIALS AND METHODS

The points outlined in the introduction will be considered separately and the solutions which we have adopted will be described.

1. Reduction of SVA and manometry signals to common factors

As outlined in chapter 2, all SVA signals were integrated over intervals of 5 seconds, which approximates to the minimum inter-contractile interval of gastrointestinal contractions (Fleckenstein P, 1978). The choice of this interval allowed recognition of distinct SVA responses to individual contractions within any single channel. Thus, for any given contraction, it became possible to show the intraluminal pressure change on manometry and, if present, any appropriate SVA response to it.

Definition of an SVA Response

An algorithm was developed to define and recognise an SVA response as an elevation of SVA signal in excess of 30 integers above baseline. This value was chosen because it approximated to 2x baseline value and could be consistently distinguished from baseline fluctuation. As outlined in chapter 2, the response range of the SVA system was 0-4096 integers within a constant linear scale and therefore the range of the SVA responses was between 30-4096 integers. A wide scatter of results between these 2 extremes has been obtained in this thesis.

2. Simultaneous recording and display of the SVA with manometry data

SVA responses, which had intervals of 5 seconds, were fed to an analogue to digital convertor and digitised at the *same sampling rate of 5 Hz* as used for the motility data. This allowed SVA signals to

be processed in exactly the same way as incoming motility data, in a simultaneous timeframe. This SVA data could then be displayed in one channel of the motility analysis program and evaluated against manometry data in the remaining channels.

The resultant SVA signal is a rectangular waveform, with minor fluctuations caused by high frequency sampling (Figure 5.1). The SVA response was then measured as the difference between maximum amplitude and the mean of baseline values, on either side of the response.

3. Differences of sensitivity and specificity for detection of contractions, between SVA and manometry

Gastrointestinal motor activity is often multifocal and contractions or contraction patterns may occur at multiple sites simultaneously or near simultaneously. While intraluminal manometry can show this multifocal activity on multiple channels, the external SVA monitor is global and currently provides only one channel of data.

Contraction patterns - the Migrating Motor Complex

The present capacity for generating only a single channel of data is arguably the greatest limitation of the SVA system. However, within the gastrointestinal tract, contractile *pattern* events occur in adjacent regions within short fixed time intervals. For example, lengthy parts of the upper gastrointestinal tract in the fasting state, may be wholly quiescent during phase I of the migrating motor complex, or wholly active during phases II and III. Although phase I may last longer in some parts than others, eg in the gastric antrum, there is a lengthy interval when all channels (antrum, duodenum and jejunum) are quiescent. There are similar intervals when all channels are active in

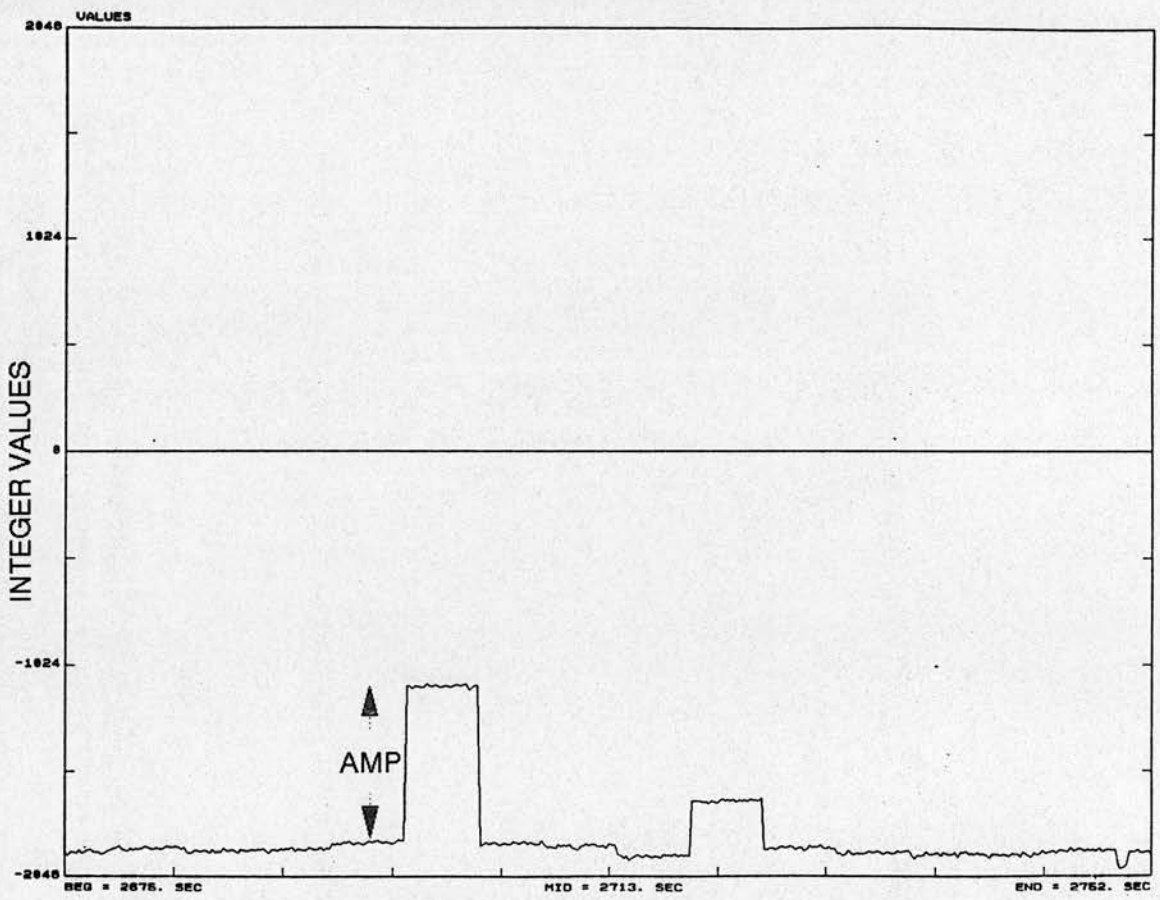

Figure 5.1. An example of the rectangular waveform of an SVA energy response to vibrational energy from the gastrointestinal tract. The minor fluctuations in the signal are caused by the high frequency sampling of the PC-Motil program and are eliminated by a smoothing routine. **AMP** represents the amplitude of the SVA response.

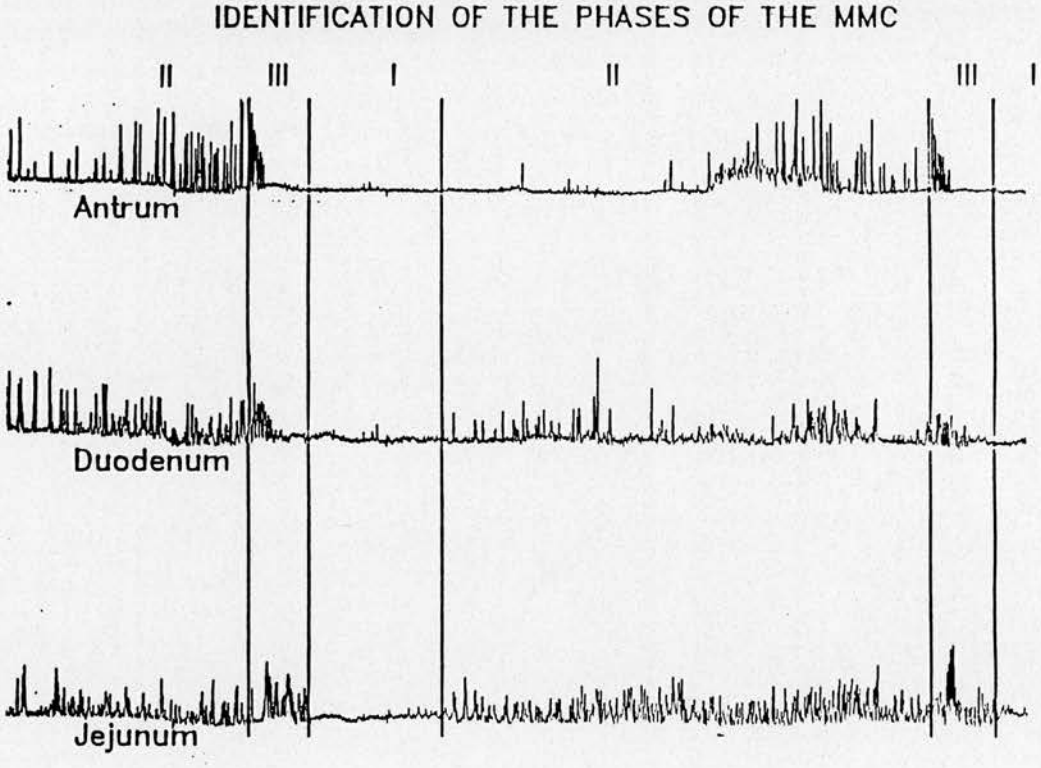

Figure 5.2. Identification of the phases of the MMC for subsequent correlation with the SVA channel. Only 3 channels of motility data are shown for clarity. The antrum, duodenum and jejunum are regarded as a *regional unit* within the upper gastrointestinal tract.

phase II or in phase III (Figure 5.2). It is thus possible to consider the upper gastrointestinal tract as a *regional unit* which may be quiescent in phase I of the MMC, or active in phases II or III.

For the purposes of the assessment described in this thesis, SVA responses were evaluated against MMC activity in the upper gastrointestinal tract, as a *regional* unit. Algorithms were constructed which defined phase I, according to characteristics described in chapter 4, as quiescence in all channels. The time of onset of phase I was defined from the end of the *last occurring* phase III, which was usually in the most distal channel. Phase II onset was timed from the first appearance of phase II *in any channel*, defined by characteristics outlined in chapter 4, to the time of onset of the first phase III *in any channel* (Figure 5.2). Individual phases were therefore assessed *without channel discrimination* and SVA responses were assessed in relation. The accumulated SVA response over each phase was divided by the duration in minutes, to give a mean SVA energy response/minute.

This approach seemed reasonable for evaluation of *contraction patterns* activity against SVA and a similar modified approach was utilised for evaluation of *individual contractions*.

Isolated Contractions

An assumption was made that the vibration energy emanating from any specific contraction would occur during the interval between the onset and end of that contraction. Since the maximum contraction frequency in the upper gastrointestinal tract is 9-12 contractions/minute (Fleckenstein P, 1978), the minimum intercontractile interval is 5 seconds. Hence, the SVA signal is integrated over a 5 second interval, in order to allow optimum discrimination between sequential contractions within the same channel.

Therefore, there may be up to a 5 second delay in the SVA response, from the time of the end of that contraction and so a time window was constructed from the beginning of the manometric contraction to its end + 5 seconds (Figure 5.3). Any SVA response occurring within that time window was considered a response to that contraction.

Multiple Contractions

The program also scans *all* other manometric channels to detect any contractions in other channels, within that time window (Figure 5.4). If multiple contractions occurred at different sites within the time window, then the SVA response was considered to be in relation to the *combination* of the contractions. Any SVA responses to single and combinations of contractions, was summated and recorded by the computer.

SVA Artefact

Any movement or cough by the subject could give an SVA artefact. Artefact removal from the SVA signal is a more difficult task than from manometry signals. At the time of the studies in this thesis, there was no automated artefact removal and hence, careful observations of the subject were carried out throughout the entire recording. The time of any such movement was noted by the observer and entered into the computer program. If an SVA response occurred within a 5 second interval of the recorded time, then this response was eliminated from the program and designated as SVA artefact.

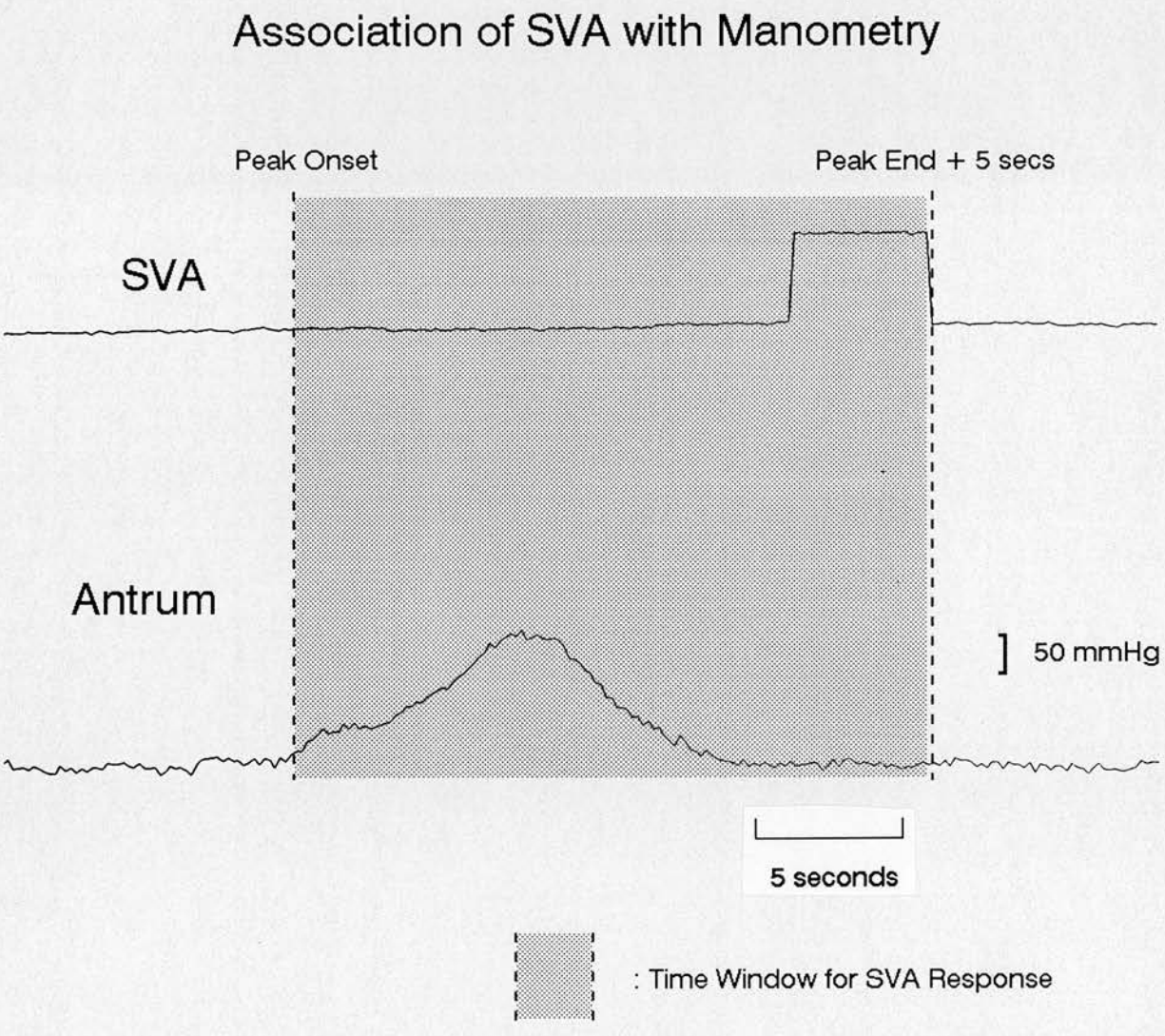

Figure 5.3. The SVA response is associated to the manometric contraction if the SVA response occurs within the above time window, related to the onset and end of the manometric contraction.

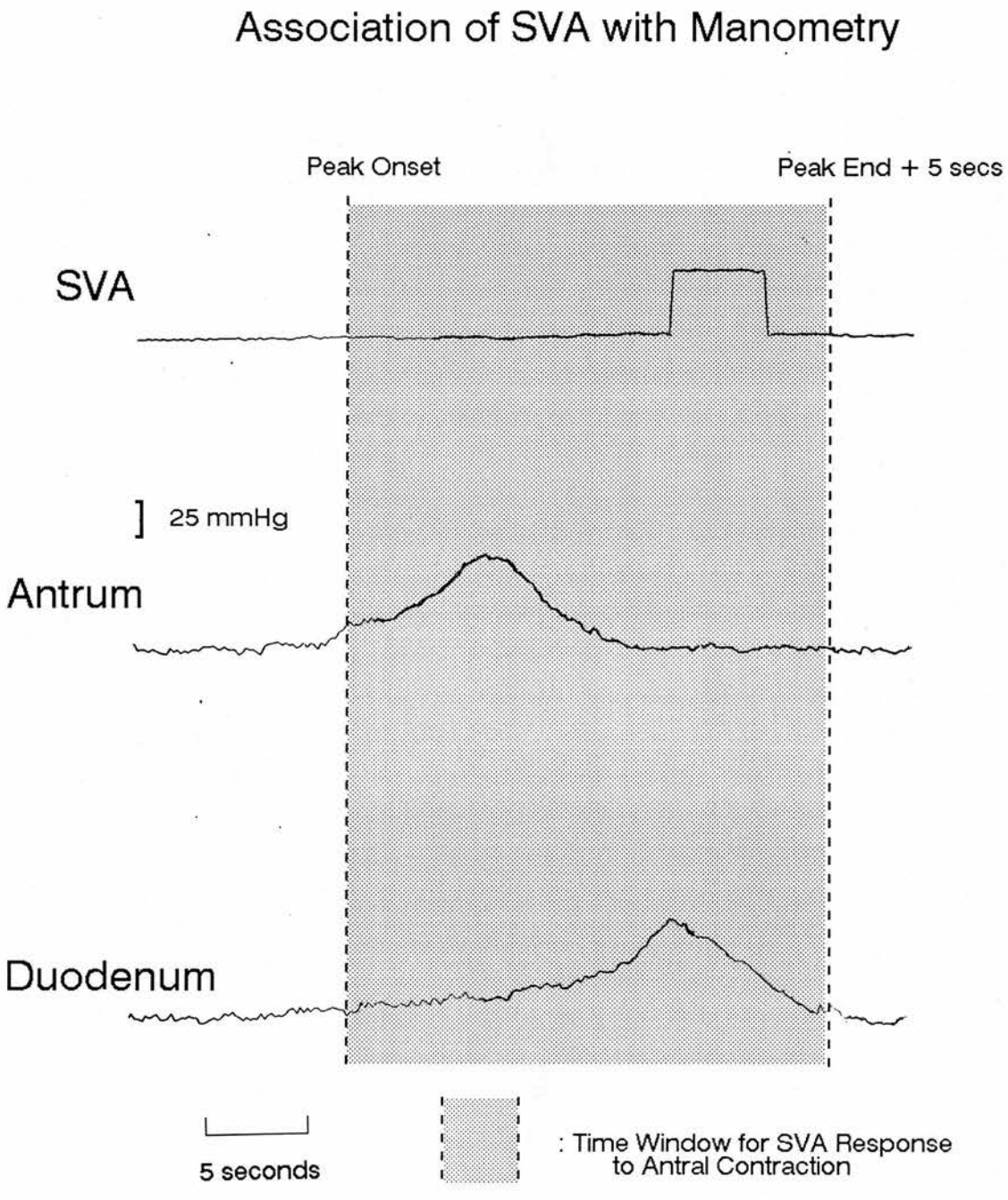

Figure 5.4. A duodenal contraction has occurred within the time window of the antral contraction. Thus the SVA response may be due to a combination of the two manometric contractions.

4. Objective correlation of events detected by both systems

i) **SVA responses to individual Migrating Motor Complex phases** in the *Upper Gastrointestinal Region.* The upper gastrointestinal MMC phases were defined as outlined previously.

The accumulated SVA response per minute (vibration energy/minute) were considered for each phase of the MMC.

ii) **Individual Contractions** - Algorithms were defined to distinguish:

(a) Single contractions in any single channel *with* an associated SVA response.

(b) Closely spaced contractions occurring within the same time window, in multiple channels *with* an associated SVA response.

Both values were expressed as the proportion of the total number of contractions within both phase II and phase III of the MMC.

iii) **Contraction Characteristics** - An evaluation of contraction amplitude, duration and motility index was made between manometric contractions and the associated SVA amplitude response. For the purposes of this correlation, only single contractions, without further contractions within the given time window, were assessed. This avoided any overlap between the manometric contractions and the associated SVA response.

RECORDING OF SVA AND INTRALUMINAL MANOMETRY

Surface Vibration Analysis was carried out on 20 volunteers undergoing intraluminal manometry recording, as described in chapter 3. The recording was carried out in the baseline fasting state (*BL*). Ethical permission was obtained from the Tayside Health Board Ethical Committee as before.

Surface Vibration Analysis

The SVA accelerometer (Bruel & Kjaer type 4370) was placed on the right upper quadrant, as used in previous experiments (Cullen PT, 1989). The signal from the accelerometer was passed to a Bruel and Kjaer amplifier (type 2626), which was in turn connected to a 4 pole high pass Butterworth filter to eliminate the aortic signal (chapter 2). From the high pass filter the signal then passed through a purpose built digital integrator which amplified and integrated the signal over 5 second intervals. The signal was then split from the digital integrator to an OPUS V microcomputer for incorporation into the PC-Motil program and also addressed to the analogue to digital converter of a BBC microcomputer, which allowed the measurement of both the minute interval SVA energy response and the accumulated SVA energy response over the individual study periods.

Data Recording

Each of the individual studies of varying intraluminal condition lasted a period of 3 hours. The accelerometer was secured to the abdominal surface using Sleek adhesive tape[13]. All clothing was removed

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[13] Johnson & Johnson Ltd., Maidenhead, UK.

from the abdominal surface and the vicinity of the accelerometer in order to avoid artefact interference from the movement of clothing adjacent to the accelerometer. At the onset of each study, the SVA signal was calibrated over a period of a minute against a fixed oscillator, which was placed in the circuit between the high pass filter and the digital integrator. The SVA energy response of this calibration signal was removed in the subsequent analysis of the accumulated SVA response. During the study period the intraluminal manometry was recorded by a water-filled catheter, perfused by a low-compliance Arndorfer system at 0.2 mls/min/channel, with manometric ports placed in the antrum, duodenum and jejunum as before (chapter 3). During the study, volunteers were asked to remain as still as possible, in order to reduce movement artefact. At the end of each study period, the volunteers were disconnected from the recording apparatus to allow some movement and gentle exercise.

Statistical Analysis

The values for the contractions associated with an SVA response and the accumulated SVA response over the individual phases were not normally distributed and therefore expressed as the median [inter-quartile range]. Comparison of differences of the SVA response between the individual phases of the MMC was by the Mann Whitney U test. The correlation between the individual contraction characteristics and the SVA energy response was by simple regression analysis with the correlation coefficient being expressed.

RESULTS

(*i*) Contractions associated with an SVA response

The proportion of the contractions associated with an SVA response during both phase II and phase III are shown in Tables 5.1 & 5.2.

(*ii*) Individual Peak Characteristics

An example of the relationship between the antral contraction amplitude and the associated SVA response is given in Figure 5.5. There was no correlation between the SVA energy response and the associated manometric contraction in terms of the contraction amplitude, duration and motility index (Table 5.3).

(*iii*) Individual Phases of the MMC

A typical tracing showing the SVA recording and the intraluminal manometry is shown in Figure 5.6. The values for the individual phases of the MMC are given in Table 5.4. The SVA response/minute for phase I was significantly less than the SVA response for phase II and phase III. There was no difference in the SVA response/minute between phase II and phase III.

Table 5.1

Proportion of Phase II Contractions associated with an SVA Response

	ANTRUM	DUODENUM	JEJUNUM
*Individual Contractions	0.71 [0.46-1]	0.61 [0.27-0.8]	0.52 [0.36-0.63]
†Multiple Contractions	0.05 [0.02-0.1]	0.25 [0.17-0.38]	0.31 [0.26-0.45]

*Individual Contractions : Contractions with an associated SVA response, *without* further contractions in the given time window.

†Multiple Contractions : Contractions with an associated SVA response, *with* further contractions in other channels in the given time window.

Table 5.2

Proportion of Phase III Contractions associated with an SVA Response

	ANTRUM	DUODENUM	JEJUNUM
*Individual Contractions	0.54 [0.33-0.6]	0.29 [0.23-0.33]	0.23 [0.16-0.38]
†Multiple Contractions	0.09 [0.06-0.13]	0.41 [0.23-0.51]	0.48 [0.29-0.62]

*Individual Contractions : Contractions with an associated SVA response, *without* further contractions in the given time window.

†Multiple Contractions : Contractions with an associated SVA response, *with* further contractions in other channels in the given time window.

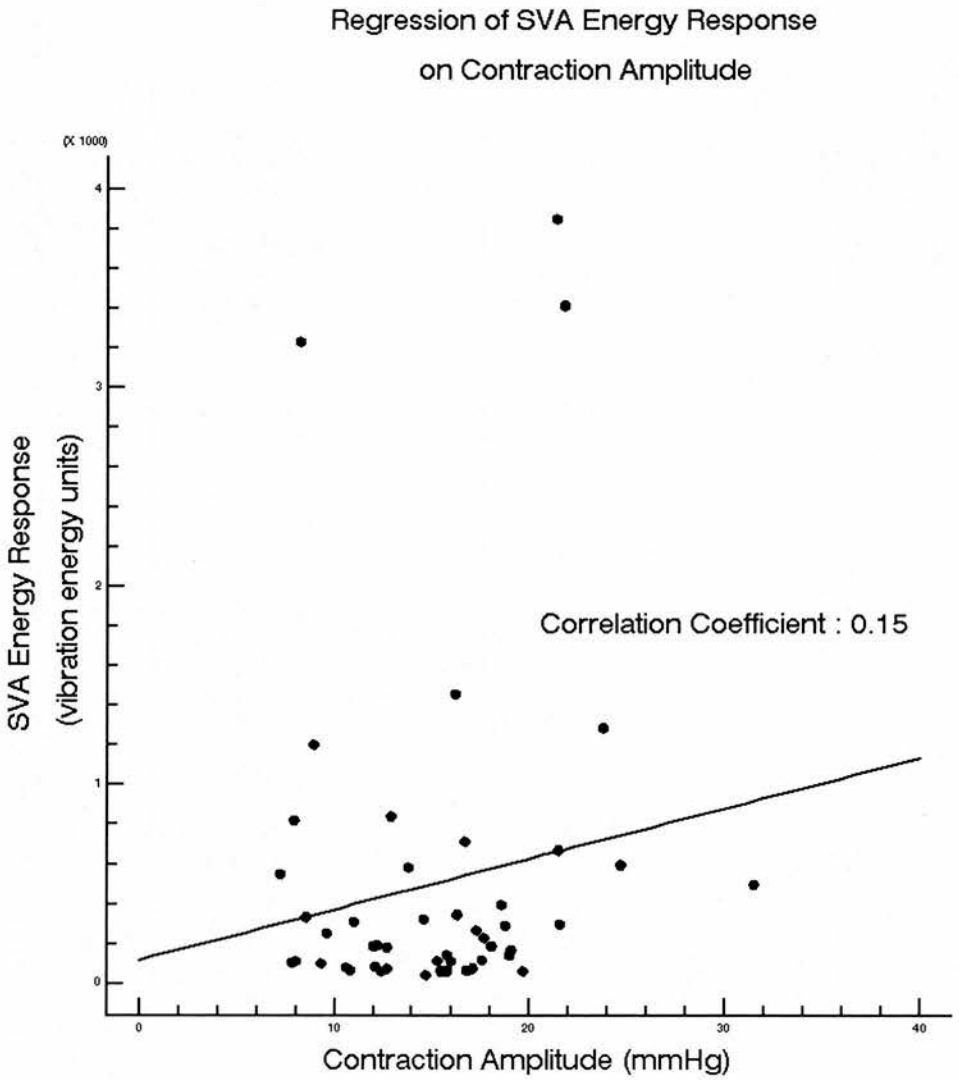


Figure 5.5. The relationship between the contraction amplitude in the antrum and the associated SVA response, showing a poor correlation.

Table 5.3.

Correlation of the SVA Energy Response with Contraction Characteristics

Value expressed is the Correlation Coefficient

	Peak Amp.	Peak Duration	Peak M.I.
ANTRUM	0.15	0.05	0.14
DUODENUM	0.09	0.09	0.17
JEJUNUM	0.14	0.12	0.07

Peak Amp. : Peak Amplitude; Peak M.I. : Peak Motility Index

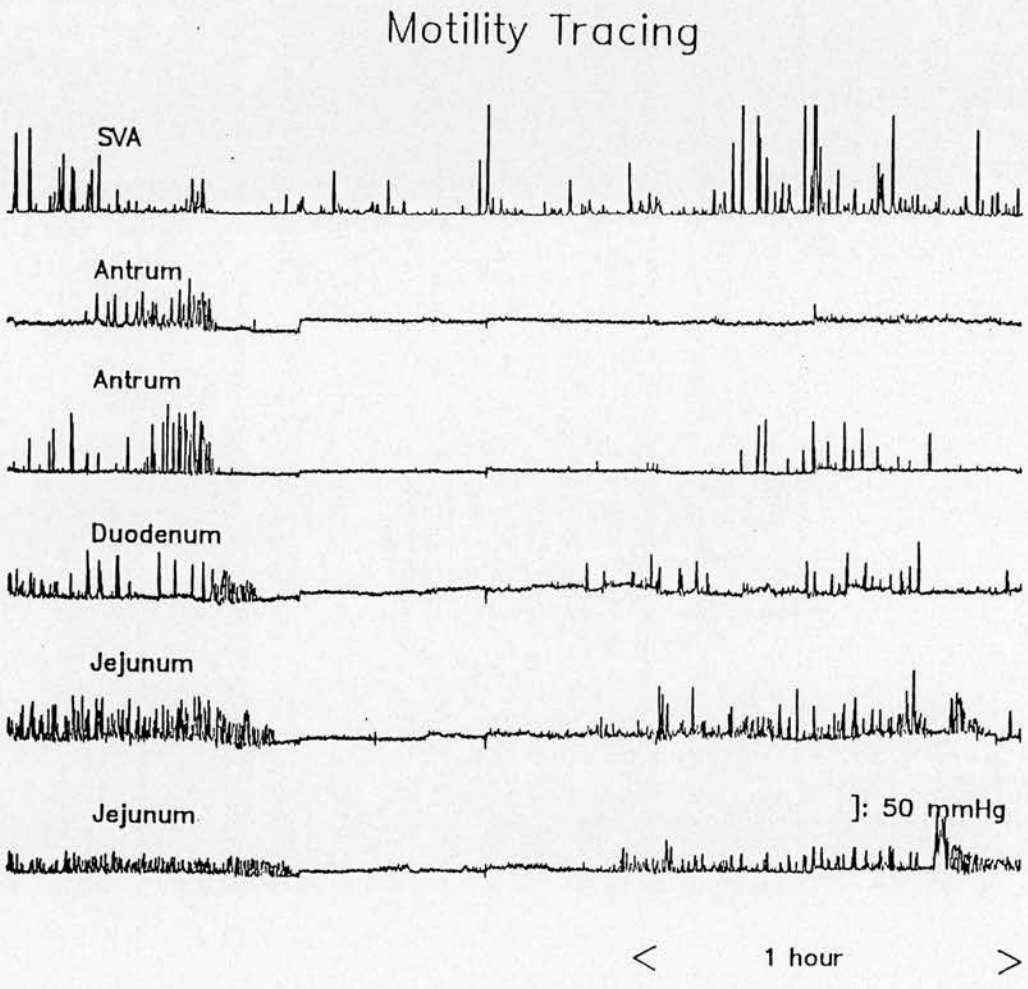


Figure 5.6. A typical tracing as recorded by the "PC-Motil" program. The first channel is that of the SVA recording, with the 5 subsequent channels being the recording from the 5 manometric ports.

Table 5.4.

Accumulated SVA Response for the Individual Phases of the MMC

SVA Response is expressed as median [IQR] X 10^2

vibration energy units/minute.

	Phase I	Phase II	Phase III
SVA Response	6.3 [4.3-8.7]	13.7 [12.3-13.9]	10.9 [9.3-13.3]

Phase I *vs* Phase II : $p < 0.001$

Phase I *vs* Phase III : $p = 0.001$

Phase II *vs* Phase III : $p = 0.12$

DISCUSSION

This chapter has explored the possible use of the measurement of vibrational energy at the abdominal surface, as detected by Surface Vibration Analysis, in the non-invasive detection of the periodic motor activity of the fasting gastrointestinal tract. This required the development of microcomputer algorithms for the comparison of the SVA signal response with the gold standard of intraluminal manometry. The algorithms developed in this chapter allowed several methods of assessment of the SVA signal response, viz the evaluation of the SVA response over the individual phases of the MMC, the association of manometric contractions with an SVA response and the correlation of contraction characteristics with the associated SVA response.

The SVA energy responses/minute during phase II and phase III of the MMC were increased as compared to phase I (Table 5.4). Thus it would appear that Surface Vibration Analysis is able to discriminate between periods of quiescence (phase I) and periods of motor activity (phases II & III) in the gastrointestinal tract. This finding may have important clinical implications, as SVA may be able to elicit noninvasively whether the bowel is hypoactive, or hyperactive. Further evaluation, however, is required to ascertain whether the differences in the SVA energy responses between periods of quiescence and activity remain despite alteration in the intraluminal milieu. This effect will be evaluated in the next chapter.

The association between isolated manometric contractions and an SVA energy response was evaluated during both phase II and phase III of the MMC, in the antrum, duodenum and jejunum. Phase I is generally devoid of contractions and was not evaluated in this context. The findings of this association show that the proportion of contractions

associated with an SVA response was higher in the antrum as compared to the duodenum and the jejunum, during both phase II and phase III of the MMC. Initially, this result was thought to be due to the higher contraction amplitude within the antrum causing increased vibrational energy emission as compared with the relatively lower contraction amplitude in the duodenum and jejunum. However, to our initial surprise, further analysis revealed that there was no correlation between the SVA energy response and the individual manometric contraction characteristics, including contraction amplitude, duration and the motility index, for any channel (Tables 5.2 & 5.3). The vibrational energy emitted from a contraction is not related to the contraction amplitude and therefore, amplitude alone would not explain the increased proportion of contractions associated with an SVA response found in the antrum. We can only speculate that the increased proportion of SVA responses to contractions within the antrum may be related to the greater intraluminal content at that site. Other factors are likely to affect vibration signals, eg if the intraluminal content is ejected through a narrow orifice, as in gastric emptying, one might expect a greater vibration signal than that of a contraction of similar amplitude or duration, but without significant movement of content. This phenomenon might be measured by assessment of contraction propagation. Evaluation of propagation requires multiple closely spaced sensors (see chapter 4), which was unsuitable for our study design which sought to address a large area of the upper gastrointestinal tract. Multiple closely spaced sensors would have used all available channels on the motility analysis program, while addressing only a short segment of the upper gastrointestinal tract.

A disappointing feature of the work in this chapter is the lack of correlation of basic contraction characteristics, viz amplitude, duration and motility index, with SVA responses. As stated, movement of the intraluminal content may be important for the generation of vibration signals. In this context, the quantity and characteristics of fasting intraluminal content could be important and will be addressed in the next chapter.

In conclusion, this chapter has described the development of algorithms capable of comparing the measurement of gastrointestinal activity by both SVA and intraluminal manometry, and carried out an initial assessment. It has shown that SVA is able to discriminate between periods of motor activity and periods of quiescence in the gastrointestinal tract. This may be useful in the clinical situation, for example in determining the return of normal bowel activity following post-operative ileus. There are disadvantages in that recording artefact remains a difficult problem, although it is only gross movement by the subject that causes significant interference and this may be excluded by both close monitoring of the patient and by keeping the recording period as short as is clinically relevant, as subject movement became more of a problem the longer the study time. This chapter has dealt with the relationship between the motor activity of the fasting gastrointestinal tract and the vibrational energy recorded at the abdominal surface. The subsequent chapter will evaluate the effect of variation of the intraluminal content on the correlation of the SVA response with manometry.

Chapter 6

Correlation of Surface Vibration Analysis and Fasting Gastrointestinal Motility : Effect of Variation in Intraluminal Content

INTRODUCTION

The Surface Vibration Analysis system detects vibration energy within the frequency range of 80 - 10000 Hz. Our hypothesis, to date, is that this vibration energy is generated by gastrointestinal contractions, but the effect of intraluminal content, whether gas or fluid, on the characteristics of this vibration signal is unknown. Farrar and Inglefinger initially held the view that the presence of intraluminal gas was an essential prerequisite for the production of bowel sounds and stated that vigorous motor activity could occur without emission of bowel sounds if the intraluminal content was free of gas (Farrar JT, 1955). However, this view was challenged by later work which stated that the prime requisite for the production of a sound wave was a vibrating object, eg the bowel wall and any transmitting medium, which was not necessarily gaseous (Watson WC, 1967). Data concerning the effects of gas or fluid intraluminal content on the characteristics of vibrational signals, generated by gastrointestinal contractions, are lacking.

The previous chapter described the development of microcomputer algorithms which allowed the comparison of the SVA signal response to both individual contractions and to contraction patterns. A preliminary assessment of this comparison was carried out in the baseline fasting state. The aim of this chapter was to further utilise these algorithms in the evaluation of the effect of variation of intraluminal content on the SVA signal response, and the correlation of this response with intraluminal manometry.

MATERIALS AND METHODS

SYNCHRONOUS RECORDING OF SVA AND INTRALUMINAL MANOMETRY

Subjects

Surface Vibration Analysis was carried out on 20 volunteers undergoing intraluminal manometry recording during all 5 studies of varying gastrointestinal content as described in chapter 3. Ethical permission was obtained from the Tayside Health Board Ethical Committee as before.

Surface Vibration Analysis and Data Recording

Intraluminal manometry and SVA recording was carried out in all 20 volunteers as previously described in chapter 5. Each of the individual studies of varying intraluminal content lasted a period of 3 hours. The intraluminal content was altered, as before, viz:

(i) **Baseline** (*BL*) fasting state (chapter 5)

(ii) **Gas and Fluid Evacuation** (*GFE*)

(iii) **Intragastric Instillation of Gas** (*IIG*)
[350 mls air]

(iv) **Intragastric Instillation of Fluid** (*IIF*) of low viscosity
[350 mls 0.5% methylcellulose solution]

(v) **Intragastric Instillation of Fluid** (*IIF*) of high viscosity
[350 mls of 5% methylcellulose solution]

GFE represents the minimum intraluminal content in the upper gastrointestinal tract. The results obtained from the *GFE* study were compared with that of the normal baseline state (*BL*) and the three instillation studies.

ANALYSIS OF THE CORRELATION OF SVA WITH MOTILITY

The algorithms developed in chapter 5 were utilised, allowing comparison of the following modules, as before, in all 5 conditions of varying intraluminal content:

(*i*) Analysis of the accumulated SVA response with the individual phases of the Migrating Motor Complex

Comparison of the response was made between the individual phases and between the different conditions of varying intraluminal content, with the results given as (vibration energy units/minute).

(*ii*) Accumulated SVA response over entire study period

The total accumulated SVA energy response was expressed over the 3 hour period of each study. This allowed comparison of the total accumulated SVA energy response between the 5 study conditions of varying intraluminal content.

(*iii*) Association of the SVA response with manometric contractions

In this chapter only the number of contractions that were associated with an SVA response, *without* further contractions in other channels within a given time window, were assessed throughout all 5 studies of varying intraluminal content. The number was again expressed as the proportion of the total number of contractions, during both phase II and phase III.

(*iv*) **Correlation of the contraction characteristics against the SVA response**

Correlation of the parameters of the individual manometric contraction, viz contraction amplitude, duration and motility index, was made with the amplitude of the SVA response, and evaluated for all 5 studies of varying intraluminal content.

Statistical Analysis

The values for the proportion of contractions with an associated SVA response and the accumulated SVA response were not normally distributed and were therefore expressed as the median [inter-quartile range]. Comparison of the intra and inter-study differences were by the Mann Whitney U test and Bonferroni's correction factor was used for repeated 2 sample testing. The correlation between the individual contraction characteristics and the SVA response was by simple regression analysis with the correlation coefficient being expressed.

RESULTS

(*i*) Individual Phases of the MMC

(a) Accumulated SVA Response between studies

The values for the individual phases of the MMC for the five studies are given in Table 6.1. Instillation of intraluminal content increased the SVA responses during all phases of the MMC, as compared to evacuation of the gas and fluid from the upper gastrointestinal tract (*GFE*). The greatest effects were seen with the instillation of gas (*IIG*) and declined with the instillation of fluid (*IIF*) and baseline (*BL*).

(b) Accumulated SVA Response within studies

Within each of the 5 studies, the SVA response/minute for phase I was less than the SVA response for phase II (Table 6.2). There was no difference in the SVA response/minute between phase II and phase III in all of the 5 studies (Table 6.2).

(*ii*) Accumulated SVA Energy Response over total study period

The accumulated SVA energy response for the total duration of the individual studies is shown in Figure 6.1. The instillation and the baseline (*BL*) studies significantly increased the total SVA response as compared to evacuation of gas and fluid from the upper gastrointestinal tract (*GFE*). There was no difference in the accumulated SVA response between the baseline (*BL*) and the 3 *instillation* studies.

Table 6.1.

Accumulated SVA Response for the Individual Phases of the MMC

SVA Energy Response is expressed as median [IQR] X 10^2 vibration energy units/minute.

	PHASE I		PHASE II		PHASE III	
	SVA Response	*p* value	SVA Response	*p* value	SVA Response	*p* value
GFE	2.9 [2.7 - 4.4]		7.3 [6.2 - 9.2]		7.4 [6.4 - 8.8]	
BL	6.3 [4.3 - 8.7]	0.001	13.7 [12.3 - 13.9]	0.001	10.9 [9.3 - 13.3]	0.001
IIG	12.9 [9.3 - 14.8]	<0.001	17.9 [16.3 - 19.4]	<0.001	13.3 [12.3 - 18.3]	<0.001
IIF (low)	8.3 [6.3 - 12.4]	<0.001	13.8 [9.6 - 17.8]	0.001	12.8 [9.4 - 16.4]	<0.001
IIF (high)	7.3 [5.3 - 11.1]	0.002	13.9 [9.3 - 19.3]	<0.001	12.4 [9.0 - 16.9]	0.003

p value indicates statistical difference from baseline value for the individual phases of the MMC (Mann-Whitney U test). $P < 0.01$ significant with Bonnferroni's correction.

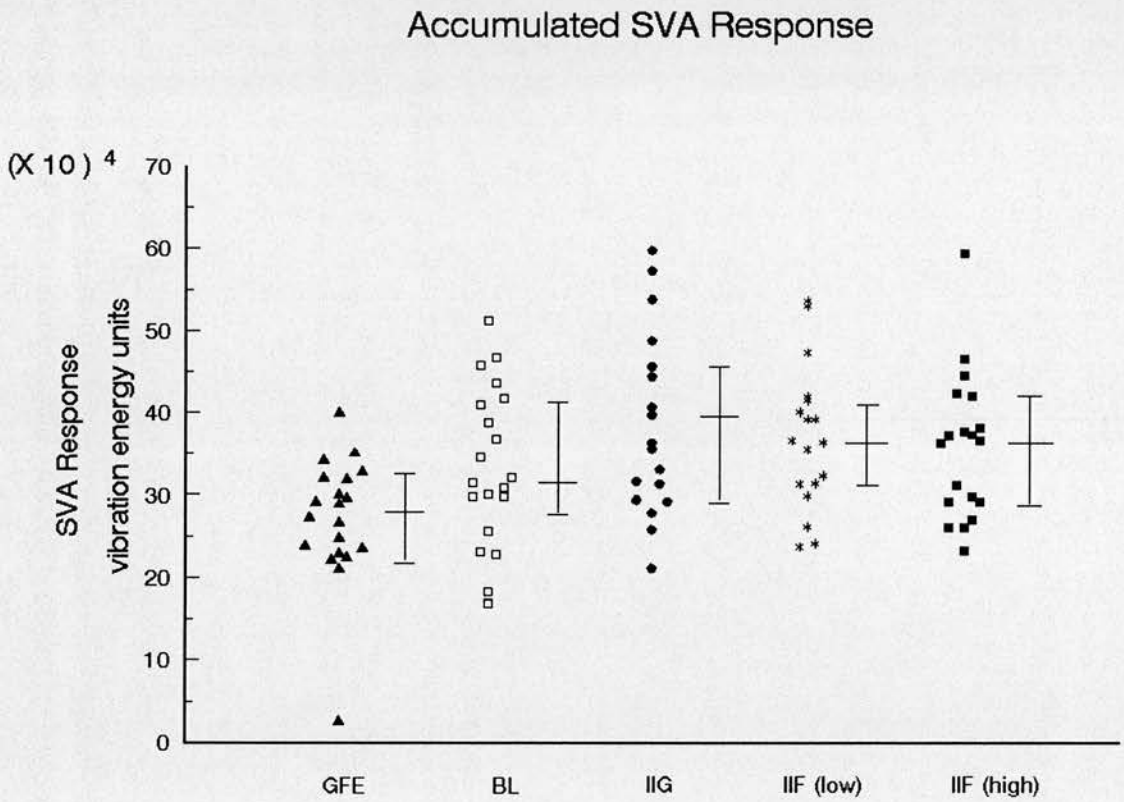
Table 6.2.

Within Study Differences of the SVA Response of the Phases of the MMC

Values for SVA responses are shown in Figure 6.1.

$p < 0.01$ taken as significant with Bonferroni's correction

	Phase I vs Phase II	**Phase I vs Phase III**	**Phase II vs Phase III**
	p value	*p* value	*p* value
GFE	<0.001	<0.001	0.96
BL	<0.001	0.001	0.12
IIG	0.005	0.5	0.03
IIF (low)	0.005	0.004	0.81
IIF (high)	0.01	0.04	0.39



GFE vs *BL* : $p = 0.01$

GFE vs *IIG* : $p < 0.001$

GFE vs *IIF(low)* : $p = 0.007$

GFE vs *IIF(high)* : $p = 0.003$

Figure 6.1. The accumulated SVA energy response for all subjects, for all 5 studies. (bar lines represent the median [inter-quartile range]).

(*iii*) **Contractions associated with an SVA response**

The proportion of the contractions associated with an SVA response during both phase II and phase III are shown in Tables 6.3 & 6.4.

(*iv*) **Individual Peak Characteristics**

There was no correlation between the SVA energy response and the associated manometric contraction in terms of the contraction amplitude, duration and motility index (Table 6.5). This lack of correlation was found in all 5 studies.

Table 6.3.

Proportion of Phase II Contractions Associated with an SVA Response (median [IQR])

	ANTRUM		DUODENUM		JEJUNUM	
		p value		*p* value		*p* value
GFE	0.58 [0.38 - 0.91]		0.59 [0.41 - 0.74]		0.64 [0.41 - 0.78]	
BL	0.71 [0.46 - 1]	0.3	0.61 [0.27 - 0.8]	0.91	0.52 [0.36 - 0.63]	0.04
IIG	0.86 [0.71 - 0.99]	0.5	0.67 [0.62 - 0.74]	0.3	0.61 [0.37 - 0.67]	0.3
IIF (low)	0.78 [0.75 - 0.91]	0.3	0.36 [0.26 - 0.61]	0.27	0.39 [0.24 - 0.62]	0.24
IIF (high)	0.64 [0.26 - 0.75]	0.1	0.31 [0.11 - 0.43]	0.01	0.39 [0.27 - 0.52]	0.36

p value indicates statistical difference from *GFE* study (Mann-Whitney U test).

$p < 0.01$ significant with Bonnferroni's correction.

Table 6.4.

Proportion of Phase III Contractions Associated with an SVA Response (median [IQR])

	ANTRUM		DUODENUM		JEJUNUM	
		p value		*p* value		*p* value
GFE	0.75 [0.65 - 1]		0.14 [0.12 - 0.45]		0.26 [0.13 - 0.39]	
BL	0.54 [0.33 - 0.6]	0.18	0.29 [0.23 - 0.33]	0.91	0.23 [0.16 - 0.38]	0.04
IIG	0.82 [0.61 - 0.9]	0.09	0.38 [0.19 - 0.49]	0.3	0.21 [0.18 - 0.33]	0.3
IIF (low)	0.6 [0.52 - 0.8]	0.56	0.15 [0.06 - 0.32]	0.27	0.15 [0.08 - 0.33]	0.24
IIF (high)	0.5 [0.43 - 0.75]	0.94	0.12 [0.06 - 0.2]	0.01	0.17 [0.08 - 0.43]	0.1

p value indicates statistical difference from baseline value (Mann-Whitney U test)

$p < 0.01$ significant with Bonnferroni's correction.

Table 6.5.

Correlation of the SVA Response with Contractions Characteristics

Value expressed is the Correlation Coefficient

	ANTRUM			DUODENUM			JEJUNUM		
	Peak Amp.	Peak Dur^n	Peak M.I.	Peak Amp.	Peak Dur^n	Peak M.I.	Peak Amp.	Peak Dur^n	Peak M.I.
GFE	0.11	0.08	0.15	0.04	0.13	0.12	0.23	0.08	0.06
BL	0.15	0.05	0.14	0.09	0.09	0.17	0.14	0.12	0.07
IIG	0.12	0.13	0.21	0.17	0.16	0.22	0.25	0.13	0.11
IIF (low)	0.21	0.09	0.26	0.13	0.08	0.18	0.07	0.06	0.2
IIF (high)	0.18	0.11	0.19	0.08	0.13	0.23	0.06	0.13	0.16

Peak Amp. : Peak Amplitude; Peak Dur^n : Peak Duration; Peak M.I. : Peak Motility Index

DISCUSSION

This chapter has utilised the algorithms developed in chapter 5, to further evaluate the relationship between the SVA signal response, gastrointestinal contractions and variation in intraluminal content.

The comparison of the total accumulated SVA response between the 5 study conditions of varying intraluminal content showed that the SVA energy response was significantly increased by the *instillation* studies as compared with *gas and fluid evacuation* (*GFE*). This finding would imply that the presence of gas and liquid in the gastrointestinal lumen is instrumental as transmitting media in the genesis of bowel sounds. The presence of any SVA response during the *GFE* study may indicate that there is not *total* removal of the intraluminal gas and fluid during the evacuation study. In addition, the large bowel may emit vibrational energy. However, no quantitative differences were found in SVA values after a standard stimulus between normal volunteers and total colectomy patients, indicating that the contribution of the large bowel to the total SVA response is likely to be small (Cullen PT, 1991). The highest SVA energy response was found in the *IIG* study, indicating that gas may be the most suitable medium for the transmission of vibration energy from the gastrointestinal tract.

The SVA energy responses during phase II and phase III of the Migrating Motor Complex (MMC) were increased as compared to phase I. This relationship existed throughout all the 5 studies of varying intraluminal content. Thus, Surface Vibration Analysis is able to discriminate between periods of quiescence (phase I) and periods of motor activity (phases II & III) in the gastrointestinal tract. There was, however, no difference in the SVA energy response between phase II

and phase III other than during the *IIG* study and hence SVA is unreliable in the discrimination of phases II and III. SVA appeared to correlate extremely well visually on several occasions with the motor activity of the gastrointestinal tract, particularly phase II activity in the antrum (Figure 6.2). However, as outlined previously, we have not been able to identify the factors associated with good as opposed to poor correlation.

The disappointing lack of correlation between the SVA energy response and the individual manometric contraction characteristics, as shown in chapter 5, persisted despite variation of the intraluminal content. Thus, alteration of the intraluminal content had no effect on the correlation of the SVA response with the characteristics of the gastrointestinal contractions and therefore, the manometric characteristics of a contraction do not correlate with the emitted vibrational energy from that contraction.

The relationship between the motor activity of the fasting gastrointestinal tract, the intraluminal content and the vibrational energy recorded at the abdominal surface has now been fully assessed, within the objectives of our initial remit. However, the optimal positioning of the SVA accelerometer on the abdominal surface for the recording of different sites within the upper gastrointestinal tract remained to be evaluated.

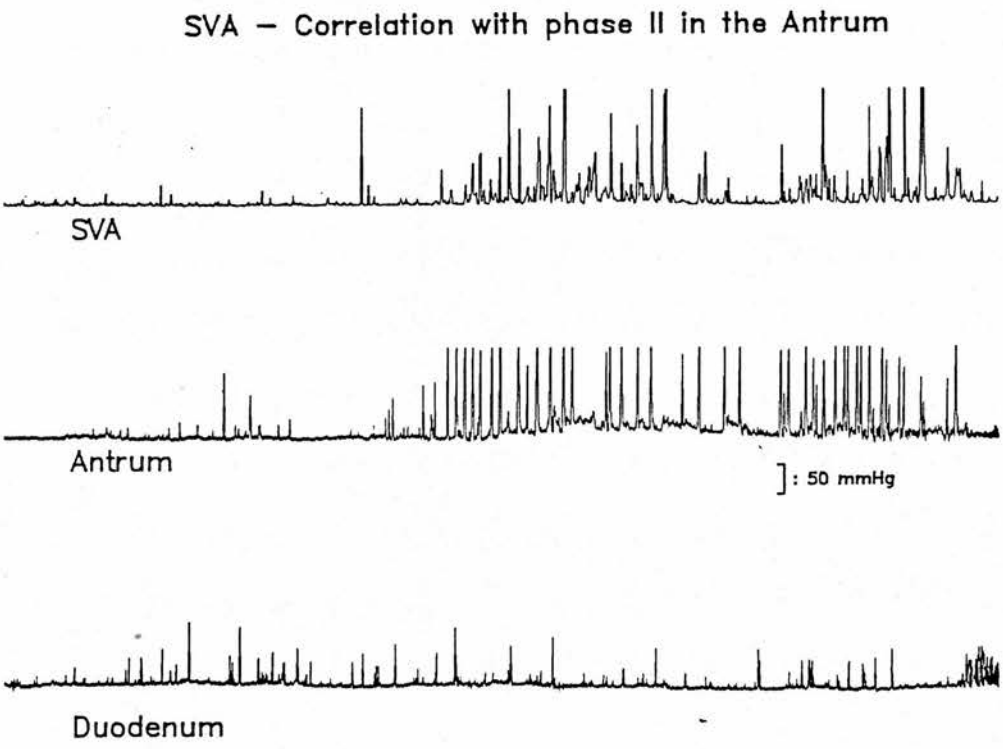


Figure 6.2. An example of good visual correlation between the SVA recording and the antral manometric recording.

Chapter 7

The Effect of Variation in Accelerometer Position on SVA Signal Response

INTRODUCTION

Vibrational energy may emanate from any peristaltic movement of the gastrointestinal tract wall from the stomach to the colon. Whilst it has been previously postulated that the stomach is the most active site in the generation of bowel sounds (Politzer JP, 1976), the relative importance of the stomach, small and large bowel in the genesis of bowel sounds has not yet been determined. Previous work placing multiple transducers on the abdominal surface has been carried out but has not shown any topographical results to indicate which area of the bowel is responsible for the genesis of a bowel sound at a particular site on the abdominal surface (Garner GC, 1989).

The aim of the work described in this chapter was to combine the recording of bowel sounds at the abdominal surface, using multiple accelerometers, together with intraluminal manometry at several sites in the upper gastrointestinal tract. This combination would help determine whether the position of the SVA accelerometer is important in the detection of signals emanating from the stomach and small intestine and if so, what position on the abdominal surface corresponds to which particular site within the upper gastrointestinal tract.

MATERIALS AND METHODS

Subjects

Studies were carried out in 10 healthy volunteers, (4 men, 6 woman, age range 20 - 32 years). In view of the requirement for fluoroscopy, a detailed menstrual and contraceptive history was taken to ensure that the risk of pregnancy was remote. None of the volunteers had any previous or current gastrointestinal complaint and were not taking any medication at the time of the studies. All volunteers gave their informed consent to the protocol, which had been approved by the Tayside Health Board Medical Ethical Committee.

Motility Studies

The perfusion catheter was constructed using 1 x 1.6 metres triple lumen pressure monitoring tubes (Internal Diameter [ID] : 0.78 mm, Outer Diameter [OD] : 2mm) and 1 x 1.6 metres radio-opaque tube (ID : 1.0 mm, OD : 2mm) bonded by tetrahydrofuran glue, as previously described in chapter 3.

Three manometry ports were utilised in this study and each marked by a metal marker. The first port was placed in the antrum and the distal 2 ports 20 cms apart for recording in the duodenum and jejunum. The total diameter of this composite tube was 4 mm and total length 1.6 metres.

After an overnight fast, the volunteers swallowed the perfusion catheter. The tube was positioned under fluoroscopic control, with the minimum field size and a maximum exposure time was 20 seconds, as before, giving a skin entrance radiation dose of 3 mGy. Gonadal shielding was provided by placing a lead apron over the pelvis. Once in its required position, with the proximal port in the antrum and the

distal port in the proximal jejunum, the tube was taped to the side of the subject's cheek. The perfusion catheter was then connected to the low compliance Arndorfer pneumohydraulic perfusion system, with a perfusion rate of 0.2 mls/min/channel. Recordings of manometry and Surface Vibration Analysis were then carried out in the fasting state over 4 hours.

SVA Studies

Two SVA accelerometers (Bruel and Kjaer, type 4370) were utilised in this study. The first accelerometer (*SVA1*) was positioned in the right upper quadrant, immediately beneath the costal margin, in the mid-clavicular line, as in previous experiments (see chapter 5). The second accelerometer (*SVA2*) was placed at varying sites on the abdominal wall surface, at an arc of 90^0 and at a radius of either 7 or 14 cms from the first accelerometer. This corresponded to 6 sites on the abdominal surface (Figure 7.1). The accelerometer was positioned at each respective site for a period of 40 minutes, during the 4 hour recording. Both accelerometers were connected to Bruel and Kjaer pre-amplifiers (type 2626). The signals then both passed through high-pass filters and then to separate digital integrators, as previously described in chapter 5. From each of the digital integrators, the signals were passed to an OPUS V microcomputer running the PC-Motil program. Two channels of the program were utilised by the SVA channels whilst the other 3 channels were used for manometry which allowed synchronous display and subsequent analysis.

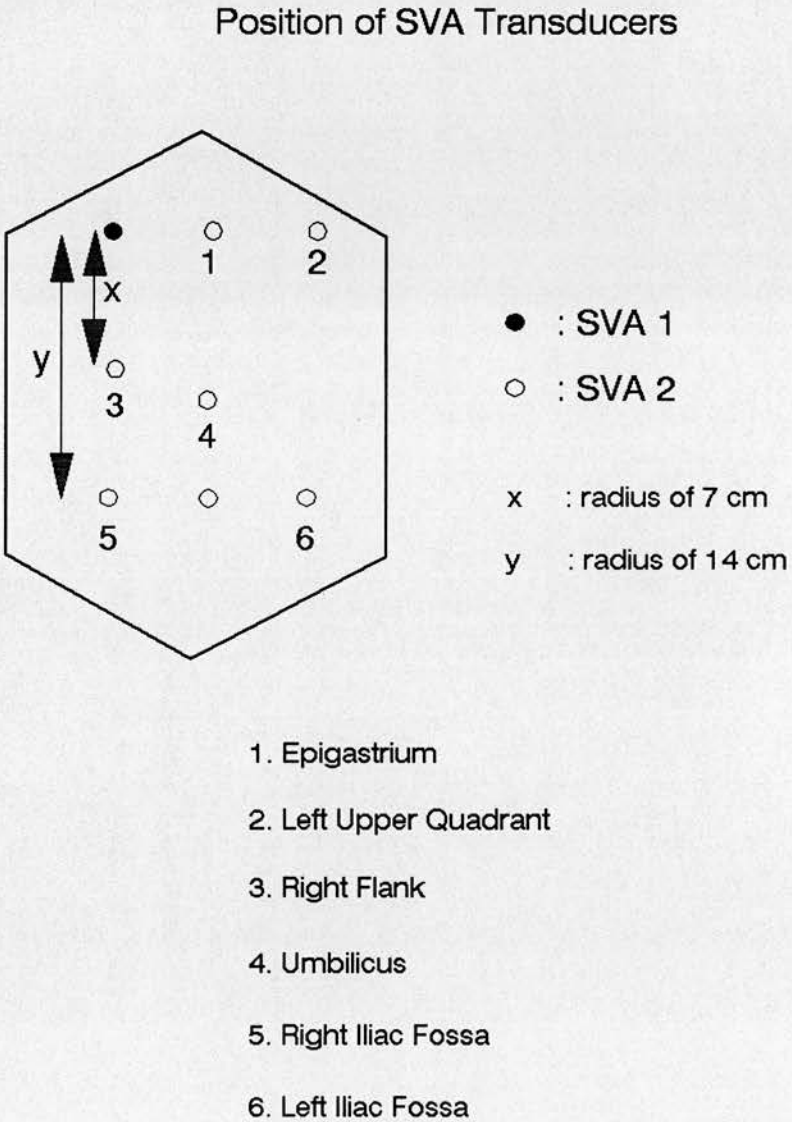


Figure 7.1. The positions of the second SVA accelerometer (*SVA2*) on the abdominal surface.

Motility and SVA signal Analysis

The 3 channel manometric recording and the 2 channels of SVA were all analysed by microcomputer, with further modifications of the software described in chapter 4. Both the SVA channels were analysed by the SVA microcomputer module as described in the chapter 5. Correlation between the SVA channel and the manometric channels was carried out utilising the same time window as described. If a manometric contraction was correlated with an SVA response in the first SVA channel then the second SVA channel was searched for a response. If there was a response in the second SVA channel then the SVA amplitude response in both SVA channels, the manometric contraction amplitude and the site of the channel were recorded and placed in a data file, for subsequent statistical analysis. If there were at least two stationary manometric contractions and simultaneous SVA responses on both the SVA channels, then this was considered as artefact and eliminated. Analysis of all 3 manometric channels was carried out for all 6 sites of the second SVA accelerometer.

The SVA energy values were pooled from all the 10 volunteers and results recorded for the three sites in the upper gastrointestinal tract, ie the antrum, duodenum and jejunum.

Statistical Analysis

The SVA energy response values were expressed as the median and inter-quartile range as appropriate for non-parametric data. The SVA energy response for each site of the second accelerometer was correlated with the SVA energy response of the accelerometer situated in the right upper quadrant, for each of the three regions, the antrum, duodenum and jejunum. Linear regression analysis gave the correlation coefficient and the R^2 value. The R^2 value is an indication of the percentage of variability of the dependent value (the second accelerometer - [*SVA2*]) on the independent variable (the right upper quadrant accelerometer - [*SVA1*]). Linear regression analysis also gives the best fit slope value (b) and the y intercept (a), as follows:

$$y = a + bx$$

RESULTS

SVA Energy Responses

The SVA energy response values for each site of the *SVA2* accelerometer are given in Table 7.1.

Correlation

The correlation coefficient and the R^2 value for the correlation between the right upper quadrant SVA accelerometer (*SVA1*) and the 6 sites of the second accelerometer (*SVA2*) are shown in Table 7.2. There was an excellent correlation between the two accelerometers for all three manometric sites. An example of the correlation graph between the *SVA1* accelerometer and the *SVA2* accelerometer placed at the umbilicus for detection of antral contractions is shown in Figure 7.2.

Comparison of the SVA response for different sites of SVA2

As the recordings for the different position of *SVA2* were not synchronous, direct comparison between the results for *SVA2* was not possible. However, comparison between the *SVA2* responses is possible by relating each of the *SVA2* responses with the associated *SVA1* response. The high correlation between *SVA1* and *SVA2* allowed comparison between the two values using the best fit slope equation:

$$SVA1 = a + b(SVA2)$$

where a represents the y intercept value and b the slope of the line. In most instances, the slope values appear essentially similar and the differences between the *SVA1* and *SVA2* values depend mainly on the y intercept value. For the positions of *SVA2* where the y intercept value is positive, the response at *SVA1* is greater than that of the *SVA2* accelerometer and similarly if the y intercept is negative, the response of the *SVA2* accelerometer is greater than that of the *SVA1*

Table 7.1.

SVA Energy Response Values - Second Transducer (*SVA2*)

SVA vibration energy units

	Epigastrium	L Iliac Fossa	L Upper Quadrant	R Flank	R Iliac Fossa	Umbilicus
ANTRUM						
median [IQR]	332 [181-697]	228 [110-487]	276 [140-495]	312 [147-1220]	326 [167-853]	252 [145-548]
range	47 - 3415	50 - 3634	45 - 3430	53 - 3678	50 - 3806	42 - 3305
DUODENUM						
median [IQR]	147 [98-405]	370 [239-729]	243 [120-514]	272 [121-645]	238 [94-808]	249 [100-870]
range	51 - 1215	100 - 2522	42 - 1910	47 - 3667	42 - 3810	42 - 3500
JEJUNUM						
median [IQR]	324 [150-824]	252 [161-462]	298 [143-852]	193 [117-497]	249 [130-536]	223 [116-504]
range	12 - 3703	43 - 3509	55 - 2662	42 - 3355	51 - 3372	54 - 2912

Table 7.2.

Correlation between *SVA1* Transducer & *SVA2* Transducer

SVA2:	Epigastrium	L Iliac Fossa	L Upper Quadrant	R Flank	R Iliac Fossa	Umbilicus
ANTRUM						
Correlation Coefficient	0.97	0.96	0.94	0.91	0.96	0.95
R^2 value	95.2	91.2	88.2	82.6	92.3	90.7
DUODENUM						
Correlation Coefficient	0.93	0.96	0.96	0.98	0.97	0.94
R^2 value	86.7	91.7	93.3	95.6	95.8	88.8
JEJUNUM						
Correlation Coefficient	0.97	0.94	0.93	0.96	0.94	0.88
R^2 value	94.9	88.7	87.2	92.4	89.3	78.1

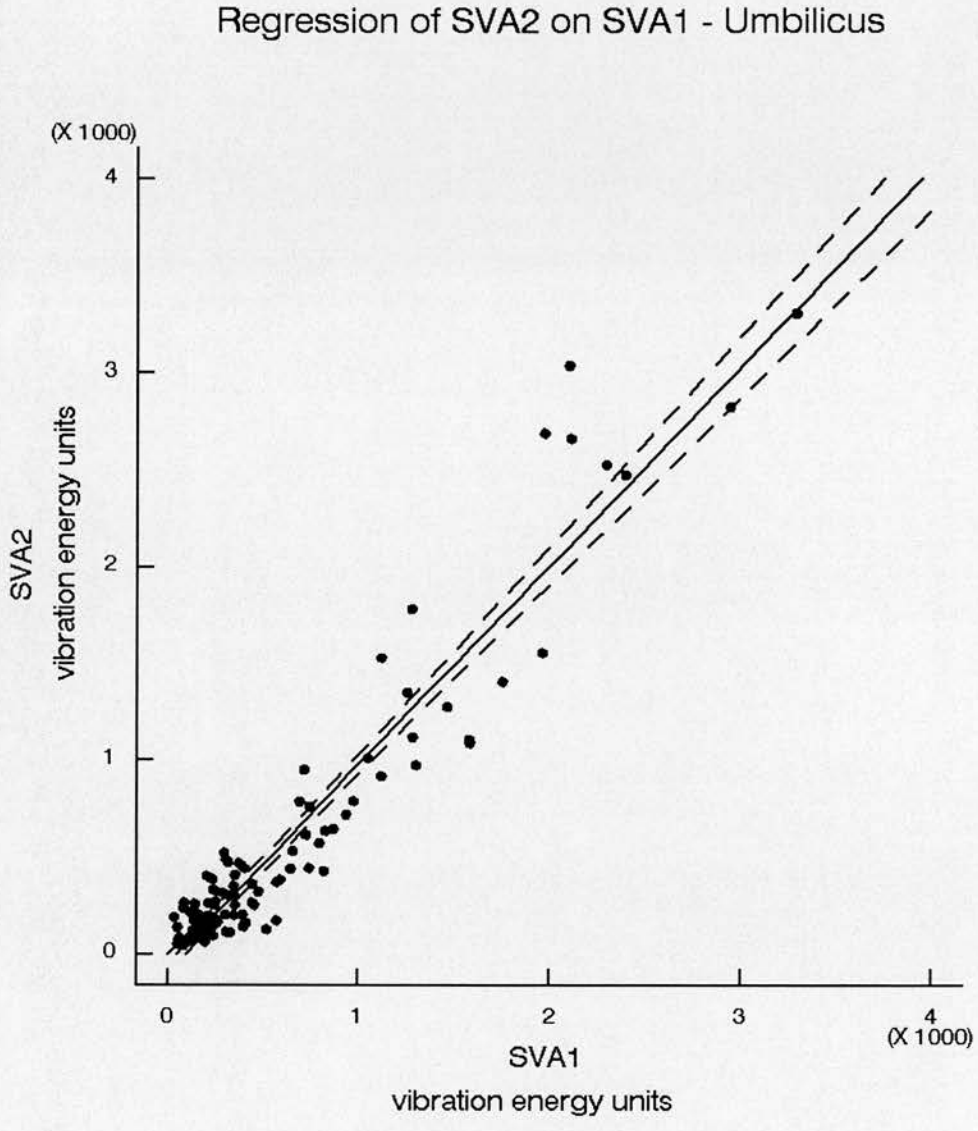


Figure 7.2. The correlation between the SVA response of the *SVA1* and *SVA2* (*umbilicus*) accelerometers for detection of antral activity. The dotted lines represent the 95% confidence limits.

accelerometer. However, differences in the slope value may account for this difference to change for certain values of the energy response of the SVA accelerometers. This cut-off value for *SVA2* response is calculated below.

From the equation $SVA1 = a + b(SVA2)$ for the slope relation between the *SVA1* and the *SVA2* accelerometers, we can rearrange the equation for the ratio of the *SVA1* value and the *SVA2* value as follows:

$$SVA1/SVA2 = b + a/SVA2$$

If we initially assume the *y* intercept to be positive, then for small values of *SVA2*, the *SVA1* value will be greater than *SVA2*. At the point where the values of *SVA2* and *SVA1* are similar, then the ratio of *SVA1* and *SVA2* will approach 1.0. Substituting this value into the above equation, we get a value for *SVA2* which then starts to exceed the *SVA1* value:

$$1 = b + a/SVA2$$

Rearranging,

$$SVA2 = a/[1 - b]$$

If we look at the relationship between for example, the antral response between *SVA1* and *SVA2* in the epigastrium (Table 6.3), in order for the epigastric value to be greater than that of the right upper quadrant, the *SVA2* value must be greater than:

$110.7/[1 - 0.86]$, ie $SVA2 \geq 790$ vibration energy units

In practice the median [IQR] for the *SVA2* response at the epigastrium was 332 [181-697] vibration energy units, which is less than that of the cut-off value above. The *SVA1* value at the *right upper quadrant* therefore gives a higher energy response within the range recorded than that of the *epigastrium.* This cut-off value for each of

the sites of *SVA2* above which the *SVA2* response is greater is shown in Table 6.3.

Conversely, if we have a negative value for the *y* intercept (*a*) then the *SVA2* response is generally better than the y response till a cutoff value of:

$$SVA1 = a/[1-b]$$

Thus *SVA1* will only exceed *SVA2* if the slope value is > 1.0. In practice, the highest slope values obtained were 1.1 in the duodenum and jejunum (see Table 6.2). A *y* intercept < 0 and a slope value > 1.0 only occurred in the duodenum between *SVA1* and *SVA2* in the *epigastrium*(a = -21.1, *b* = 1.1). Thus, the *SVA1* value would have to be ≥ 211 (-21.1/-0.1) vibration energy units. The median [IQR] for the *epigastric* recording was 147 [98-405] vibration energy units, suggesting that the *epigastric* recording is similar to the *right upper quadrant* recording, for values of *SVA1* up to 211 SVA vibration energy units.

These cut-off limits and the *y* intercept values thus enable the comparison of the different sites of the SVA accelerometer position (*SVA2*) as follows:

Antrum

The SVA response at the *umbilicus* has a slope value of 1.0 with a *y* intercept of -54.1 and therefore the response is higher at the *umbilicus* by value of the intercept. The *y* intercept values for the *left iliac fossa, right flank* and *right iliac fossa* were negative but smaller than that of the *umbilicus*, whereas the *y* intercept of the *epigastrium* and the *left upper quadrant* were positive, with cut-off values of 790 and 443 SVA vibration energy units respectively.

Duodenum

The SVA response at the *umbilicus* again had a slope value of 1.0 with a negative *y* intercept of -38.1 SVA vibration energy units and the response at the *umbilicus* is again higher than that of the antrum. The values obtained at the *epigastrium, left upper quadrant* and right flank are similar to the response at the *right upper quadrant*, with cut-off values within the median [IQR] of the respective responses (Tables 7.2 & 7.3).

Jejunum

The values obtained at the 6 sites of the *SVA2* accelerometer consistently had positive *y* intercept values, with high cut-off values for those slope values which were < 1.0 (Table 7.3). Thus the highest SVA response was obtained at the *right upper quadrant.*

Table 7.3.

Values for Second Transducer Position (*SVA2*)

SVA2:	Epigastrium	L Iliac Fossa	L Upper Quadrant	R Flank	R Iliac Fossa	Umbilicus
ANTRUM						
y Intercept	110.7	-22.1	57.6	-4.2	-26.0	-54.1
Slope Value	0.86	0.99	0.87	0.96	0.92	1.0
Cut-off value	790	—	443	—	—	—
DUODENUM						
y Intercept	-21.1	166.3	25.2	6.9	207.1	-38.1
Slope Value	1.1	1.04	0.83	0.98	1.03	1.0
Cut-off value	211*	—	148	345	—	—
JEJUNUM						
y Intercept	128.8	145.3	100.4	39.1	88.2	80.8
Slope Value	1.0	1.1	1.1	0.96	0.93	1.0
Cut-off value	—	—	—	977.5	1260	—

y intercept and cut-off values are given as SVA vibration energy units

Cut-off values are the value for the *SVA2* energy response beyond which the *SVA2* > *SVA1* response

* represents the cut-off value for the *SVA1* energy response beyond which the *SVA1* > *SVA2* response

DISCUSSION

Auscultation of bowel sounds has a decisive role to play in the management of the patient with paralytic ileus, although subjective interpretation and documentation may give rise to discrepancies. There is as yet no previous work on determining which site on the abdominal surface corresponds to which particular region of the gastrointestinal tract. In general terms, bowel sounds are classified collectively and terminology such as active, quiet, tinkling and sparse used in our description of these collective sounds. But regionalisation of these sounds may be important in determining for example whether small bowel or gastric activity has returned in post-operative ileus.

This chapter has shown the regional difference in the detection of vibration signals at the abdominal surface. The *umbilicus* appeared the most suitable site for the detection of signals emanating from the antrum and the duodenum, with the jejunal activity being detected with the highest energy response at the *right upper quadrant.* The findings that the response to the antrum and duodenum is greater at the *umbilicus* is reasonable as the position of the antrum and duodenum are essentially fixed and do not vary greatly between subjects. The finding that the proximal jejunum is best detected at the *right upper quadrant* is less easy to comprehend. However, during the fluoroscopic positioning of the manometric catheter at the onset of the study, the tip of the catheter usually crossed the midline having passed through the duodeno-jejunal flexure, indicating that in most of the subjects, the first loop of the jejunum was situated in the right side of the abdomen. This may explain as to why the jejunal response was maximal in the *right upper quadrant* accelerometer. However, in 4 of the 10 subjects, the catheter tip remained on the left side of the abdomen at

fluoroscopy, demonstrating the relatively inconstant position of the small bowel. Thus in this study, whilst we have shown that the SVA response to the proximal jejunum is greatest in the *right upper quadrant*, this finding may not be consistent in larger studies, due to the inconstant position of the jejunum.

As noted in chapter 5, the greatest limitation of the SVA system is its ability to generate only one channel of data. The high correlation between signals obtained by the reference sensor in the *right upper quadrant* and a second sensor at multiple different sites suggests that multiple sensors may have no advantage. SVA signals extend within limited margins outside of the acoustic spectrum and hence, their velocity and transmission characteristics through the different media of the tissues of the abdomen are likely to be similar to that of sound. Since the velocity of sound waves is 800 metres/second, the time lag between detection at *SVA1* and *SVA2*, over distances of 7 and 14 cms, will be very short. Exploitation of this time lag to pinpoint the source of the contractions within the abdomen is unlikely to be possible.

In conclusion, this chapter has shown that the positioning of the SVA accelerometer is best at the *umbilicus* for the recording of vibrational energy from the antrum and duodenum. This position may be important in determining the motor activity in the upper gastrointestinal tract non-invasively, for example in the return of normal motor activity in post-operative ileus. However, a single site on the abdominal surface is unsuitable for detection of the jejunal response, due to its variable position. The siting of the accelerometer at the *umbilicus* would therefore appear to be a reasonable compromise in the detection of the response from the upper gastrointestinal tract.

Chapter 8

Evaluation of Surface Vibration Analysis in Clinical Conditions

INTRODUCTION

The diagnosis of partial or chronic intestinal obstruction remains a difficult clinical problem in view of the paucity of objective investigations (Jones PF, 1985). Recently, the presence of cluster contractions, as detected by manometry, have been demonstrated in bowel proximal to a partial obstruction, following a meal challenge (Summers RW, 1983). These cluster contractions consist of intense contractile activity, lasting one to three minutes, which alternate with similar periods of quiescence. Distal to the obstruction, the bowel shows reflex inhibition and quiescence (Kendall G, 1987). We have previously shown that SVA is able to detect a typical pattern of alternating hyperactivity and quiescence in volunteers with induced intestinal obstruction, in response to the presence of the cluster contractions and a preliminary study showed that this approach could be of value in clinical subacute and chronic intestinal obstruction (Cullen PT, 1989).

This chapter describes the application of SVA, in the clinical situation, to the diagnosis of subacute and chronic intestinal obstruction in a large cohort of patients, in order to define the sensitivity and specificity of the test. The SVA findings in patients were compared to those of normal healthy volunteers. In addition, the small bowel transit time, as measured by the hydrogen breath test, was determined in both patients and volunteers, in order to ascertain differences in the transit time of a test meal. Assessment of the patient in the *fed* state allowed the evaluation of both the presence of cluster contractions and the small bowel transit time.

MATERIALS AND METHODS

Subjects - Patients

Forty-six patients, 33 female, (age median : 56 years, range 21-86), with suspected chronic partial intestinal obstruction, were entered into the study. All patients, except one, had previously undergone at least one laparotomy. The types of operations previously performed are listed in Table 8.1. The mean duration since the last abdominal operation was 8.5 years (range 1-40 years). All patients underwent thorough clinical investigations including plain abdominal X-rays and barium studies where appropriate. The patients were also investigated by SVA (vide infra). The results of the SVA test were available to the clinician responsible for the patient and the decision as to whether a patient required a laparotomy for chronic adhesions was based on clinical grounds. At the time of the test, none of the patients had vomiting as a predominant symptom and all were eating and drinking normally.

Subjects - Volunteers

Control studies were also performed in 18 volunteers, 11 male (age: median 26 years, range 21-51). All volunteers were healthy, free of any gastrointestinal symptoms and none were taken any medication that would affect the gastrointestinal tract. None of the volunteers had undergone any previous laparotomy, including appendicectomy. All volunteers gave their informed consent, which had been approved by the Tayside Health Board Medical Ethical Committee.

Table 8.1.

Patient Details

	Patient	Last Operation	Time Elapsed (years)	Sex
1.	DL	Hysterectomy	18	F
2.	MM	Panproctocolectomy	6	F
3.	JM	Division adhesions	4	F
4.	AS	Strang. Femoral hernia	1	M
5.	PK	Antrectomy	10	M
6.	MC	Appendicectomy	11	F
7.	DE	Right Hemicolectomy	1	M
8.	AM	Cholecystectomy	7	F
9.	JH	Division adhesions	2	M
10.	MM	Sterilisation	20	F
11.	RK	Gastrectomy	20	M
12.	PM	Cholecystectomy	6	F
13.	JS	Sigmoid colectomy	2	M
14.	ME	Vagotomy/enterostomy	14	F
15.	IK	Hysterectomy	12	F
16.	JP	Vagotomy/enterostomy	4	M
17.	AF	Right hemicolectomy	4	F
18.	JR	Appendicectomy	40	M
19.	GL	Vagotomy/pyloroplasty	2	M
20.	CY	Nissen fundoplication	3	F
21.	DD	Division of adhesions	6	F
22.	PR	Division of adhesions	5	F
23.	WC	Cholecystectomy	6	F
24.	MK	Division of adhesions	5	F
25.	TS	Cholecystectomy	4	F
26.	JF	Hysterectomy	11	F
27.	JL	Gastrectomy	2	M
28.	JM	Cholecystectomy	2	F
29.	DM	Division of adhesions	4	F
30.	TF	Hysterectomy	20	F
31.	MT	Gastrectomy	2	F
32.	LM	Division of adhesions	20	F
33.	DF	Division of adhesions	10	F
34.	TB	Sigmoid colectomy	4	M
35.	JA	Appendicectomy	2	F
36.	KF	Appendicectomy	6	F
37.	MH	Vagotomy/pyloroplasty	30	F
38.	GS	Sterilisation	12	F
39.	NM	NIL		F
40.	AC	Sigmoid colectomy	2	F
41.	DN	Gastrectomy	4	M
42.	PP	Division of adhesions	2	F
43.	YM	Appendicectomy	10	F
44.	JM	Cystectomy/conduit	3	F
45.	AB	Appendicectomy	20	F
46.	DW	Anterior Resection	3	M

Study Protocol

The protocol for the SVA study was similar for both the patient and the volunteer groups. After a 12 hour overnight fast, SVA recordings were carried out for 30 minutes before and 180 minutes after a standard meal. The SVA accelerometer was placed in the right upper quadrant and all subjects lay supine for the duration of the study.

Standard Meal

The standard meal consisted of 200g mashed potato, 100g baked beans and 25 ml of water with 5.25 g glucose. This meal had a total caloric content of 273 kCal. All the patients in this study were able to tolerate the test meal and were eating and drinking normally at the time of the study.

SVA Recording

The SVA accelerometer was amplified at a set gain for all the studies and processed by the digital integrator as described in chapter 5. The output from the integrator was addressed to the in-built analogue to digital convertor of a BBC microcomputer, which provided sequential and accumulated SVA amplitude measurements over the study period.

Hydrogen Breath Test

The orocaecal transit time in both patients and volunteers was evaluated by the hydrogen breath test. After an overnight fast, each subject was given a chlorhexidine mouth wash to eliminate oral bacteria. Three end expiratory breath samples were then taken in order to assess the baseline value, using a modified Haldane Priestly tube

(Metz G, 1976). The baseline value was taken as the average of the 3 samples. Following the ingestion of the test meal, breath samples were taken every 15 minutes. Baked beans contain indigestible oligosaccarides which are rapidly fermented by the anaerobic bacteria present in the large bowel, generating hydrogen gas which diffuses rapidly into capillaries and is excreted in the breath (Levitt MD, 1969). Breath hydrogen concentration in parts per million (ppm) was evaluated using a GMI exhaled hydrogen monitor[14]. The orocaecal transit time was defined as the interval between meal ingestion and the first rise of breath hydrogen concentration in excess of 10 ppm, which was required to be sustained for at least 3 successive readings (Campbell FC, 1984).

A dual peak rise of breath hydrogen was regarded as showing evidence of small bowel bacterial overgrowth (Rhodes JM, 1979). The first peak (>10 ppm than the previous reading), which was usually detected within 30 minutes of meal ingestion and was sustained for at least 3 successive readings, represented hydrogen release due to fermentation by small bowel bacteria and the second peak which occurred later represented the fermentation by colonic bacteria after the arrival of the substrate at the caecum. Rapid initial rises in the breath hydrogen which were not sustained for 3 successive readings were considered to be due to failure to eliminate normal mouth bacterial flora, and were ignored in regards to the evaluation of the oro-caecal transit time.

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[14]GMI Instruments, Renfrew, Scotland.

Data Analysis

All graphic printouts of the SVA studies were studied by one independent observer acquainted with the SVA system (F.C. Campbell) and assessed visually for the presence of alternating hyperactivity or quiescence. The presence of this pattern was taken as a positive result for the presence of subacute intestinal obstruction. The observer was blind as to whether the study was from the patient or volunteer group. In addition, the total accumulated SVA energy response for each study was compared between the patient and the volunteer group.

Patient Group

Following the SVA study, the patients were then followed up clinically for a median period of 18 months (range 6 - 28 months). Patients either underwent a laparotomy or were followed up at 4 monthly intervals in the outpatient clinic. Those patients who underwent a laparotomy were divided into two groups - those in whom obstruction was proven and those in whom there was no evidence of obstruction. The decision as to whether there was any evidence of obstruction was made by the senior surgeon at each laparotomy. The patients who did not undergo laparotomy were categorised as being persistently symptomatic, with symptoms suggestive of partial intestinal obstruction, or those in whom symptoms resolved.

Statistical Analysis

The SVA energy values and the oro-caecal transit time were expressed as the median and the inter-quartile range, as appropriate for non-parametric data. Comparison of patient values against that of the volunteers was by the Mann-Whitney U test. Assessment by visual analysis allowed description of the sensitivity and specificity of SVA in the detection of partial intestinal obstruction.

RESULTS

Patient Group - Clinical Outcome

Twenty-eight patients underwent laparotomy with a suspected diagnosis on clinical grounds of partial intestinal obstruction. The diagnosis was confirmed in 14 patients at laparotomy, whilst the remaining 14 patients showed no gross evidence of intestinal obstruction. The cause of the intestinal obstruction was adhesions in 11 patients, a sigmoid volvulus in one patient, a colonic carcinoma in another patient and metastases from a carcinoid tumour in the one patient who had not previously undergone a laparotomy.

In the group of patients who did not undergo a laparotomy (n : 18), 8 patients remain symptomatic at follow-up, whilst in 10 patients their symptoms have resolved and the patients are now asymptomatic.

Visual Analysis

The pattern of alternating hyperactivity and quiescence was found in 12 of the 14 patients who were subsequently proven to have evidence of intestinal obstruction at laparotomy (Figure 8.1), whilst the pattern was found in only three of the non-obstructed patients. None of the volunteers demonstrated any evidence of this obstructive pattern. This gives the test a sensitivity of 0.86 and a specificity of 0.79. The normal SVA response in a non-obstructed patient is shown in Figure 8.2.

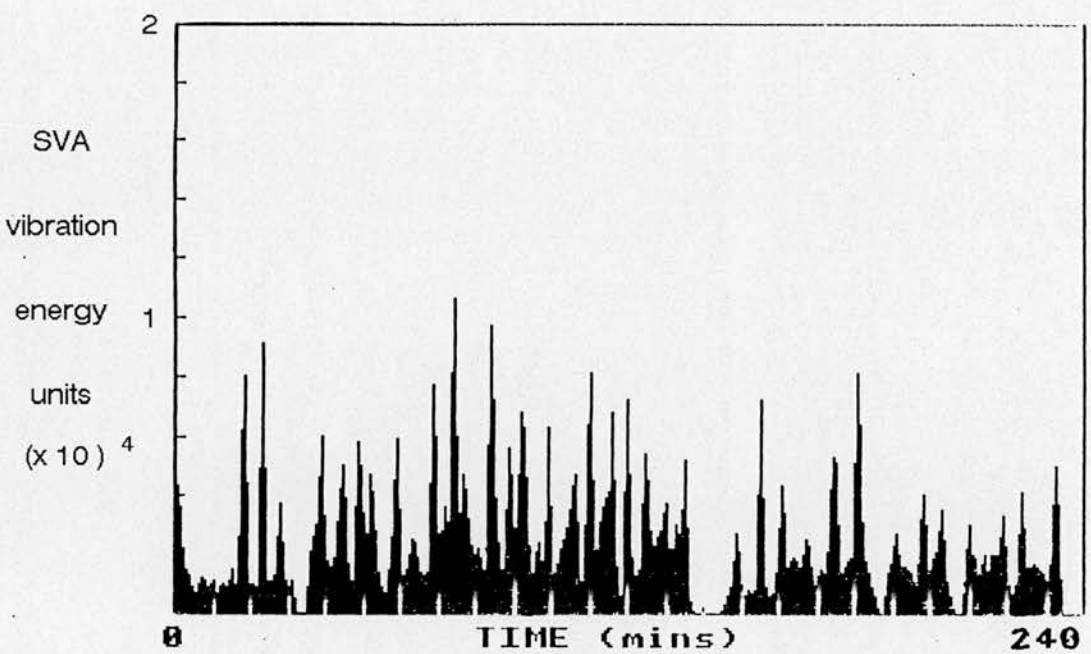

Figure 8.1. A typical pattern of alternating hyperactivity and quiescence as detected by SVA in a patient with intestinal obstruction subsequently proven at laparotomy.

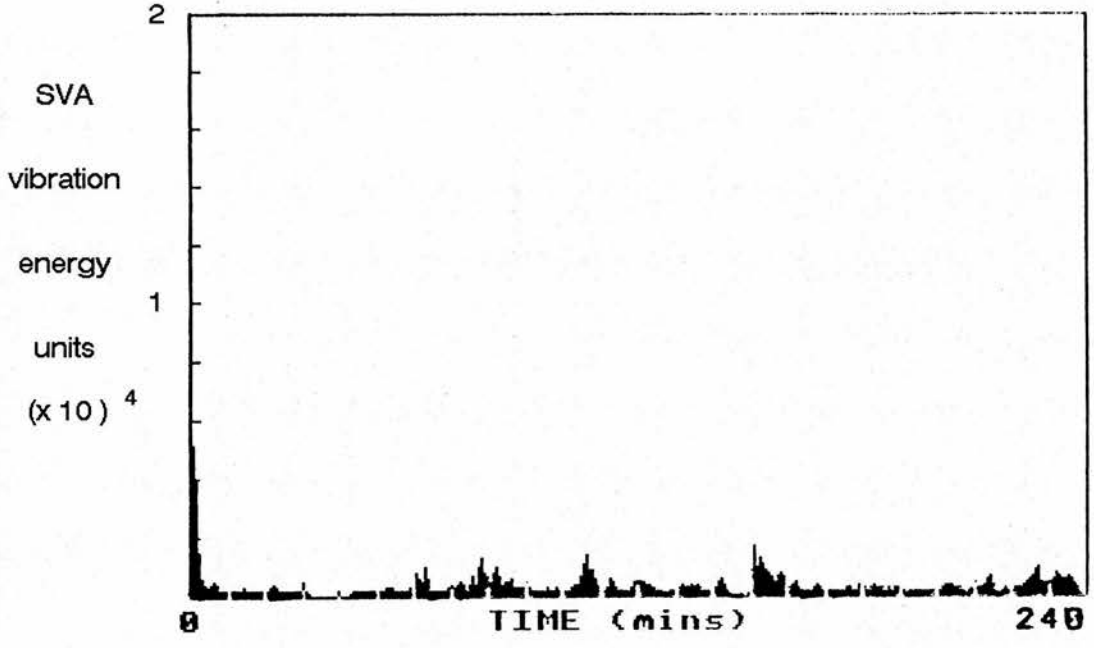

Figure 8.2. A normal response by SVA in a patient whose symptoms resolved at follow-up and classified as asymptomatic.

Accumulated SVA Amplitude Measurements

The accumulated SVA energy values were increased in the obstructed patients (439873 [386551-667646]) as compared to both the non-obstructed patients (192463 [172388-290729]) and the volunteers (156145 [113808-250154]) ($p < 0.001$) (Figure 8.3). In the conservatively treated group, SVA energy values were greater in the symptomatic patients (313087 [223197-479257]) as compared to the volunteers and asymptomatic patients (160525 [114722-345973]) ($p < 0.02$) (Figure 8.4).

Oro-caecal transit time

There were no differences in the transit time between the volunteers (225 [195 -365] minutes) and either the obstructed patients (247 [165 - 295] minutes, $p = 0.47$) or the non-obstructed patients (290 [190 - 370] minutes, $p = 0.65$) (Figure 8.5). Similarly there were no differences between the volunteers and the patients who did not undergo a laparotomy (symptomatic group : 210 [150 - 325] minutes, ($p = 0.38$), asymptomatic group : 350 [250 - 395] minutes, $p = 0.09$) (Figure 8.6). Evidence of small bowel bacterial overgrowth was found in 4 patients - 2 with no evidence of obstruction at laparotomy, one symptomatic and one asymptomatic patient who did not undergo laparotomy. In addition, 2 of the volunteers had a dual hydrogen peak rise, suggestive of bacterial overgrowth.

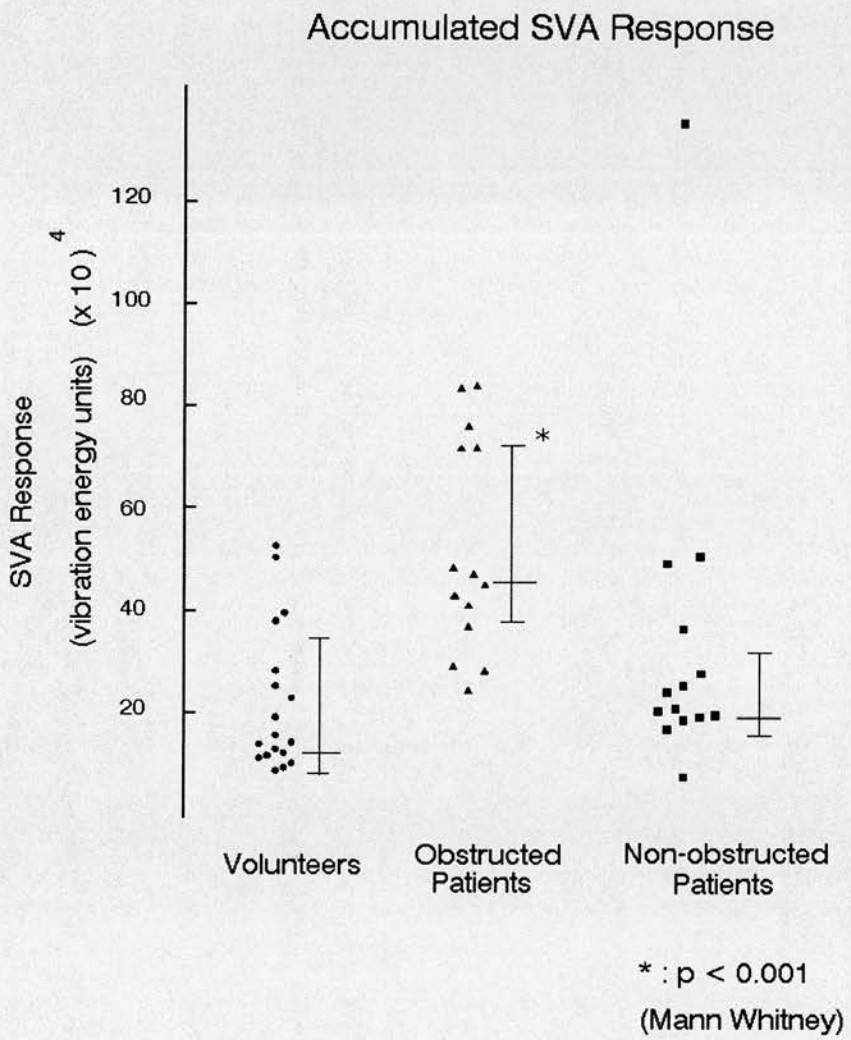

Figure 8.3. Accumulated SVA Energy Response - Volunteers vs patients who underwent laparotomy. Bar lines represent the median [IQR]

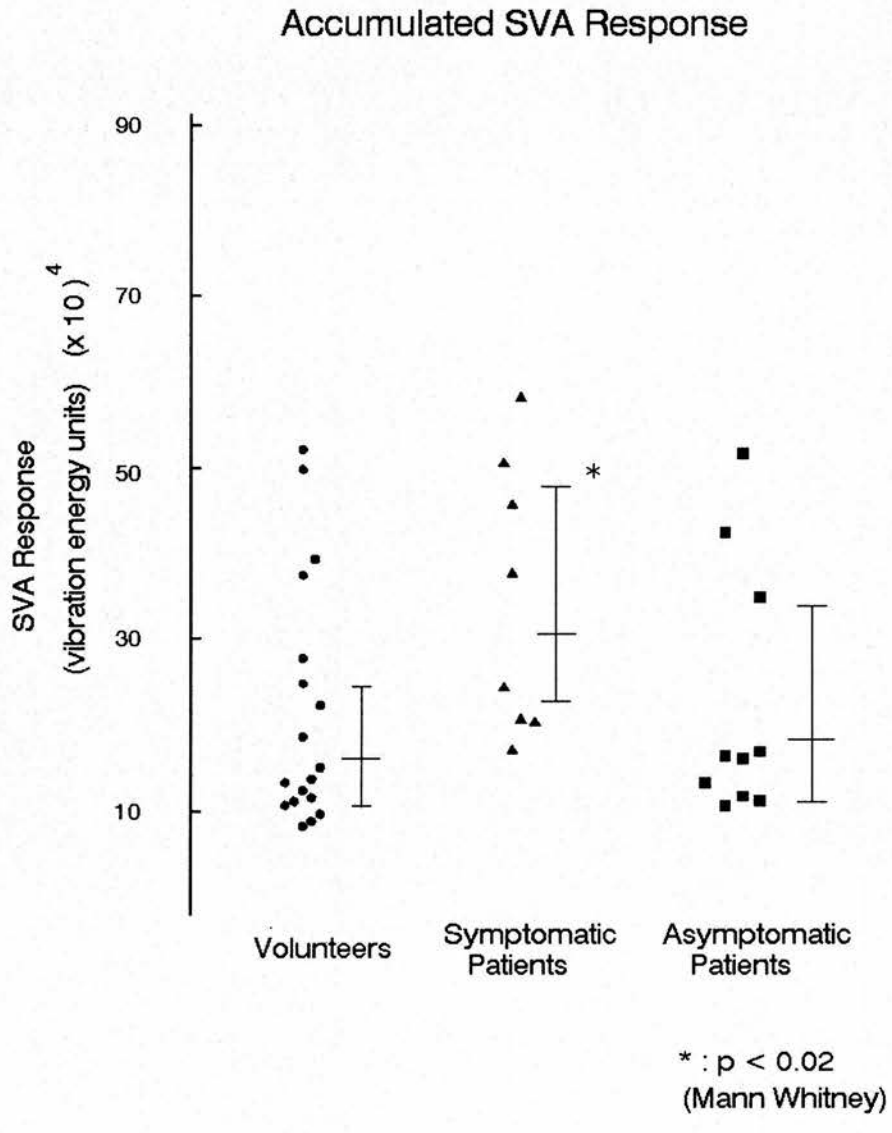

Figure 8.4. Accumulated SVA Energy Response - Volunteers vs patients who did not undergo laparotomy. Bar values represent the median [IQR].

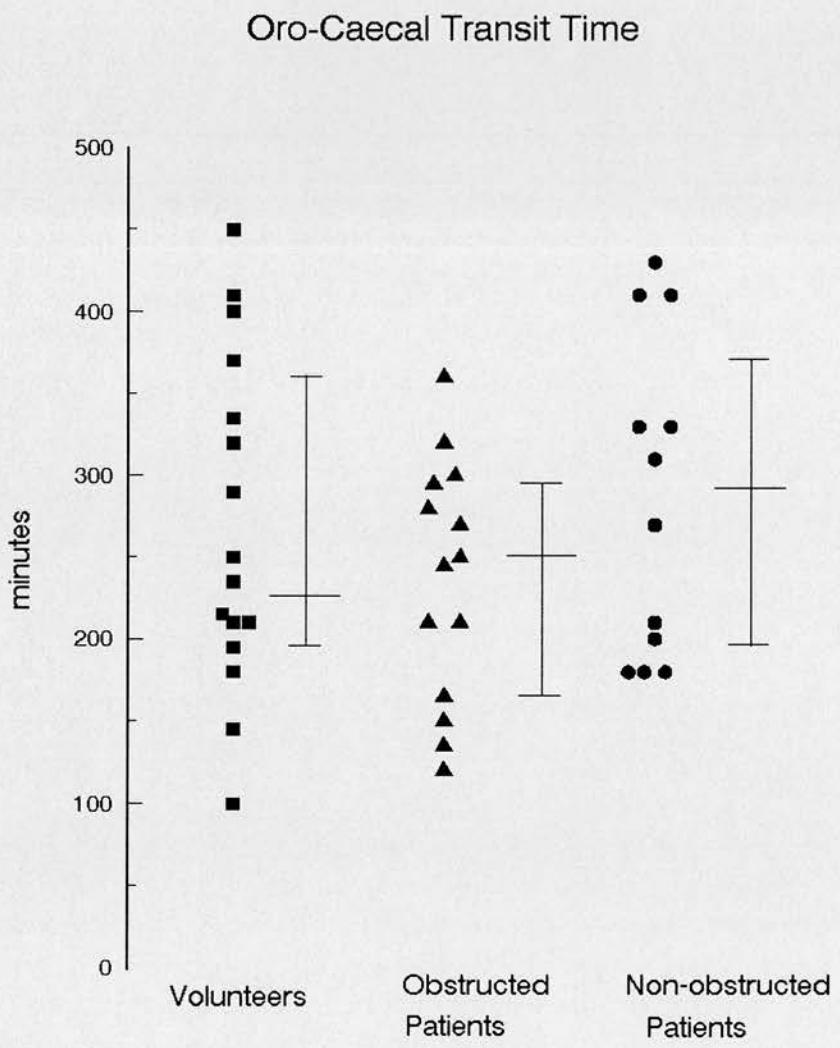

Figure 8.5. Oro-caecal transit time of volunteers vs patients who underwent a laparotomy. Bar values represent the median [IQR].

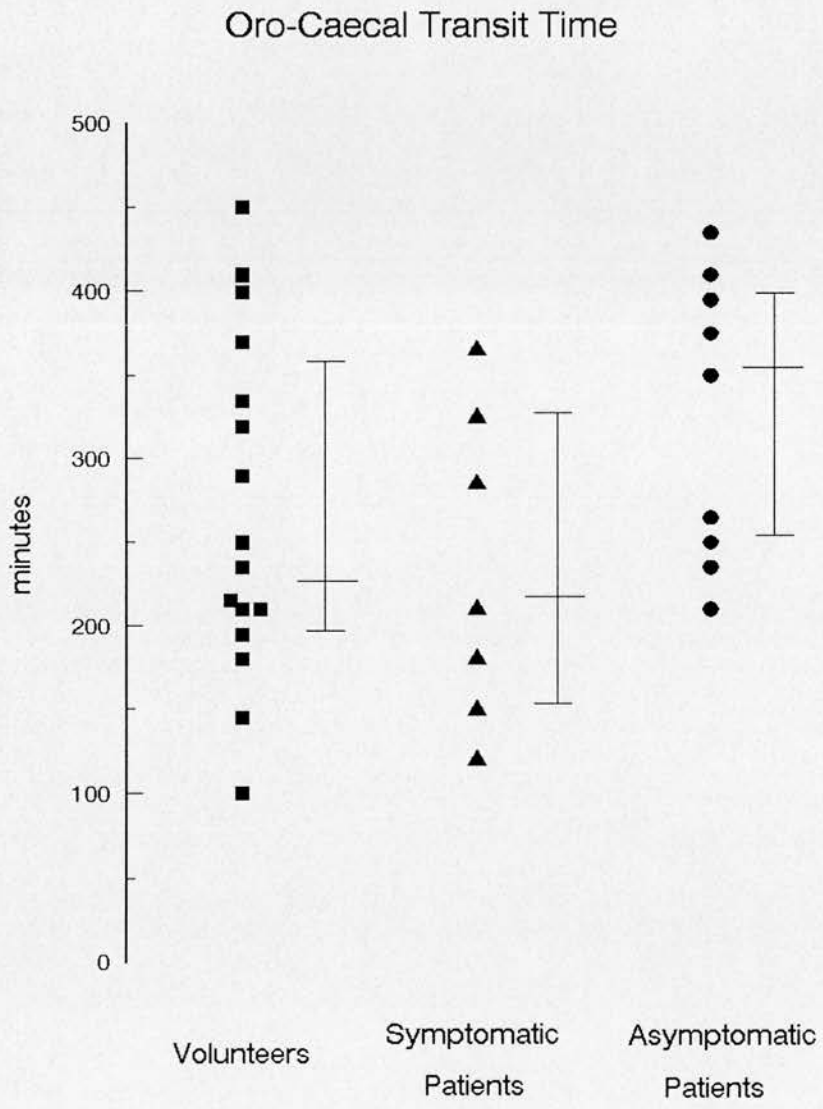

Figure 8.6. Oro-caecal transit time of volunteers vs patients who did not undergo a laparotomy. Bar lines represent the median [IQR].

DISCUSSION

The diagnosis of acute intestinal obstruction is an easily recognised symptom complex involving abdominal distension, nausea and vomiting and obstipation. However the signs and symptoms of partial intestinal obstruction are more often unreliable (Arnbjornsson A, 1976). Currently available methods of investigating partial small bowel obstruction are subjective and inadequate and often the surgeon is forced into an exploratory laparotomy on the basis of unexplained symptomatology. Small bowel contrast radiography is increasingly being performed (Dunn JT, 1984), although some reports have shown that only 50% of these studies are useful in determining the clinical outcome of the patient (Lo AM, 1966). A definitive method of diagnosing the condition pre-operatively is therefore very desirable.

Summers *et al* have shown the existence of cluster contractions in the small bowel in the patients with partial intestinal obstruction. These cluster contractions were defined as periods of motor activity consisting of 3 - 10 contractions, with a contraction frequency of 12 contractions/minute, which were followed by 1 minute of quiescence. They may occur in normal subjects in the fasting state during phase II of the MMC, but are most strikingly found in the post-prandial state in the patient with a partial mechanical intestinal obstruction or pseudoobstruction (Summers RW, 1983). Patients with pseudoobstruction, however, tended to have lower amplitude contractions and, in addition, had abnormal fasting motility, with absence of the MMC. However, although it was felt to be a useful adjunct to radiological investigation, some of the patients were intolerant of the invasive nature of the manometry tubing. SVA has been shown to be able to detect the presence of cluster contractions with a typical pattern

of alternating hyperactivity and quiescence in volunteers with intraluminal balloon induced intestinal obstruction (Cullen PT, 1989). The use of a meal challenge in this chapter allowed the assessment of the presence of cluster contractions in the post-prandial state and the measurement of the oro-caecal transit time in both patients with presumed partial intestinal obstruction and healthy volunteers.

The SVA response was assessed by two methods: visual inspection and the accumulated SVA energy response. Twelve out of fourteen patients diagnosed to have evidence of partial intestinal obstruction at laparotomy had SVA energy patterns of alternating hyperactivity and quiescence, consistent with an SVA diagnosis of obstruction. The accumulated SVA energy response was also increased in these patients, as compared to that of the volunteers. The sensitivity and specificity of the visual analysis of the SVA response would appear to be reasonable and the overall accuracy may be improved by taking the visual assessment in conjunction with the accumulated SVA response. The patients with persistent symptomatology at follow-up were found to have a significantly raised accumulated SVA response, similar to the response in the patients with confirmed obstruction. This finding may point to these patients having as yet undiagnosed partial intestinal obstruction as the cause of their symptomatology.

The oro-caecal transit time was not significantly delayed in patients with partial intestinal obstruction. This may be due to the fact that the patients in this study were able to tolerate the test meal and may represent a subgroup of the total population of patients with undiagnosed intestinal obstruction. Evidence of small bowel bacterial overgrowth was found in 4 patients who did not undergo laparotomy. This may possibly account for some of their symptoms,

as two of these patients experienced intestinal colic, relieved by diarrhoea. However there was also evidence of bacterial overgrowth in 2 volunteers, who were otherwise healthy, confirming that the hydrogen breath test lacks absolute specificity, as found in previous studies (O'Connor MP, 1987). Thus the hydrogen breath test would not appear to be applicable to the diagnosis of partial intestinal obstruction.

The clinical results of the use of SVA in the clinical context is encouraging. The pattern of alternating hyperactivity is not entirely specific, but this specificity may be improved in conjunction with the accumulated SVA response, in order to discriminate from patients with pseudoobstruction. Further volunteer studies are needed in order to evaluate more fully the normal range for the accumulated SVA response to the test meal. This will enable us to improve the discrimination of the values obtained in patient studies. In addition this study has only assessed those patients who were able to tolerate the test meal, which is not possible in all patients with partial intestinal obstruction. Further patient studies with a liquid test meal are obviously required in this context.

CONCLUSIONS

CONCLUSION

Motility disorders of the upper gastrointestinal tract remain a difficult diagnostic challenge. They are common and may represent up to 20% of attendances at a General Practitioner (Loof I, 1985). The symptomatology of these disorders is variable, with considerable overlap between pyschosomatic and organic symptoms.

To date, intraluminal manometry remains the most effective method available for the purposes of investigating patients with possible gastrointestinal motility disorders. The analysis of these disorders is facilitated in the fasting state by the well defined parameters of the Migrating Motor Complex (MMC). Furthermore, pattern abnormalities may occur in the fasting state in patients with functional bowel disorders (Kellow J, 1990). Hence, it is appropriate that studies of fasting motility be included in the investigation of the patient with a suspected gastrointestinal motility disorder.

This thesis has assessed a novel method for the detection of gastrointestinal motor physiology and evaluated this method against the conventional gold standard of intraluminal manometry. In order to improve the usage of this gold standard, we set out to assess a potential cause of the known inter-subject variation of normal fasting motility and to refine the analysis of motility. The novel method of Surface Vibration Analysis was firstly assessed against intraluminal manometry and secondly, its potential value was evaluated in patients with chronic intestinal obstruction, who have well characterised motility disturbances, involving periodic high amplitude contraction clusters. This disturbance appeared theoretically suitable for investigation by SVA.

The objectives of this thesis were addressed in the following modules, viz:

I. **The relationship of the intraluminal milieu to fasting motor activity.**

II. **Computerised Analysis of fasting motor activity.**

III. **Evaluation of SVA against manometry.**

IV. **Effect of the intraluminal milieu on SVA response.**

V. **Evaluation of SVA in clinical disorders**

I. The relationship of the intraluminal milieu to fasting motor activity

The factors controlling the MMC require full evaluation to justify its use as a clinical parameter in the diagnosis of motility abnormalities. Previous studies have demonstrated a considerable variation in the parameters of fasting motor activity in normal healthy volunteers (Vantrappen G, 1977, Thompson DG, 1980), which has hampered the use of the Migrating Motor Complex in the appraisal of clinical motility disturbances.

This thesis has evaluated a full range of intraluminal content from evacuation of both gas and liquid from the upper gastrointestinal tract to the instillation of both gas and liquid of different viscosity. The parameters of the MMC were then comprehensively analysed for each variation in the intraluminal milieu. We have shown that these parameters are affected by alteration in the intraluminal milieu, with increasing contraction amplitude and duration of phase II following the instillation of both gas and liquid.

We feel that differences in the intraluminal milieu between volunteers may in part account for the wide variability of the

parameters of fasting motor activity found in normal volunteers. It would seem therefore logical to standardise the intragastric milieu within the gut when performing manometric studies, by repeated gastric aspiration. This technique may be impractical for ambulatory studies, but standardisation of the intraluminal content during bedside motility studies may reduce the variability of normal volunteers and thus improve the assessment of abnormal motility.

II. Computerised analysis of fasting motor activity

We have developed and validated a microcomputerised method of analysing the manometric recordings of fasting motor activity. This program is able to handle large data files, beyond that capable of normal conventional manual analysis. The parameters measured include:

Contraction amplitude, duration & motility index

Duration of the individual phases of the MMC

Migration velocity of the MMC

Propagation of individual contractions

Recognition of various causes of artefact, including respiration, cough/sneeze/movement and movement of manometric ports

This new methodology has vastly improved our ability to analyse motility tracings. Previous detailed manual analysis of a 3 hour recording of 5 channels of manometric tracing would take on average 3 days to complete. Computer analysis of the same tracing takes around 5 minutes on a PC-AT 386 with 80387 maths coprocessor. In addition the computer is both consistent and objective.

III. Evaluation of SVA against manometry

Non-invasive methods of investigating gastrointestinal motor disorders confer benefit to patients in terms of comfort and ease of the motility studies, but require comparison with intraluminal manometry to assess their efficacy in determining gastrointestinal motor activity. This thesis has shown that SVA is able to discriminate between periods of motor activity (phases II and III of the MMC) and periods of quiescence (phase I). The disadvantages of SVA are that it cannot reliably discriminate between phase II and phase III of the MMC in the small bowel, and also, at the present time, an observer requires to be present throughout the study period, in order that periods of movement artefact be accurately recorded.

IV. Effect of the intraluminal milieu on SVA response

The SVA response would appear to be related to the intraluminal milieu, as evacuation of the intraluminal content (*GFE*) caused a significant decrease in the SVA response, as compared to both the baseline state (*BL*) and the *instillation* studies. The response difference was greatest with the *instillation of gas* (*IIG*) and declined with the *instillation of fluid* (*IIF*). Thus, the presence of gas in the gastrointestinal tract conferred the most benefit in the SVA response to gastrointestinal contractions.

V. Evaluation of SVA in clinical disorders

Furthermore, SVA is able to detect discrete pattern abnormalities such as cluster contractions in patients with partial intestinal obstruction. The levels of sensitivity and specificity achieved by SVA are acceptable, but require further validation in

larger cohorts of both patients and volunteers. Nevertheless, SVA may have a potential use as a supplementary investigation in the patient with subacute intestinal obstruction.

This thesis has attempted to evaluate an alternative methodology for the assessment of gastrointestinal motility. It has been ambitious in that the field of the thesis is novel and uncharted. It has improved the usage of intraluminal manometry, by firstly providing an objective and consistent, automated method of analysis of motility recordings and secondly, by demonstrating a potential cause of the normal variability of the MMC. In addition, Surface Vibration Analysis is able to to discriminate periods of motor quiescence and motor activity, which has a potential clinical application in the post-operative state. It is also able to demonstrate the presence of high amplitude cluster contractions, as seen in patients with subacute intestinal obstruction.

PROPOSALS FOR THE FUTURE

(*i*) To investigate, using conventional manometry, a large cohort of normal volunteers in whom the intraluminal milieu is standardised by repeated aspiration of the gastric content. This would allow assessment as to whether standardisation of the intraluminal milieu would decrease the variability of the parameters of the MMC.

(*ii*) SVA has been shown to detect the pattern abnormality of cluster contractions found in partial subacute intestinal obstruction. Pattern abnormalities also exist in patients with functional bowel disorders (Kellow J, 1990) and it would be potentially beneficial if SVA could be applied to the investigation of these patients, as there tends to be poor tolerance of invasive intubation in this group of patients. It may be possible to detect whether the patients motility is hypoactive or hyperactive, with important therapeutic consequences.

(*iii*) The use of the microcomputer analysis should allow manometric studies to be performed over longer periods of time, as the duration of recording periods were previously hampered by the requirement for laborious manual analysis. Further algorithms could be formulated to recognise various pattern abnormalities that can occur during fasting motility, such as bursts of non-propagated phasic pressure activity and sustained incoordinated phasic pressure activity (Malagelada J-R, 1986). This would allow easy and objective analysis of of both normal volunteers and patients with functional bowel disorders.

(*iv*) The relationship between the SVA response and gastrointestinal motility may be more related to the movement of the intraluminal content, as discussed in chapter 6. Future assessment of this relationship may be carried by the evaluation of contraction propagation, using closely spaced manometric channels, with the associated SVA response.

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PUBLICATIONS ARISING FROM THESIS

PUBLICATIONS

1. Response of the Migrating Motor Complex to variation of fasting intraluminal content.
   Smith D, Waldron B, Campbell FC.
   Am J Physiol 1992; **263:** G533-G537.

2. Development and validation of microcomputer analysis of gastric and small bowel manometry.
   Waldron B, Smith D, Storey BE, Campbell FC.
   J Gastroint Motility 1992; **4: (Dec)** 301-315.

PUBLISHED ABSTRACTS

1. The influence of fasting, acaloric intraluminal content on motility patterns.
   British Society of Gastroenterology, Southampton, 1990
   Smith D, Waldron B, Campbell FC.
   Gut 1990; **31:** A1195.

2. Is fasting small bowel motility affected by variation of resting intraluminal content?
   American Association of Gastroenterology, New Orleans, 1991
   Smith D, Waldron B, Campbell FC.
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3. Phase characteristics of the human migrating motor complex (MMC) and fasting intraluminal content.
   International Symposium on Gastrointestinal Motility,
   Kobe, Japan, 1991
   Smith D, Waldron B, Campbell FC.
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4. The response of the human migrating motor complex to fasting gas and secretion.
British Society of Gastroenterology, London, 1991
Smith D, Waldron B, Campbell FC.
Gut 1991; **32:** A1215.

5. Development and validation of a microcomputer technique for analysis of gastric and small bowel manometry.
British Society of Gastroenterology, London, 1991
Smith D, Waldron B, Storey BE, Loudon M, Campbell FC.
Gut 1991; **32:** A1216.

APPENDICES

Appendix I.

Bruel & Kjaer Model 4370 Accelerometer

Weight	54 g
Voltage Sensitivity	10 mV/ms^{-2}
Charge Sensitivity	10 ± 2% pC/ms^{-2}
Mounted Resonance	18 kHz
Frequency Range	0.2-6000 Hz
Capacitance inc Cable	1200 pF
Max Transverse Sensitivity	<4%
Base Strain Sensitivity	0.003 $ms^{-2}/\mu strain$
Temp Transient Sensitivity (3HzLLF)	0.08 $ms^{-2}/^{0}C$
Magnetic Sensitivity (50Hz-0.03T)	1.2 ms^{-2}/T
Acoustic Sensitivity	0.001 ms^{-2}
Max. Ambient Temp	250 ^{0}C
Base Material	Stainless Steel

Appendix II.

Bruel & Kjaer Model 2626 conditioning amplifier

Measurement Modes	Charge
Acceleration Sensitivity	3 Digit Conditioning
(with 1 nF transducer)	0.1 mV/pC to 1 V/pC
	(-20dB to + 60dB)
Rise Time	2.5 V/μs
Frequency Range	0.3 Hz to 100 KHz
Input Impedence	>10 GΩ
Maximum Input	$1^{10^{5}}$ pC
Maximum Output	10 V (10mA) pK
Noise (1Hz to 22Hz)	$<3^{10^{-3}}$ pC

Appendix III.

Example of Computer Printout of Analysis of One Study

********** MOTILITY ANALYSIS **********

With Detailed Phase 2 printout

Subject Filename : DS5

Analysis of Channels:

ds502.ils : ANTRUM
ds503.ils : ANTRUM
ds504.ils : DUODENUM
ds505.ils : JEJUNUM
ds506.ils : JEJUNUM

********** Channel 1 : ANTRUM **********

		Interval minutes	Contractions No.	Frequency No./min	Mean Amplitude mmHg
	Phase 1	1.51	---	---	---
	Phase 2	16.31	6	0.37	22.78
	No Phase 3 present.		Time is	17.82 minutes.	
	Phase 1	25.15	---	---	---
	Phase 2	12.26	6	0.49	17.90
	Time at onset of phase 3 is			50.24 mins.	
MMC (1)	Phase 3	4.24	10	2.36	24.77
	Phase 1	120.52	(1)	---	---

********** Channel 2 : ANTRUM **********

		Interval minutes	Contractions No.	Frequency No./min	Mean Amplitude mmHg
	Phase 1	2.79	---	---	---
	Phase 2	9.67	4	0.41	16.98
	No Phase 3 present.	Time is	12.46 minutes.		
	Phase 1	15.28	---	---	---
	Phase 2	22.39	13	0.58	27.43
	Time at onset of phase 3 is	52.13 mins.			
MMC (1)	Phase 3	9.92	32	3.23	30.60
	Phase 1	92.20	(2)	---	---
	Phase 2	42.03	15	0.36	26.50

******** Channel 3 : DUODENUM *******

		Interval minutes	Contractions No.	Frequency No./min	Mean Amplitude mmHg
	Onset of fasting activity at time	0.00 minutes.			
	Phase 1	1.05	---	---	---
	Phase 2	58.86	77	1.31	20.91
	Time at onset of phase 3 is	59.90 mins.			
MMC (1)	Phase 3	6.56	69	10.52	13.39
	Phase 1	51.66	(1)	---	---
	Phase 2	64.79	42	0.65	16.30

---

* Velocity (Ch. 2 - 3) of Phase 3 (1 - 1) is 1.23cms/min. **

******** Channel 4 : JEJUNUM *******

		Interval minutes	Contractions No.	Frequency No./min	Mean Amplitude mmHg
	Phase 1	0.91	---	---	---
	Phase 2	1.50	7	4.66	43.08
	Time at onset of phase 3 is	2.42 mins.			
MMC (1)	Phase 3	4.64	32	6.90	23.44
	Phase 1	1.22	---	---	---
	Phase 2	47.07	177	3.76	16.99
	Time at onset of phase 3 is	61.34 mins.			
MMC (2)	Phase 3	13.83	105	7.59	17.25
	Phase 1	48.21	---	---	---
	Phase 2	48.72	87	1.95	15.22
	Time at onset of phase 3 is	166.47 mins.			
MMC (4)	Phase 3	4.17	39	9.36	19.68
	Phase 1	5.70	(1)	---	---

* Velocity (Ch. 3 - 4) of Phase 3 is 2.63 cms/min.

******** Channel 5 : JEJUNUM ********

		Interval minutes	Contractions No.	Frequency No./min	Mean Amplitude mmHg
	Onset of fasting activity at time	0.00 minutes.			
	Phase 1	3.00	---	---	---
	Phase 2	60.46	136	2.25	12.28
	Time at onset of phase 3 is	63.46 mins.			
MMC (1)	Phase 3	7.98	64	8.02	11.52
	Phase 1	48.78	---	---	---
	Phase 2	46.25	62	1.34	12.75

Time at onset of phase 3 is 168.66 mins.

MMC (2)	Phase 3	8.16	65	7.96	18.20
	Phase 1	5.36	(1)	---	---

---

* Velocity (Ch. 4 - 5) of Phase 3 (1 - 1) is 1.48cms/min. **

* Velocity (Ch. 4 - 5) of Phase 3 (2 - 2) is 2.75cms/min. **

	Ch. 1:	Ch. 2:	Ch. 3:	Ch. 4:	Ch. 5:
No. of peaks detected:	24	67	192	475	330
After artefact excluded:	23	66	189	472	328

End of Analysis