NON-INVASIVE MONITORING OF GASTRIC MOTILITY IN HUMANS

by

Koray Özcan

M.D. degree in Medicine,
Faculty of Medicine, Marmara University, 1998

Submitted to the Institute of Biomedical Engineering
in partial fulfillment of the requirements
for the degree of
Master of Science
in
Biomedical Science

Boğaziçi University
January, 2005

NON-INVASIVE MONITORING OF GASTRIC MOTILITY IN HUMANS

APPROVED BY:

Assistant. Prof. Dr. Ata Akın (Thesis Supervisor)	...…….
Prof. Dr. Yekta Ülgen	.....
Dr. Halil Coşkun	…….

DATE OF APPROVAL: 18/ 01/2005

ACKNOWLEDGMENTS

Firstly, I would like to thank to my supervisor Assist. Prof. Dr. Ata Akın for his help and interest, not only during this study, but also during my graduate education in Institute of Biomedical Engineering.

I would like to thank my dear colleagues Dr. Mehmet Susam, Dr. Hisham Alsaher, Yasemin Keskin M.S for their support in technical details that concerned me during my master education and thesis.

I would like to thank also to Assoc. Prof. Dr. Semra Doğru Abbasoğlu for her great help in the statistical analysis of the data and her valuable advices. I also thank to my friend, Gürkan Çelik for sharing his great mathematics knowledge with me and for his technical support.

Lastly, I would like to thank my parents and my dear wife Duygu, who supported me with great patience and to all my friends who have helped during this work of thesis.

ABSTRACT

NON-INVASIVE MONITORING OF GASTRIC MOTILITY IN HUMANS

Stomach is an organ of gastrointestinal system where the food coming from the mouth through the esophagus is mixed by the rhythmic contractions of the smooth muscles, with acid and other gastric secretions. The control of motility of the stomach is performed by neuronal and hormonal factors that modulate the smooth muscles in generating muscular contractions. *Electrogastrography* is a procedure for recording gastric myoelectrical activity either invasively by placing electrodes on serosal lining of the stomach or non-invasively by using electrodes located on the skin of the abdomen. Compared with the development of other surface electrophysiological measurements, such as Electrocardiogram (ECG) and Electroencephalogram (EEG), the progress of the EGG has been very slow. The main problems include: (1) difficulty in data acquisition and analysis because of the low signal-to-noise ratio of the EGG; (2) difficulty in interpreting EGG data and extracting useful and relevant information from the EGG; and (3) lack of understanding of the correlation between the EGG and gastric motility. Today, numerous clinical and animal studies are being carried out by using EGG in order to have reliable, scientific data which can help the interpretation of the findings. The frequency of gastric contractions is controlled by the gastric slow wave, which is around 3 cycles per minute (cpm) and the appearance of gastric contractions is associated with spike activities. Today, conventional EGG devices are collecting data related with the lower frequency signals but it was shown on the animal models that higher frequency signals observed during peristaltic contractions can also be detected and quantified from EGG recordings by using a suitable method and perhaps, the patterns of this high frequency components can be correlated with the pathological processes related with the stomach. Our main interest arises on the collection and interpretation of the high frequency peristaltic contractions signals in humans using EGG.

Keywords: Electrogastrography (EGG), spike potential, gastric motility, gastric slow waves

ÖZET

MİDE HAREKETLİLİĞİNİN İNSANLARDA MÜDAHALESİZ ÖLÇÜMÜ-ELECTROGASTROGRAFİ

Mide, sindirim sisteminin önemli organlarından birisidir ve midenin temel görevi, yemek borusu yoluyla kendisine aktarılan yiyecekleri, yapısında bulunan düz kas hücrelerinin ritmik kasılmaları ve salgıladığı asit içerikli sıvıyı ve sindirim enzimlerini kullanarak sindirime uygun hale getirmektir. Mide motilitesinin kontrolü, salgılanan hormonlar ve mide düz kaslarının nöral kontrolü yoluyla sağlanmaktadır. Elektrogastrografi (EGG), mide düz kas hücrelerinin sergilediği, mide motilitesine yol açan elektriksel aktiviteyi, gerek serozal elektrotlar kullanarak invaziv, gerekse karın duvarına yerleştirilen yüzeysel elektrotlar kullanılarak non-invaziv olarak ölçülmesi yöntemidir. Elektrokardiyografi (EKG) ve Electroensefalografi (EEG) gibi diğer yüzeysel elektrofizyolojik ölçüm teknikleriyle karşılaştırıldığında, EGG çok yavaş gelişim göstermiştir. Bunun nedenleri (1) mideden gelen elektriksel sinyallerin oldukça zayıf olması ve düşük sinyal/gürültü oranı nedeniyle veri toplamanın güç olması, (2) EGG ile kullanılabilir veri elde etmenin ve elde edilen verilerin, klinikle olan ilişkilerinin yorumlanmasının oldukça güç olması, (3) EGG verileri ile gastrik motilite arasındaki ilişkinin tam olarak anlaşılıp ortaya konulamamış olmasıdır. Gastrik kasılmaların frekansı, "yavaş dalgalar" olarak nitelendirilen ve frekansı genelde 0,05 Hz olan elektriksel sinyaller tarafından kontrol edilmektedir. Gastrik kasılmaların şekli ise diken dalga aktivitesi ile ilgilidir. Günümüzde, konvansiyonel EGG tekniği ile daha çok düşük frekanslı sinyallerin toplanması hedeflenmektedir ancak yapılan bazı hayvan çalışmalarında peristaltik kasılmalar sırasında yüksek frekanslı sinyallerinde görülebildiği tespit edilmiştir. Bizim de, bu çalışmadaki temel amacımız, EGG kullanarak insanlarda, yüksek frekanslı peristaltik kasılma sinyallerini toplamak ve yorumlamaktır.

Anahtar Sözcükler: Elektrogastrografi (EGG), diken dalga potansiyeli, gastrik motilite, gastrik yavaş dalgalar

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

EGG	Electrogastrography
EEG	Electroencephalography
ECG	Electrocardiography
GER	Gastric Electrical Rhythm
GIS	Gastrointestinal System
UES	Upper Esophageal Sphincter
LES	Lower Esophageal Sphincter
HCl	Hydrochloric acid
GERD	Gastroesophageal Reflux Disorder
FFT	Fast Fourier Transform
DF	Dominant Frequency
PDF	Power of Dominant Frequency
PS	Power of Signal
cpm	cycles per minute

1. INTRODUCTION

1.1 Background

The living organisms need energy to maintain their life and this energy is obtained from the foods that are taken into the body through the digestive organs of the organism and processed by the digestive system of the living organism. This digestive process is a complex procedure, which requires synchronic function of a series of organs and digestive activity of some chemicals, and enzymes that are released into the foods through the digestive tract.

The gastrointestinal system provides the body with a continuous supply of water, electrolytes and nutrients. In order to achieve this goal, movement of the food through the lumen of the gastrointestinal organs, absorption of the digestive products, water and various electrolytes, circulation of blood through the GI tract to transport the absorbed substances and control of all these functions by the nervous and hormonal system are required.

Motility, secretion, digestion and absorption are the main actions of the Gastrointestinal System. Motility can be defined as the movement of lumened organs of the GI tract by which the eaten food is precisely mixed with digestive juices and enzymes and propelled through the lumen of the system from mouth to anus. Secretion is the production and release of some chemicals such as hydrochloric acid (HCl) and some biochemically active enzymes such as trypsin, pepsin etc. Digestion is the procedure of degradation of the foodstuffs from large molecules into the small micromolecules, which can be absorbed through the GI system walls, and absorption is the activity related with the passage of the micromolecules formed at the end of the digestion from the lumen of the GI tract into the blood stream.

1.2 State-of-Art of Motility Measurement

The early and exact diagnosis of GIS diseases is very important for a physician, especially in order to prevent any kind of malignant transformation that can occur because of an ongoing physical damage. The diagnostic tools in hand are however somewhat invasive ones and require insertion of a probe or direct visual fiberoptic endoscopes into

the gut and his may be an unpleasant experience for the patient. Another important disadvantage for these diagnostic invasive procedures is the cost. The diagnostic value of these techniques for the patients with motility problems is controversial, too. The physician can only obtain some indirect knowledge about the characteristic propulsive movement (peristalsis) of the GIS organs. GIS is mostly under control of autonomic nervous system and a constant electrical activity, which initiates and maintains the peristalsis throughout the system occurs between the neurons of the autonomic nervous system and GIS smooth muscle. The electrical activity of the stomach can be monitored by Electrogastrography. This instrument works in a similar manner with other electrophysiological activity detection instruments like ECG, EGG, etc. EGG can be applied via intraluminal, serosal and surface routes and the nature of the data from each route is somewhat different from each other.

Today, there are some problems, which cause some limitations for the clinical application of EGG as a diagnostic and monitoring tool. These problems can be listed as follows [1, 2]:

Data Acquisition

During collection of the signals, many physiological noise signals like heart, breathing, intestinal motility may alter the quality of the data and need an appropriate filtering. EGG signals are low frequency signals caused by slow wave contractions of the stomach, thus there is a difficulty in data acquisition and analysis because of the low signal-to-noise ratio.

Correlation and Standardization

Due to the nature of the EGG signals, it is very difficult to interpret the EGG data and take the necessary information from it. In literature, there are numerous studies using the EGG but the correlation of EGG with gastric motility and gastric motility disturbances is not well understood yet. Lack of standardization is another problem, which prevents the use of EGG as a widespread clinical tool.

Spike Activity

The spike activity is the electrical response activity with higher frequency content, which is responsible for triggering the peristaltic contractions. The duration and strength of this spike activity signals determines the force of the muscular contraction [3]. The spike activity, as being the high frequency component of the EGG signal, may be the important electrical activity, which can be used for the determination of the pathological processes. It is difficult to detect this higher frequency signals through the surface but it was shown that higher frequency signals of the antrum observed during peristaltic contractions can also be detected and quantified from surface EGG recordings using an appropriate wavelet transform.

When we consider about the conventional EGG techniques, generally, researchers preferred to work on the analysis of the lower frequency signals, as the expected frequency for the stomach is around 3 cpm. The higher frequency components of the signal are usually filtered by the EGG device itself or by some analytical computer programmes.

In an animal study, it was shown that the higher frequency signals from the stomach, which is generally collected from serosal electrodes, are related with the spike activity of the stomach and this activity may be the triggering factor for the gastric smooth muscle contraction. In fact, the magnitude of FFT of the signal is slightly increased during this spike activity. In another animal study, by using both serosal and surface electrodes, it was shown that, the surface electrodes could also detect the spike activity signals by using an appropriate detection algorithm [3].

1.3 Objectives

Main objective of this study is to monitor gastric motility non-invasively in human subjects. This study will be a continuation of the studies of Akin and Sun, in which the possibility of detecting the spike activity of the serosa in dogs from surface electrodes [4] is mentioned and the spike activity signals from the abdominal surface recordings in dogs is detected with an accuracy of 96% using a new detection algorithm based on a continuous wavelet transform [3]. At our study, we aim to apply a similar approach based on spectral estimation to the recordings from the abdominal surface electrodes in the

healthy human subjects and try to determine whether any discernable changes are observed in spectral bands for the EGG recordings in human objects.

1.4 Outline of the Study

In Chapter 2, the basic physiology and anatomy of the stomach is explained including the electrical activity of the smooth muscle cell and neuroendocrine control of the gastrointestinal system function. Chapter 3 presents conventional methods used for the diagnosis of the motility disorders. In Chapter 4, EGG device and EGG technique are explained and basic information about the EGG parameters and EGG application fields are is given. Chapter 5 presents the experimental procedure that we have used for EGG data collection and data analysis technique. Technical and statistical results of the experiments are presented in Chapter 6. Discussion of experimental results and conclusions reached on the basis of these results are given in Chapter 7 and Chapter 8, respectively.

2. ANATOMY AND BASIC PHYSIOLOGY OF THE STOMACH

2.1 Digestive Process

The organs of the GI tract are shown in Figure 2.1. As soon as the food enters the mouth, the digestive process begins. The food is chewed by the teeth and mixed with the saliva from salivary glands by the help of the tongue. The food is then swallowed and under the reflex control, the upper end of the esophagus relaxes to let the food inside the lumen. This upper end of the esophagus is called upper esophageal sphincter (UES) and this entrance point prevents the reflux of the swallowed food back to the mouth and airways and entrance of the air into the esophagus. The rhythmic contractions of GI tract start in order to propel the food into the stomach and these contractions are known as *peristalsis*. By the beginning of a peristaltic movement at the esophagus, the lower end of the esophagus, called as lower esophageal sphincter (LES), relaxes and the food enters into the stomach. The stomach has a large lumen, which stores food, mix it with hydrochloric acid and degrade into smaller particles. So formed mixture is called chymus and when chymus is ready for further digestion, the antrum of the stomach relaxes and chyme enters into small intestine. In small intestine, the digestive chemicals and enzymes from pancreas and gallbladder are added into the chymus and carbohydrates, proteins and lipids are degraded into micro molecules which can be absorbed through the GI tract walls into the blood stream. After absorption of the useful molecules, the wastes are collected in the lumen of the colon and are thrown out by the voluntary relaxation of the anus.

2.2 Anatomy of Stomach

Anatomically, the stomach can be divided into three major regions: Fundus (the most proximal), Corpus and Antrum (Figure 2.2). Histologically, Fundus and Corpus are hardly separable. In the Antral area, the density of the smooth muscle cells increases. The area in the corpus around the greater curvature, where the split of the longitudinal layers takes place, is considered to be anatomically correlated with the origin of gastric electrical activity. The circular layer of the muscularis is continuous with the circular layer of the esophagus, but is absent in the fundus. The thickness of the circular layer increases in the antrum and especially in the pyloric sphincter. It does not continue into the duodenum. The oblique layer of the muscularis is clearly seen in the fundus and near the lesser curvature of

the corpus, but the oblique fibers disappear distally (towards the antrum). The outermost layer is the serosa [5, 6].

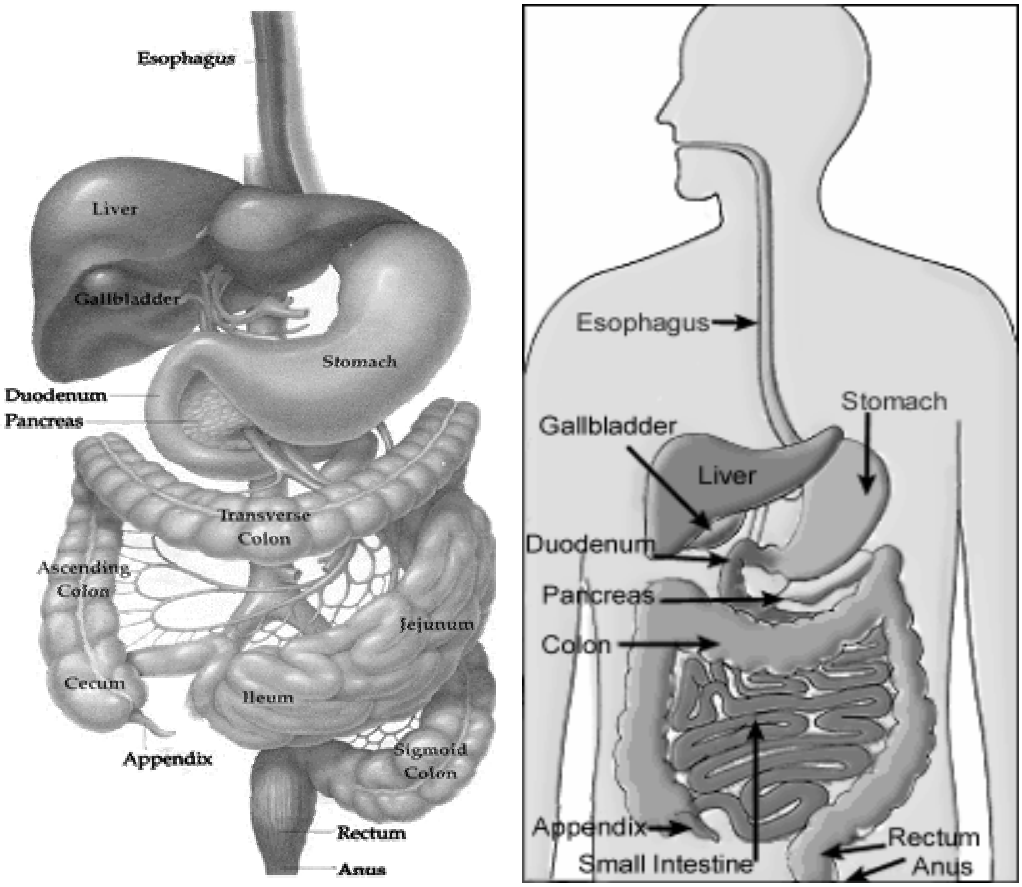

Figure 2.1 A. Anatomic Locations of GIS Organs and B. Schematic of GIS [5]

2.3 Characteristics of GIS Muscle Wall

If we look at the cross section of the gut, typically five layers are encountered from outside to inside: 1) Serosa 2) Longitudinal muscle layer 3) Circular muscle layer 4) Submucosa; that contains major nerves and blood vessels which travel through entire GIS and 5) Mucosa. In addition, a sparse layer of smooth muscle fibers, the muscularis mucosa, lies in the deeper layers of the mucosa. The motor functions of the gut are performed by different layers of the smooth muscle. (Figure 2.3)

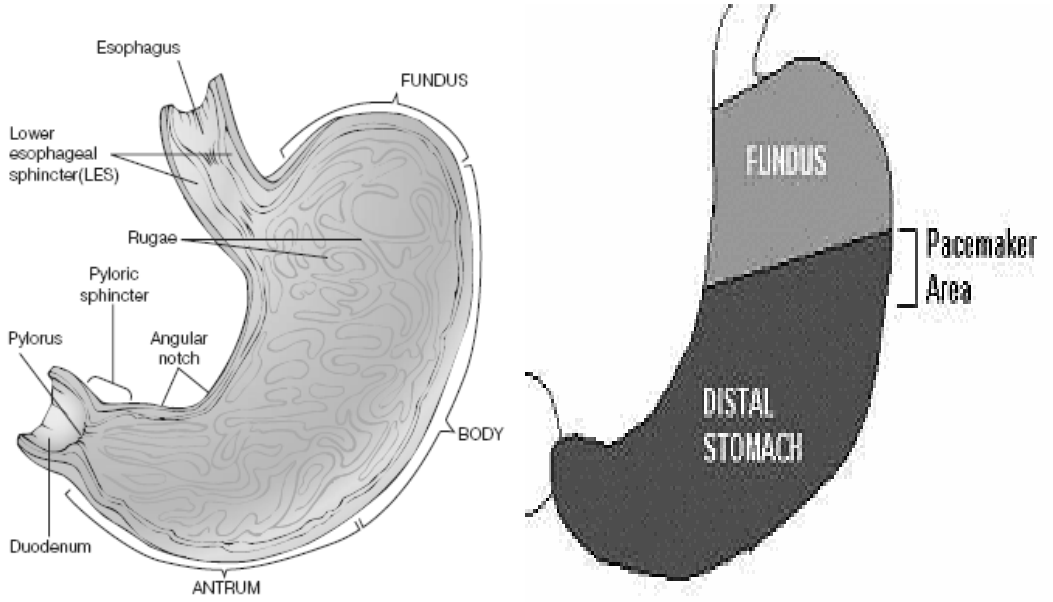

Figure 2.2 Gross and Physiological Anatomy of Stomach [5, 7]

2.4 Physiology of Gastrointestinal Smooth Muscle Cell

In order to understand the physiological activity of the GIS organs, we have to focus on the physiology of the smooth muscle.

Smooth muscle contains both actin and myosin filaments having chemical characteristics similar to but not exactly the same as those of the actin and myosin filaments in skeletal muscle. However, it does not contain troponin so that the mechanism for control of contractions is entirely different. Smooth muscle does not have the same striated arrangement of the actin and myosin filaments as that found in skeletal muscle. Large numbers of actin filaments are attached to *dense bodies*. Some of these bodies are attached to the cell membrane and others are dispersed inside the cell and are held in place by a scaffold of structural proteins linking one dense body to another. It is mainly through these bonds that the force of contraction is transmitted from one cell to the next [8].

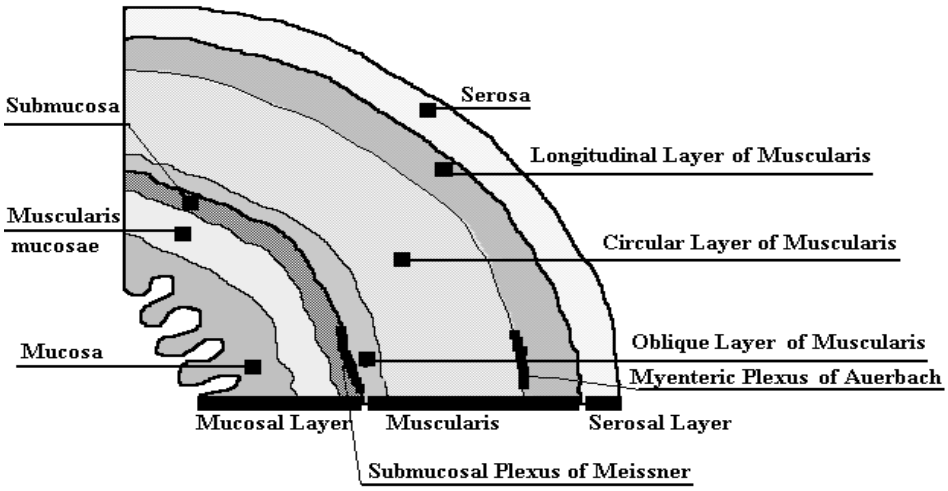

Figure 2.3 Layered Structure of the GIS Smooth Muscle [7]

The individual smooth muscle fibers in the GI tract are between 200 and 500 micrometers in length and 2 and 10 micrometers in diameter and they are arranged in bundles of as many as 1000 parallel fibers. Within each bundle, the muscle fibers are electrically connected with each other through large numbers of gap junctions that allow low resistance movement of ions from one cell to the next. Therefore, electrical signals can travel readily from one fiber to the other.

The surface/volume ratio of the gastrointestinal cells is larger than the skeletal muscle cells. The range of the resting membrane potential of the gastrointestinal smooth muscle cell is from about –40 mV to around –80 mV. Gastrointestinal smooth muscle cells have a higher ratio of Na^+ conductance to K^+ conductance than skeletal muscle cells; thus they have a smaller resting membrane potential.

During depolarisation, the rising phase is caused by entry of Ca^{2+} or of Na^+ and Ca^{2+} through voltage-gated channels. The balance between the influx of Na^+ and Ca^{2+} and the efflux of K^+ via Ca^{2+} activated K^+ channels is responsible for the plateau phase.

The resting membrane potential of gastric muscle cells lies negative to –60mV distal to the region of the gastric pacemaker. At this potential the open probability of voltage

dependent Ca^{2+} channels is very low. Therefore, there is little resting leak of Ca^{2+} into the cells, and the mechanical tone of gastric muscle is low.

The smooth muscle of the GI tract undergoes almost continual but slow electrical activity. This activity tends to have two basic types of electrical waves: 1) slow waves 2) spikes. In addition, the voltage of the resting potential of the gastrointestinal smooth muscle can change to different levels without the generation of waves and this can have important effects in controlling motor activity of the GI tract [9].

Gastric emptying depends upon the orderly propagation of electrical slow waves from the pacemaker region to the pylorus. Due to the differences in propagation velocity in the long axis of the circular muscle fibers versus the transverse axis, slow waves rapidly spread circumferentially around the stomach, organizing the electrical activity into a band of excitation that spreads distally. Each slow wave propagating through individual fibers, results in Ca^{2+} influx. The rise in intracellular Ca^{2+} activates myosin light-chain kinase, leading to cross bridge formation and contraction.

2.4.1 Slow Waves

Most gastrointestinal contractions occur rhythmically and this rhythm is determined mainly by the frequency of the so-called “slow waves” in the smooth muscle membrane potential. These waves are not action potentials. Instead, they are slow, undulating changes in the resting membrane potential. Their intensity usually varies between 5 mV and 15 mV and their frequency ranges in different parts of the human GI tract between 3 cycles per minute (cpm) and 12 cpm: about 3 cpm in the body of the stomach., as much as 12 cpm in the duodenum and changing about 8 or 9 cpm in the terminal ileum.

The slow waves themselves do not directly cause muscle contraction. However, they do control the appearance of intermittent spike potentials and the spike potentials in turn cause the muscle contraction.

2.4.2 Spike Potentials

The spike potentials are true action potentials. They occur automatically when the resting potential of the gastrointestinal smooth muscle becomes more positive than about –40mV (the normal resting potential is between –50 and –60mV). Thus, each time the peaks

of the slow waves rise temporarily above the –40mV, spike potentials appear on these peaks. Also, the higher the slow wave potential raises above this level, the greater the frequency of the spike potentials, usually ranging between 1 and 10 spike per second. The spike potentials last 10 to 40 times as long in the gastrointestinal muscle as the action potentials as the action potentials in large nerve fibers each lasting as long as 10 to 20msec.

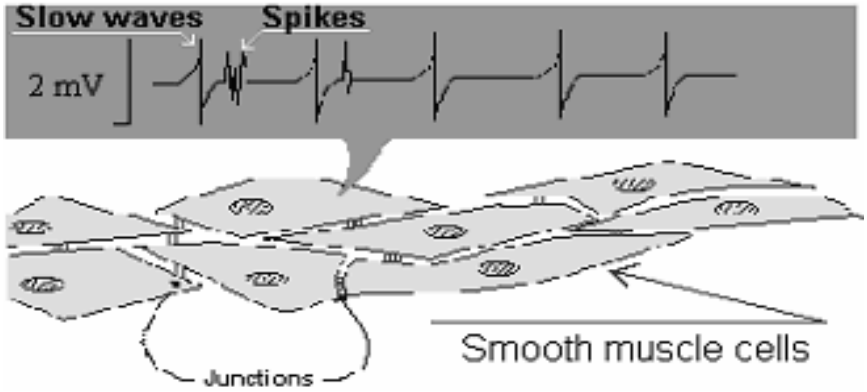

Figure 2.4 Propagation of Slow Waves and Spike Potentials Throughout Gastric Smooth Muscle Cells [7].

2.4.3 Tonic Contraction of Gastrointestinal Smooth Muscle

The smooth muscle of the GI tract usually exhibits tonic contraction as well as rhythmical contractions. Tonic contraction is continuous, not associated with the basic electrical rhythm of the slow waves, but instead often lasting several minutes or even several hours. The tonic contraction is sometimes caused by repetitive series of spike potentials – the greater the frequency, the greater the degree of contraction [8]. However, at other times tonic contraction is caused by hormones or other factors that bring about continuous depolarization of the smooth muscle membrane without causing action potentials.

2.5 Neural Control of Gastrointestinal Function

The enteric system is composed mainly of two plexi; an outer plexus lying between the longitudinal and circular muscular layers, called the myenteric plexus or Auerbach plexus and an inner plexus, called the submucosal plexus or Meissner plexus that lies in the submucosa. The myenteric plexus controls mainly the gastrointestinal movements and the submucosal plexus controls mainly gastrointestinal secretion and local blood flow. Also,

the sympathetic and parasympathetic nervous systems have connections with this internal neural network. Although the enteric nervous system can function on its own, independently of these extrinsic nerves, stimulation of the parasympathetic and sympathetic system can further activate or inhibit gastrointestinal functions.

2.6 Motor Functions of Stomach

The motor functions of the stomach may be summarized as 1) storage of large quantities of food until it can be accommodated into the duodenum 2) mixing of this food with gastric secretions until it forms a semi-fluid called chyme 3) slow emptying of the food from the stomach into the small intestine at a rate suitable for proper digestion and absorption by the small intestine [8].

Physiologically the stomach can be divided into two major parts; the corpus or the body and the antrum. Fundus of the stomach may be classified as another part of the stomach anatomically but it is a part of the body of the stomach physiologically.

2.7 Storage function of Stomach

As food enters the stomach, it forms concentric circles in the body and the fundus of the stomach. The newest food lies closest to the esophageal opening and the oldest food lies nearest the wall of the stomach. Normally when food enters the stomach, a vagal reflex greatly reduces the tone in the muscular wall of the body of the stomach so that the wall can bulge progressively outward, accommodating greater and greater quantities of food up to 1.5 liters. The pressure in the stomach remains low until this limit is approached.

2.8 Mixing and Propulsion of Food in Stomach

The digestive juices of the stomach are secreted by the gastric glands, which cover almost the entire wall of the body of the stomach except along a strip on the small curvature of the stomach. These secretions come immediately contact with that portion of the stored food lying against the mucosal surface of the stomach; when the stomach is filled, weak peristaltic constrictor waves also called mixing waves, move toward the antrum along the stomach wall approximately once every 20 seconds. These waves are initiated by the Basic Electrical Rhythm (BER) consisting of electrical slow waves that

occur spontaneously in the stomach wall. In most parts of the GI tract, these waves are not strong enough to cause contractions unless they first elicit action potentials but in the stomach their positive peaks do rise above the threshold for excitation even without action potentials.

As slow waves move down the stomach, they not only cause the secretions to mix with the upper portions of the stored food but also provide weak propulsion to move the food toward the antrum. When the stomach is full, these mixing contractions usually begin near the midpoint of the stomach but as the stomach empties, the contractions become stronger and also originate farther back up the stomach wall, thus propelling the last vestiges of the stored food into the stomach antrum. Then when completely empty, the stomach becomes mainly quiescent until new food enters.

As the constrictor waves progress from the body of the stomach into the antrum, they become more intense, some becoming extremely intense and providing powerful peristaltic rings that force the antral contents under high pressure toward the pylorus. Each time a peristaltic wave passes over the antrum toward the pylorus, it digs deeply into the contents of the antrum. Yet the opening of the pylorus is small enough that only a few millimetres of antral contents are expelled into the duodenum with each peristaltic wave. Also, as each peristaltic wave approaches the pylorus, the pyloric muscle itself contracts, which further impede emptying through the pylorus. Therefore, most of the antral contents are squirted backward through the peristaltic ring toward the body of the stomach [8].

2.9 Hunger Contractions

Besides the peristaltic contractions that occur when food is present in the stomach, another type of intense contractions occurs when stomach has been empty for a long time and they are called *hunger contractions*. These are rhythmic peristaltic contractions in the body of the stomach. However, when they become extremely strong, they often fuse together to cause a continuing titanic contraction lasting for as long as 2 to 3 minutes.

Hunger contractions are usually most intense in young, healthy people with high degrees of gastrointestinal tonus and they are also greatly increased by a low level of blood glucose.

2.10 Emptying of Stomach

Mainly, stomach emptying is promoted by the intensity of the peristaltic contractions of the stomach antrum. At the same time emptying is opposed by varying degrees of resistance to the passage of the chyme at the pylorus. Most of the time the antral peristaltic contractions are weak and function mainly to cause mixing of the food and gastric secretions. However, about 20 percent of the time while the food is in the stomach, the antral contractions become very intense, beginning at the incisura angularis of the stomach and then spreading through the antrum no longer as weak mixing contractions but instead as strong peristaltic, ring like contractions. As the stomach becomes progressively more and more empty, these constrictions begin farther and farther up the body of the stomach, gradually pinching off the lowermost portions of the stored food and adding this food to the chyme in the antrum. These intense peristaltic contractions often create as much as 50 to 70 cm of water pressure, which is about six times as powerful as the usual mixing type of peristaltic waves. Thus, the intensity of this antral peristalsis is the principal factor that determines the rate of the stomach emptying. When pyloric tone is normal, each strong antral peristaltic wave forces several millilitres of chyme into the duodenum. Thus, the peristaltic waves provide a pumping action that is frequently called the *pyloric pump*.

2.11 Regulation of Stomach Emptying

The rate at which the stomach empties is regulated by signals both from the stomach and from the duodenum. The stomach signals are; 1) nervous signals caused by distension of the stomach by food 2) the hormone gastrin released from the antral mucosal in response to the presence of certain types of food in the stomach. Both these signals mainly increase pyloric pumping force and at the same time slightly inhibit the pylorus thus promoting stomach emptying.

On the other hand, signals from the duodenum depress the pyloric pump and usually increase pyloric tone at the same time. In general, when an excess volume of chyme or excessive amounts of certain amounts of chyme enter the duodenum, strong negative feedback signals, both nervous and hormonal, depress the pyloric pump and enhance pyloric sphincter tone. Obviously, these feedback signals allow chyme to enter the duodenum only as rapidly as it can be processed by the small intestine [8].

3. TECHNIQUES USED FOR DIAGNOSIS OF UPPER GASTROINTESTINAL SYSTEM MOTILITY DISORDERS

3.1 Motility Disorders

Upper gut motility disorders involve functional disorders within the esophagus, stomach and small intestine. Approximately 35 million Americans suffer from gastrointestinal motility disorders. These disorders range from gastroparesis, affecting a small number each year, to common gastrointestinal disorders — Irritable Bowel Syndrome (IBS), gastroesophageal reflux disease (GERD), and fecal incontinence. There are three primary components to functional gastrointestinal disorders: *motility*, *GI tract sensation*, and *brain-gut dysfunction*. All of which affect both the lower and upper gut [10].

Normal motility or *peristalsis* is an orderly sequence of muscular contractions from top to bottom. In functional GI disorders, muscular spasms can cause pain, or contractions can be very rapid or very slow altering gut transit. *Sensation*; refers to the visceral sensation problems. The stomach nerves are sometimes so sensitive that even normal contractions can induce pain or discomfort in response to physiological stimuli, such as digesting a meal. *Brain-Gut Dysfunction* is functional problem in which the regulatory connection between brain and gut function may be impaired causing disharmony in the way the brain and gastrointestinal system communicate [11].

3.2 Motility Disorder Testing

Motility disorders result when any chronic abnormal muscular activity such as muscular spasms or irregular contractions start causing pain, diarrhea, constipation, indigestion, vomiting or abdominal bloating. Since these disorders are functional, not structural, they cannot usually be identified by x-ray, blood tests or endoscopy. In general practice, these patients usually are sent to invasive diagnostic techniques of investigation, such as upper GI endoscopy and usually nothing pathological is found in such examinations. Even though many of these disorders are accentuated by stress and emotional upset, they are physical conditions and not psychological [10].

3.3 Motility Problems Related with Stomach

Gastroparesis-delayed Gastric Emptying: Many of these patients have difficulty eating, experiencing severe, chronic vomiting and nausea. Some patients may even require tube feeding to ensure adequate nutrition. There are a number of causes for gastroparesis including diabetes mellitus, anorexia, bulimia, lupus and brain disorders. However, nearly 60% of the cases have an unknown origin.

Functional Dyspepsia (Non-Ulcer Dyspepsia): Abnormal gastric accommodation reflex or low gastric relaxation may cause functional dyspepsia. Patient's symptoms include pain or discomfort and bloating in the upper abdomen, fullness, and nausea.

3.4 Techniques for Investigation of Gastric Motility Disorders

Upper GIS Endoscopy: This test actually does not actually show any motility disorder directly, but it is a gold standart technique for directly observing the inner structure of the stomach and diagnosis any organic disorder, such as peptic ulcer. In diagnosis of motility disorder, this technique may be used to exclude any organic pathology that may cause symptoms in the patient and may route the physician to other diagnostic methods, which are listed below.

Manometric Studies: This technique measures the tone and compliance (stretch) of the esophagus and upper stomach. It also measures gastric accommodation and gastric sensation. Manometric studies can show whether the upper stomach relaxes adequately during eating and how much filling of the stomach it takes to cause pain or discomfort. An intragastric balloon is inserted into the stomach of the patient through the esophagus and resistance and volume changes are measured by using this balloon. Filling the balloon bit by bit with air, the motility specialist is able to determine volume related abdominal pressure pain levels, in addition to esophageal and stomach muscle tone and elasticity. In some patients, a manometry is used to diagnosis GERD and GERD related conditions that may be due to altered esophageal and stomach pressures. An advantage of this technique is its close contact with the stomach wall. Manometry testing can accurately detect stomach wall contractions in the esophagus, pylorus and small intestine, however, does not accurately measure gut tone.

24-hours pH Monitoring: Patients who suffer from GERD are under risk of carcinomatous changes in their esophagus. This disorder is encountered because of dysfunction of LES and the golden standart technique for diagnosis is to show the acid reflux into the esophagus. A pH sensitive electrode is inserted into the esophagus of the patient and it is connected to a recording device. The recording device is worn around the waist. Patients are able to continue their regular daily routine and consume a normal diet. After 24 hours, the patient simply returns the recording device for data analysis.

Gastric Emptying Studies: Gastric emptying studies measure the flow of solid or liquid meals as they empty into the small intestine. Gastric emptying is controlled by contraction and tone of the stomach wall. A computer controlled pump is used which shows whether the upper stomach relaxes adequately during eating and how much filling of the stomach it takes to cause pain or discomfort. A special sleeve manometer is used to measure the pressure in the pyloric sphincter, the hard ring of smooth muscle creating the boundary between the stomach and the small intestine. Pressure sensors in the manometer can also measure contractions of the stomach and upper intestine.

Antroduodenal manometry: This test measures the pressure waves in the stomach and adjacent small bowel, recording the pressure changes in the antrum and duodenum. Part of diagnostic testing includes measuring muscle contraction and responses to physiological stimuli (i.e. meals, erythromycin) using a manometer. Additional diagnostic testing, in conjunction with nuclear medicine, includes measuring stomach emptying and transit in the small intestine using a nuclear medicine scan.

Electrogastrography: This technique will be described in details in the next chapter.

3.5 Gastric Dysrhythmia

The normal Gastric Electrical Rhythm (GER) is three cycles per minute 3 cpm (0.05 Hz). Any other disturbance in this basic rhythm is called as dysrhythmia. Dysrhythmias can be classified as 1) tachygastria, which refers to the state of having a higher frequency of GER than normal, 2) bradygastria, which refers to the state of having a lower frequency of GER that normal and 3) arrhythmia which is a state of having irregular slow waves with no constant frequency.

Table 3.1 Types of Gastric Electrical Rhythm

Types of Gastric Electrical Rhythm	
Type of the rhythm	**Frequency**
Normal	3 cycles/min (0.05 Hz)
Bradygastria	≤ 2 cycles/min (≤ 0.03 Hz)
Tachygastria	≥5 cycles/min (≥ 0.083 Hz)

4. ELECTROGASTROGRAPHY: DATA COLLECTION AND INTERPRETATION

Electrogastrography is a term given to the measurement of human or animal gastric electrical activity. It has been known since the 1920's but has not received widespread acceptance, especially as a clinical diagnostic tool in gastroenterology. In 1922, Walter Alvarez, using cutaneous electrodes applied to the epigastric region, intentionally recorded the first EGG. Since this first application, EGG has been an area of interest for many physiologists, psychophysiologist and gastroenterologists. Parallel to the development in the technology of the electronic equipment and electrical instrumentation, the interest for the cutaneous EGG has also increased. This increment was partially due to the association of some electrogastrographic abnormalities with many clinical syndromes, which stimulated much more studies with the EGG in both clinical and physiological areas.

Gastric myoelectrical activity can be measured serosally, intraluminally, or cutaneously. When serosal or intraluminal electrodes are used, signal collection is performed via the electrodes that are placed directly to the serosa or mucosa of the organ. The electrode is placed to the serosa by piercing the needle electrodes directly to the serosa during that abdominal surgery. The mucosal recording is obtained by the electrodes that are located on a tube, which is similar to nasogastric tube and these electrodes collects the signals from mucosal by direct contact. This invasive way of recording has the advantage of collecting data directly from the target organs so that the effect of the noise from the environment and nearby organs is minimum and recording both slow waves and spikes, since these recordings represent myoelectrical activities of a small number of smooth muscle cells. However, application of invasive recording can cause pain and stress in human subjects and is usually preferred for experimental studies in animals. Non-invasive (cutaneous) recording technique is simply the collection of the electrical signals from the abdomen via the surface electrodes located on the skin of the abdomen.

There are some major differences between the internal recording techniques and cutaneous EGG [12, 13]. The shape and the waveform that is obtained from the recording significantly depends on the way of the recording. As the signals are collected from the organ directly in internal methods, the amplitude of the waveform may be as high as 2 mV; on the other hand the amplitude in cutaneous EGG recording may vary from -100 μV to

500 μV because of the distance through which the electrical signals must travel. Serosal recordings are usually carried out by implanting pairs of stainless steel (or silver) wire, 2-5 mm with short distance bipolar (SDB) electrode technique. In view of the nature of gastric electrical activity, these recordings can be qualified as differential. In addition, the active surface are of the wire is very small. The SBD signals have well-defined time characteristics but their frequency spectra are quite broad and the signal period cannot be recognized in them unless sharp and very narrow band-pass digital filtering is done. Spike activity, which is defined related to gastric contractions, can be clearly seen in internal SDB recordings, but it was shown that cutaneous techniques might also pick up the spikes, as well [1, 14, 15].

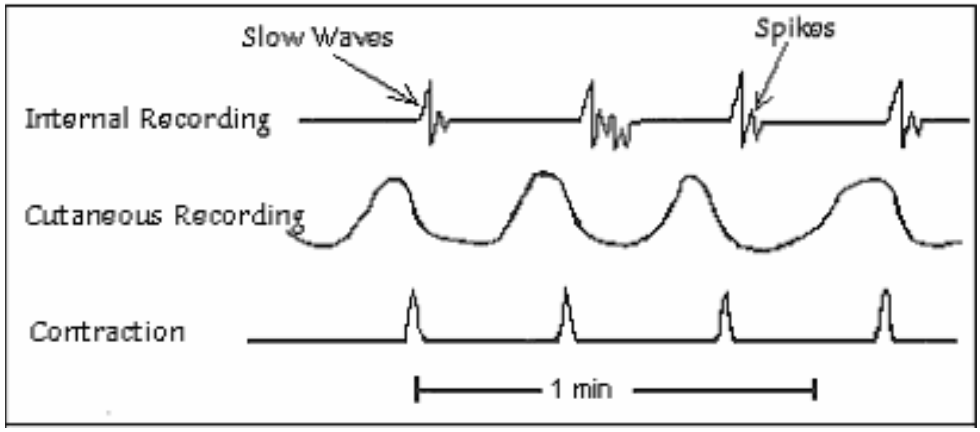

Figure 4.1 Comparision of Electrogastrograms Recorded via Internal and Surface Electrodes [16]

Unlike ECG, EGG is not an easy type of recording method because of the anatomical and physiological nature of the target organ and other interference factors. The interfering signals from abdominal organs like small intestine, colon and duodenum and extra-abdominal organs such as heart, diaphragm may affect the signal that is obtained from stomach. In order to collect the right and proper data from the stomach, the technician must follow the correct way of recording and must use a proper technique for data collection. The details of a suitable EGG recording technique will be given in the following part

4.1 EGG Device

The EGG device may resemble to an ECG instrument in some ways but as the signals from the stomach has much lower amplitude and different frequency than the heart; instrument must be configured in an appropriate manner. An EGG instrument must mainly

contain pre-amplification, isolation, filtering, analog-to-digital conversion and process and display compartments. The signal must be amplified during data collection and as the gastric electrical signals has the frequency of nearly 0.05 Hz; the collected data must be filtered in such a way that high frequency signals, such as cardiac, duodenal, colonic and diaphragmatic signals, must be eliminated from the raw data. The filtering operation may also be carried out after data collection by using some computer programmes.

The filtered EGG signal is then amplified by using high-impedance amplifiers. These amplifiers must be electrically isolated in a convenient way in order to prevent any possible electrically shock hazard. For this isolation, some designers have used fiber-optic cables while some preferred photo-couplers or some different electronical measures in order to achieve the isolation.

The amplified signals are analog signals and must be converted into digital numbers, which may ease the data processing procedure. Analog-to-digital converters are used for this purpose. The digital values are processed in personal computers by using different data analysis software according to different analytical parameters.

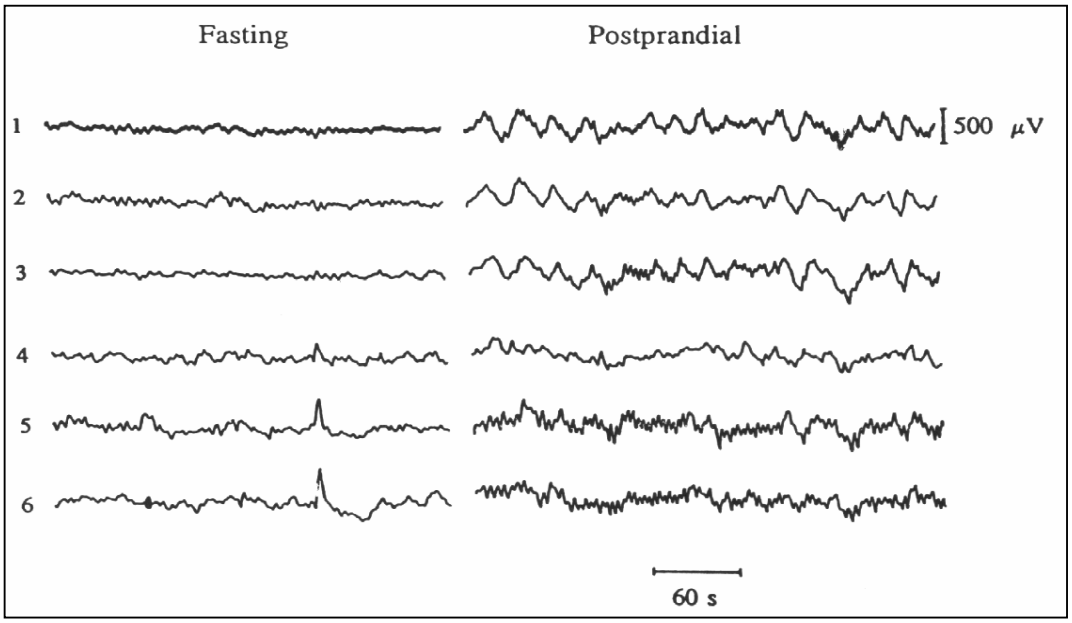

Figure 4.2: An Example of Six Unipolar EGG Signals, Recorded from Six Electrodes on the Abdomen, Referenced to an Electrode on the Right Ankle [17]

4.2 Position of Patient

Supine position of the patient is preferred for EGG recording as sitting or upright position may lead small intestines to come forward position at which they will be much more in front of the stomach, thus will prevent and disturb the data collection. The subject must be relaxed, must stand still as much as he/she can and must not talk during recording. For an ideal recording, the room should be electrically shielded, sound diminished, and dimly illuminated.

4.3 Electrode Placement

As the signals recording in the EGG are very weak signals, the electrodes applied must procedure as little noise as possible. Commercially available, pre-gelled silver/silver-chloride electrodes, which are already being used for ECG, may be suitable for EGG, too. Skin abrasion with sand paper is a crucial part of the procedure. After proper skin preparation, the impedance of a pair of electrodes placed on the human body is slightly <10 kΩ and this impedance will be suitable for a good EGG recording.

The cutaneous EGG may be applied by using either monopolar or bipolar electrode configurations. In monopolar configuration, there are two electrodes; one of them is used as an active electrode while the other one is the reference. In bipolar configuration, there are two active electrodes against a reference electrode. The placement of the cutaneous electrodes on the abdomen is a very important part of the recording process and is still a question of doubt. The anatomy of the abdomen and stomach complicates the exact localization of the electrically active areas of the organ. The antral electrical activity is the main target of EGG and electrode locations, which will focus on this area, must be preferred. The location of the stomach may be radiologically determined by barium contrast techniques or by using ultrasound and electrodes may be placed according to this localization. These efforts for the exact localization of the stomach is crucial as the electrical signals from stomach are very tiny signals and must be collected as pure as possible. Also, the proper localization of these electrodes will decrease the artefacts caused by different physiological signals from the abdominal organs and from the environment and any subjective difference in size and shape of the organ may lead to wrong data collection and misinterpretation of the electrical activity of stomach [17,18].

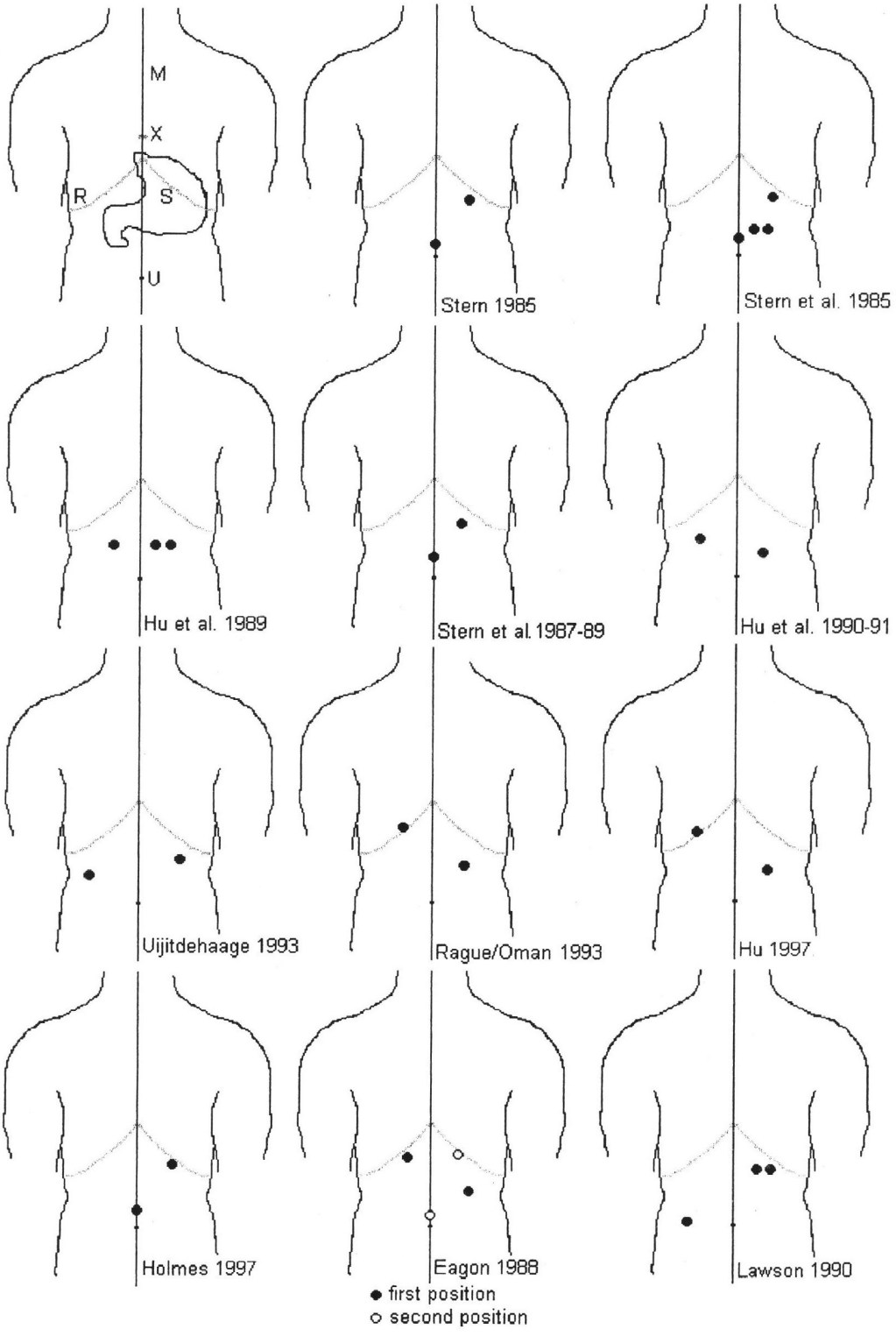

Figure 4.3 Alternative Electrode Positions Used for EGG Recording [19]

In fact, in daily practice, some authors used roughly the antral axis for electrode placement. In Dutch EGG studies, the transpyloric line of Addison is defined, which runs halfway between the distal end of the sternum and the umbilicus and this line is preferred to be used as a landmark of the antral axis in a EGG electrode placement on the guess basis [17]. We also preferred to use this imaginary line for determining the antral axis in our EGG recordings.

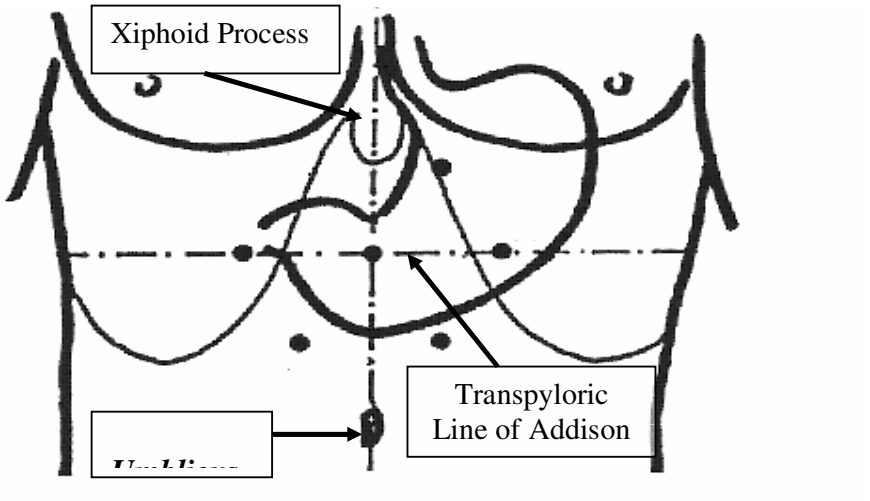

Figure 4.4 Transpyloric Line of Addison and Anatomic Localization of Electrodes on the Abdomen [17].

4.4 Frequency Ranges

The EGG signals, in fact is a collection of a mixture of signals and noises from abdominal and environmental sources and has a low S-to-N ratio when compared to other recording techniques. The researcher must set the instrument in such a way that the noise and artefacts will be blocked and the suitable data from the stomach will be collected. The composition of the EGG data and sources of artefacts are listed in Table 4.1.

4.5 EGG Parameters

When data are collected by EGG, the next step requires the appropriate analysis of the data. At this step, a researcher must decide 1) which EGG parameters will be used for a specific study 2) what the meaning and clinical significance of each EGG parameter is and how the necessary data can be extracted from this raw data. This important signal-

processing step is the vital part of the test and needs to be carefully planned. Below, we will give information about the EGG parameters, which are used for evaluation [17].

Table 4.1 Composition of EGG Signal

	Component	**Frequency Range**
EGG Signal	Normal Gastric Slow Waves	0.033 – 0.066Hz (2-4 cpm)
Noise	Motion Artefacts	Whole range
	Dermal Noise	<0,033Hz (<2cpm)
	Small Intestine	0.15 – 0.2Hz (9 – 12cpm)
	Respiration	0.2 – 0.4Hz (12 – 25cpm)
	Heart	1 – 1.5Hz (60 – 90cpm)

Dominant Frequency and Power: As EGG is a multi-component signal and in the time domain, these multiple components are superimposed on each other and make accurate quantitative analysis of the data impossible. However, in the frequency domain, the signal and noise are usually separated and if the EGG recording is correct, gastric signal is the main (dominant) component. The frequency, believed to be of gastric origin and at which the power has a peak value is called *the dominant frequency*. *Dominant power* is the power at the dominant frequency. The dominant frequency and power are computed from the power spectrum analysis of the data. Power spectrum analysis of a data sequence is defined as the Fourier transform of the autocorrelation function of the data sequence or the squared magnitude of the Fourier transform of the infinite data sequence with appropriate statistical averaging.

Relative Changes of Dominant Power or Frequency: This is the ratio of power before and after certain stimulation. This is a useful parameter for determining the changes in the motility behaviour against certain types of stimuli.

Percentage of Normal Slow Waves: This is a quantitative assessment of the regularity of gastric slow waves measured from the EGG. It is defined as the percentage of time during which normal slow waves are observed in the EGG recording. This is computed by using running power spectra of EGG:

Percentage of Gastric Dysrhythmia: This is defined as the percentage of time during which gastric dysrhythmia is observed in the EGG. It is computed in the same way with the computation of percentage of the normal slow waves.

Instability Coefficients: For calculation of this parameter, dominant frequencies and power for a period is calculated and the changes are observed. The ratio between the standart deviation and the mean of dominant frequencies and corresponding dominant power is called the instability.

4.6 Applications of Electrogastrography

In literature, there are numerous studies, which have used EGG on clinical grounds [20, 21, 22]. The main topics were:

a. Effects of gut hormones and pharmacological and prokinetic agents on gastric myoelectrical activity

b. Gastric myoelectrical activity in pregnant women

c. Gastric myoelectrical activity in patients with motion sickness

d. Gastric myoelectrical activity with suspected gastroparesis

e. Gastric myoelectrical activity in diabetic gastroparetic patients

f. Detection of slow wave propagation from the EGG

g. Prediction of gastric emptying using the EGG

h. Forms of gastric dysrhythmia

i. Gastric myoelectrical activity in some systemic diseases like systemic sclerosis

j. Recovery of Gastrointestinal tract motility and myoelectrical activity change after abdominal surgery

4.6.1 Effects of Gut Hormones and Pharmacological and Prokinetic Agents

Since EGG is a reliable measure of the frequency of gastric myoelectrical activity, it can be used to investigate whether certain hormones or prokinetic agents enhance slow waves or induce gastric dysrhythmias [23]. Hormones like Glucagon, Epinephrine and pharmacological agents like Domperidone [24], Erythromycin [11] have become the subjects of such kind of studies. In these studies, it has been shown that opioid peptides have potent effects on gastric slow waves [10]. Other peptides including Insulin, Secretin, Cholecystokinin and Pentagastrin have also been demonstrated to induce gastric dysrhythmias [25]. There are several studies, which have reported that some prokinetic agents, such as Cisapride [16] and Erythromycin may be able to convert gastric dysrhythmias into normal slow waves [11].

4.6.2 Nausea and Vomiting of Pregnancy

In EGG studies, some abnormalities were found in symptomatic pregnant women and these abnormalities have disappeared after the termination of the pregnancy. The main abnormalities were instability of EGG and less responsiveness of the EGG to the test meal. Some differences in EGG between patients with nausea and without nausea were observed. Through these results, it can be concluded that abnormalities in the EGG are objective pathophysiological events associated with nausea and vomiting in pregnant women [23]. EGG may be the technique of choice for such studies as it is a non-invasive method.

4.6.3 Motion Sickness

Motion sickness is another clinical entity in which EGG can be used as a tool for gastric myoelectrical activity measurement. In one study, an alteration of normal 3 cpm activity to tachygastria (4-9 cpm) was observed in subjects with motion sickness during rotation where as a continuation of 3 cpm activity was noted in subjects without motion sickness during rotation [26].

4.6.4 Gastroparesis

The EGG may be used to differentiate between normal subjects and patients with gastroparesis [23]. This is important for patients with diseases like Diabetes Mellitus that can cause some autonomic nervous system abnormalities, which can present itself as a kind

of gastric motility problem. Also, due to induction of anaesthesia, the patients who undergo a surgical procedure may face the gastroparesis problem and EGG may be helpful for the physician to determine and document the gastric myoelectrical activity.

4.6.5 Gastric Emptying

The studies related with gastric emptying have variable results. Some studies have shown that there was no evidence of an association between EGG and gastric emptying [24] while some authors found a good correlation between dysrhythmic EGG's and delayed gastric emptying [27]. More studies are needed so that the correlation between the EGG and gastric emptying can be understood well. A normal EGG recording may not guarantee normal gastric emptying while an abnormal EGG may predict delayed gastric emptying [23].

5. EXPERIMENTAL PROCEDURE

5.1 Subjects

The studies were performed in 6 healthy volunteers with a mean age of 28.3 years. There were 3 male and 3 female subjects. The subjects had no history of symptoms related with stomach and had no history of gastrointestinal tract related disease. Demographic data, such as age, gender, body weight, body height, were recorded. All the subjects are informed about the experimental procedure in detail and their informed consents are taken.

5.2 EGG Instrument

In our study, we used Biopac® MP30 hardware systems for EGG data acquisition. This is a multipurpose system, which can be adjusted according to the characteristics of the physiological signal to be measured [28]. In the system menu of the software, we made the precise set up for our experimental procedure and designed the instrument in such a way that we can collect the electrical signals with frequencies between 0-35 Hz by using a bipolar electrode. Our sampling rate was 200 samples/sec. After data collection before and after ingestion of a standart meal, we processed the data by using the software tools in the Biopac® system.

5.3 EGG Procedure

The patients did not eat or drink anything for 12 hours before the pre-prandial recordings. The patients lied supine on a bed in a quiet room, and are told to stand still without talking or any extremity movement throughout the recording process in order to prevent the noise as much as possible. We used commercial Ag/Ag-Cl ECG electrodes for sampling signals. In our study, we have experienced some problems for gathering the appropriate signals and tried different ways of electrode placement and we saw that the electrode placement defined in the Dutch experience was suitable for our instrument data collection capacity and placed our electrodes on the transpyloric line of Addison.

The time for electrogastrographic data collection varies from 15 minutes to 2 hours in different studies and we decided that a 20-minute data collection would be suitable for our study. After the placement of the electrodes, a pre-prandial recording for a period of 20

minutes is performed. After this initial recording, the patient is de-connected from the instrument to eat the meal. In literature, the content of the standart meal was given as a diet which contains 500 kcal energy, %50 carbohydrates, % 30 fats and %20 protein [29] and diet given to the subjects are arranged according to this knowledge (a ham-sandwich with cheese, 200 ml apple juice). After a 10 minutes waiting time, post-prandial recording for 20 minutes is carried out and the procedure is finished.

5.4 Data Analysis

The raw EGG signal of a subject is given in Figure 5.1. This raw signal is firstly down- sampled to 5samples/sec. Then, it is filtered by a band-pass (0.01 - 1.5Hz) IIR filter. The resultant EGG wave is given in Figure 5.2.

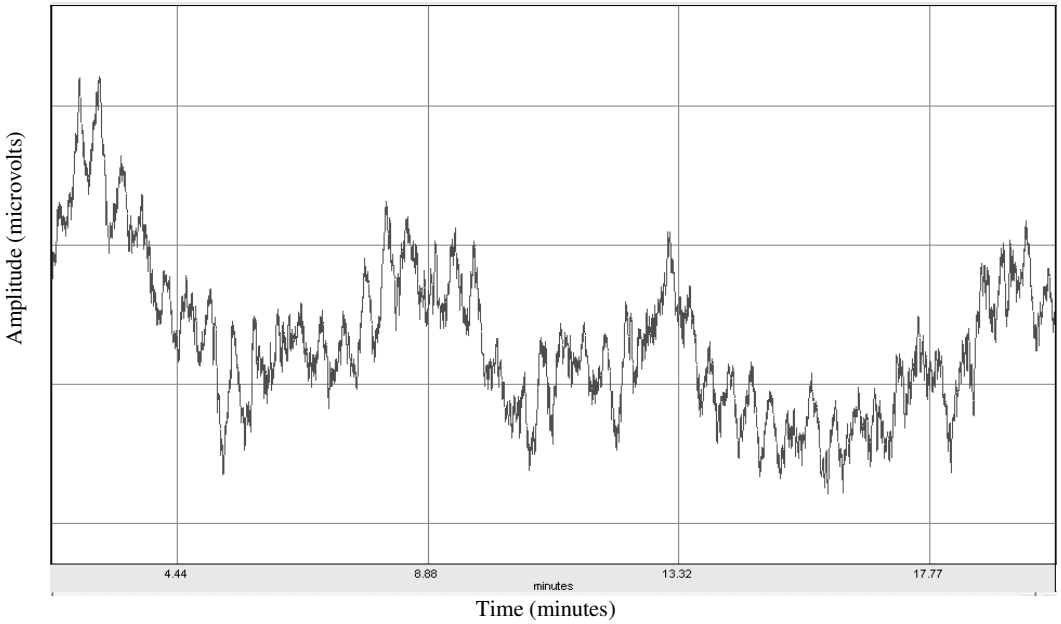

Figure 5.1 Raw EGG Signal of a Subject

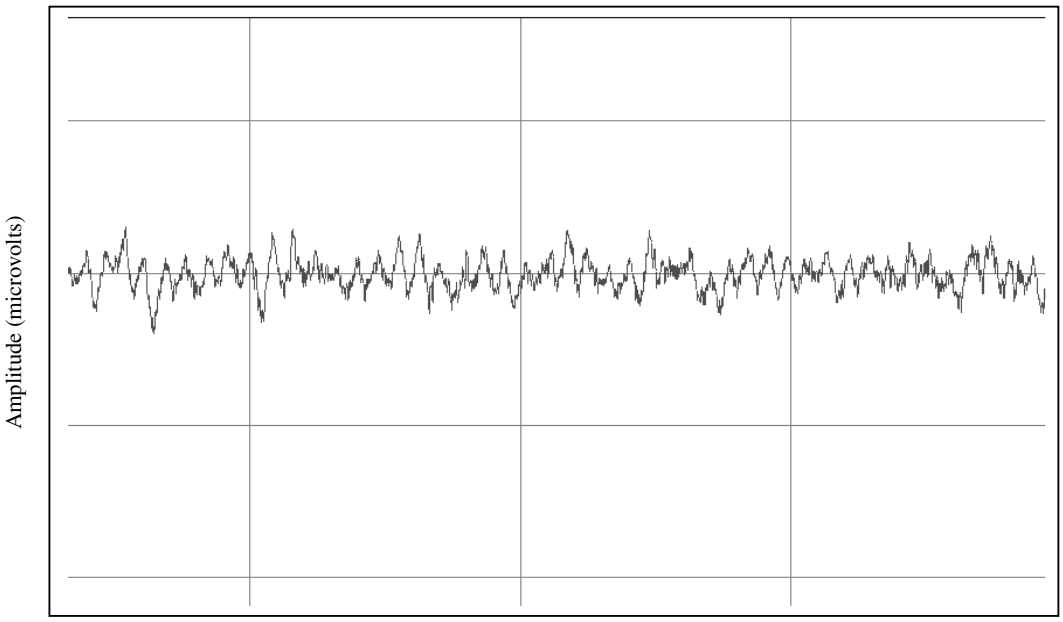

Figure 5.2 EGG Data that is Down-sampled to 5Hz and Filtered by Bandpass Filter

Then, data is transformed into frequency domain by Fast Fourier Transform. The FFT of the EGG of a subject is given in Figure 5.3:

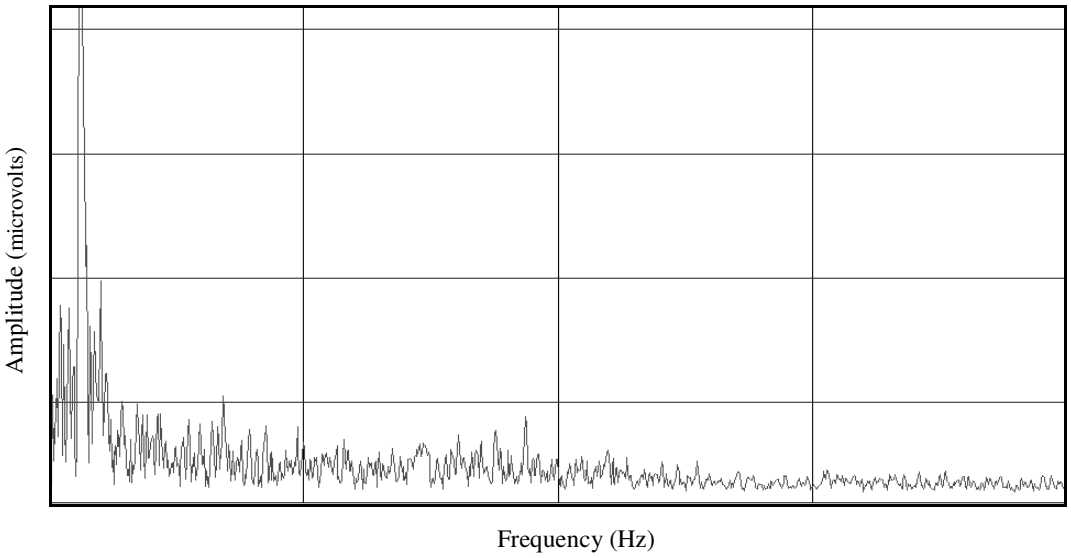

Figure 5.3 FFT of Processed Signal

These procedures are repeated for post-prandial recordings and by using the FFT data, dominant frequency, power of dominant frequency and area is calculated for both recordings. The statistical analysis is carried out on SPSS 11.5 for Windows statistical

analysis programme and nonparametric Wilcoxon Analysis Test is used to determine the statistical significance of the changes that occur between pre-prandial and post-prandial recording data.

6. RESULTS

For every subject, a pre-prandial recording of 20 minutes, followed by a post-prandial recording of 20 minutes is carried out. Biopac® system BSL pro 3.6.7 software is used for the analysis of the data. For every recording, firstly, data is down-sampled to 5Hz and is filtered by a bandpass IIR filter (0.01-1.5 Hz). Next, Fast Fourier Transform of the resultant wave is generated. This FFT is used for the determinations of Dominant Frequency (DF), Power of Dominant Frequency (PDF) and Power of Signal (PS) for each subject.

In general, the parameters that we have used are applied to entire signal. In our study, besides determining these parameters for whole wave, we examined every subject's FFT graph and try to plot some common regions of frequency for each and we examined all these for parameters for each of these bands and determine the changes between the pre-prandial and post-prandial recordings. Some of these bands correspond to physiological signals while some do not. After the determination of the changes in the parameter, statistical evaluation is carried out. The frequency bands that we have determined are given on Table 6.1.

Table 6.1 Table of Frequency Bands Used for Parameter Calculation

BANDS	FREQUENCY (Hz)	FREQUENCY (cpm)
A	**0.02 – 0.03**	**1.2 – 1.8**
B	**0.03 – 0.07**	**1.8 – 4.2**
C	**0.12 – 0.16**	**7.2 – 9.6**
D	**0.24 – 0.44**	**14.4 – 26.4**
E	**0.44 – 0.71**	**26.4 – 42.6**
F	**0.71 – 1**	**42.6 – 60**
G	**1 – 1.5**	**60 – 90**
H	**0.83 – 1.5**	**49.8 – 90**

6.1 Dominant Frequency

6.1.1 Dominant Frequency for Individual Subject

The dominant frequencies for both pre-prandial and post-prandial recordings were compatible with gastric electrical activity, which is between 2 to 4 cpm. Detecting this competence was important for us in order to confirm the correctness of our recordings. Dominant frequencies for each subject are given below on Table 6.2;

Table 6.2 Table of Pre-prandial and Post-prandial Dominant Frequencies for Each Subject

	Dominant Frequency (DF) (Hz)	
	Pre-prandial	**Post-prandial**
1	0.044	0.051
2	0.046	0.046
3	0.051	0.054
4	0.032	0.038
5	0.033	0.026
6	0.054	0.054

Mean pre-prandial DF and mean post-prandial DF were 0.043 Hz (2.6 cpm) and 0.045 Hz (2.68 cpm), respectively. An increment of %3, 11 in DF was seen in post-prandial recordings with respect to pre-prandial ones but this was not statistically important ($p > 0.05$).

6.1.2 Dominant Frequencies for Different Frequency Bands

The pre-prandial DF values and post-prandial DF values for each band are given in Table 6.3 and Table 6.4, respectively. Post-prandially, there is an increment in DF values for bands A, B, C, D and H (%1.83, %50.2, %104.9, %27.7 and %2.58 respectively) but this was statistically non-significant ($p > 0.05$). The highest post-prandial change was seen on band C (0.12 - 0.16 Hz). In bands E, F and G, there was a decrement in post-prandial DF values with respect to pre-prandial DF values (%-10.5, % -18, and % -1.6 respectively) but these decrements in the DF values were also statistically non-significant ($p > 0.05$). The post-prandial changes in the DF for each frequency band are shown in Figure 6.1.

Table 6.3 Table of Pre-prandial Dominant Frequencies for Different Frequency Bands

		A	B	C	D	E	F	G	H
Dominant Frequency (Hz)	**1**	0.021	0.044	0.127	0.247	0.490	0.847	1.068	1.041
	2	0.027	0.046	0.135	0.288	0.640	0.881	1.450	0.904
	3	0.025	0.051	0.147	0.334	0.499	0.986	1.008	0.911
	4	0.029	0.032	0.142	0.242	0.478	0.964	1.013	0.964
	5	0.026	0.033	0.149	0.344	0.447	0.933	1.279	1.279
	6	0.020	0.054	0.135	0.394	0.693	0.742	1.306	1.306

Table 6.4 Table of Post-Prandial Dominant Frequencies for Different Frequency Bands

		A	B	C	D	E	F	G	H
Dominant Frequency (Hz)	**1**	0.025	0.051	0.126	0.353	0.446	0.742	1.279	0.911
	2	0.030	0.046	0.147	0.358	0.534	0.735	1.080	1.111
	3	0.025	0.054	0.146	0.348	0.495	0.712	1.066	1.069
	4	0.024	0.038	0.121	0.277	0.440	0.723	1.210	1.210
	5	0.026	0.045	0.134	0.241	0.452	0.452	1.020	0.914
	6	0.021	0.054	0.160	0.307	0.485	0.930	1.186	1.186

6.2 Power of Dominant Frequency (PDF)

6.2.1 Power of Dominant Frequency for Individual Subject

Power of Dominant Frequency is power at the dominant frequency. PDF values for each subject are given in Table 6.5. The mean values for PDF were 0.0308 μV and 0.0428 μV for pre-prandial and postprandial recordings, respectively ($p > 0.05$). The postprandial power has increased by a mean of %67.6 ($p > 0.05$).

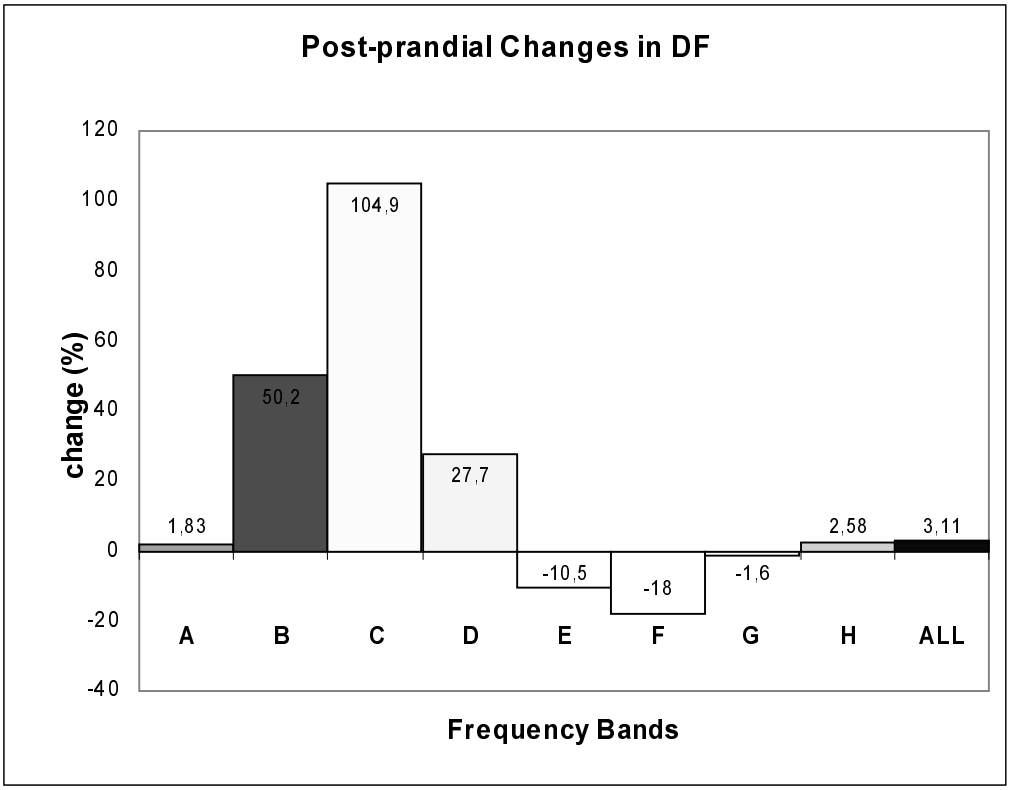

Figure 6.1 Post-prandial Changes in Dominant Frequencies (DF) for Different Frequency Bands

Table 6.5 Table of Pre-prandial and Post-prandial Power of Dominant Frequencies for Each Subject

	Power of DF (μV)	
	Pre-prandial	**Post-prandial**
1	0.0837	0.0664
2	0.0104	0.0090
3	0.0510	0.1084
4	0.0100	0.0341
5	0.0113	0.0228
6	0.0187	0.0158

6.2.2 Power of Dominant Frequency for Different Frequency Bands

PDF values for each band have increased in the post-prandial recordings and some of these increments were statistically significant. The highest increase was seen on band C (%122) and this was a statistically significant increase ($p < 0.05$). The increase in band A was also significant (%51, $p < 0.05$). PDF values for pre-prandial and post-prandial recordings and percentage of increase are given on Table 6.6, Table 6.7 and Figure 6.2, respectively.

Table 6.6 Table of Pre-prandial PDF Values for Different Frequency Bands

		A	B	C	D	E	F	G	H
Power of DF (μV)	1	0.0183	0.0837	0.0068	0.0055	0.0020	0.0011	0.0014	0.0024
	2	0.0049	0.0104	0.0010	0.0007	0.0006	0.0010	0.0005	0.0015
	3	0.0387	0.0510	0.0066	0.0049	0.0024	0.0016	0.0013	0.0024
	4	0.0095	0.0100	0.0052	0.0088	0.0041	0.0055	0.0049	0.0055
	5	0.0114	0.0113	0.0063	0.0054	0.0050	0.0050	0.0071	0.0071
	6	0.0105	0.0187	0.0056	0.0055	0.0051	0.0049	0.0068	0.0068

Table 6.7 Table of Post-prandial PDF Values for Different Frequency Bands

		A	B	C	D	E	F	G	H
Power of DF (μV)	1	0.0258	0.0864	0.0100	0.0107	0.0067	0.0029	0.0022	0.0041
	2	0.0090	0.0090	0.0036	0.0017	0.0010	0.0009	0.0010	0.0018
	3	0.0496	0.1084	0.0134	0.0081	0.0040	0.0035	0.0016	0.0031
	4	0.0130	0.0241	0.0093	0.0046	0.0038	0.0025	0.0028	0.0028
	5	0.0228	0.0197	0.0132	0.0080	0.0064	0.0064	0.0042	0.0049
	6	0.0123	0.0158	0.0074	0.0045	0.0049	0.0059	0.0076	0.0076

6.3. Power of Signal (PS) (Area of Wave)

6.3.1. Power of Signal for Individual Subjects

Power of Signal is defined as the area under the FFT curve of the signal and shows the magnitude of the defined signal. The mean pre-prandial and mean post-prandial PS values were 0.004050 μV-Hz and 0.012087 μV-Hz; respectively and the pre-prandial and post-prandial PS values are given in Table 6.8. Post-prandially, we observed a mean increase of %179.4 in PS values and this was statistically significant ($p < 0.05$).

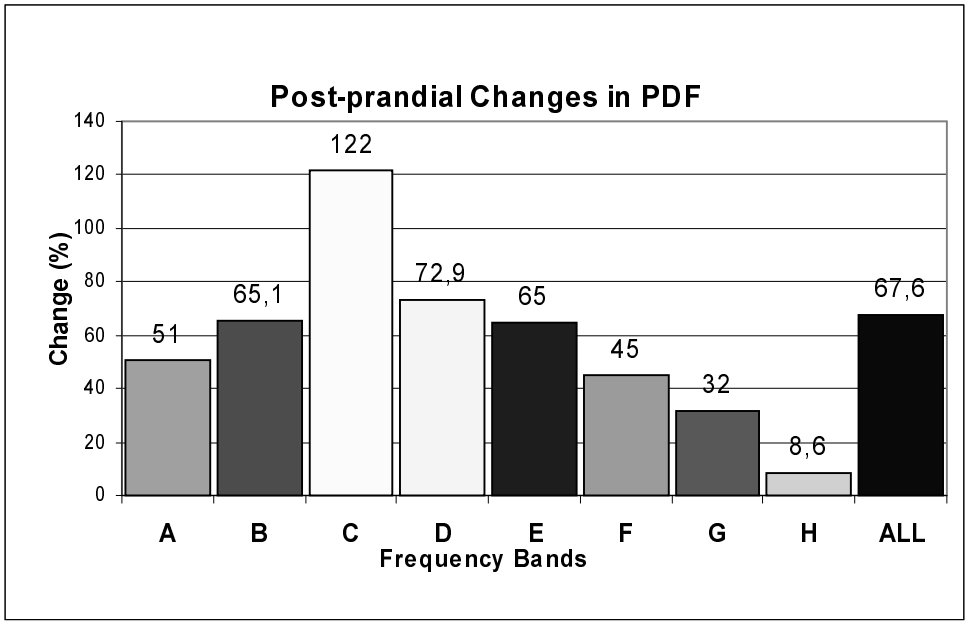

Figure 6.2 Post-prandial Changes in Power of Dominant Frequency (PDF) for Different Frequency Bands

6.3.2 Power of Signal for Different Frequency Bands

On every frequency band, there was an increase in PS values. The highest increases are seen on bands D and E (%117.7 and %109.7, respectively). Although the increase in band C was very slight, it was statistically important ($p < 0.05$). The pre-prandial PS values and post-prandial PS values are given on Table 6.9 and Table 6.10, respectively. The post-prandial changes in the PS for each frequency band are shown in Figure 6.3.

Table 6.8 Table of Pre-prandial and Post-prandial Power of Signal Values for Each Subject

	Power of Signal (μV-Hz)	
	Pre-prandial	**Post-prandial**
1	0.007864	0.033180
2	0.002300	0.002411
3	0.004608	0.015722
4	0.002290	0.004825
5	0.002286	0.011330
6	0.004949	0.005052

Table 6.9 Table of Pre-prandial PS Value for Different Frequency Bands

		A	B	C	D	E	F	G	H
Power of Signal (µV-Hz)	1	0.000048	0.000298	0.000039	0.000117	0.000058	0.000069	0.000057	0.000188
	2	0.000016	0.000046	0.000005	0.000030	0.000017	0.000038	0.000069	0.000142
	3	0.000082	0.000309	0.000035	0.000149	0.000077	0.000051	0.000074	0.000350
	4	0.000017	0.000199	0.000039	0.000626	0.000119	0.000157	0.000169	0.000667
	5	0.000029	0.000092	0.000060	0.000326	0.000207	0.000213	0.000578	0.001092
	6	0.000005	0.000064	0.000048	0.000165	0.000208	0.000260	0.000652	0.000574

Table 6.10 Table of Post-prandial PS Value for Different Frequency Bands

		A	B	C	D	E	F	G	H
Power of Signal (µV-Hz)	1	0.000104	0.000267	0.000047	0.000285	0.000211	0.000112	0.000128	0.000490
	2	0.000037	0.000068	0.000023	0.000045	0.000032	0.000027	0.000043	0.000132
	3	0.000120	0.000443	0.000076	0.000245	0.000268	0.000231	0.000072	0.000363
	4	0.000051	0.000647	0.000047	0.000236	0.000160	0.000092	0.000196	0.000263
	5	0.000017	0.000084	0.000102	0.000243	0.000281	0.000248	0.000373	0.000628
	6	0.000010	0.000124	0.000119	0.000159	0.000183	0.000238	0.000581	0.000798

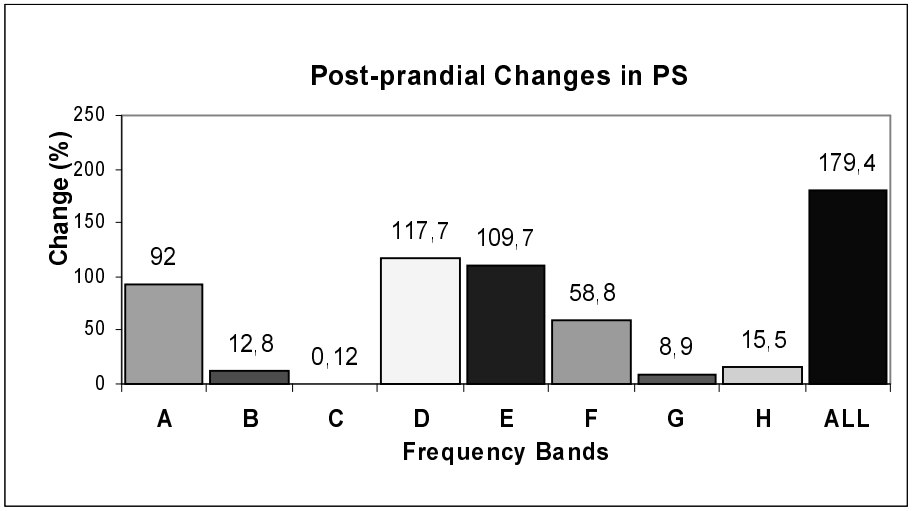

Figure 6.3 Post-prandial Changes in Power of Signal (PS) for Different Frequency Bands

In Table 6.11, the statistical evaluation and significance of the examined EGG data are given.

Table 6.11 Statistical Analysis of EGG Parameters

Band A			
Variable	***Preprandial (mean±SD;median)***	***Postprandial (mean±SD;median)***	***p***
DF	24.6 ± 3.5; **25.5**	25.2 ± 2.9; **25.0**	> 0.05
PDF	155.5 ± 121.3; **109.5**	354.1 ± 237.6; **362**	**0.03**
PS	32.8 ± 28.1; **23**	56,5 ± 45.6; **44**	> 0.05
Band B			
DF	43.3 ± 9.1; **45.0**	48.0 ± 6.2; **48.5**	> 0.05
PDF	308.5 ± 302; **150**	472 ± 389; **419**	> 0.05
PS	168 ± 117.6; **145.5**	272.2 ± 231.8; **195.5**	> 0.05
Band C			
DF	139.2 ± 8.3; **138.5**	139 ± 14.6; **140.0**	> 0.05
PDF	52.5 ± 21.6; **59.5**	94.8 ± 36.9; **96.5**	**0.03**
PS	37.6 ± 18.3; **39**	69 ± 36.6; **61.5**	**0.03**
Band D			
DF	308.1 ± 59.7; **311.0**	314 ± 47.6; **327.5**	> 0.05
PDF	51.3 ± 25.8; **54.5**	62.6 ± 32.4; **63**	> 0.05
PS	235.5 ± 214; **157**	202.2 ± 87.2; **239.5**	> 0.05
Band E			
DF	541 ± 100; **494.5**	475.3 ± 36.2; **468.5**	> 0.05
PDF	32 ± 18; **32.5**	44.6 ± 20.7; **44.5**	> 0.05
PS	114.3 ± 79.2; **98**	189.2 ± 90.2; **197**	> 0.05
Band F			
DF	892 ± 89.8; **907**	715.6 ± 152.7; **729**	> 0.05
PDF	31.8 ± 21.5; **32.5**	36.8 ± 21; **32**	> 0.05
PS	131.3 ± 92.6; **113**	158 ± 93.2; **171.5**	> 0.05
Band G			
DF	1187.3 ± 183.4; **1173**	1140.2 ± 99.8; **1133**	> 0.05
PDF	36.5 ± 29.5; **31**	32.3 ± 24, **25**	> 0.05
PS	266.5 ± 273.8; **121.5**	232.2 ± 207.4; **162**	> 0.05
Band H			
DF	1067 ± 181.2; **1002.5**	1066.8 ± 129.8; **1090**	> 0.05
PDF	42.8 ± 24.7; **39.5**	40.5 ± 20.4; **36**	> 0.05
PS	502.2 ± 355.4; **462**	445.6 ± 244; **426.5**	> 0.05
Whole Band			
DF	43.3 ± 9.1; **45**	44.8 ± 11; **48.5**	> 0.05
PDF	308.5 ± 302.7; **150**	477.5 ± 385.7; **434.5**	> 0.05
PS	4049 ± 2233; **3454**	12086 ± 11441; **8191**	**0.03**

7. DISCUSSION

The early diagnosis of GIS diseases is a crucial step for determining the appropriate treatment strategy for the patient. The signs and symptoms of the GIS diseases are usually non-specific and sometimes can not be able to localize the problem source. The conventional methods of diagnosis for GIS diseases, like gastroscopy, 24-hours pH monitoring, etc. are usually invasive methods. These invasive methods are very useful tools for diagnosis but they may be expensive and sometimes may not be well tolerated by the patients. These methods, also may give little information about the diseases of the patients with motility problems in whom the electrophysiological activity of the gastrointestinal system organs is sometimes disturbed for some reason, causing symptoms of the patient [30]. The electrogastrography is a non-invasive procedure like ECG, EEG and deals specifically with the electrical activity of the stomach. It was first defined by Walter Alvarez in 1922 and in his first practice, Alvarez has defined the gastric pacemaker localization, types of peristalsis and some problems related with data collection [31]. Since that time, it was used by many researchers for examining electrical activity of the stomach. In time, the data acquisition and processing methods have improved and by the force of this improvement, researchers tried to comprehend the nature of the EGG signal. But there were great limitations with the processing, understanding and clinical application of the signal [18, 23, 32, 33, 34]. The EGG signal is very small, the noises from nearby organs disturb the signal and the collected data are not much correlated with the peristaltic activity of the organ, thus the information gathered by EGG is not useful for clinical application.

Different parameters about EGG was defined and studied by different researchers [32]. Dominant frequency, power of dominant frequency, power of signal, instability coefficient and determination of slow waves are the parameters that were mostly used by researchers. These parameters ere examined by using different analysis methods like frequency analysis, Fast Fourier Transform, Running Spectrum Analysis and Waveform Analysis. In our study, we decided to perform a spectral analysis of dominant frequency, power of dominant frequency and power of signal on the entire wave and on the frequency bands that we have arbitrarily defined. The purpose for defining such frequency bands was to observe the post-prandial changes in the defined parameters in the low and high frequency components of EGG signal. The high activity signals, namely spike potentials

are responsible for the smooth muscle contraction of the stomach and can only occur during a portion of the slow wave [15]. The correlation of the spike activity to the clinical problems is a problem to solve. Another problem is the availability of the spike activity only on serosal or intraluminal electrodes. However, Akin and Sun have reported that, spike activity of the serosa can be detected on the surface electrodes by using an algorithm based on a continuous wavelet transform [3, 4, 34]. In our study, we focused on several frequency bands and determined whether any change has occurred on signals post-prandially in these different frequency bands.

The Dominant Frequency of EGG signal reflects the frequency of the gastric slow waves [17]. In studies, where different types of solid and liquid meals are used, it was found that the DF decreases after a liquid meal and increases after a solid meal [14,35, 36]. In another study, it was reported that EGG frequency decreases from the baseline for a short period after eating and then gradually increases to above the baseline level [37, 38]. In our study, the subjects ingested both solid and liquid meal and when we consider about whole signal, we have encountered a %3.11 of DF increase post-prandially but this was statistically non-significant. For all subject, DF were in between 2-4 cpm for both pre-prandial and post-prandial recordings. When different frequency bands are considered, DF is increased in bands A, B, C, D and H while it has decreased in the other bands. As Band B contains the frequency of the gastric slow wave, the increase in this band is compatible with the increase in the whole signal.

Power of Dominant Frequency reflects the amplitude and regularity of the gastric slow waves. Dominant power increases as the amplitude of the signal increases and it decreases when the signal is less regular or has more noise [17]. In another study, a significant difference in PDF was found in different motility period and the results showed that PDF was statistically higher during gastric contraction than motor quiescence [31]. In our study, we encountered a %67.6 increase in the whole signal, besides this there was an increase in PDF in bands A and C, which was statistically important. The increase in Band C may be related to increased intestinal activity, which corresponds to that frequency band.

Power of Signal (PS) shows the magnitude of the signal. The magnitude of the signal is reported to increase by some authors but this may be due to some other reasons. The distension of stomach due to the ingested food may cause a decrease in the thickness of the

abdominal distance at which the signal will travel to electrode and a relative increase in power may occur. Likewise, in the patients with a thick belly, the magnitude of the signal may be smaller when compared to the patients whose belly is thin. Akin and Sun reported an increase in PS at high frequency region of 0.83-1.5 Hz (Band H in our study) by using serosal electrodes in an animal study. PS for whole signal and Band C have increased in our study. The increase in Band C was statistically important and can again be explained by the increase in intestinal activity. The increase in PS for whole signal was also statistically important, but we did not see any statistically significant rise in PS for higher frequencies (Band H particularly).

This study was a continuation of the study of Akin and Sun and we tried to detect changes in some analytical parameters against a triggering effect, ingestion of a meal. We divided the FFT of the signal into some frequency bands in order to examine the higher frequency component of the signal, as well as the lower frequency component. Another aim of this study was to detect any additional frequency zone(s) in which a statistically significant change in the examined parameters post-prandially. This was a preliminary study and the experimental group was small. This small group size limited our capacity for generalization and statistical analysis of the data. In the next step, we will evaluate our experience in the EGG for this study and plan new studies with larger experimental groups. New algorithms or parameters can be planned to use in the analysis of the electrogastrographic examination of the subjects, like the algorithm that was formed by Akin and Sun [3]. The different demographic properties of the subjects, such as body-mass index, abdominal circumference can be taken into consideration in the computation of the EGG parameters. The final step will be the use of these findings and algorithms in the interpretation of the EGG data from the people with gastrointestinal diseases and trials to correlate the results with the findings from these people.

8. CONCLUSION

As being a non-invasive procedure, electrogastrography will be a better choice for the diagnosis of the GIS diseases but there is still no consensus about the correlation of the EGG data with the symptoms of the patients. The nature of the EGG signal makes the normalization and standardization of the data very difficult and the widespread use of this device is still not possible and limited to research purposes. In our study, we tried to analyze the electrogastrographic data from abdominal surface electrodes, with spectral analysis by using some frequently used parameters. We examined the changes of parameters in not only the whole signal, but also in some frequency bands we have defined, as well. Our aim was to see first; the changes in high frequency component of the signal and second; the changes in different frequencies. We have seen increases in DF, PDF and PS values in each subject but these increases were not statistically important. In band analysis, we could not observe the statistically significant increase in magnitude (PS) of the higher frequency components but a statistically important increase for PS in whole signal was detected. The other increases in PDF and PS values may be compatible with the intestinal activity. The limited group size was our defect in the standardization and statistical analysis of our findings. However, this study is a preliminary study and we plan to get new recordings and increase our sample size. We also plan to make some trials by having multi-side abdominal recordings in order to achieve a good standart electrode positioning technique for our future studies. If we can reach to some meaningful results, the next step will be the analysis of the electrogastrographic recordings from the patients with gastrointestinal system diseases.

9. REFERENCES

1. Smout A.J., E.J. Van Der Schee and J.L. Grashuis, "What is measured in electrogastrography?" *Dig. Dis. & Sci*., vol.25, pp.179-187, 1980.
2. Pezzola F., G. Riezzo, I. Giorgio and J. Thouvenot, "Electrogastrography; possibilities and limits", *Acta Gastro. Belgica*, vol.LII, pp.421-28, 1980.
3. Akin A., H. Sun, "Non-invasive gastric motility monitor: fast electrogastrogram", *Physiol. Meas*. Vol.23, pp.505-519, 2002
4. Akin A., H. Sun, "Time frequency methods for detecting spike activity of stomach" *Med. Biol. Eng. Comput.* vol.37, pp.381-90, 1999.
5. http:// www.cpmc.org (Web Site of California Pacific Medical Center)
6. Moore L K., *Clinically Oriented Anatomy*, Third Edition, Williams & Wilkins-Baltimore, 1992.
7. http:// www.irccsdebellis.it (Web Site of S.de Bellis National Medical Research Gastroenterology Institute)
8. Guyton A., *Textbook of Medical Physiology*, Eighth edition, W.B. Saunders Company-Philadelphi*a*, 1991.
9. Sanders M., N. G. Publicover, "Excitation-Contraction coupling in Gastric Muscles", *Dig. Dis. & Sci*., vol.39, pp.69-72, 1994.
10. Kim C.H., A.R. Zinsmeister and J.R. Malagelada, "Mechanism of canine gastric dysrhythmia", *Gastroent.*, vol.92, pp.993-9, 1987.
11. Chen J., R.W. McCallum and K.G. Davenport, "Erythromycin enhances the gastric slow waves in gastroparetic patients", *Gastroent.,* vol.99, pp.1207, 1990.
12. Lin Z., Z. Chen, B. Schirmer and R. McCallum, "Postprandial response of gastric slow waves: correlation of serosal recordings with the electrogastrogram", *Dig. Dis. & Sci*., vol.45, pp.645-651, 2000.
13. Familoni B O., Y J. Kingma, "Study of transcutaneous and intraluminal measurement of gastric electrical activity in humans", Med. & Biol. Eng. & Comput., vol.25, pp.397-402, 1987.
14. Takehito K., I. Shimoyama, Y. Nakajima and T. Ochiai, "Gastric and non-gastric signals in Electrogastrography", *Journ. Autono. Nerv. Syst*., vol.79, pp.60-66, 2000.
15. Chen J., R. W. McCallum and R. Richards, "Frequency components of the electrogastrogram and their correlations with gastrointestinal contractions in human", *Med. & Biol. Eng. & Comput*., vol.31, pp.61-67, 1993.
16. Koch K.L., S. Bingaman and N. Sperry, "Effect of cisapride on gastric electromechanical activity in healthy volunteers: A double-blind, placebo controlled study", *Gastroent.*, vol.100, pp.A459, 1991.
17. Chen Z., R. McCallum, *Electrogastrography: Principles and Applications*, *Raven Press-New York*, 1994.
18. Soysal I., "Electrogastrography And The Analysis Using The Adaptive Spectral Analysis Method", Master Thesis, Boğaziçi University, Istanbul, Turkey, 1995.

19. Cheung B., P. Vaitkus, "Perspective of Electrogastrography and Motion Sickness", *Brain Res. Bull*. vol.47, pp.421-431, 1998.

20. Leahy A., K. Besherdas and C. Clayman, "Abnormalities of Electrogastrogram in Functional Gastrointestinal Disorders", *Am. J. Gastr*., vol.94, pp. 1023-28, 1999.

21. Chen J., R. W. McCallum, "Electrogastrography: measurement, analysis and prospective applications", *Med. & Biol. Eng. & Comput*., vol.29, pp. 339-350, 1991.

22. Abell L T., J. Malagelada, "Electrogastrography current assessment and future perspectives", *Dig. Dis. & Sci*., vol.33, pp.982-992, 1988.

23. Chen Z., R. McCallum, "Clinical applications of Electrogastrography", *Am. J. Gastr*., vol.88, pp.1324-1336, 1993.

24. Koch K.L., R. M. Stern and W. R. Stewart, "Gastric emptying and gastric myoelectrical activity in patients with diabetic gastroparesis: Effect of long-term domperidone treatment", *Am J Gastroent.*, vol.84, pp.1069-75, 1989.

25. Hasler W., C. Owyang, "Peptide-induced gastric arrhythmias: A new cause of gastroparesis", *Regulat. Pept. Lett*, vol.2, pp. 6-11, 1990.

26. Stern R.M., K. L. Koch and W. R. Stewart, "Spectral analysis of tachygastria recorded during motion sickness", *Gastroent.*, vol.92, pp.92-7, 1987.

27. Abell T.L., M. Camilleri and V. S. Hench, "Gastric electromechanical function and gastric emptying in diabetic gastroparesis", *Eur. J. Gastroent. Hepatol.*, vol.3, pp.163-7, 1991.

28. http:// www.biopac.com (Web Site of Biopac Health Sciences Inc.)

29. Baysal A., P. Arslan, G. Pekcan and M. Yurttagül, "Besinlerin Bileşimleri", Diyetisyenler Derneği Yayını, 3.Baskı, Ankara, 1993.

30. http://www.rah.sa.gov.au (Web Site of Royal Adelaide Hospital-Australia)

31. Alvarez W., "The electrogastrogram and what it shows", *Jour. A M A*, vol.74, pp.1116-1119, 1922.

32. Chen J., R. Richards and R. McCallum, "Identification of gastric contractions from the cutaneous electrogastrogram", *Am. J. Gastr*., vol.89, pp.79-85, 1994.

33. Mintchev M., J. Kingma and K. Bowes, "Accuracy of cutaneous recordings of gastric electrical activity", *Gastroent.* vol.104, pp.1273-1280, 1993.

34. Wang Z., Z. Chen, "Blind separation of slow waves and spikes from gastrointestinal myoelectrical recordings", *Trans. Inform. Tech. Biomed.* vol.5, pp.133-37, 2001.

35. Chen J., R.W. McCallum, "The response of electrical activity in normal human stomach to water and solid meals", *Med. & Biol. Eng. & Comput*., vol.29, pp.351-57, 1991.

36. Geldof H., E. J. Van der Schee, "Myoelectrical activity of the stomach in gastric ulcer patients: An EGG study", *J. Gastrointest. Mot.* , vol.1, pp. 122-30, 1989.

37. Hamilton J W., B. Bellahsene, M. Reichelderfer, J. G. Webster and P. Bass, "Human Electrogastrograms: Comparision of surface and mucosal recordings", *Dig. Dis. & Sci*., vol.31, pp.33-39, 1986.

38. Hamilton J W., B. Bellahsene, M. Reichelderfer, J. G. Webster and P. Bass, “Human Electrogastrograms: Comparision of Techniques of Recording”, *Am. J. Gastr*., vol.83, pp.806-811, 1988.