Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.
THE DEVELOPMENT AND USE OF RADIOPAQUE MARKERS FOR THE ASSESSMENT OF GASTRIC EMPTYING IN DOGS

A THESIS PRESENTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF VETERINARY SCIENCE AT MASSEY UNIVERSITY

FRAZER JAMES ALLAN 1995
Abstract

Currently, there is no suitable technique that can be used by veterinarians in private practice to assess the rate of emptying of solids from the stomach of dogs. Radiographic studies using barium sulphate suspension are commonly employed by veterinarians to assess gastric emptying. However, these methods are qualitative and assess the gastric emptying of liquids not solids. Diseases which affect gastric emptying are more likely to affect the emptying of solids rather than liquids. The objective of this study was to develop a technique that the practising veterinarian could use to assess the rate of gastric emptying of solids in dogs.

The study was divided into two parts, the development of radiopaque markers and the development of a method utilising these radiopaque markers that could be used in veterinary practice to assess the gastric emptying of solids.

A 1.5 mm diameter (small) marker and a 5.0 mm diameter (large) marker were developed based on studies by other investigators. It was anticipated that the small marker would empty from the stomach with food and the large marker would empty with the onset of the migrating motility complex. Both markers were made from a compound containing high density polyethylene and barium sulphate.

The gastric emptying of both sizes of marker was then assessed in 20 healthy, mixed breed dogs. Studies were performed on days one, six and nine of the investigation. After a 24 hour fast, thirty small and ten large markers were placed into a standard meal comprising of canned Prescription Diet® d/d. With the dogs restrained in ventrodorsal and left lateral recumbency, radiographs were taken hourly until all, or most of, the markers had emptied from the stomach. Percent gastric emptying of the markers versus time curves (GEvT curves) were then generated from this data. The time taken to reach the point of inflection on the GEvT curve (the lag phase), and the times taken to empty 25%, 50% and 75% of the markers (T_{25}, T_{50} and T_{75} respectively) were calculated from the GEvT curves. The sex and age of the dogs and training the dogs to the radiographic procedure did not have a significant effect on the gastric emptying parameters. There was a weak but significant positive correlation between dog weight and the T_{50}. 
There were no significant differences in the $T_{25}$, $T_{50}$ and $T_{75}$ between the large and small markers. Contrary to their anticipated behaviour, the large markers left the stomach during the fed motility pattern. A larger, 7 mm diameter marker, may be required to mark the onset of the MMC in dogs.

The mean GEvT curve of the small markers on day one (with 95% confidence intervals) was considered to represent the most appropriate gastric emptying reference curve for clinical use. The lag phase of the small markers on day one was $2.45 \pm 2.04$ hours, the $T_{25}$ was $4.85 \pm 2.15$ hours, the $T_{50}$ was $6.05 \pm 2.99$ hours and the $T_{75}$ was $8.32 \pm 2.72$ hours. If delayed gastric emptying is suspected, taking two or three sets of radiographs at regular intervals from 6-16 hours after feeding and comparing the results with the reference curve is probably the most appropriate method of assessing gastric emptying in a patient. Conversely, if excessively rapid gastric emptying is suspected, taking two or three sets of radiographs at regular intervals from 0-5 hours after feeding and comparing the results with the reference curve is most appropriate.

In conclusion, radiopaque markers provide a simple quantitative method of evaluating the gastric emptying rate of dogs. However, the results of this study have not established that the gastric emptying of the small markers occurs at the same rate as the gastric emptying of food. In addition, the sensitivity and specificity of this diagnostic procedure still needs to be determined. These steps in the validation process are currently being carried out at the Department of Veterinary Clinical Sciences at Massey University.
Acknowledgements

I would like to thank my supervisors, Grant Guilford and Boyd Jones, for their guidance, patience and support. In particular, Boyd's constructive comments on the finer points of the English language and Grant's endless enthusiasm and optimism were of great help to me.

To Ian Robertson, thank you for your expert advice and for the many hours you spent poring over radiographs on my behalf. Special thanks also to Marge Chandler and Phillip Judge for sacrificing many nights of sleep to help me collect data through the "graveyard shift".

This thesis would not have been possible without the loving support of my wife, Rebecca, who helped me collect data, proof-read the text and encouraged me through this project.

Thank-you to Fiona Dickinson for assisting me with the graphics and the trickier aspects of word-processing. I extend my appreciation to the staff of the small animal hospital, in particular, Jill Hogan and Pauline Gordon for their expert attention to the dogs during the study. Thank-you to the radiology staff, Hilary Burbidge, Nicki Moffat and Su Jenkins for their professional advice and for sharing the radiology suite with me during the data collection.

I acknowledge the generous support of the Comparative Gastroenterology Society for funding this study, Stallion Plastics who supplied the radiopaque markers at cost price and Friskies Pet Care for providing the maintenance dog food ration.
Table of Contents

Chapter One Introduction

1.1 General Introduction ................................................. 1
1.2 Physical Obstructions ............................................. 1
1.3 Gastric Motility Disorders ........................................ 2
    Gastric motility disorders resulting in delayed gastric emptying . 4
    Gastric motility disorders resulting in excessively rapid gastric emptying .. 9
1.4 Diagnosis of Gastric Emptying Disorders ....................... 10
1.5 Gastric Emptying Studies- The ideal technique? .............. 12
1.6 A Veterinary Perspective on Gastric Emptying Studies- Justification for the study . 14
1.7 Radiopaque Markers ............................................... 15
1.8 Study Objectives .................................................. 16

Chapter Two Anatomy of the Canine Stomach

2.1 General Description ................................................ 18
2.2 Nerves of the Stomach ............................................. 20
2.3 Layers of the Stomach ............................................. 21
    The serosa ..................................................... 21
    The muscularis ............................................... 23
    The submucosa ............................................... 24
    The mucosa ................................................. 24
### Chapter Three Physiology of Gastric Emptying in Humans and Monogastric Animals

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1</td>
<td>General Introduction</td>
<td>25</td>
</tr>
<tr>
<td>3.2</td>
<td>Electromechanical Properties of Gastric Smooth Muscle</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>The isolated gastric smooth muscle cell</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>The gastric pacemaker and the gastric slow wave</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Electromechanical properties of the proximal stomach</td>
<td>32</td>
</tr>
<tr>
<td>3.3</td>
<td>Gastric Accommodation and Receptive Relaxation</td>
<td>33</td>
</tr>
<tr>
<td>3.4</td>
<td>Gastric Emptying of Liquids</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Role of the proximal stomach</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Role of the distal stomach and small intestine</td>
<td>37</td>
</tr>
<tr>
<td>3.5</td>
<td>Intestinal Feedback Inhibition</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>&quot;The intestinal brake&quot;</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Neurohormonal control of intestinal feedback inhibition</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Intestinal feedback inhibition- Summary</td>
<td>48</td>
</tr>
<tr>
<td>3.6</td>
<td>Gastric Emptying of Solids</td>
<td>49</td>
</tr>
<tr>
<td>3.7</td>
<td>Neural Control of Distal Stomach Motility</td>
<td>54</td>
</tr>
<tr>
<td>3.8</td>
<td>The Pylorus and Gastric Emptying</td>
<td>56</td>
</tr>
<tr>
<td>3.9</td>
<td>Control of Pyloric Contractility</td>
<td>58</td>
</tr>
<tr>
<td>3.10</td>
<td>The Hydrodynamic Model of Gastric Emptying</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Preliminary observations</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Hydrodynamic theory</td>
<td>63</td>
</tr>
<tr>
<td>3.11</td>
<td>The Migrating Motility Complex</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Introduction</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Description of the migrating motility complex</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td>Function of the migrating motility complex</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>Control of the migrating motility complex</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>The migrating motility complex- Summary</td>
<td>73</td>
</tr>
<tr>
<td>3.12</td>
<td>Converting from the MMC to the Fed Pattern</td>
<td>73</td>
</tr>
<tr>
<td>3.13</td>
<td>Control of the Fed Pattern</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>Hormonal control</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>Neural control</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>Control of the Fed Pattern- Summary</td>
<td>78</td>
</tr>
</tbody>
</table>
Chapter Four

Techniques for Assessing the Rate of Gastric Emptying

4.1 General Introduction ................................................................. 79
4.2 Positive Contrast Radiography .................................................. 79
4.3 Plain Radiography ................................................................. 83
4.4 Scintigraphy ........................................................................... 85
4.5 Real-time Ultrasound .............................................................. 93
4.6 Applied Potential Tomography .................................................. 96
4.7 Biomagnetic Techniques .......................................................... 99
4.8 Magnetic Resonance Imaging .................................................... 100
4.9 Radiotelemetry ..................................................................... 102
4.10 Indirect Methods ................................................................. 103
4.11 Carbon-labelled Octanoic Acid Breath Test ............................. 105
4.12 Intubation Methods .............................................................. 107

Chapter Five

Materials and Methods

Phase One - Radiopaque Marker Development and Selection of the Test Meal

5.1 Objectives ............................................................................ 111
5.2 Background ........................................................................ 112
5.3 Selection of the Material for the manufacture of Markers ....... 115
5.4 Selection of the Shape of the Markers ..................................... 118
5.5 Selection of the Size of the Markers ........................................ 118
5.6 Selection of the Test Diet ......................................................... 119
5.7 Quantity of the Test Meal ....................................................... 120
5.8 Number of Markers Per Test Meal .......................................... 121
Chapter Six

Materials and Methods

Phase Two- Gastric Emptying Studies
Using Radiopaque Markers in Healthy Dogs

6.1 Radiopaque Markers .................................................. 122
6.2 The Test Meal ......................................................... 123
6.3 Prescription Diet® canine/feline d/d Formulation Change ........ 124
6.4 Study Animals .......................................................... 126
6.5 Experimental Method .................................................. 128
6.6 Radiographic Equipment ............................................ 131
6.7 Radiographic Interpretation .......................................... 132
6.8 Observer Variation ................................................... 133
6.9 Statistical Methods ................................................... 134

Chapter Seven

Results

7.1 Experimental Protocol ................................................ 135
7.2 Observer Variation and Radiograph Interpretation ............ 136
7.3 Effects of Variables on Gastric Emptying Parameters .......... 138
7.4 Individual GEVT Curves and Lag Phases ......................... 141
   Small markers ................................................................ 141
   Large markers ................................................................ 142
7.5 Clinical Data ............................................................... 144

Chapter Eight

Discussion

8.1 Experimental Protocol ................................................ 145
8.2 Observer Variation and Radiograph Interpretation ............ 146
8.3 Effects of Variables on Gastric Emptying Parameters .......... 152
8.4 Gastric Emptying of the Small Markers ......................... 154
8.5 Gastric Emptying of the Large Markers ......................... 156
8.6 Clinical Implications ................................................... 158
8.7 Validation of the Technique ........................................... 160
8.8 Summary ................................................................. 161

Bibliography ................................................................. 164
### List of Tables

**Table 1.1** Conditions which can cause abnormal gastric emptying in humans and animals ........................................ 3  
**Table 1.2** Features of the ideal gastric emptying study .......................................................... 12  
**Table 4.1** Characteristics of the ideal radioisotope .......................................................... 86  
**Table 4.2** Summary of the advantages and disadvantages of the techniques used to determine the rate of gastric emptying .................................................. 110  
**Table 5.1** Summary of the physical properties of an indigestible solid and their relative importance to the rate of gastric emptying of indigestible solids .................................................. 114  
**Table 6.1** Summary of the physical properties of the radiopaque markers used in this study .......................................................... 123  
**Table 6.2** A comparison of the nutritional analyses of the old canned Prescription Diet® canine/feline d/d and the new canned Prescription Diet® canine d/d diets .......................................................... 125  
**Table 6.3** Summary of the sexes, ages and weights of the dogs used in the study and the type of test meal fed .......................................................... 127  
**Table 6.4** Typical Proximate Analysis of Friskies Go Dog® .......................................................... 128  
**Table 7.1** Summary of the mean $T_{25}$, $T_{50}$ and $T_{75}$ for the small and large markers on days 1, 6 and 9 .......................................................... 140  
**Table 7.2** Lag phases for the small and large markers on days 1, 6 and 9 .......................................................... 142  
**Table 8.1** An example of how a large number of markers of indeterminate location can cause substantial errors in gastric emptying calculations .......................................................... 150
List of Figures

Figure 2.1. Diagram showing the important anatomical landmarks of the stomach .......................................................... 19
Figure 2.2. Diagram showing the layers of the stomach .......................................................... 21
Figure 2.3. Musculature of the stomach .......................................................... 22
Figure 3.1. The electrical activity recorded from individual gastric smooth muscle cells from nine regions of the canine stomach .......................................................... 27
Figure 5.1. Diagram representing how prospective marker material was assessed for radiopacity .......................................................... 116
Figure 6.1. Photograph showing the two sizes of radiopaque marker used in the study .......................................................... 122
Figure 6.2. Photographs of the ventrodorsal radiograph and the left lateral radiograph of Dog E on day 1 at 5 hours .......................................................... 130
Figure 7.1 Histograms showing the observer variation between two radiologists for the small and large markers .......................................................... 137
Figure 7.2 Mean percent gastric emptying versus time curves for the male and female dogs .......................................................... 138
Figure 7.3 Mean percent gastric emptying versus time curves for the old and new diets .......................................................... 138
Figure 7.4. Scattergram and line of best fit showing the effect of age on $T_{50}$ for the small and large markers .......................................................... 139
Figure 7.5 Scattergram and line of best fit showing the effect of weight on $T_{50}$ for the small and large markers .......................................................... 139
Figure 7.6 Mean percent gastric emptying versus time curves for days 1, 6 and 9 .......................................................... 140
Figure 7.7 Percent gastric emptying versus time curves for the small markers in dog Q on days 1, 6 and 9 .......................................................... 141
Figure 7.8 Percent gastric emptying versus time curves for the large markers in dog N on day 9 and dog F on day 1 .......................................................... 143
Figure 7.9 Mean percent gastric emptying versus time curves for the small markers and large markers on day one .......................................................... 144
Figure 8.1 The four overlay regions where interpretive errors can be made .......................................................... 148