

Intraluminal, self-expanding metallic stents in canine  
trachea

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by

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A Thesis Submitted to the  
Graduate Faculty in Partial Fulfillment of the  
Requirements for the Degree of  
MASTER OF SCIENCE

Major: Biomedical Engineering

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Iowa State University  
Ames, Iowa  
1989

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## TABLE OF CONTENTS

1	INTRODUCTION . . . . .	1
2	OBJECTIVES . . . . .	2
3	TRACHEA . . . . .	3
3.1	Anatomy of the Trachea . . . . .	3
3.2	Histology . . . . .	3
3.3	Physiological Function . . . . .	5
3.4	Bacterial Flora . . . . .	7
4	CAUSES OF TRACHEAL LUMEN REDUCTION IN HUMANS . . . . .	9
4.1	Methods of Correction . . . . .	9
5	TRACHEAL COLLAPSE IN DOGS . . . . .	11
5.1	Etiology . . . . .	11
5.2	Pathology . . . . .	12
5.2.1	Pathophysiology . . . . .	12
5.2.2	Histochemical study . . . . .	13
5.3	Clinical Features . . . . .	13

<b>6</b>	<b>MANAGEMENT</b>	<b>14</b>
6.1	Resection and Anastomosis	14
6.2	Chondrotomy	15
6.3	Dorsal Tracheal Membrane Plication	15
6.4	Intraluminal Prosthetic Dilators (IPD)	16
6.5	Montgomery T-Tube	17
6.6	Extraluminal Supports	17
6.6.1	Tracheal Prosthetic Ring	18
6.6.2	Polypropylene Spiral Prosthesis	20
6.7	Self-expanding Metallic Stents	20
<b>7</b>	<b>MATERIALS AND METHOD OF STUDY</b>	<b>24</b>
7.1	Stent	24
7.2	Coating	27
7.3	Stent Placement in the Trachea	27
7.4	Experimental Study	28
7.4.1	Phase 1	28
7.4.2	Phase 2	30
<b>8</b>	<b>RESULTS</b>	<b>33</b>
8.1	Phase 1	33
8.1.1	Clinical examination	33
8.1.2	Radiographic examination	33
8.1.3	Pathological findings	35

8.2	Phase 2 . . . . .	43
8.2.1	Clinical examination . . . . .	43
8.2.2	Radiographic examination . . . . .	49
8.2.3	Pathological findings . . . . .	66
8.2.4	Bacterial culture . . . . .	77
9	<b>DISCUSSION AND CONCLUSION . . . . .</b>	<b>80</b>
10	<b>BIBILOGRAPHY . . . . .</b>	<b>85</b>
11	<b>APPENDIX A . . . . .</b>	<b>89</b>
12	<b>APPENDIX B . . . . .</b>	<b>95</b>
13	<b>ACKNOWLEDGEMENT . . . . .</b>	<b>106</b>

## LIST OF TABLES

Table 3.1:	Results of Tracheal Flora and Tracheal-Pharyngeal (T-P) comparison in healthy dogs . . . . .	7
Table 11.1:	Phase 1: Tracheal lumen (TL) and stent measurements for groups 1 and 2 . . . . .	90
Table 11.2:	Phase 1: Tracheal lumen (TL) and stent measurements for groups 3 and 4 . . . . .	91
Table 11.3:	Phase 1: The initial and final tracheal lumen (TL) and stent measurements in percentages of initial tracheal diameter cranial to the stent . . . . .	92
Table 11.4:	Phase 1: Microscopic reaction in the trachea at the stent level for various time periods . . . . .	93
Table 12.1:	Phase 2: Internal tracheal <i>dv</i> diameter at the stent level for plain stent group . . . . .	96
Table 12.2:	Phase 2: Internal tracheal <i>dv</i> diameter at the stent level for the hooked stent group . . . . .	97
Table 12.3:	Phase 2: Internal tracheal <i>dv</i> diameter two cm from the stent	98

Table 12.4:	Phase 2: <i>Dv</i> diameter of tracheal lumen (TL) and the stent after eight weeks for the plain stent group . . . . .	99
Table 12.5:	Phase 2: <i>Dv</i> diameter of tracheal lumen (TL) and the stent after eight weeks for the hooked stent group . . . . .	100
Table 12.6:	Phase 2: Stent diameter within the trachea during the eight week period . . . . .	101
Table 12.7:	Phase 2: Displacement measurements of the stents . . . . .	102
Table 12.8:	Phase 2: Microscopic reaction in the trachea at the stent level in the plain stent group at eight weeks . . . . .	103
Table 12.9:	Phase 2: Microscopic reaction in the trachea at the stent level in the hooked stent group at eight weeks . . . . .	104
Table 12.10:	Phase 2: Microorganisms cultured from the trachea at the stent level, at necropsy . . . . .	105

## LIST OF FIGURES

Figure 3.1:	Trachea in normal configuration . . . . .	4
Figure 3.2:	Normal appearing tracheal section. The tracheal wall consists of ciliated, pseudostratified columnar epithelium (1); subepithelial lamina propria composed of collagen bundles, blood vessels, and submucosal glands (2); cartilaginous rings (3); and adventitia . . . . .	6
Figure 6.1:	Collapsed trachea with plicated dorsal membrane . . . . .	16
Figure 6.2:	TPR made from a polypropylene syringe case . . . . .	18
Figure 6.3:	Porous polypropylene implants . . . . .	19
Figure 6.4:	Polypropylene spiral prosthesis made from a syringe case . .	21
Figure 6.5:	Gianturco endovascular stent . . . . .	23
Figure 7.1:	Plain stent . . . . .	25
Figure 7.2:	Hooked stents. 1. Hooked stent used in Phase 1, has both the hooks on one end, but on the opposite sides; 2. Hooked stent used in Phase 2, has one hook on each end . . . . .	26

Figure 7.3:	Radiograph of the thorax showing the levels at which the measurements were taken. 1. Dv diameter above the stent level; 2. Stent diameter within the trachea; 3a. Internal dv diameter at the cranial end of the stent; 3b. Internal dv diameter at the center of the stent; 3c. Internal dv diameter at the caudal end of the stent . . . . .	32
Figure 8.1:	Phase 1, dog 9: Endoscopic view of the stent on the eighteenth day . . . . .	34
Figure 8.2:	Phase 1, dog 10: Endoscopic view of the completely covered stent on the twenty-fifth day showing multiple nodules on the mucosal surface . . . . .	34
Figure 8.3:	Phase 1, Dog 9: Radiograph of the thorax showing the plain stent on the first day . . . . .	36
Figure 8.4:	Phase 1, Dog 9: Radiograph of the thorax showing the plain stent on the eighth day . . . . .	37
Figure 8.5:	Phase 1, Dog 9: Radiograph of the thorax showing the plain stent on the eighteenth day . . . . .	38
Figure 8.6:	Phase 1, Dog 6: Radiograph of the thorax showing the hooked stent on the first day . . . . .	39
Figure 8.7:	Phase 1, Dog 6: Radiograph of the thorax showing the hooked stent on the eighth day . . . . .	40
Figure 8.8:	Phase 1, Dog 6: Radiograph of the thorax showing the hooked stent on the eighteenth day . . . . .	41

Figure 8.9:	Phase 1, tracheal specimens: Ventral view. From left to right: Dog 2 from group 1 (three days), dog 5 from group 2 (eight days), dog 6 from group 3 (eighteen days), and dog 10 from group 4 (twenty-five days) . . . . .	44
Figure 8.10:	Phase 1, tracheal specimens: Lateral view . . . . .	45
Figure 8.11:	Phase 1, tracheogram: Ventral view. From left to right: Dog 2 from group 1 (three days), dog 5 from group 2 (eight days), dog 6 from group 3 (eighteen days), and dog 10 from group 4 (twenty-five days) . . . . .	46
Figure 8.12:	Phase 1, tracheogram: Lateral view . . . . .	47
Figure 8.13:	Phase 2, Dog 1: Endoscopic view of the stent after four weeks	48
Figure 8.14:	Phase 2, Dog 1: Endoscopic view of the stent after eight weeks	49
Figure 8.15:	Phase 2, Dog 7: Endoscopic view of the stent after four weeks	50
Figure 8.16:	Phase 2, Dog 2: Endoscopic view of the stent after four weeks	51
Figure 8.17:	Phase 2, Dog 2: Endoscopic view of the stent after eight weeks	51
Figure 8.18:	Phase 2, Dog 2: Radiograph of the thorax showing the plain stent on the first day . . . . .	52
Figure 8.19:	Phase 2, Dog 2: Radiograph of the thorax showing the plain stent after two weeks . . . . .	53
Figure 8.20:	Phase 2, Dog 2: Radiograph of the thorax showing the plain stent after six weeks . . . . .	54
Figure 8.21:	Phase 2, Dog 2: Radiograph of the thorax showing the plain stent after eight weeks . . . . .	55

Figure 8.22: Phase 2, Dog 1: Radiograph of the thorax showing the hooked stent on the first day . . . . .	56
Figure 8.23: Phase 2, Dog 1: Radiograph of the thorax showing the hooked stent after two weeks . . . . .	57
Figure 8.24: Phase 2, Dog 1: Radiograph of the thorax showing the hooked stent after six weeks . . . . .	58
Figure 8.25: Phase 2, Dog 1: Radiograph of the thorax showing the hooked stent after eight weeks . . . . .	59
Figure 8.26: Phase 2: Mean <i>dv</i> diameter of the tracheal lumen within the stent . . . . .	61
Figure 8.27: Phase 2: Mean lumen and stent measurements after 8 weeks	62
Figure 8.28: Phase 2: Mean <i>dv</i> diameter of the tracheal lumen cranial to the stent . . . . .	64
Figure 8.29: Phase 2: Mean diameter of the stents within the trachea . .	65
Figure 8.30: View of the thorax taken at the time of necropsy. Arrow shows the site of the stent; T - Trachea, L - Lungs . . . . .	67
Figure 8.31: Phase 2, tracheal specimens of plain stent group: Ventral view. From left to right: Dog 2, dog 5, dog 6, dog 8, and dog 10 . . . . .	68
Figure 8.32: Phase 2, tracheal specimens of the plain stent group: Lateral view . . . . .	69

Figure 8.33: Phase 2, tracheal specimens of the hooked stent group: Ventral view. From left to right: Dog 1, dog 3, dog 4, dog 7, and dog 9 . . . . .	70
Figure 8.34: Phase 2, tracheal specimens of the hooked stent group: Lateral view . . . . .	71
Figure 8.35: Phase 2, tracheogram of the plain stent group: Ventral view. From left to right: Dog 2, dog 5, dog 6, dog 8, and dog 10 .	72
Figure 8.36: Phase 2, tracheogram of the plain stent group: Lateral view	73
Figure 8.37: Phase 2, tracheogram of the hooked stent group: Ventral view. From left to right: Dog 1, dog 3, dog 4, dog 7, and dog 9	74
Figure 8.38: Phase 2, tracheogram of the hooked stent group: Lateral view	75
Figure 8.39: Mild tracheal tissue reaction to the stent wires in dogs 4 and 10	78
Figure 8.40: Severe tracheal tissue reactions to the stent wires in dogs 7 and 8 . . . . .	79

## 1 INTRODUCTION

In patients with a reduced tracheal lumen, correction of the obstruction may be life saving. The necessity to reestablish a respiratory pathway has stimulated the search for an adequate prosthesis or a surgical procedure. In the past decade many new surgical techniques have been described and several prostheses have been developed for the tracheobronchial tree. The endovascular stent seems to be the latest promising development.

Dr. Wallace and his group found the self-expanding stainless steel stent designed by Dr. Gianturco for intravascular use to be applicable in human patients with tracheobronchial stenosis. They published their research on stents placed in the trachea of dogs in 1986. Their biggest problem was stent migration, and they suggested further research with a tracheal stent design that would provide better fixation. This research initiated my study which used a modified Gianturco intraluminal stent in the canine trachea.

## 2 OBJECTIVES

The purposes of this experimental study are:

1. To use the Gianturco endovascular stent as an intraluminal tracheal prosthesis and study the clinical reaction
2. To modify the original Gianturco stent for better fixation and compare it to the original stent design.

This study was initiated with an interest to develop a prosthesis for tracheal collapse in toy breed dogs. This experimental tracheal prosthesis could be used, however, in any form of tracheal lumen reduction since the basic idea is to maintain the airway.

### 3 TRACHEA

#### 3.1 Anatomy of the Trachea

The canine trachea is a flexible tubular organ extending from the cricoid cartilage to the bifurcation into two main bronchi. There are approximately 35 - 45 C-shaped, semicircular cartilages, interconnected by annular ligaments. The fibroelastic bands of tissue are approximately 1 mm wide, while the cartilages are 4 mm wide [Evans and Christensen, 1979]. The transverse trachealis muscle, called the dorsal membrane and present at the dorsal aspect of the trachea, bridges the cartilage segments and forms a lumen. The tracheal width is regulated by this transverse band of muscle. Figure 3.1 shows the anatomy of the trachea.

#### 3.2 Histology

Histologically, the wall of the trachea is organized in four layers: Mucosa, submucosa, muscle and cartilage, and adventitia as shown in Figure 3.2 [Dellmann, 1987]. The mucosal lining of the trachea consists of a pseudostratified columnar epithelium with cilia and goblet cells. Beneath this layer is the lamina propria, composed of loose connective tissue with many subepithelial longitudinal fibers. The lamina propria also contains small blood and lymph vessels and nerve endings.

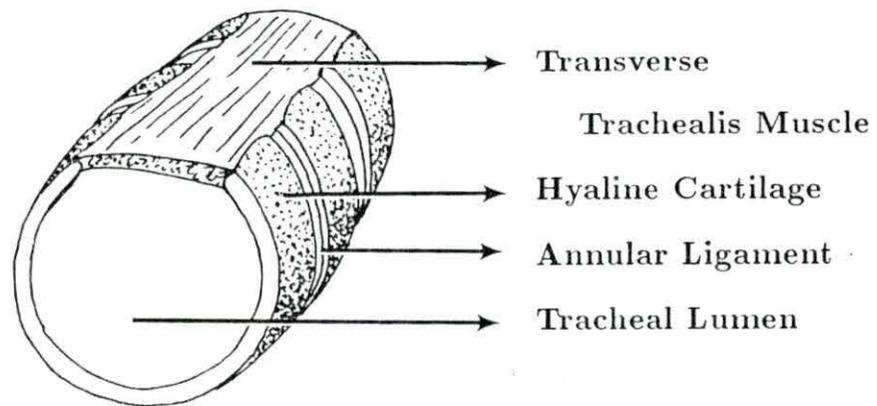


Figure 3.1: Trachea in normal configuration

Tubuloacinar mucous glands open into the tracheal lumen and are extensions of the surface epithelium into the subepithelial connective tissue. Hyaline cartilage rings are the supporting tissue of the trachea. The rings are connected dorsally by the transverse trachealis muscle. Both the muscle and the cartilage are surrounded by the adventitia in which numerous fat cells, blood vessels and nerves are located [Dellman, 1987].

### 3.3 Physiological Function

The major function of the trachea is a conduction tube for the transport of respiratory gases. The particulate matters are also removed from the respiratory tree. The mucociliary function of the trachea and the cough reflex are very important in the removal of particulates from the tracheobronchial tree. The mucociliary function is an important consideration when resecting a portion of the trachea when utilizing a prosthetic material for internal support. The mucociliary transport depends not only on the beating characteristics of the cilia but also on the composition and thickness of the periciliary mucous layer. Under optimal conditions in the respiratory tract, mucus is propelled at a velocity of 10 mm / min by cilia beating at about 20 Hz. About 50 % of the particulate introduced into the respiratory tract of healthy individuals is cleared in 30 minutes by ciliary action [Satir and Dirksen, 1987]. However, there are large individual variations and environmental and physiological factors which influence mucociliary transport.

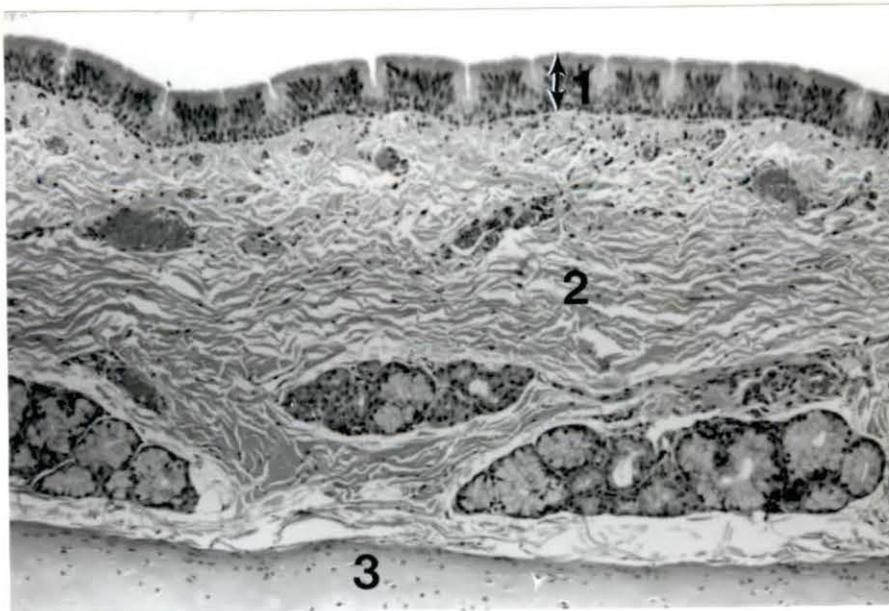


Figure 3.2: Normal appearing tracheal section. The tracheal wall consists of ciliated, pseudostratified columnar epithelium (1); subepithelial lamina propria composed of collagen bundles, blood vessels, and submucosal glands (2); cartilaginous rings (3); and adventitia

Table 3.1: Results of Tracheal Flora and Tracheal-Pharyngeal (T-P) comparison in healthy dogs

Source	Number of Animals	Positive Tracheal Cultures	Sterile Tracheal Culture (%)	Identity between T-P Cultures (%)
McKiernan et al., 1982	33	12	63.6	80
Lindsey and Pierce, 1978	19	9	52.6	78
Creighton and Wilkins, 1974	5	0	100	ND <sup>a</sup>
Pecora, 1976	62	44	29.0	ND

<sup>a</sup>Not Done.

### 3.4 Bacterial Flora

It has been hypothesized that the lower part of the canine trachea and the lungs are sterile, in spite of evidence in the literature to support the presence of bacteria [Creighton and Wilkins, 1974; Lindsey and Pierce, 1978; McKiernan et al., 1982]. These studies were specifically designed to identify the bacterial flora from the lower part of trachea, using techniques (i.e., guarded culture swabs, transtracheal aspiration, open lung biopsy and lung aspiration) to avoid the potential for contamination from the upper airway. They reported that the resident tracheal flora are similar to the pharyngeal flora in many cases. This is probably due to introduction of normal pharyngeal flora into the lower respiratory tract by aspiration during sleep [Lindsey and Pierce, 1978].

Table 3.1 [McKiernan et al., 1982] summarizes the results of four different bacteriologic studies done in healthy dogs. The common bacterial isolates from the trachea were *Streptococcus* spp., *Staphylococcus*, *Klebsiella pneumoniae*, and

*Pasturella multocida*. Most of these bacterial isolates from the trachea were in pure culture [McKiernan et al., 1982].

## 4 CAUSES OF TRACHEAL LUMEN REDUCTION IN HUMANS

In humans, tracheal stenosis has resulted from vehicular accidents, prolonged tracheal intubation, extensive burns and tumor resection. Extrinsic compression secondary to mediastinal and neck neoplasm, vascular rings and anomalous vessels also may be responsible for tracheal stenosis [Wallace et al., 1986]. Tracheomalacia, either primary or secondary, may cause physiologic stenosis, and maneuvers such as crying, straining and coughing increase the likelihood of tracheal collapse [Vinograd et al., 1987]. Collapse of the airway following tracheobronchial reconstructive surgery is also a common cause of tracheal lumen reduction [Wallace et al., 1986].

### 4.1 Methods of Correction

Tracheal resection and end-to-end anastomosis is the treatment of choice for stenotic lesions of the trachea [Grillo, 1979]. In addition, intrinsic mural or external supportive stents composed of auricular cartilage, hyaline rib cartilage, urinary bladder graft with associated osteogenesis, tibial periosteal graft [Vinograd et al., 1987], and tubes made of Teflon<sup>R</sup> [Amemiya et al., 1985], polyethylene or silicone rubber [Gleeson and Westaby, 1984; Westaby et al., 1982] have been used to maintain the patency of the reconstructed trachea. None of the above mentioned corrective methods has been useful in the long-term management of tracheal steno-

sis. Laser surgery done for tracheal stenosis was often complicated by restenosis [Amemiya et al., 1985].

## 5 TRACHEAL COLLAPSE IN DOGS

Collapsed tracheal rings in dogs have received increased attention because of the increased frequency of the diagnosis in veterinary practice. There are two types of tracheal collapse (TC): Dorsoventral and lateral [Ettinger and Ticer, 1983]. The lateral collapse rarely occurs spontaneously, although it is commonly seen following central chondrotomy, a procedure used for the treatment of dorsoventral TC. Dorsoventral flattening of the trachea is the most commonly described lesion and is often associated with a pendulous dorsal membrane. Tracheal collapse is frequently reported in the toy breeds of dogs such as Chihuahuas, Pomeranians, Toy Poodles and Yorkshires. Rarely, the condition has been diagnosed in bassets and greyhounds [Done, 1978].

Tracheal collapse may involve the thoracic or the cervical region and is frequently seen at the thoracic inlet. Cases of TC involving the whole length of the trachea have also been reported. Extension of TC into the bronchi has been described [Ettinger and Ticer, 1983].

### 5.1 Etiology

The cause of a collapsed trachea is not usually known and may be acquired or congenital [Done and Drew, 1976]. The acquired disease occurs in middle to late life

while the congenital lesion is described in young dogs. In dogs with acquired TC the potential tracheal ring size is not lost, rather the rings lose their ability to remain firm and they subsequently collapse [Bojrab, 1981; Done, 1978; Ettinger and Ticer, 1983]. In congenital TC there is a malformation of the rings, and in the presence of a concurrent lung disease as a triggering factor, clinical signs develop because of compression at the thoracic inlet [Walker and Hobson, 1983]. The congenital form may have an associated neurologic deficiency of the trachealis muscle. Some investigators [Hobson, 1976] believe that a neurologic deficiency of the trachealis muscle could be the primary cause of the TC .

## 5.2 Pathology

Normally, air moves through the open, unobstructed trachea with minimal resistance. When the tracheal cartilage loses the ability to remain firm, with or without the presence of weakened trachealis muscle, the trachea collapses dorsoventrally assuming a lunate configuration. This severely compromises the lumen with a significant increase in the ratio of the width to the height of the cartilage from 1:1 to 4:1. There is also a 40 - 80 % reduction in the length of the affected tracheal cartilage. The dorsal tracheal membrane was found to be up to four times longer than in the normal trachea and prolapsed into the lumen [Done and Drew, 1976].

### 5.2.1 Pathophysiology

Flattening of the trachea changes the dynamics of the air flow through the upper conductive airway. In the case of cervical collapse, the negative intrapleural pressure expands the intrathoracic airway lumen during inspiration while the

cervical trachea stays collapsed, resulting in an inspiratory dyspnea. But in thoracic collapse, on expiration the intrathoracic trachea is narrowed by the positive intrapleural pressure resulting in a forced expiration and a honking cough. When both thoracic and cervical portions are involved, expiratory dyspnea becomes clinically predominant.

### 5.2.2 Histochemical study

Histologically the collapsed tracheal cartilage is less homogeneous, with reduced numbers of chondrocytes. The cartilage varies from normal hyaline cartilage to fibrocartilage. The hyaline cartilage is occasionally replaced by collagen fibers. Histochemically, collapsed tracheal cartilage has less chondroitin sulfate and calcium, attributable to the reduced number of chondrocytes [Dallman et al., 1988].

## 5.3 Clinical Features

Dogs with collapsed trachea are asymptomatic initially and able to move air through the narrow tracheal lumen under normal conditions. When there is an associated lung disease or a need for an increased minute volume as in exercising, TC becomes clinically significant and is described as 'Respiratory distress syndrome' [Walker and Hobson, 1983]. The affected dog suffers from a harsh, dry cough (goose honk sound) and dyspnea which can be easily initiated by any pressure on the neck, such as from a leash or mere palpation. The dog may show any of the following signs: Low exercise tolerance, labored breathing, wheezing, stridor or bronchopneumonia [Walker and Hobson, 1983; Done and Drew, 1976].

## 6 MANAGEMENT

Medical management with bronchodilators, antitussives, corticosteroids and the symptomatic control of respiratory disease is usually the first line of treatment. When conservative therapy fails, surgical correction with or without the use of a prosthetic device is considered [Walker and Hobson, 1983]. The primary goal of surgery is to increase the tracheal lumen area and keep the airway patent without disrupting the mucociliary flow. The recommended surgical procedures include resection and anastomosis, tracheal ring chondrotomy, plication of the trachealis muscle and application of extraluminal or intraluminal prosthesis. In general, treatment of TC with surgery alone has not been uniformly successful.

### 6.1 Resection and Anastomosis

Resection of tracheal lesions received attention in the late 1970s in both the human and veterinary medical literature. Although the primary indications for tracheal resections are stenosis and neoplasm, removal and end-to-end anastomosis is a possibility whenever a short segment of the trachea is collapsed. Unfortunately, most dogs with TC have a longer section of affected trachea than can be removed safely. Moreover, tracheal anastomosis is difficult to perform, especially at the thoracic inlet and is associated with major postoperative complications [Fingland

et al., 1987].

## 6.2 Chondrotomy

Chondrotomy for management of TC, described by Knowles and Snyder in 1967 involves bisection of the cartilaginous tracheal rings on the ventral midline, leaving the mucosa intact. This allows the trachealis muscle to draw together the incomplete dorsal portion and increase the lumen diameter by converting the elliptical shape of the lumen into a triangular shape. As mentioned in the previous chapter, lateral TC is a common complication following transection of every tracheal ring. In an attempt to prevent this, a modified procedure which involved transection of every other ring was suggested by Leonard in 1971 [Done, 1978]. Transection of alternate rings allows the dorsal tracheal membrane to shorten and pull the ends of the tracheal rings toward the midline while the intact rings prevent the lateral collapse of the trachea. This procedure is effective only if the tracheal cartilages are rigid. Since the majority of the dogs with TC have extremely soft and flaccid tracheal cartilage, chondrotomy alone is usually of little value.

## 6.3 Dorsal Tracheal Membrane Plication

In 1973, Bojrab proposed plication of the dorsal membrane to shorten the gap between the tracheal ring ends [Hobson, 1976; Done, 1978]. Plication with horizontal mattress sutures was used to pull the tips of the cartilage rings closer together and form a more circular lumen as shown in Figure 6.1. This technique may be used with reasonable success in dogs that have rigid tracheal cartilage rings of near normal length and a lax dorsal membrane. Plication fails to reshape the malformed

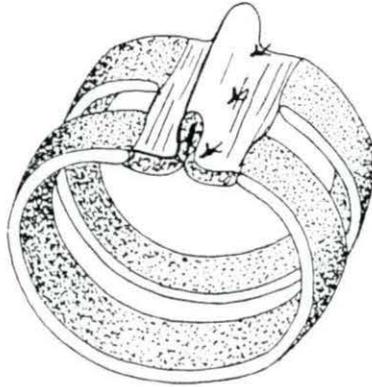


Figure 6.1: Collapsed trachea with plicated dorsal membrane

rings, and leads to a significant decrease in the tracheal lumen diameter. In dogs with complete dorsoventral flattening, plication of the dorsal tracheal membrane is contraindicated.

#### 6.4 Intraluminal Prosthetic Dilators (IPD)

Teflon-coated springs, Teflon cuffs and silastic tubes with or without fenestrations were used as IPDs by Leonard and Wright [Leonard and Wright, 1978]. Although the IPDs yielded poor results, they did provide a life - prolonging procedure for refractory cases of TC. They were uniformly unsuccessful because of their inherent disadvantages which are lack of flexibility, potential ulceration or erosion

of the tracheal wall, granuloma formation and interference with mucociliary flow. Moreover, application of an IPD requires a tracheostomy which increases the likelihood of post operative complications. These IPDs should be used only as an emergency support for maintaining the airway.

### 6.5 Montgomery T-Tube

The silicone rubber T-tube was introduced in 1968 by Montgomery [Gleeson and Westaby, 1984] for relief of subglottic stenosis and subsequently was used by other researchers for tracheal stenosis and collapse. The Montgomery T-tube was utilized alone or as an adjunct to extensive tracheal reconstruction. The shortness of the inferior limb limits the application of this prosthesis to inlet level tracheal collapse. In 1982, Westaby et al. designed a silicone rubber T-Y stent based on the Montgomery tube. This T-Y stent is bifurcated inferiorly and possessed a side arm in the upper half. Although it resembles the Montgomery tube, the increased length and bifurcated lower end extended the range of use to the carina and main bronchus. It has been tried by several researchers [Westaby et al., 1982; Gleeson and Westaby, 1984]. Like the IPDs these rubber stents interfere with flexibility and mucociliary flow and need a permanent tracheostomy.

### 6.6 Extraluminal Supports

Some investigators believe that extraluminal prostheses are the most suitable for prolonged tracheal support, since lumen diameter is restored during respiration without interfering with the mucociliary flow. A number of different extraluminal prosthesis have been described in recent years, and they all carry the risks of thoracic

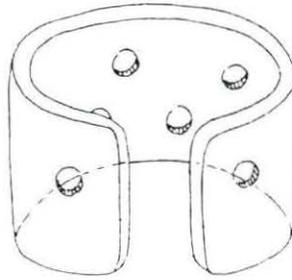


Figure 6.2: TPR made from a polypropylene syringe case

surgery along with other inherent disadvantages. Polypropylene syringe cases and Teflon<sup>R</sup> tubing have been the devices used to support the tracheal rings. High density porous polyethylene is used for smaller airways [Nelson, 1985].

The attempts to use relatively long sections of plastic tubing as extraluminal prostheses to support the trachea remain unsuccessful because they interfere with the tracheal mobility [Boyd and Hanselka, 1976].

### 6.6.1 Tracheal Prosthetic Ring

The most commonly used extraluminal prosthesis is the polypropylene tracheal prosthetic ring (TPR) [Hobson, 1976]. These prostheses are made from 3 ml polypropylene syringe holders (Figure 6.2) or purchased as porous polypropylene

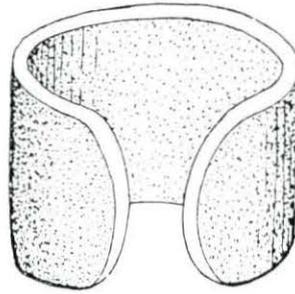


Figure 6.3: Porous polypropylene implants

implants<sup>1</sup> (Figure 6.3). The porous implant allows tissue growth over the entire surface and suture passage at any point, while the implants made from syringe cases rely on holes drilled through the ring. The open ends of the TPR are sutured to the ventral surface to partially encircle the trachea or mainstem bronchus and are placed one to three tracheal rings apart to provide flexibility. However, they tend to span two or three annular ligaments, thereby inhibiting the tracheal flexibility to some degree. Other potential disadvantages of TPRs are:

1. The TPR may fail to contact the trachea uniformly and the resulting kink may cause the edge of the ring to erode the tracheal wall.

---

<sup>1</sup>Monoject, Sherwood Medical Industries Inc., Deland, FL [Hobson, 1976].

2. The sections of collapsed trachea left unsupported between the rings may cause a postoperative tracheal collapse and coughing.
3. Isolating the collapsed trachea by blunt dissection to place the TPR may endanger the neurovascular integrity of the trachea since the innervation and vascularization to a large extent are segmental in the trachea [Kirby et al., 1989].

### 6.6.2 Polypropylene Spiral Prosthesis

At the College of Veterinary Medicine at Ohio State University, a polypropylene spiral prosthesis (PSP) [Figure 6.4] was devised from the barrel of a 3 cc syringe for extraluminal support of the collapsed trachea [Fingland et al., 1987]. Although these PSPs appear to provide uniform support to the trachea while maintaining the flexibility, they significantly decrease tracheal blood flow predisposing the trachea to necrosis, and they have the other disadvantages of TPRs [Kirby et al., 1989].

### 6.7 Self-expanding Metallic Stents

The self-expanding stainless steel stents devised by Gianturco and reported by Wright et al. in 1985 are popular endoprotheses that are being used by several researchers. They were successfully used to maintain patency in canine large veins and aortas [Wright et al., 1985] and also in small vessels less than 5 mm in diameter [Duprat et al., 1987]. They were used to correct experimentally induced vena caval stenoses and to relieve the symptoms in patients with superior vena caval syndrome [Charnsangavej et al., 1986]. In vitro, they had been utilized to expand an aortic

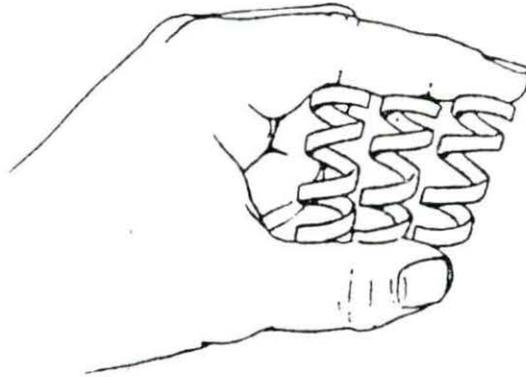


Figure 6.4: Polypropylene spiral prosthesis made from a syringe case

lumen that had been compromised by dissection [Charnsangavej et al., 1985]. These metallic stents have also been used as vehicles for the placement of intravascular grafts [Lawrence et al., 1987]. They have also proved to be useful in patients with recurrent benign strictures and malignant obstructions of the biliary ducts [Coons, 1989].

The successful use of these stents in blood vessels and biliary tracts initiated an investigation of their possible use in the tracheobronchial tree. Wallace et al. from M. D. Anderson Hospital and Tumor Institute, Houston, Texas, experimented with self-expanding stainless steel endovascular stent (Figure 6.5) for the purpose of maintaining the airway in patients with tracheal stenosis. The stainless steel stents they used in their study were 2 and 4cm in diameter. They introduced the stents into the tracheobronchial trees of healthy dogs weighing 15-25 Kg using a special Teflon<sup>R</sup> catheter system. The stents experienced migration ranging from two to nine cms in both directions, indicating the need for a better stent design. They also reported the use of these stainless steel stents as a life supporting measure in two clinical patients with tracheal stenosis.

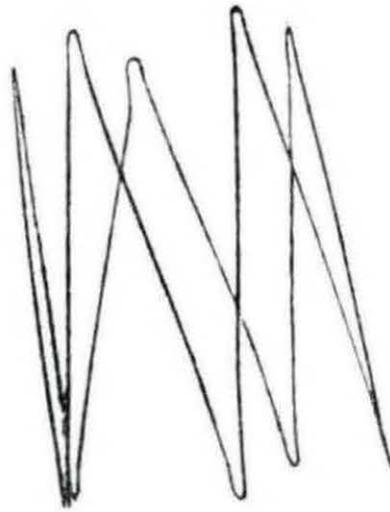


Figure 6.5: Gianturco endovascular stent

## 7 MATERIALS AND METHOD OF STUDY

This experimental study was divided into two phases to obtain a better understanding of the clinical and pathological reaction caused by placing stents in the trachea. Phase 1 was a preliminary, short term study in which ten inert metallic stents were introduced into the thoracic tracheas of ten adult dogs and left in place for a varying periods of three to twenty-five days. The results of Phase 1 were promising and encouraging to continue with Phase 2 which was an eight-week study involving ten dogs in which we compared the long-term effects of two types of stents. Mixed breeds of dogs weighing 15 to 20 Kg were used in both phases.

### 7.1 Stent

The stent design was based on the original Gianturco endovascular stents, and they were made in the Engineering Research Institute Machine Shop, at the Iowa State University, Ames. The stents were made from 0.022 in. spring steel wire (AISI 9260), constructed in the form of a cylinder, with loops bent in a zig-zag configuration. Totally 20 stents were made and nine of these 20 were revised by attaching two hooks to anchor the stent. These hooks were designed to have rounded ends and to protrude beyond the stent surface by  $<0.5$  mm. The stents without hooks were called *plain stents* (Figure 7.1) while the stents with hooks were called

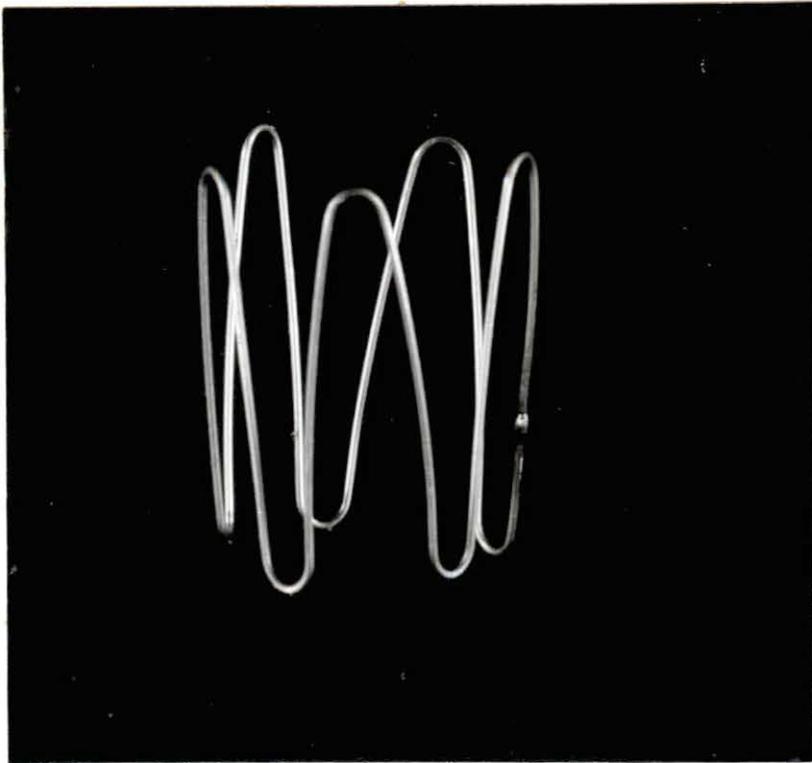


Figure 7.1: Plain stent

*hooked stents* (Figure 7.2). The hooked stents used in the two phases differed by the site of the hook attachments (shown in Figure 7.2). The dilating force of the stent can be varied by manipulating the wire size, the number of wire loops, angle of the loops, and the stent length. The dilating force increases when one or more of these factors are increased [Wright et al., 1985].

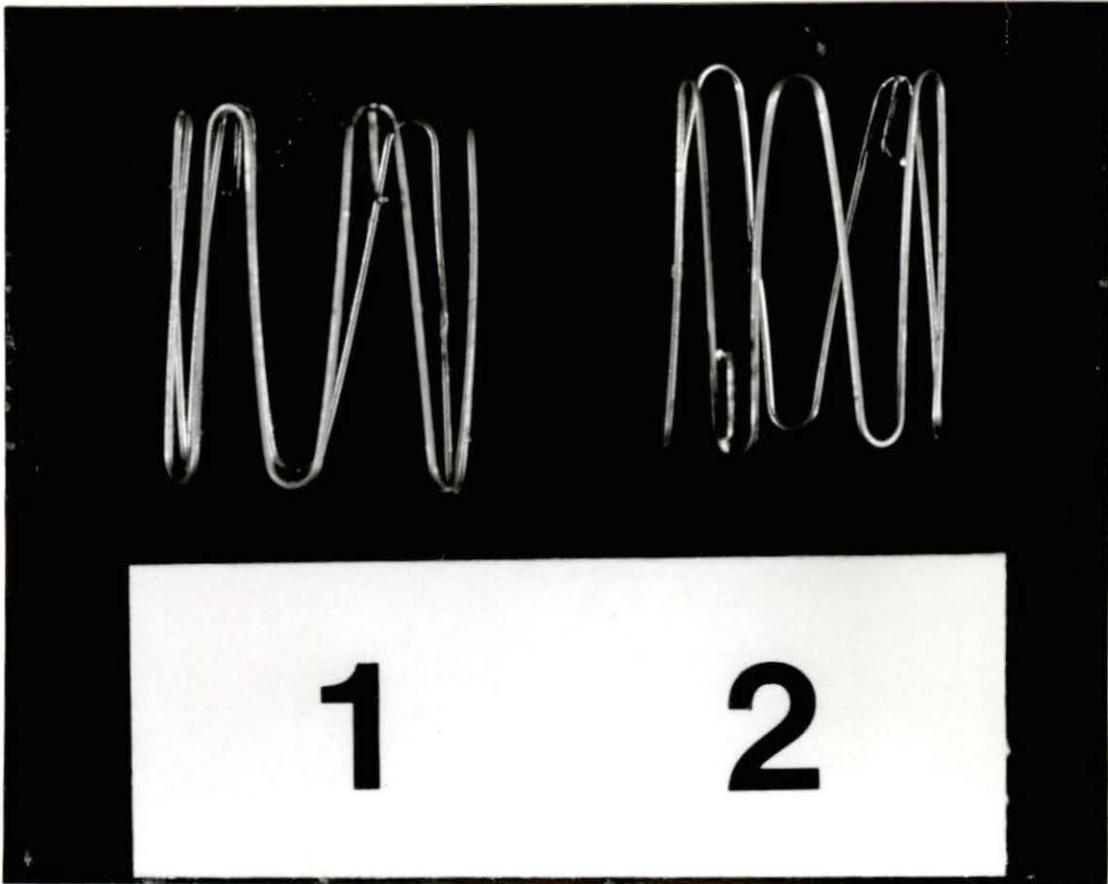


Figure 7.2: Hooked stents. 1. Hooked stent used in Phase 1, has both the hooks on one end, but on the opposite sides; 2. Hooked stent used in Phase 2, has one hook on each end

In Phase 1, four hooked stents and six plain stents were used. The stents were 3 cm in length, 2.5 - 3 cm in diameter, and had six loops. The four hooked stents had both the hooks on one end but on opposite sides. Five plain and five hooked stents of smaller diameter (2 - 2.5cm), with a fewer number of loops (five instead of six) but of the same length were used in Phase 2. The five hooked stents used in Phase 2 had one hook on one end and one on the opposite end. This revision in the hooked stents was to overcome the change noticed in the expansile property of the hooked stents used in Phase 1.

## 7.2 Coating

Silastic<sup>R</sup> medical adhesive silicone type A<sup>1</sup>, a biocompatible rubber, was used to coat all the metallic stents since it is nonpyrogenic, noncytopathic and recommended for dip coating applications. The stents were prepared for coating by cleaning them thoroughly in a hot water - mild soap solution and rinsing them several times in hot water. The dispersion used for dip coating the stents was obtained by dissolving the medical adhesive in hexane (1gm of adhesive in 50 ml of solvent). The stents were dipped briefly into the silicone dispersion and were then air-dried. This process was repeated five or six times to ensure a thin layer of silastic on the stents [Dow Corning Co., 1980].

## 7.3 Stent Placement in the Trachea

The stents were introduced through the endotracheal route using a rigid, hollow delivery tube and a piston-like rod. The delivery system and the stents were

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<sup>1</sup>Dow Corning Corporation, Midland, Michigan.

sterilized before use.

Each dog was anesthetized and endotracheally intubated. A stent was squeezed to reduce its diameter small enough to be placed inside the tip of the hollow delivery tube. The dog's endotracheal tube was withdrawn from the trachea momentarily and the hollow delivery tube was passed through the larynx and advanced into the trachea. Using fluoroscopic guidance the tip of the delivery tube was positioned at the level of the first or second rib. Then the piston-like rod was introduced through the tube and held against the stent while the delivery tube was withdrawn, leaving the stent exposed. The tube and the rod were pulled out immediately after the stent was placed. The dog was reintubated immediately and radiographs of the thorax, both lateral and dorsoventral views, were taken prior to recovery from anesthesia. The position of the stent could be altered as long as it remained partially within the delivery tube. However, once it was released only slight adjustment could be accomplished.

## 7.4 Experimental Study

### 7.4.1 Phase 1

In this phase the stents were left in the trachea for a varying period of three to twenty-five days. Ten dogs each received a stent: Four hooked and six plain. The dogs were divided into four groups depending upon the duration of the study. In two dogs the stents were left in for three days (group 1), in three dogs for eight days (group 2), in four dogs for eighteen days (group 3) and in the last dog for 25 days (group 4).

**7.4.1.1 Observation period** During this time the dogs were clinically assessed for cough, hemoptysis, respiratory distress and difficulty in swallowing. Radiological monitoring for changes in size and position of the stents was done periodically. Dogs in groups 1 and 2 were radiographed on the first and the last day of their trial period. The dogs in group 3 were radiographed on the eighth day, in addition to the radiographs taken on the first and last day. The dog in group 4 which had the stent for 25 days was radiographed on the first, eighth, fifteenth and twenty-fifth day. The measurements of the tracheal lumen were taken from these radiographs (Figure 7.3), for quantitative analysis. The initial lumen diameter was also taken from the first day radiographs, within two cm cranial to the stent. The stent movement was also measured for these time periods. On the last day of the observation period, a fiberoptic endoscope<sup>2</sup> was passed into the trachea of the anesthetized dogs to view the mucosal changes caused by the stents in the dogs in groups 3 and 4. At the termination of the trial periods the dogs were euthanatized<sup>3</sup> using an intravenous injection of sodium pentobarbitol<sup>4</sup>, and necropsies were performed. At the time of necropsy microbial swabs were taken for aerobic bacterial culture. After gross examination the tracheas were preserved in 5% buffered formalin. Multiple samples were taken across the wire at the stent site and two cm from the cranial end of the stent for future histological examination. One tracheal specimen from each group (dog 2 from group 1, dog 5 from group 2, dog 6 from group 3 and dog 10 from group 4) was photographed. Later tracheograms were performed

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<sup>2</sup>Olympus model GIF-XP.

<sup>3</sup>Euthanization was done according to the requirements of Animal Care Society of the Iowa State University.

<sup>4</sup>Sleepaway, Fort Dodge Labs, Fort Dodge, IA.

on these formalin fixed specimens by first blotting them dry and then coating the luminal as well as the serosal surface with liquid barium. Ventral and lateral view of radiographs were obtained.

#### 7.4.2 Phase 2

Phase 2 was an eight-week study in which five plain stents and five hooked stents were used in ten healthy adult dogs. The stents were placed individually, in the thoracic part of the trachea. This phase of the experimental study was similar to Phase 1 except for the following:

- The dogs were divided into two groups depending on the type of stent used.
- The duration of the study was longer.
- The hooked stent's size and design were changed as mentioned above.

**7.4.2.1 Observation period** During the eight week observation period the dogs were clinically assessed for normal respiratory function. To visualize the stents and measure the internal tracheal lumen, follow-up radiographs, both lateral and dorsoventral views, were taken. The required measurements were taken from these radiographs (Figure 7.3). The measurements of interest were the diameter of the tracheal lumen within the stent and one to two cm cranial to the stent, the actual diameter of the stent and the migration of the stent. All of these were measured on the first day, immediately after stent placement, and again during the second, sixth and eighth weeks (on the last day) from the radiographs taken on those days. The dorsoventral (dv) diameter of the tracheal lumen at the stent level was the average

of diameters measured at three levels, the caudal end, the center and the cranial end of the stent. The initial tracheal lumen diameter was also taken from the first day radiographs within two cm cranial to the stent. Figure 7.3 shows the diameters measured and the levels from which they were taken. These diameter values in cm were then converted into percent of the initial tracheal diameter as measured two cm cranial to the stent on the first day. The original diameter was kept as 100%. The mean value of each of these measurements for the plain and the hooked groups was calculated. These mean values were statistically compared (Student's t-test) to their initial value (100%) as well as to the opposite group to find out the statistical significance ( $P < 0.05$ ) of the changes caused by the stents. The standard error of the means were also calculated for each mean.

To follow the gross mucosal changes, two dogs from each group were examined endoscopically during the fourth and eighth weeks. Photographs were taken during these procedures. On the last day of the trial period the dogs were euthanized using sodium pentobarbitol. This was followed by a necropsy to examine the trachea and mediastinum grossly and to preserve the trachea for further studies. During the necropsy, swabs were also taken from the mucosal surface of the trachea, at the level of the stent for culture studies.

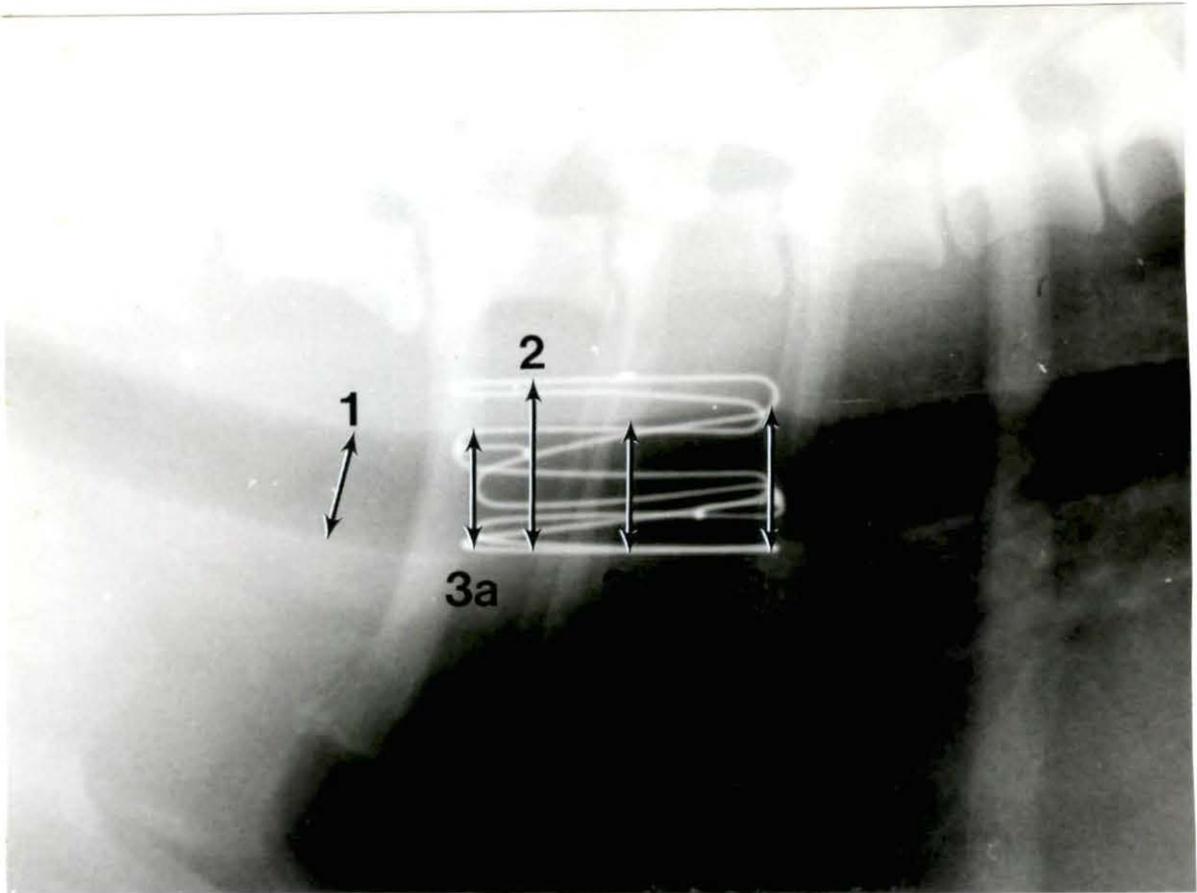


Figure 7.3: Radiograph of the thorax showing the levels at which the measurements were taken. 1. Dv diameter above the stent level; 2. Stent diameter within the trachea; 3a. Internal dv diameter at the cranial end of the stent; 3b. Internal dv diameter at the center of the stent; 3c. Internal dv diameter at the caudal end of the stent

## 8 RESULTS

### 8.1 Phase 1

#### 8.1.1 Clinical examination

Two dogs (4 and 6) experienced moderate coughing while one (dog 7) suffered from severe coughing and mild respiratory distress. All these three dogs had hooked stents but these findings did not show any correlation to the pathological reaction that was elicited by the stents. There was no hemoptysis or difficulty in swallowing. The other seven dogs were normal and active throughout the observation period. Endoscopic examination of the group 3 dogs on the last (eighteenth) day of the trial period revealed that approximately one-half of the stent wires were covered with tissue (Figure 8.1). Dog 10 which had the stent in place for twenty-five days, had many mucosal nodules at the stent site (Figure 8.2). The adjacent mucosa appeared normal with occasional hyperemia.

#### 8.1.2 Radiographic examination

The various measurements taken from the radiographs in Phase 1 are summarized in Table 11.1 and Table 11.2. These measurements were expressed as a percentage of the initial tracheal lumen diameter as shown in Table 11.3.



Figure 8.1: Phase 1, dog 9: Endoscopic view of the stent on the eighteenth day



Figure 8.2: Phase 1, dog 10: Endoscopic view of the completely covered stent on the twenty-fifth day showing multiple nodules on the mucosal surface

The tracheal lumen at the site of the stent was dilated in all the dogs immediately after stent placement. Dilatation progressed in most dogs during the course of the observation period. Figure 8.3, Figure 8.4 and Figure 8.5 show an increase caused by the plain stents while Figure 8.6, Figure 8.7 and Figure 8.8 show the same for the hooked stents. The eighteenth day radiographs showed that the two hooked stents in group 3 had a cone-like shape instead of the original cylindrical form, with the hooked end being narrower (Figure 8.8). The tracheal lumen diameter cranial to the stent varied from 95% to 117% (Table 11.3) regardless of the duration. Of the ten stents, seven moved cranially and one caudally. The plain stents moved a maximum of ten cm, while the hooked stents moved a maximum of 0.5 cm.

### 8.1.3 Pathological findings

**8.1.3.1 Gross pathology** The site of the stent could be easily identified in the dogs when the thorax was examined. The stents of dogs 6 and 8 were found to extend dorsally into the trachealis muscle thereby making a prominence on the dorsal aspect of the trachea. Dogs 3 and 5 had dilated vessels on the outer surface of the trachea around the stent site. Copious mucus was found collecting in the trachea in the two dogs with three day duration (group 1); there was none found in the rest of the dogs. The tracheal lumen was dilated in all the dogs and the mucosal surface was smooth except in the group 4 dog (twenty-five days) which showed multiple small nodules. Occasionally the mucosa showed hyperemia and other signs of acute inflammation.

The wires were partially covered by tissue depending on the duration of the experiment. In dogs 4 and 7 (had hooked stents) a loop of the stent was found



Figure 8.3: Phase 1, Dog 9: Radiograph of the thorax showing the plain stent on the first day

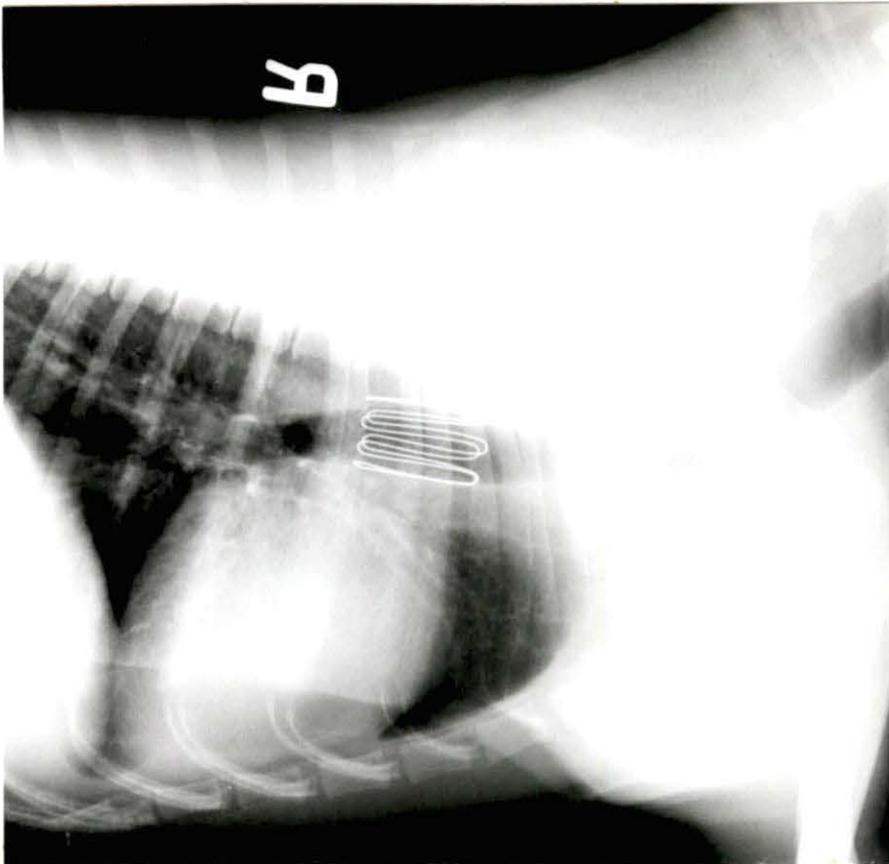


Figure 8.4: Phase 1, Dog 9: Radiograph of the thorax showing the plain stent on the eighth day

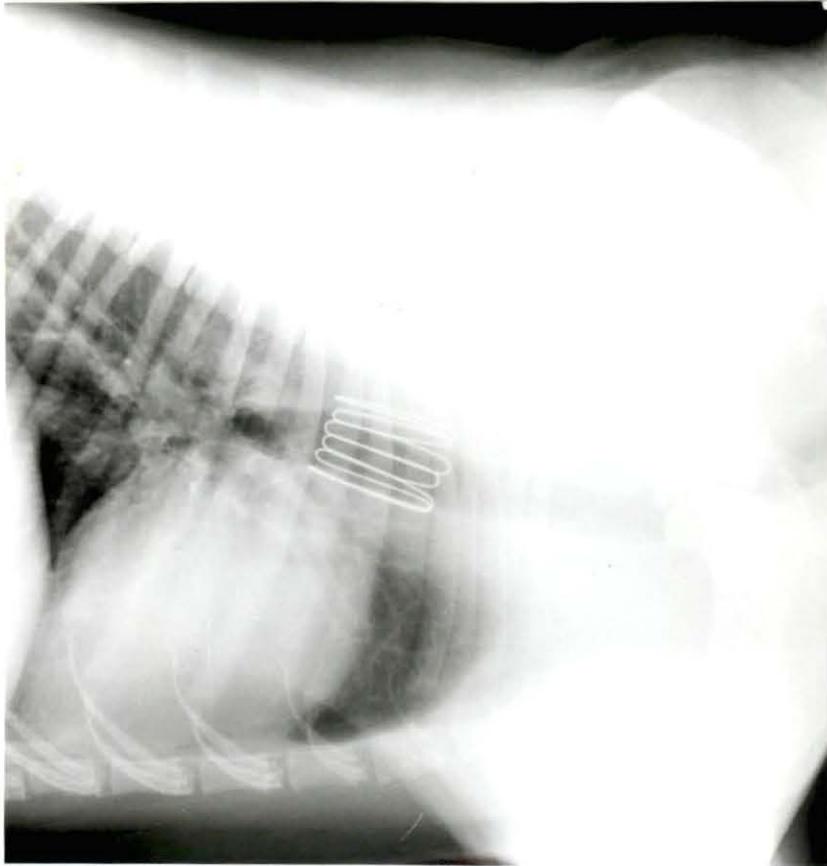


Figure 8.5: Phase 1, Dog 9: Radiograph of the thorax showing the plain stent on the eighteenth day

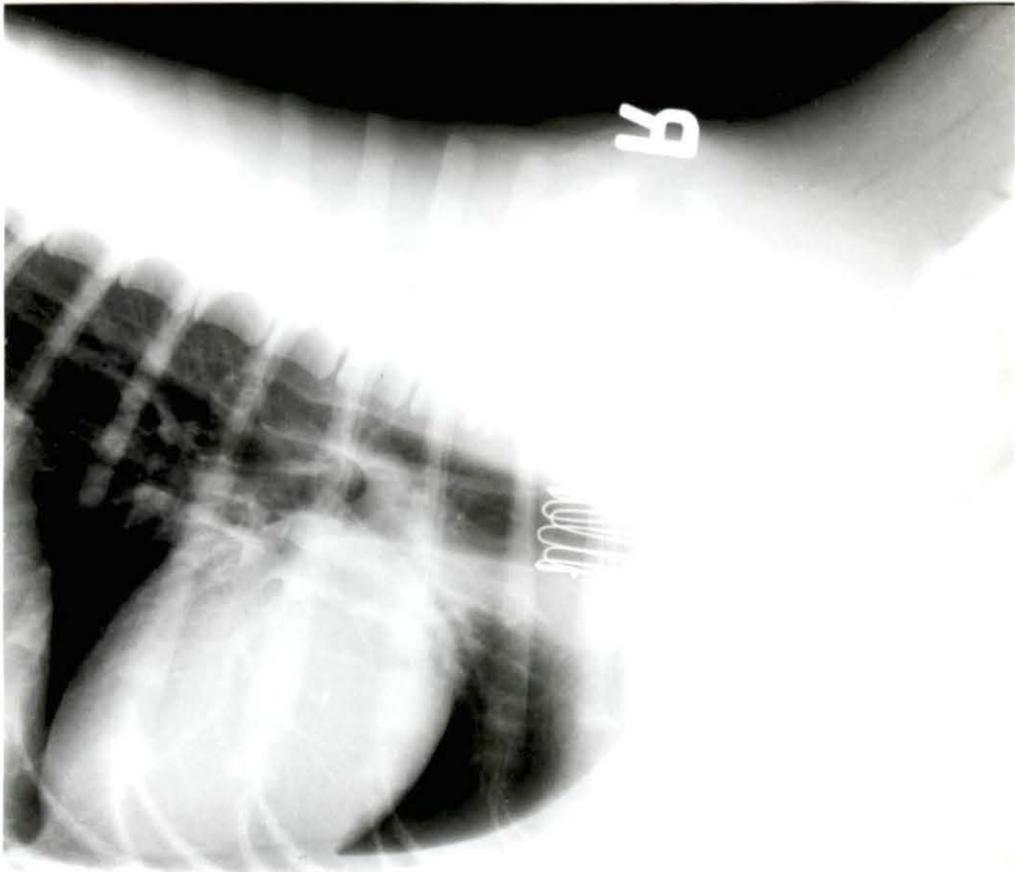


Figure 8.6: Phase 1, Dog 6: Radiograph of the thorax showing the hooked stent on the first day



Figure 8.7: Phase1, Dog 6: Radiograph of the thorax showing the hooked stent on the eighth day



Figure 8.8: Phase 1, Dog 6: Radiograph of the thorax showing the hooked stent on the eighteenth day

to be protruding into the lumen. Figure 8.9 and Figure 8.10 show the ventral and lateral views of the tracheal specimens from dog 2, 5, 6 and 10 and Figure 8.11 and Figure 8.12 are the ventral and lateral views of the tracheograms.

**8.1.3.2 Microscopic lesions** Microscopic lesions associated with stent wires consisted of focal necrosis and inflammation with edema and hyperemia extending into the adjacent mucosa. The severity of the inflammatory response varied moderately among dogs within the same group. The principal variables in the tissue response included mucosal thickness, necrosis, edema, composition of exudates, lymphoid response and degree of fibrosis (Table 11.4).

Lesions in the two dogs euthanatized three days after placement of the stents could be classified as acute focal fibrinopurulent tracheitis with necrosis around the wires. The tracheal mucosa was moderately thickened by fluid and cellular exudates. The exudate surrounding the wires in the lamina propria consisted of fibrin and neutrophils with fewer macrophages. Nearby venules and lymphatics were dilated; fibrosis and lymphoid nodules were absent.

Microscopic lesions in dogs euthanatized eight to 25 days after placement of the stents were qualitatively similar but variable among dogs. The general tissue response would be classified as chronic multifocal pyogranulomatous tracheitis. The tracheal mucosa of most dogs was extremely irregular in thickness depending on the proximity of stent wires. Around the wires was a band of necrotic cell debris and neutrophils surrounded by a broad band of neutrophils, macrophages, and lymphocytes intermixed with spindle-shaped fibroblasts. In some dogs immature fibrous connective tissue formed concentric rings around wires. In some sections a refrac-

tile material, assumed to be silicone coating from wire stents, was intermixed with cell debris implying that the silicone coating separated and lodged in the tracheal wall, probably happened at time of stent placement. Lymphoid nodules were rarely present in the lamina propria and adventitia of the sections. The chronic inflammatory response was particularly severe in dog with fractured tracheal rings. In this dog, pyogranulomatous exudate and fibrosis formed a tract along the wire from the tracheal mucosa through the tracheal wall to the adventitia. The tracheal epithelium was complete over many of the wires, but varied from nonciliated immature cells to more fully differentiated ciliated columnar cells and goblet cells.

The bacterial cultures revealed isolation of *Pseudomonas aeruginosa* in two dogs (dogs 6 and 8), *Pseudomonas fluorescens* in two dogs (dog 7 and 9), and *Staphylococcus epidermis* in one dog (dog 10).

## 8.2 Phase 2

### 8.2.1 Clinical examination

Clinically the observation period was uneventful except for mild coughing experienced by dogs 3 and 10. Pathologically dog 3 which had a hooked stent, showed severe reaction and dog 10 which had a plain stent, showed mild reaction. Dog 3 was pregnant during the trial period and delivered puppies uneventfully. In general the dogs were active and functioning normally through out the eight week period.

**8.2.1.1 Tracheal endoscopy** Dog 1 which had a hooked stent showed healthy mucosa with the stent partially covered (about 50%) during the fourth week (Figure 8.13). This covering was almost complete by the eighth week as shown in

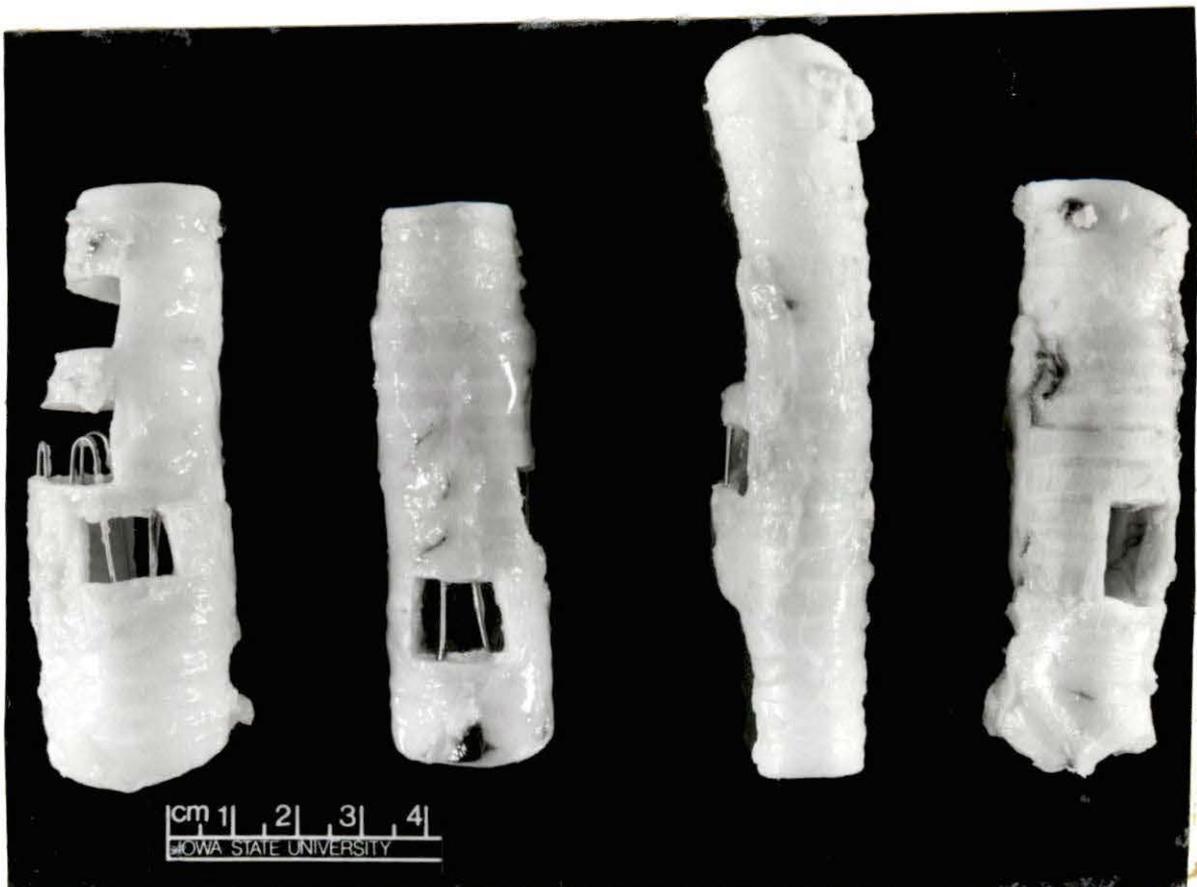


Figure 8.9: Phase 1, tracheal specimens: Ventral view. From left to right: Dog 2 from group 1 (three days), dog 5 from group 2 (eight days), dog 6 from group 3 (eighteen days), and dog 10 from group 4 (twenty-five days)



Figure 8.10: Phase 1, tracheal specimens: Lateral view

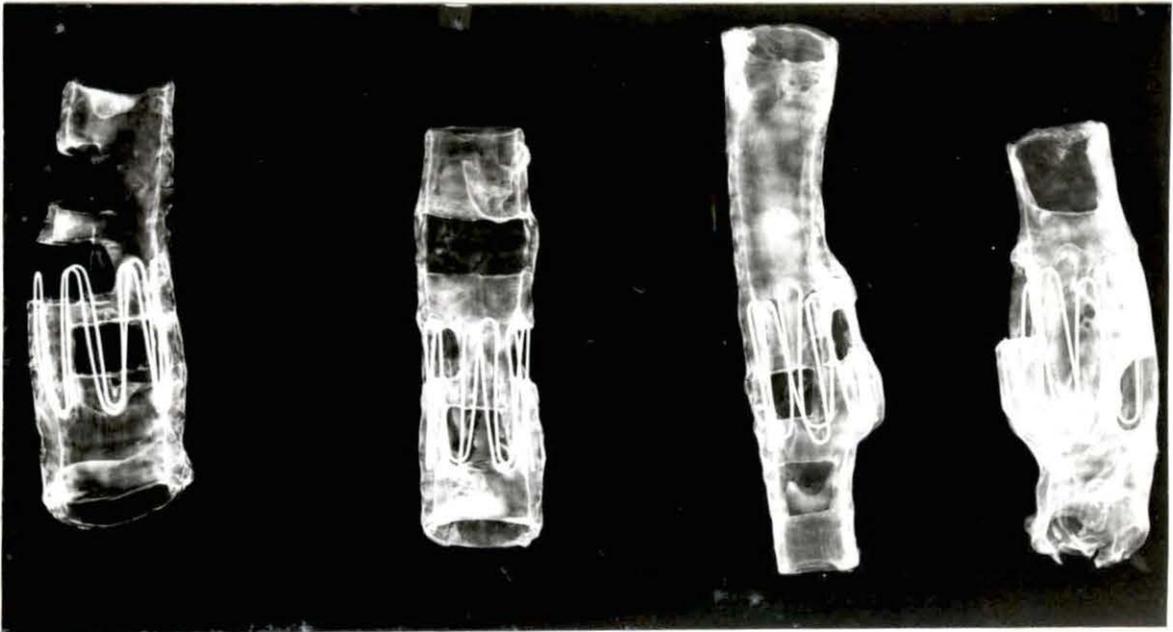


Figure 8.11: Phase 1, tracheogram: Ventral view. From left to right: Dog 2 from group 1 (three days), dog 5 from group 2 (eight days), dog 6 from group 3 (eighteen days), and dog 10 from group 4 (twenty-five days)

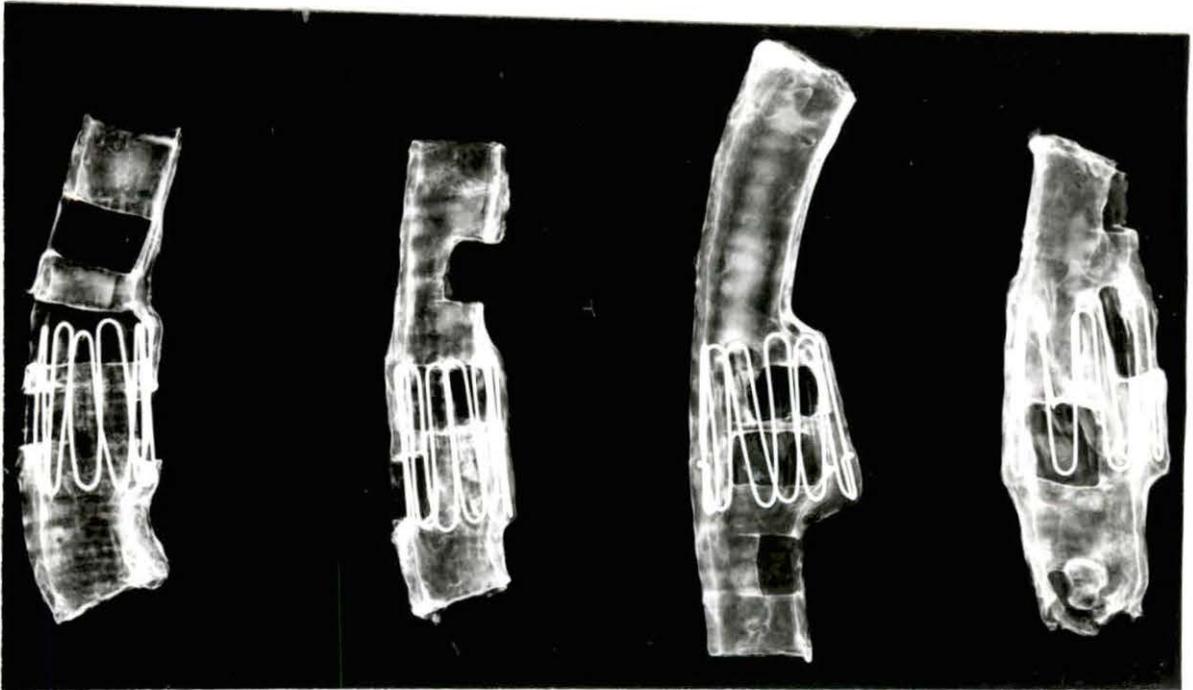


Figure 8.12: Phase 1, tracheogram: Lateral view



Figure 8.13: Phase 2, Dog 1: Endoscopic view of the stent after four weeks

Figure 8.14. In dog 7 which also had a hooked stent, there were two uncovered loops protruding into the lumen at four weeks (Figure 8.15), and the mucosa was hyperemic with surface irregularities. This was still present after eight weeks. Thickening of the tracheal wall with associated lumen narrowing was suspected for this dog and it was evident on the radiographs.

In dogs 2 and 6 with the plain stents, endoscopy during the fourth week showed that the stents were about 50% covered with healthy mucosa and that small nodules were present. There was one mucosal nodule, about 3 mm in size in dog 2 and three nodules, of sizes varying from 1 - 3 mm in dog 6. During the eighth week these nodules were found to have receded in size, and the stents were 80% covered by mucosa. The mucosal surface of the trachea at and above the level of the stent



Figure 8.14: Phase 2, Dog 1: Endoscopic view of the stent after eight weeks

was normal. Figure 8.16 and Figure 8.17 are photos taken during endoscopy, of the mucosal surface on the fourth and eighth week respectively, for dog 2. In none of the four dogs was excess mucus visible, implying that the mucociliary function was clinically normal.

### 8.2.2 Radiographic examination

In this phase the tracheal lumens within the stents were altered in both the groups by the tissue reaction while the stents expanded progressively with time. Figure 8.18, Figure 8.19, Figure 8.20 and Figure 8.21 are the radiographs taken on the first day, and second, sixth and eighth weeks respectively, of dog 2 with a plain stent. Figure 8.22, Figure 8.23, Figure 8.24 and Figure 8.25 are the comparable



Figure 8.15: Phase 2, Dog 7: Endoscopic view of the stent after four weeks

radiographs for dog 1 with a hooked stent.

**8.2.2.1 Internal tracheal diameter within the stent** Table 12.1 and Table 12.2 show the measured values of the lumen diameter within the stent and the corresponding percentages when compared to the initial lumen diameter (taken two cm cranial to the stent, Table 12.3). The averages of these values are plotted in Figure 8.26. The graph indicates that although the lumen diameter increased over 125% in the first two weeks for both the groups, the diameter after eight weeks was close to the initial value. The increase was statistically significant for the plain stents ( $P < 0.05$ ) for each of the four periodic measurements, while it was found to be significant only for the second week measurement for the hooked stent group.



Figure 8.16: Phase 2, Dog 2: Endoscopic view of the stent after four weeks



Figure 8.17: Phase 2, Dog 2: Endoscopic view of the stent after eight weeks

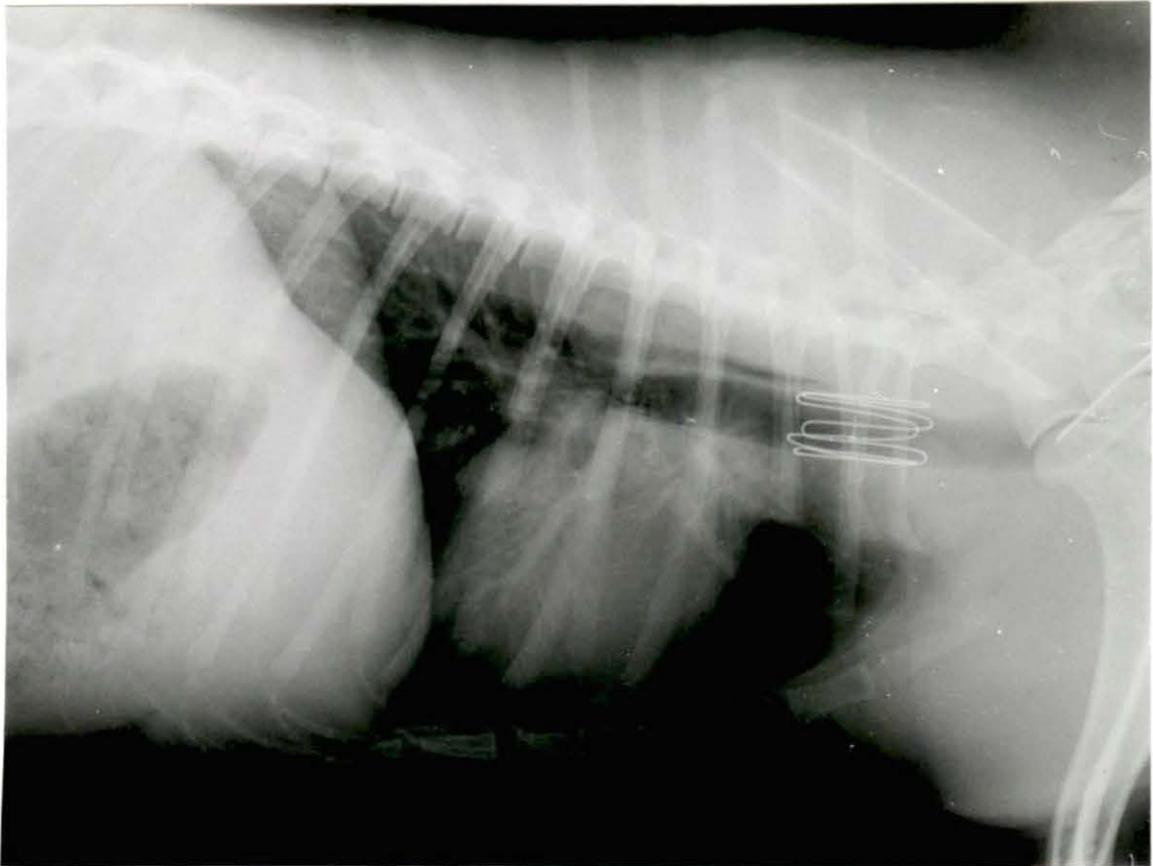


Figure 8.18: Phase 2, Dog 2: Radiograph of the thorax showing the plain stent on the first day

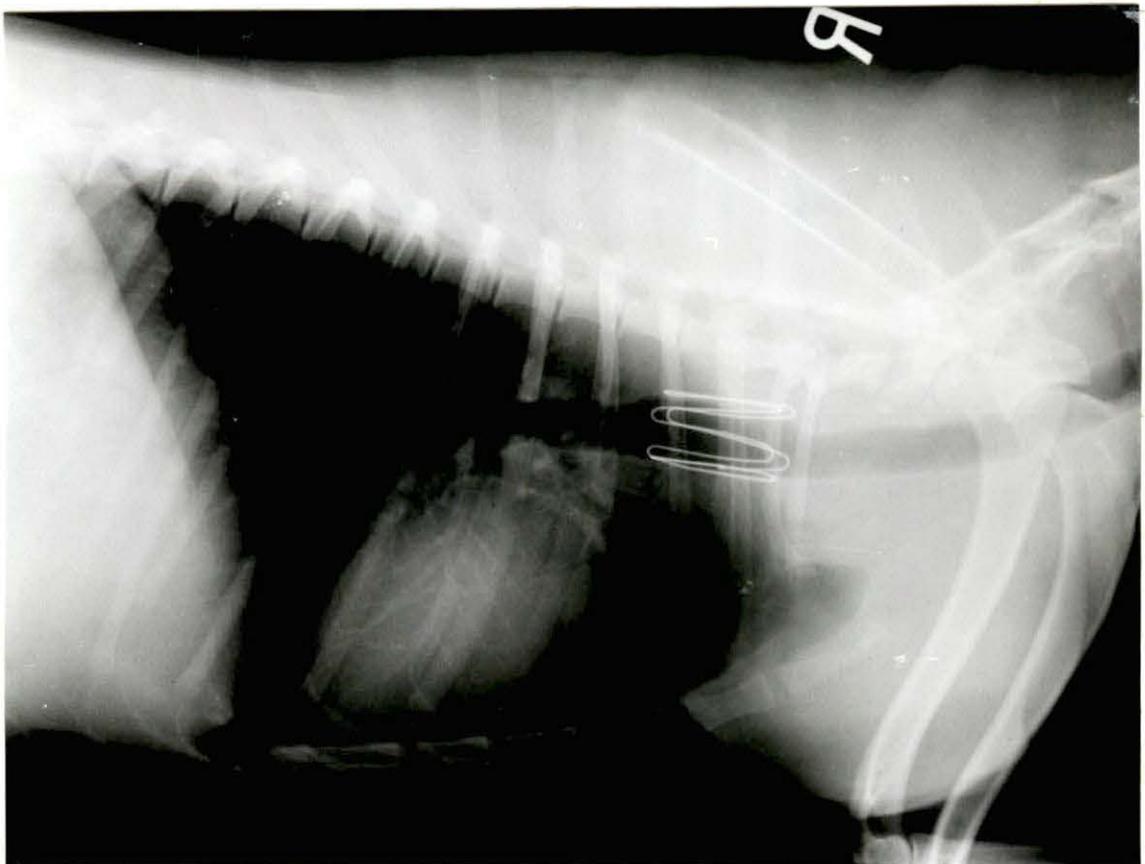


Figure 8.19: Phase 2, Dog 2: Radiograph of the thorax showing the plain stent after two weeks



Figure 8.20: Phase 2, Dog 2: Radiograph of the thorax showing the plain stent after six weeks



Figure 8.21: Phase 2, Dog 2: Radiograph of the thorax showing the plain stent after eight weeks



Figure 8.22: Phase 2, Dog 1: Radiograph of the thorax showing the hooked stent on the first day

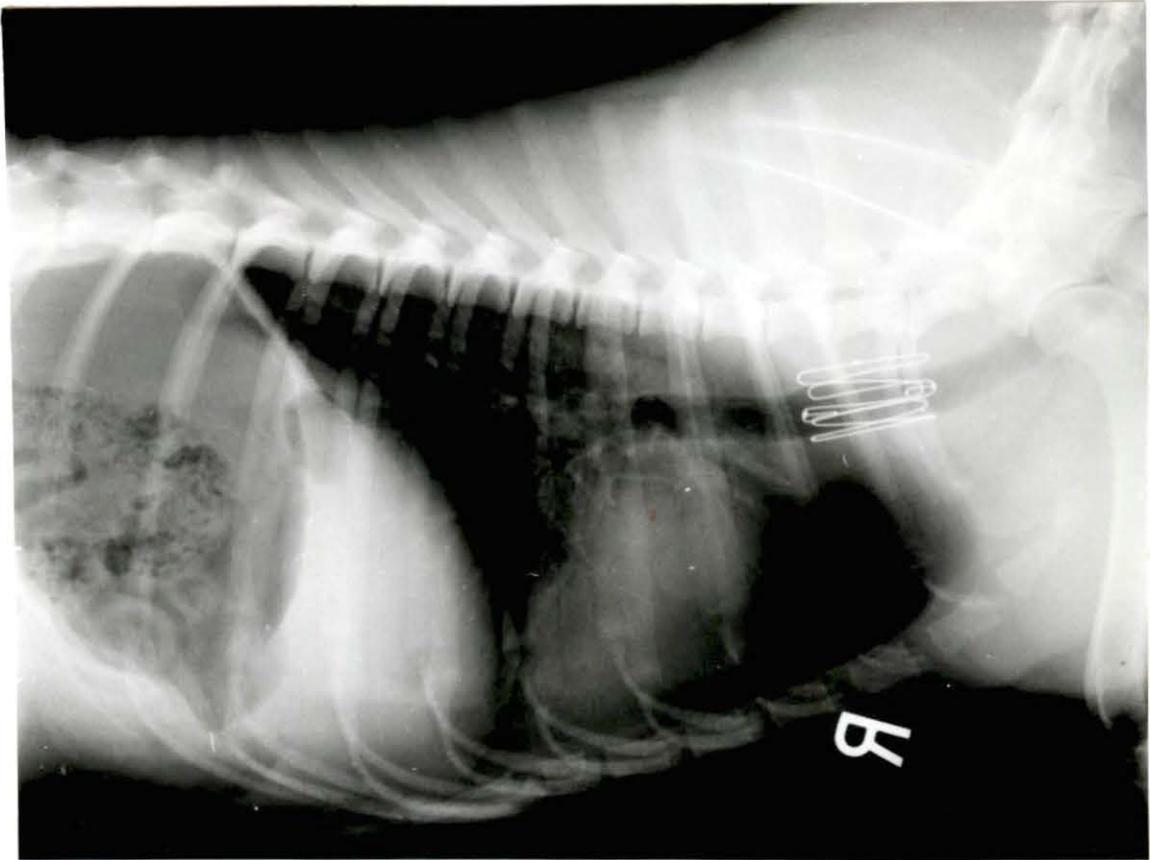


Figure 8.23: Phase 2, Dog 1: Radiograph of the thorax showing the hooked stent after two weeks

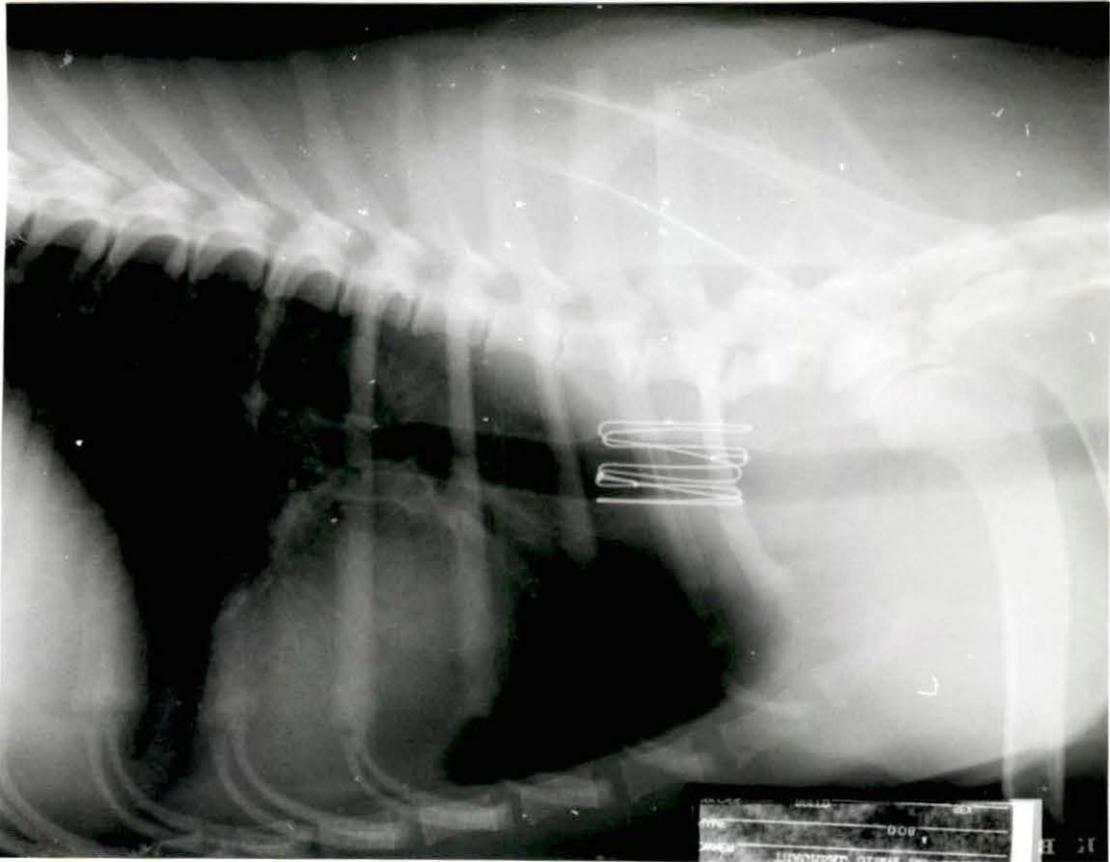


Figure 8.24: Phase 2, Dog 1: Radiograph of the thorax showing the hooked stent after six weeks



Figure 8.25: Phase 2, Dog 1: Radiograph of the thorax showing the hooked stent after eight weeks

After eight weeks, the mean lumen diameter was increased more in the plain stent group (114%) than in the hooked stent group (106%), but this difference was not statistically significant ( $P > 0.05$ ). The values after eight weeks for the the stent diameters, plus the above mentioned tracheal diameters at various levels are summarized in the Table 12.4 and Table 12.5. For convenience of understanding, the means for each group are plotted in Figure 8.27. The tracheal lumen diameters within the stent, at the cranial end, center and caudal end were compared during the eight week period. It was obvious that the lumen was wider at the center than at the ends in the plain stent group after eight weeks; the mean diameters of the cranial end, center and caudal end of the stents were 105%, 139% and 103% respectively. The hooked stent group behaved differently. The diameter increased gradually from the cranial end; the tracheal lumen at the cranial end was 94%, center 101% and caudal end 124%.

**8.2.2.2 Tracheal lumen diameter cranial to the stent** This measurement was included in the study since it reflects the effect of the stent on the neighboring segments of trachea. Table 12.3 shows how this measurement varied over the period of eight weeks for the two groups. For the plain stent group, the lumen cranial to the stent was less than the initial percentage (100%) for the second (89%), sixth (91%) and eighth weeks (92%). This reduction is significant ( $P < 0.05$ ) for the last two values. The mean values for the hooked stent group were 104%, 110% and 120% for the second, sixth and eighth week respectively, but the differences were not significant. As shown in Figure 8.28 there was a significant difference in the lumen size above the stent level between the two groups at each time period.

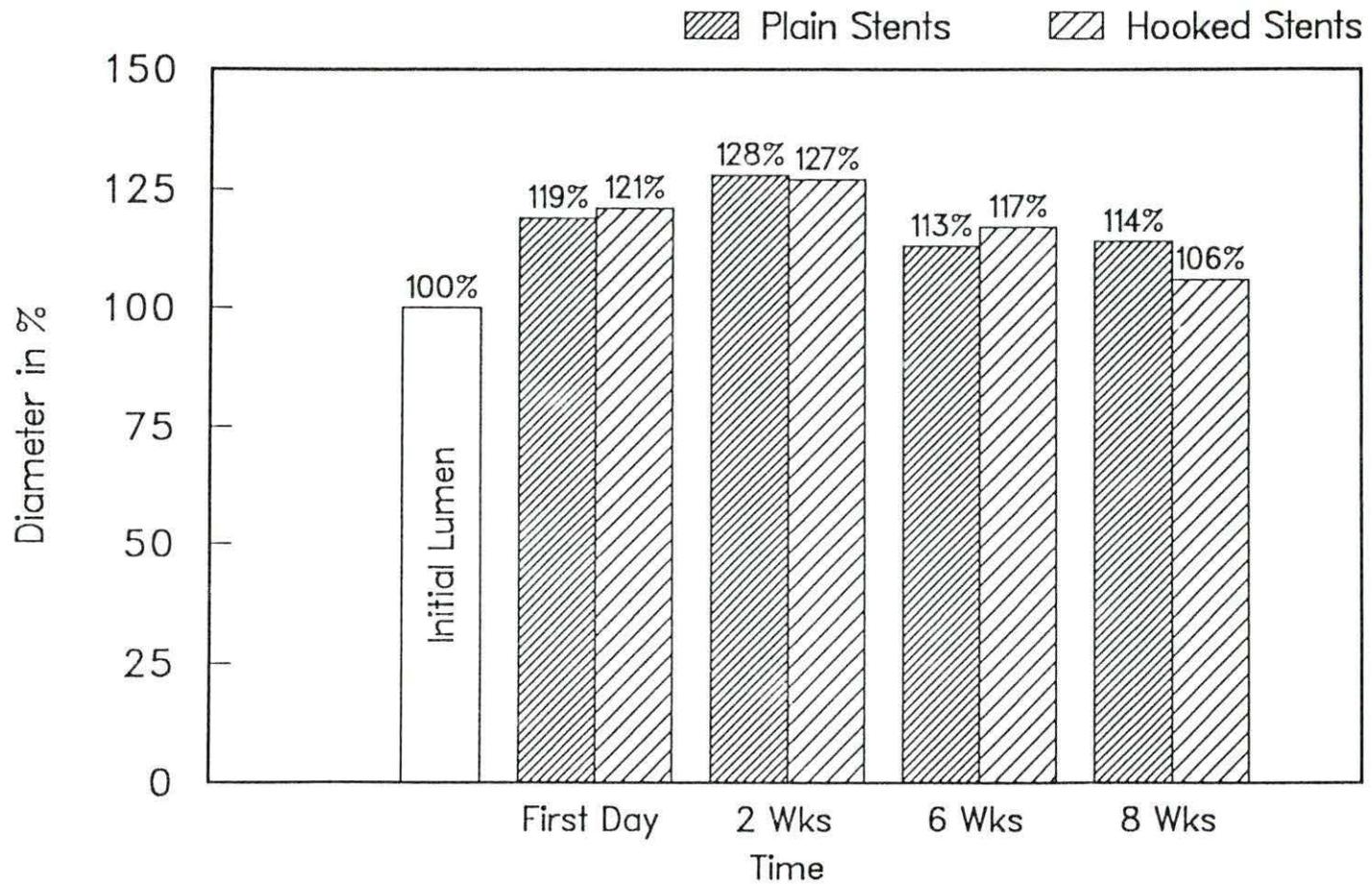


Figure 8.26: Phase 2: Mean *dv* diameter of the tracheal lumen within the stent

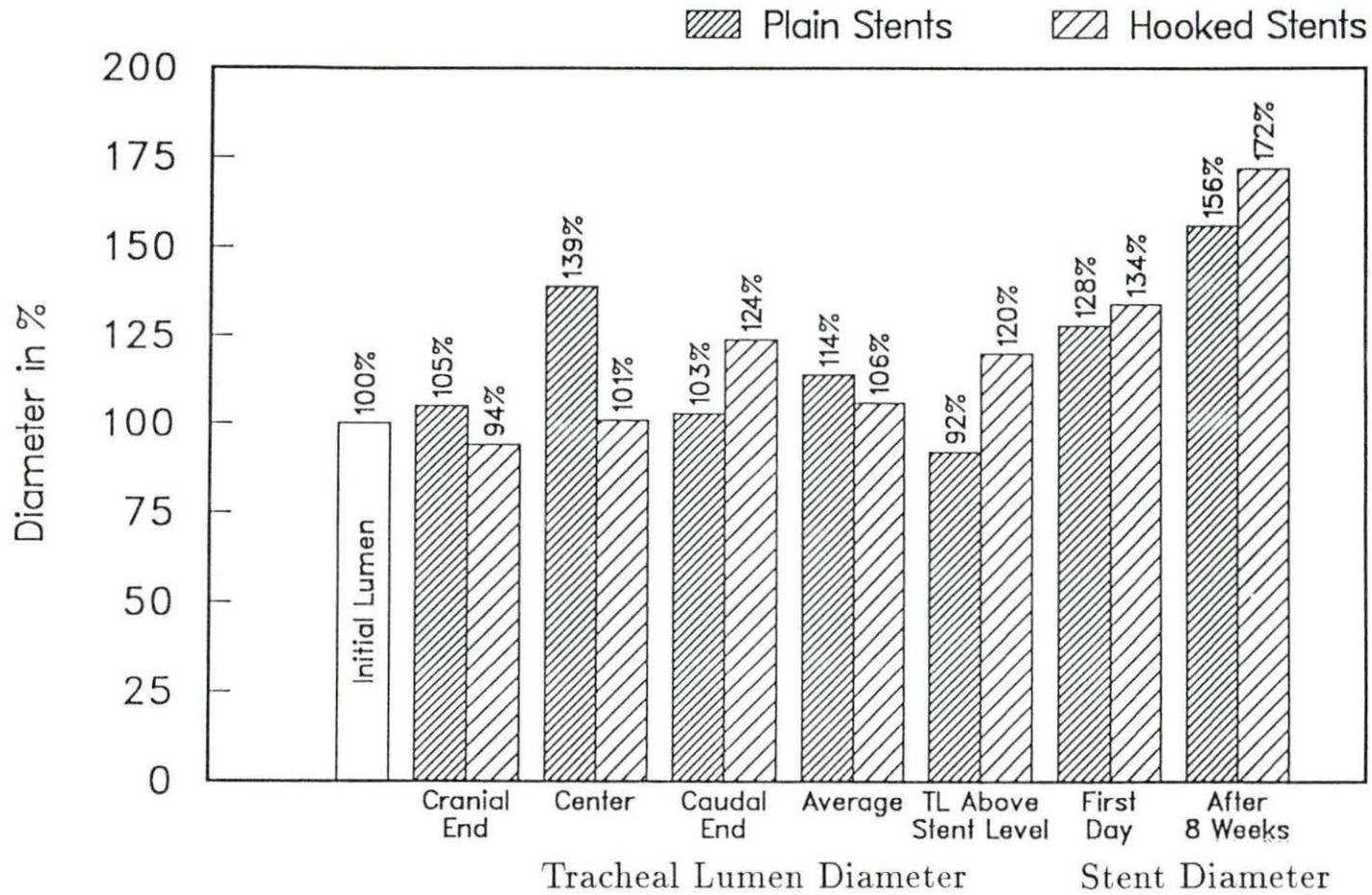


Figure 8.27: Phase 2: Mean lumen and stent measurements after 8 weeks

**8.2.2.3 Diameter of the stents** As expected, due to the springy quality of the wire, the actual diameters of the stents after placement in the trachea increased over the period of eight weeks. This is shown in Table 12.6 for both plain and hooked stents. After eight weeks within the trachea, the plain stents averaged 2.13 cm in diameter and the average for the hooked stents was 2.05 cm. The diameters of the plain stents and the hooked stents were significantly larger than the original tracheal diameters throughout the trial period. The mean stent diameters for both the groups are plotted in Figure 8.29. This increase in the percentage was higher for the hooked stents (172%) than for the plain stents (158%), but the actual stent diameter after eight weeks remained lower than the plain stents. There was no statistically significant difference between these two groups ( $P > 0.05$ ).

**8.2.2.4 Stent migration** Displacement of the stents took place mostly in the first two weeks and occurred in both directions though caudal displacement was predominant. As shown in Table 12.7 four plain stents and three hooked stents moved during the eight week period. The maximum migration was less than 2 cm for the plain stents and 1 cm for the hooked stents. This displacement was found to be significant for the plain stents while it was not ( $P > 0.5$ ) for the hooked stent group. There was no significant variation in the stent migration between the plain and the hooked stent groups.

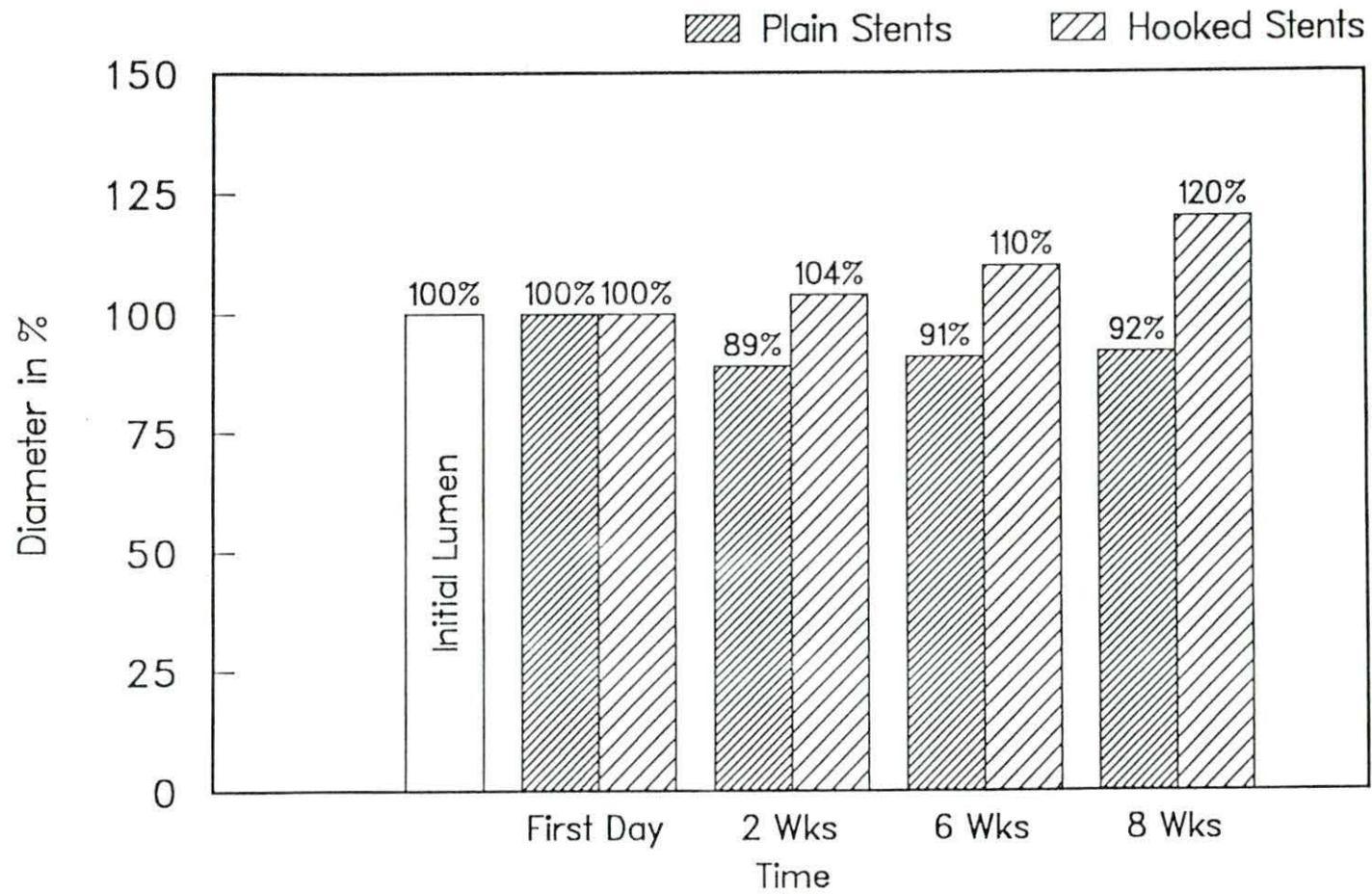


Figure 8.28: Phase 2: Mean *dv* diameter of the tracheal lumen cranial to the stent

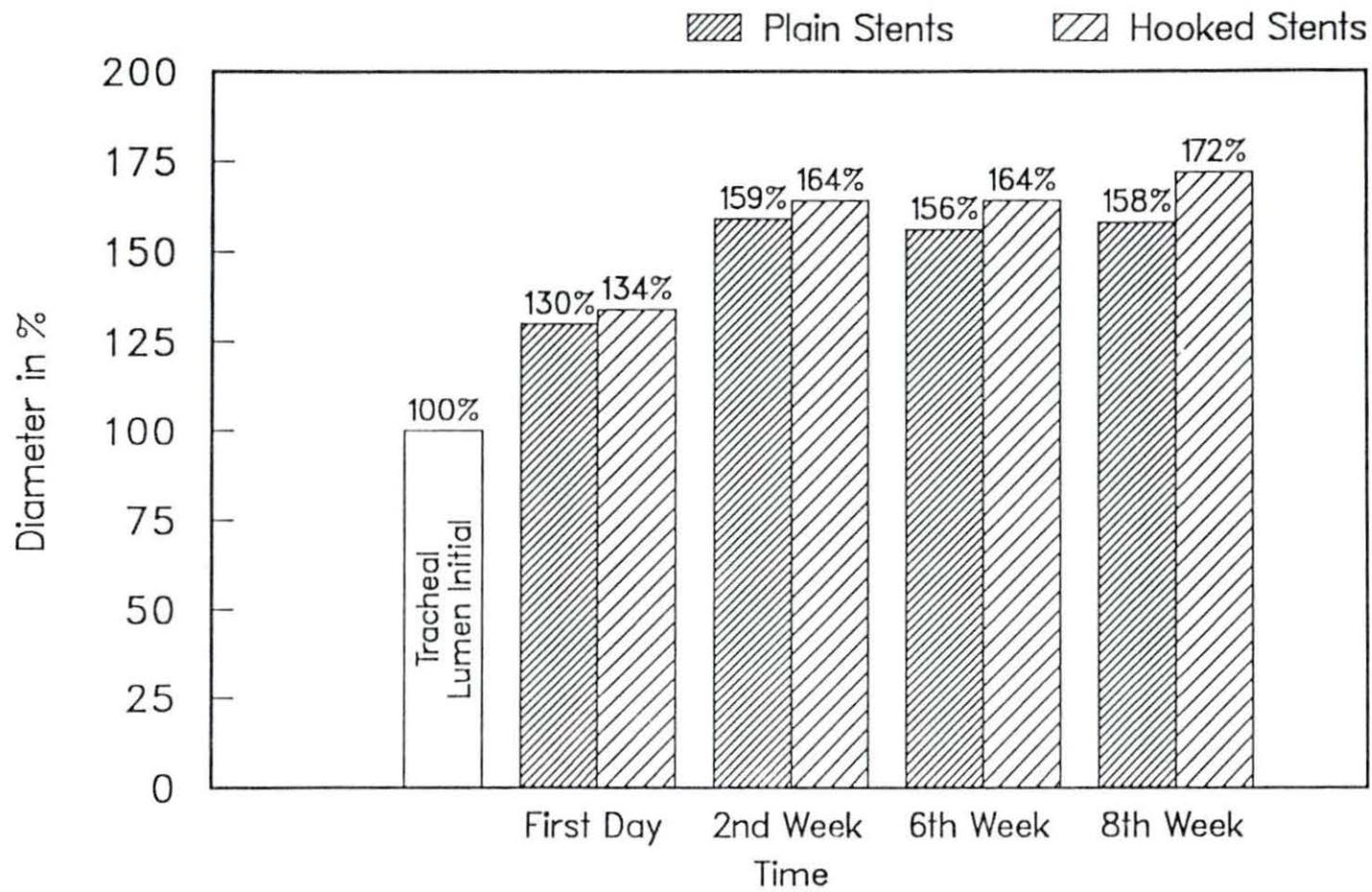


Figure 8.29: Phase 2: Mean diameter of the stents within the trachea

### 8.2.3 Pathological findings

**8.2.3.1 Gross pathology** When the trachea and the mediastinum were examined at necropsy there was no gross pathological difference found between the two groups. The stent could be easily identified since the trachea seemed dilated at that site. Figure 8.30, a photo of the thorax taken at the time of necropsy shows a trachea with a stent. In general the mediastinum was normal except in one dog (dog 3) with a hooked stent, which showed mediastinal adhesions along with many enlarged lymph nodes at the carina. In the same dog there was a severe tissue reaction causing lumen narrowing and mucosal irregularities. Invariably all the dogs had a thickened tracheal wall and six (three plain and three hooked) showed a dilated lumen with a smooth mucosal surface at the stent site. In dog 6 (plain stent) three mucosal nodules were seen at the cranial end of the stent while dog 2 (plain stent) had a single nodule; this confirmed the endoscopic findings. Dog 7, which had a flattened trachea with wider dorsal membrane, showed an uncovered loop protruding into the narrowed lumen as found during endoscopy. None of the dogs showed mucus accumulation in the trachea. Figure 8.31 and Figure 8.32 show the ventral and lateral views of the tracheal specimens of the plain stent group respectively while Figure 8.33 and Figure 8.34 are the ventral and lateral views of the tracheal specimens from the hooked stent group. Tracheograms of the specimens outline the details of the mucosal surface and indicate the tracheal wall thickness. Figure 8.35 and Figure 8.36 show the ventral and lateral views of the tracheogram pictures for the plain stent group while Figure 8.37 and Figure 8.38 are from the hooked stent group.



Figure 8.30: View of the thorax taken at the time of necropsy. Arrow shows the site of the stent; T - Trachea, L - Lungs

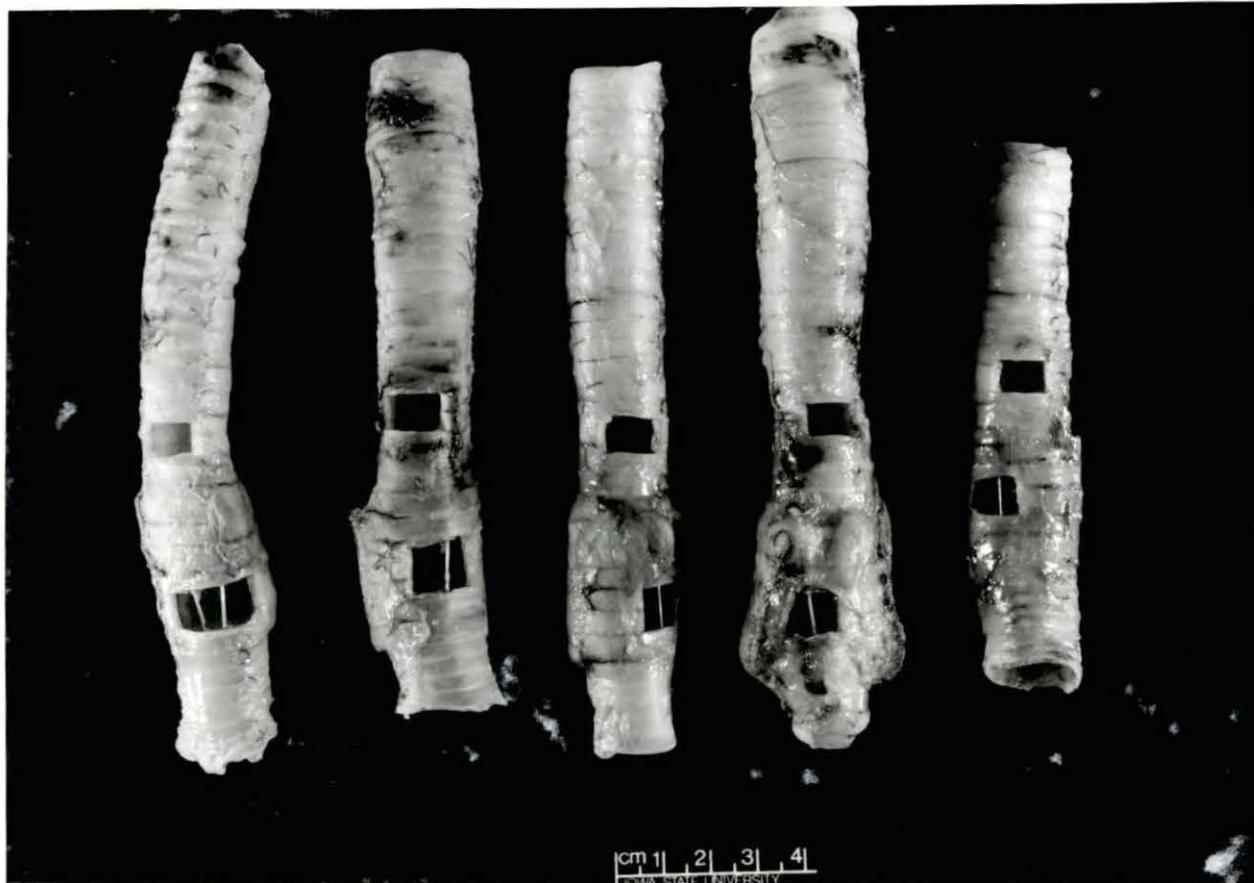


Figure 8.31: Phase 2, tracheal specimens of plain stent group: Ventral view. From left to right: Dog 2, dog 5, dog 6, dog 8, and dog 10



Figure 8.32: Phase 2, tracheal specimens of the plain stent group: Lateral view



Figure 8.33: Phase 2, tracheal specimens of the hooked stent group: Ventral view.  
From left to right: Dog 1, dog 3, dog 4, dog 7, and dog 9



Figure 8.34: Phase 2, tracheal specimens of the hooked stent group: Lateral view

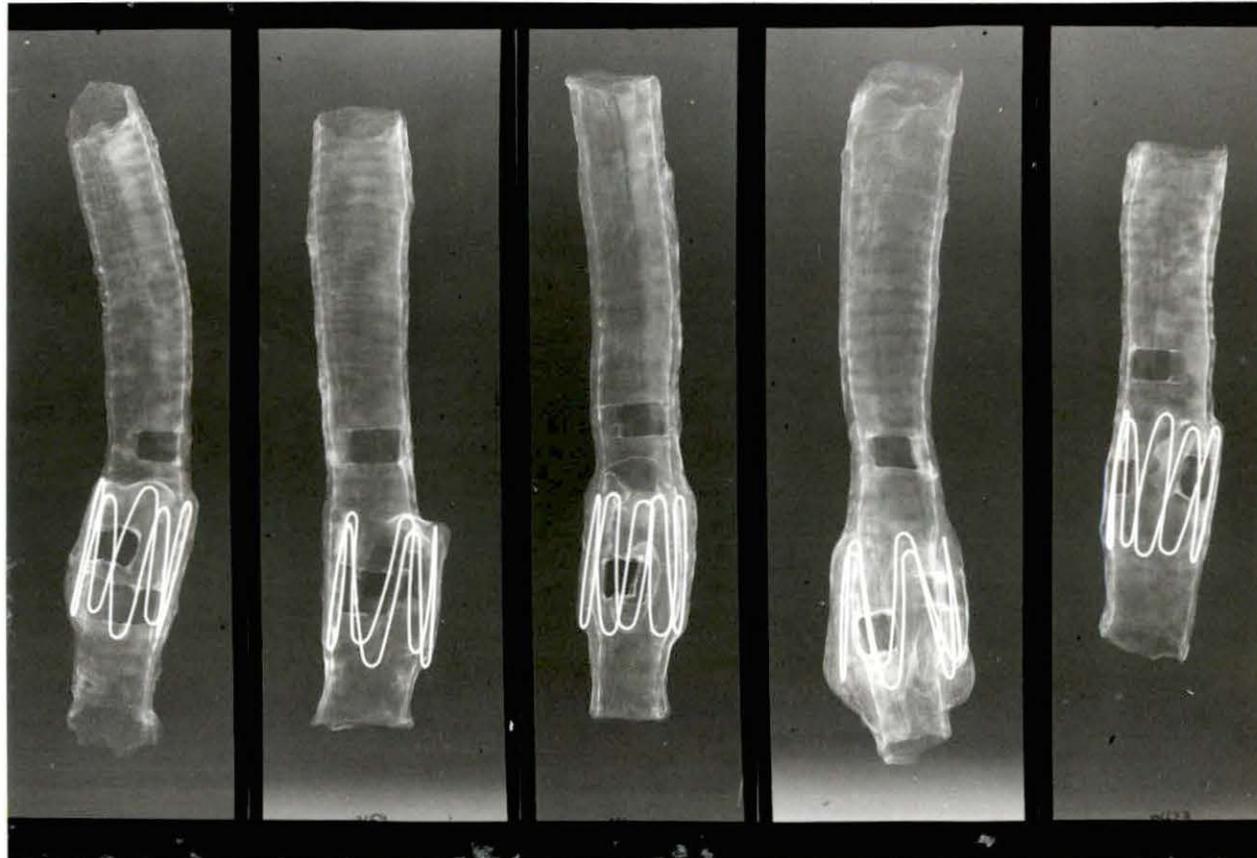


Figure 8.35: Phase 2, tracheogram of the plain stent group: Ventral view. From left to right: Dog 2, dog 5, dog 6, dog 8, and dog 10

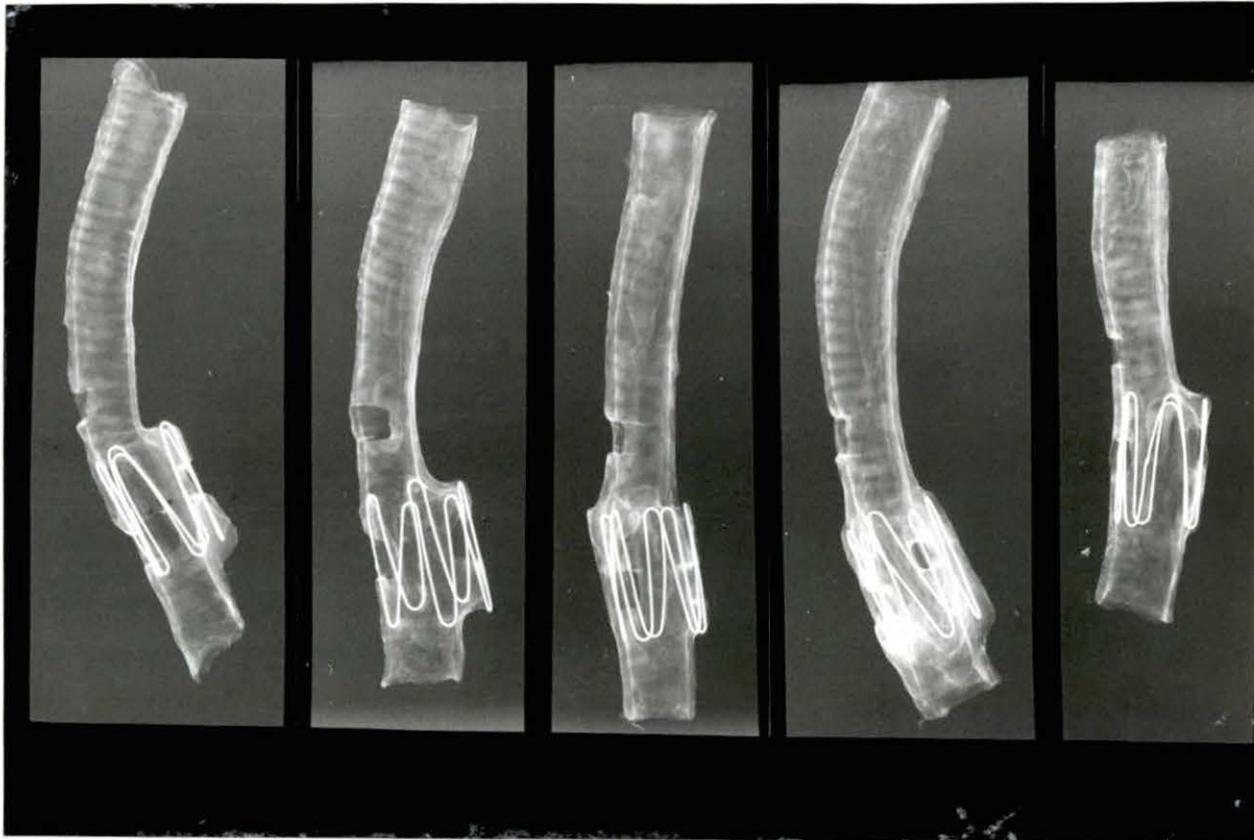


Figure 8.36: Phase 2, tracheogram of the plain stent group: Lateral view

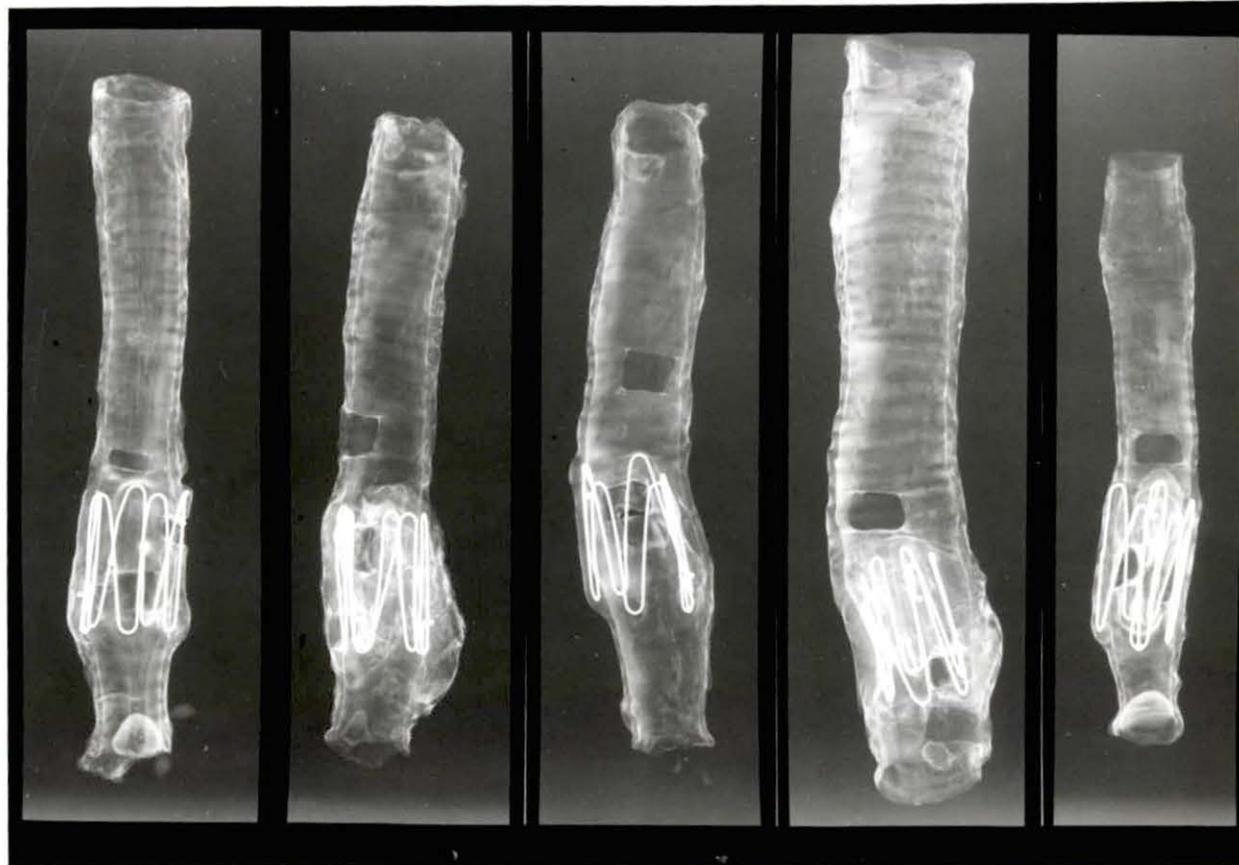


Figure 8.37: Phase 2, tracheogram of the hooked stent group: Ventral view. From left to right: Dog 1, dog 3, dog 4, dog 7, and dog 9



Figure 8.38: Phase 2, tracheogram of the hooked stent group: Lateral view

**8.2.3.2 Microscopic reaction** Microscopic lesions were very similar in nine of the ten dogs and were classified as chronic proliferative pyogranulomatous tracheitis of varying degrees, with lymphoid nodules (Table 12.8 and Table 12.9). The typical reaction around wires consisted of a small amount of cell debris and a purulent exudate immediately around the wires. The wire and cell debris were surrounded by a concentric band of immature granulation tissue infiltrated with a large numbers of neutrophils, macrophages, eosinophils, and plasma cells (Figure 8.39A). Mucosal edema and hyperemia were mild. Most sections contained variable numbers of lymphoid nodules within the mucosa and adventitia within several millimeters of the wires. infiltration of neutrophils between tracheal epithelial cells and other inflammatory cells in the lamina propria (Figure 8.39B). One of the ten dogs had an extremely mild tissue response to the stent wires. In this dog (dog 4), wires were surrounded by a thin layer of fibrous connective tissue with minimal cellular exudate (Figure 8.39B). The inflammatory reaction was particularly severe where the wires were in contact with the tracheal muscle or in sites of tracheal ring fracture (Figure 8.40A). There was also occasional necrosis of tracheal ring chondrocytes (Figure 8.40B). In some sections a clear to eosinophilic refractile material was surrounded by foreign body giant cells and purulent exudate to form the center of microgranulomas. This refractile material was interpreted to be possible coating from the wire stents.

The refractile materials occasionally found in the tissue sections were interpreted as possible coating from the wire stents. This indicated that the coating separated from the stents, probably when the stents were released from the tip of the metal delivery tube into the tracheal lumen, at the time of placement of the

stent in the trachea.

#### 8.2.4 Bacterial culture

Several organisms were cultured from the mucosal surface of the trachea, in both mixed and pure cultures. All ten dogs had positive cultures. The organisms isolated were alpha-hemolytic *Streptococcus*, *Bordetella bronchoseptica*, *Pseudomonas* spp, Micrococci and *Stahylococcus intermedius*. Among the above, *bordetella bronchoseptica* was predominant and was cultured in five of the ten dogs. Table 12.10 gives the details of the culture results.

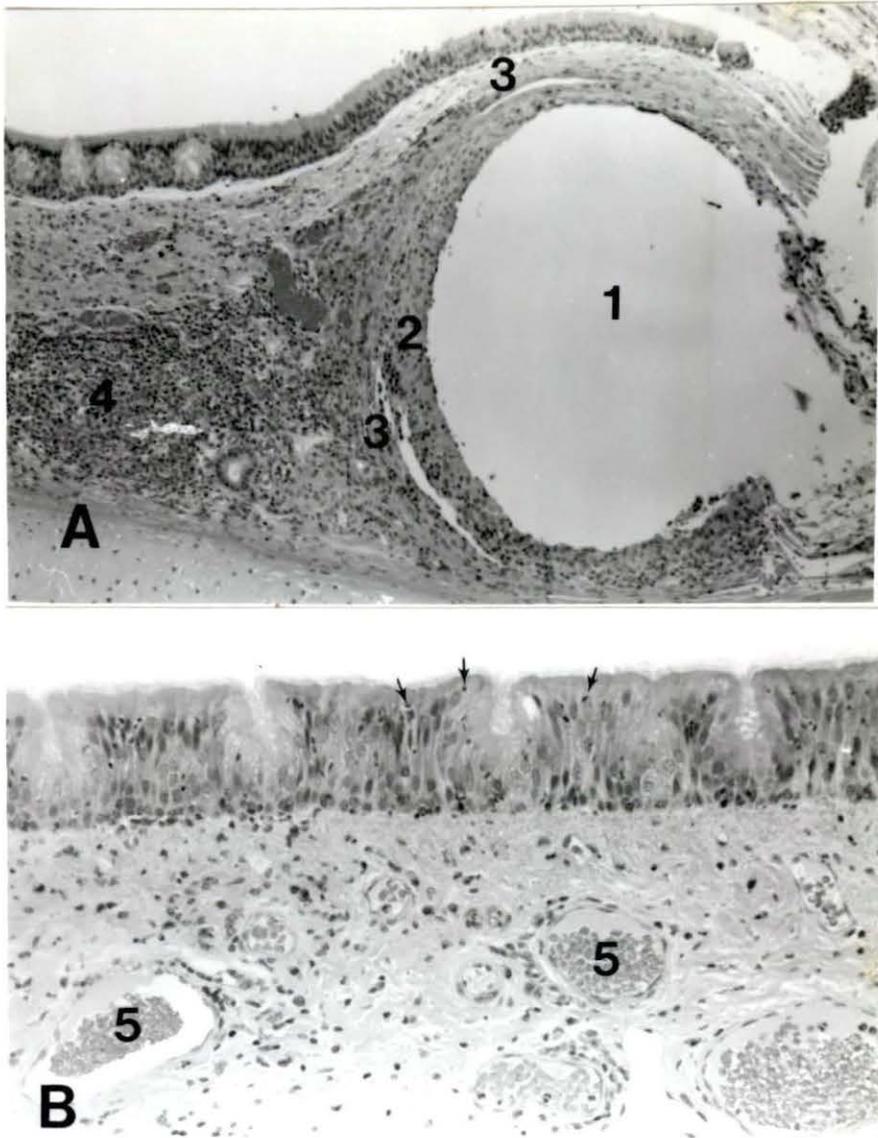


Figure 8.39: Mild tracheal tissue reaction to the stent wires in dogs 4 and 10. Figure A shows the round space (1) left by the stent wire in dog 10, surrounded by a zone of macrophages (2) and a thin band of mature fibrous connective tissue (3). Adjacent to the space, the lamina propria is thickened by a mild diffuse infiltration of mononuclear leukocytes and lymphoid nodules (4). Figure B shows the mild tissue reaction in dog 4, characterized by a mild infiltration of neutrophils (arrows) between tracheal epithelial cells, a diffuse mixture of inflammatory cells in the lamina propria, and dilated capillaries and venules (5)

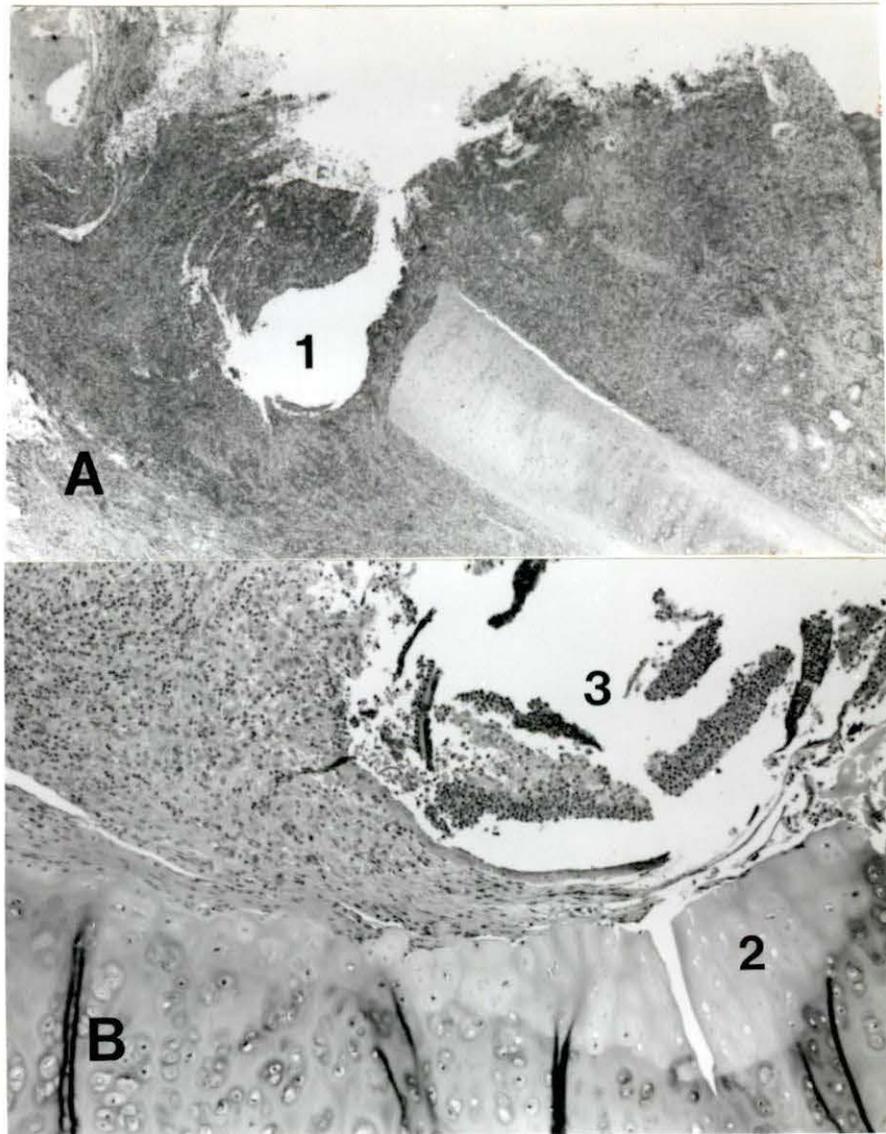


Figure 8.40: Severe tracheal tissue reactions to the stent wires in dogs 7 and 8. Figure A shows severe tissue reaction around ends of a fractured tracheal ring in dog 8. The round space (1) left by the stent wire is surrounded by a dense exudate consisting of neutrophils, macrophages, and lymphocytes supported by immature and developing granulation tissue. Figure B shows the necrosis of tracheal ring chondrocytes (2) in dog 7, adjacent to the space left by the stent wire (3). The dense pyogranulomatous exudate around the space is similar to that described in Figure A

## 9 DISCUSSION AND CONCLUSION

This research was begun as an attempt to devise a biocompatible stainless steel stent to be used as a prosthesis in tracheal collapse. Two stents were made of surgical<sup>1</sup> stainless steel based on the original Gianturco endovascular stent and were inserted into the trachea of two normal dogs. These trials were not successful because the stainless steel stents failed to expand in the trachea after they had been compressed for insertion and hence they moved freely within the trachea. A stent made of spring steel was designed; it expanded satisfactorily when introduced in a trial dog. Since movement of the stents after insertion needed to be minimized, the stents produced for the experimental study were made of spring steel. They were coated with silicone rubber for biocompatibility. Some of the stents had hooks attached to determine if this would further reduce the stent movement.

**In Phase 1**, the acute reaction elicited by the stents seemed severe, and there were occasional ring fractures. This severe reaction was localized and may have been caused by overdistention of the trachea. Though the mucosa ulcerated at the contact sites in the beginning, the stents were partially covered in two weeks by the regrowing mucosa. The associated disruption of the mucociliary function of the trachea in the first few days, due to mucosal cell attenuation and loss of cilia, was

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<sup>1</sup>Kirshner wire.

also regained after the first week. Some dogs developed coughing in the first two weeks which may have aided the function of the cilia. This coughing may also be due to tracheitis and the irritation caused by the stents. The hooked stents used in Phase 1 experienced a change in their expansile property, a cone like formation of the stent occurred after two weeks. This change was probably due to weakening at the point where the hook was welded to the stent. This weakening caused a narrow loop angle which in turn resulted in a widening of the opposite end (the end without the hooks). In this phase the hooked stents moved less than the plain stents. Moreover one of the plain stents moved 10 cm, showing the plain stents instability. The results of this phase gave an initial indication of the adequacy of the stent design and of the clinical and pathological reactions that would be elicited in the long-term phase (Phase 2).

**In Phase 2** to control overdilatation, the stents were made smaller with fewer loops. The hooked stents were constructed with hooks on each end to prevent the cone-like disfiguring that occurred in the first phase. The problem was only partially solved since weak sites remained at the welding points. For this reason some of the hooked stents would not stay perfectly cylindrical.

*Tracheal endoscopy* showed nodules at the ends of the stents in two dogs with a plain stent and in one dog with a hooked stent. Histologically these nodules were found to be granulomatous lumps. The mucosal covering of the stents was found to be complete on the dorsal aspect of the trachea, where the trachealis muscle is present.

*The internal tracheal diameter* at the stent level increased to approximately 125% of the initial value in the first two weeks for both the groups; it decreased in

the next few weeks probably due to tissue reaction resulting in a thickened tracheal wall. The unique behavior of the trachea at various levels (cranial end, center and caudal end) within that section (at the stent level) could not be explained.

*The tracheal lumen diameter cranial to the stent* was significantly different between the two groups. one of the very few that was found. The reason for this difference is unclear because histopathological study revealed the same reaction, diffuse fibrosis in the lamina propria at this level of the trachea, in both the stent groups.

*The actual stent diameter* within the lumen progressively increased during the eight week period for both plain and hooked stent groups. At the end of the study the stent diameter expressed as a percent of the initial tracheal lumen diameter remained higher (172%) for the hooked stents than for the plain stents (158%), but the difference was not significant. This difference may be due to the difference in the mean initial lumen diameter of the two groups of dogs used. The plain stent group dogs had a mean initial dv diameter of 1.36 cm while it was 1.22 cm for the hooked stent group (statistically they were found to be comparable groups). This is also supported by the fact that the actual diameter measurements (in cm) after eight weeks remained lower for the hooked stents (2.05 cm) than the plain stents (2.13 cm).

In Phase 2, of the seven stents that migrated from the original site of placement, six moved caudally. This is in contrary to the Phase 1 stents in which cranial movement was predominant. This shows that the stents have the tendency to move in both directions. Though three of the five hooked stents moved in this phase, the migration was found to be insignificant statistically.

There was no difference in the pathological reaction elicited by the stents between the two groups. It was evident that even in a dog that developed a severe reaction to the stent, the reaction was localized to a short tracheal segment. The absence of mucus accumulation in the trachea indicated normal mucociliary function. Dog 3 had a hooked stent and developed a severe reaction with tracheal ring fracture and enlarged mediastinal lymph nodes. One possible explanation could be that the stent was found to be much larger than the dog's trachea. This dog was the smallest of the ten dogs used in phase 2 and after eight weeks the ratio of the initial lumen diameter to the stent diameter was 1:2.13; this was probably too high. Dog 8 had a plain stent and also developed a severe reaction due to overdistention; lumen/stent ratio was 1:1.96. Dog 7 (lumen/stent ratio was 1:1.44) had a hooked stent and developed a severe reaction similar to dogs 3 and 8. This may be partially attributable to the fact that the stent failed to completely contact the mucosal surface which is necessary for mucosal covering. Later it was found that the orientation of the stent was not aligned perfectly with that of the trachea, which could have happened at the time of placement. Also as mentioned earlier, the hooked stent was not perfectly cylindrical. All these factors added together probably elicited a severe tissue reaction in an attempt to bridge the gap between the wall and the stent. In the other dogs the lumen/stent ratio varied from 1:1.37 to 1:1.59 except in dog 9 which had a ratio of 1:1.91 and these dogs showed mild to moderate reaction.

The refractile materials occasionally found in the tissue sections were interpreted as the coating from the wire stents. This indicated that the coating separated from the stents, probably when the stents were released from the tip of the metal delivery tube, into the tracheal lumen, at the time of placement of the stent

in the trachea. The cell reactions that were seen surrounding the coating materials were probably caused by the microorganisms. All the dogs had positive bacterial cultures of the trachea. Some of the organisms cultured were normal inhabitants of the oral cavity and upper respiratory tract.

In this study, though the stents elicited severe microscopic reactions, they were mostly localized and may have been due to a high lumen/stent diameter ratio. In spite of the tissue reactions, the stents dilated the trachea in most of the cases. The degree of reaction may be controlled by increasing the lumen/stent ratio. In this experimental study, there were few advantages of using hooked stents. The controlled displacement and dilated tracheal lumen cranial to the stent level were insufficient to support the use of the hooked stents over the plain stents.

With these results the experimental study could be extended using a controlled expansion stent in:

- differing stent/lumen ratios
- experimental dogs for much longer periods
- dogs with surgically simulated tracheal collapse
- severe clinical cases, as a life supporting measure.

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11 APPENDIX A

Table 11.1: Phase 1: Tracheal lumen (TL) and stent measurements for groups 1 and 2

Group no.	Dog no.	No. of days	Stent type	Displacement (cm)	Initial TL cranial to the stent (cm)	TL within stent		Final TL cranial to the stent (cm)	Stent diameter	
						Initial (cm)	Final (cm)		Initial (cm)	Final (cm)
1	1	3	plain	+ <sup>a</sup> 10.0	1.60	1.85	2.40	1.70	1.85	2.50
	2	3	plain	+2.2	1.90	2.20	2.30	1.80	2.20	2.30
2	3	8	hooked	0.0	1.20	1.20	1.65	1.40	1.40	1.65
	4	8	hooked	+0.5	1.30	1.60	1.90	1.35	1.60	1.90
	5	8	plain	+2.0	1.30	1.70	2.50	1.30	1.70	2.50

<sup>a</sup>Denotes cranial displacement.

Table 11.2: Phase 1: Tracheal lumen (TL) and stent measurements for groups 3 and 4

Group no.	Dog no.	No. of days	Stent type	Displacement (cm)	Initial TL cranial to the stent (cm)	TL within stent			Final TL cranial to the stent (cm)	Stent diameter		
						Initial (cm)	inter-mediate <sup>a</sup> (cm)	Final (cm)		Initial (cm)	Inter-mediate (cm)	Final (cm)
3	6	18	hooked	+ <sup>b</sup> 0.5	1.30	1.75	2.10	2.15	1.30	1.75	2.10	2.15
	7	18	hooked	+0.4	1.55	2.10	2.10	1.80	1.50	2.10	2.15	2.00
	8	18	plain	- <sup>c</sup> 0.2	1.25	1.90	1.70	1.75	1.45	1.90	2.00	2.30
	9	18	plain	0.0	1.65	2.10	2.10	2.20	1.90	2.10	2.20	2.40
4	10	25	plain	+1.5	1.40	2.20	2.30	2.10	1.40	2.20	2.20	2.40

<sup>a</sup>Intermediate measurements were taken on the eighth day for group 3 dogs and on the fifteenth day for the group 4 dog.

<sup>b</sup>Denotes cranial displacement.

<sup>c</sup>Denotes caudal displacement.

Table 11.3: Phase 1: The initial and final tracheal lumen (TL) and stent measurements in percentages of initial tracheal diameter two cm cranial to stent

Group no.	Dog no.	No. of days	Stent type	Displacement (cm)	TL at stent level		Final TL cranial to stent (%)	Stent diameter	
					Initial (%)	Final (%)		Initial (%)	Final (%)
1	1	3	plain	+ <sup>a</sup> 10.0	116	150	106	116	156
	2	3	plain	+2.2	116	121	95	116	121
2	3	8	hooked	0.0	100	138	117	117	138
	4	8	hooked	+0.5	123	146	104	123	146
	5	8	plain	+2.0	131	192	100	131	192
3	6	18	hooked	+0.5	135	165	100	135	165
	7	18	hooked	+0.4	135	116	97	135	165
	8	18	plain	-0.2 <sup>b</sup>	152	140	116	152	184
	9	18	plain	0.0	128	133	115	127	145
4	10	25	plain	+1.5	157	150	100	157	171

<sup>a</sup>Cranial displacement.

<sup>b</sup>Caudal displacement.

Table 11.4: Phase 1: Microscopic reaction in the trachea at the stent level for various time periods

Group no.	Dog no.	No of days	Mucosal thickness/ Nodularity	Tracheal rings/ Trachealis muscle	Lamina propria				
					Necrosis	Edema	Exudate composition	Lymphoid response	Fibrosis
1	1	3	500 $\mu\text{m}$	acute inflam. of trachealis muscle	yes	yes	N <sup>a</sup> , few M <sup>b</sup>	no	no
	2	3	1.1 mm	acute inflam. of adventicia	yes	yes	N, few M	no	no
2	3	8	300 $\mu\text{m}$	normal	no	no	minimal; N, M	no	yes
	4	8	700 $\mu\text{m}$	inflammation of trachealis muscle	no	slight around wires	L <sup>c</sup> , M, N, Pc <sup>d</sup>	no	yes
	5	8	1.4 mm	severe inflam.; necrosis of muscle and adventicia	yes	yes	N, L, M	no	yes

<sup>a</sup>Neutrophils.

<sup>b</sup>Macrophages.

<sup>c</sup>Lymphocytes.

<sup>d</sup>Plasma cells.

Table 11.4: Continued

Group no.	Dog no.	No of days	Mucosal thickness/ Nodularity	Tracheal rings/ Trachealis muscle	Lamina propria				
					Necrosis	Edema	Exudate composition	Lymphoid response	Fibrosis
3	6	18	300 $\mu$ m	hyperplastic perichondrium ; muscle bulged	around wires	no		yes small	yes mature
	7	18	2.5 mm	muscle infiltrated; obliterated by fibrosis;	no	no	N,M,L,Pc	numerous	extensive
	8	18	300 $\mu$ m few nodules	chronic inflam. extending into adventicia and muscle	no	no	N,M,L	no	extensive
	9	18	1.8 mm	chronic inflam. extending through ring and muscle	around wires wires	mild	pyogranulomatous	few	moderate
4	10	25	6 mm	fractured rings	around wires	multifocal	severe; N,M	some	severe

12 APPENDIX B

Table 12.1: Phase 2: Internal tracheal *dv* diameter at the stent level for plain stent group

Dog no	Diameter at	First day		2 Weeks		6 Weeks		8 Weeks	
		cm	%	cm	%	cm	%	cm	%
2	cranial end	1.50	107.1	1.50	107.1	1.40	100	1.35	96.4
	center	1.60	114.3	1.90	135.7	1.75	125.0	1.80	128.6
	caudal end	1.55	110.7	1.70	121.4	1.30	92.9	1.30	92.9
	average	1.55	110.7	1.70	121.4	1.48	105.9	1.48	105.9
5	cranial end	1.50	115.4	1.70	130.8	1.40	107.7	1.50	115.4
	center	1.80	138.5	2.30	176.9	1.90	146.2	2.10	161.5
	caudal end	1.60	123.1	1.80	138.5	1.50	115.4	1.50	115.4
	average	1.63	125.6	1.93	148.7	1.60	114.3	1.70	121.4
6	cranial end	1.60	114.3	0.90	64.3	1.75	125.0	1.30	92.9
	center	1.60	114.3	1.70	121.4	1.65	117.9	1.90	135.7
	caudal end	1.60	114.3	1.40	100.0	1.30	92.9	1.60	114.3
	average	1.60	114.3	1.33	95.2	1.52	108.4	1.60	114.7
8	cranial end	1.70	141.6	1.30	108.3	1.00	83.3	1.30	108.3
	center	1.70	141.6	2.00	166.7	1.60	133.3	1.60	133.3
	caudal end	1.50	125.0	2.00	166.7	1.50	125.0	1.05	87.5
	average	1.63	136.1	1.77	147.3	1.37	114.2	1.32	109.8
10	cranial end	1.50	100.0	1.80	120.0	1.70	113.3	1.70	113.3
	center	1.70	113.3	2.10	140.0	1.90	126.7	2.00	133.3
	caudal end	1.70	113.3	1.90	126.7	1.80	120.0	1.60	106.7
	average	1.63	108.9	1.93	128.9	1.80	120.0	1.77	117.8
mean		1.61	119.1	1.73	128.3	1.55	112.6	1.57	113.8
SEM <sup>a</sup>		-	5.142	-	9.799	-	2.477	-	2.760

<sup>a</sup>Standard error of the mean.

Table 12.2: Phase 2: Internal tracheal *dv* diameter at the stent level for the hooked stent group

Dog no	Diameter at	First day		2 Weeks		6 Weeks		8 Weeks	
		cm	%	cm	%	cm	%	cm	%
	cranial end	1.30	104.0	1.35	108.0	1.40	112.0	1.20	96.0
	center	1.50	120.0	1.60	128.0	1.40	112.0	1.30	104.0
	caudal end	1.40	112.0	1.50	120.0	1.50	120.0	1.40	112.0
	average	1.40	112.0	1.48	118.6	1.43	114.6	1.30	104.0
3	cranial end	1.10	110.0	1.30	130.0	1.00	100.0	0.55	55.0
	center	1.40	140.0	1.70	170.0	0.95	95.0	0.80	80.0
	caudal end	1.40	140.0	1.60	160.0	1.80	180.0	1.40	140.0
	average	1.30	130.0	1.53	153.0	1.25	125.0	0.92	92.0
4	cranial end	1.10	100.0	1.30	118.2	1.20	109.1	1.10	100.0
	center	1.25	113.6	1.40	127.3	1.45	131.8	1.20	109.1
	caudal end	1.25	113.6	1.30	118.2	1.15	104.5	1.40	127.3
	average	1.20	109.1	1.33	121.2	1.27	115.2	1.23	111.8
7	cranial end	1.70	100.0	1.70	100.0	1.70	100.0	1.10	64.7
	center	2.10	123.5	2.15	126.0	1.50	88.0	1.20	70.5
	caudal end	2.30	135.3	2.00	117.6	1.90	111.8	1.85	108.8
	average	2.17	128.0	1.95	114.7	1.70	100.0	1.38	81.4
9	cranial end	1.15	109.5	- <sup>a</sup>	-	1.50	142.9	1.60	152.4
	center	1.50	142.9	-	-	1.40	133.3	1.50	142.9
	caudal end	1.30	123.8	-	-	1.20	114.3	1.40	133.3
	average	1.32	125.5	-	-	1.37	130.2	1.50	142.9
mean diameter		1.48	120.9	1.57	126.9	1.40	117.0	1.27	106.4
SEM <sup>b</sup>		-	4.318	-	8.810	-	5.178	-	10.486

<sup>a</sup>Exact measurements could not be taken due to the poor quality of the radiographs.

<sup>b</sup>Standard error of the mean.

Table 12.3: Phase 2: Internal tracheal *dv* diameter two cm from the stent

Stent type	Dog no	First day		2 Weeks		6 Weeks		8 Weeks	
		cm	%	cm	%	cm	%	cm	%
plain	2	1.40	100.0	1.20	85.7	1.30	92.9	1.40	100.0
	5	1.30	100.0	1.20	92.3	1.15	88.5	1.25	96.2
	6	1.40	100.0	1.00	71.4	1.20	85.7	1.25	89.3
	8	1.20	100.0	1.20	100	1.15	95.8	1.05	87.5
	10	1.50	100.0	1.40	93.3	1.40	93.3	1.30	86.7
mean		1.36	100	1.20	88.5	1.24	91.2	1.25	91.9
SEM <sup>a</sup>		0.050	-	-	4.847	-	1.816	0.057	2.619
hooked	1	1.25	100.0	1.25	100.0	1.25	100.0	1.25	100.0
	3	1.00	100.0	1.15	115.0	1.15	115.0	1.30	130.0
	4	1.10	100.0	1.15	104.5	1.20	109.1	1.25	113.6
	7	1.70	100.0	1.70	100.0	1.75	103.0	1.80	105.9
	9	1.05	100.0	1.05	100.0	1.30	123.8	1.60	152.4
mean		1.22	100	1.26	103.9	1.33	110.2	1.44	120.4
SEM		0.127	-	-	2.908	-	4.272	0.111	9.457

<sup>a</sup>Standard error of the mean.

Table 12.4: Phase 2: *Dv* diameter of tracheal lumen (TL) and the stent after eight weeks for the plain stent group

Dog no.	Values in	TL cranial to the stent Initial	TL within stent 8 weeks later				TL cranial to the stent Final	Stent diameter	
			Cranial end	Center	Caudal end	Average		First day	Final
2	cm	1.40	1.35	1.80	1.30	1.48	1.40	1.65	2.05
	%	100.0	96.4	128.6	92.9	105.9	100.0	117.9	146.4
5	cm	1.30	1.50	2.10	1.50	1.70	1.25	1.78	2.15
	%	100.0	115.4	161.5	115.4	121.4	96.2	127.0	153.6
6	cm	1.40	1.30	1.90	1.60	1.60	1.25	1.65	2.05
	%	100.0	92.9	135.7	114.3	114.3	89.3	117.9	146.4
8	cm	1.20	1.30	1.60	1.05	1.32	1.05	1.90	2.35
	%	100.0	108.3	133.3	87.5	109.8	87.5	158.3	195.8
10	cm	1.50	1.70	2.00	1.60	1.77	1.30	1.80	2.05
	%	100.0	113.3	133.3	106.7	117.8	86.7	120.0	136.7
mean	%	100.0	105.3	138.5	103.4	113.8	91.9	128.0	155.8

Table 12.5: Phase 2: *Dv* diameter of tracheal lumen (TL) and the stent after eight weeks for the hooked stent group

Dog no.	Values in	TL cranial to the stent Initial	TL within the stent 8 weeks later				TL cranial to the stent Final	Stent diameter	
			Cranial end	Center	Caudal end	Average		First day	Final
1	cm	1.25	1.20	1.30	1.40	1.30	1.25	1.45	1.90
	%	100.0	96.0	104.0	112.0	104.0	100.0	116.0	152.0
3	cm	1.00	0.55	0.80	1.40	0.92	1.30	1.50	2.13
	%	100.0	55.0	80.0	140.0	92.0	130.0	150.0	212.5
4	cm	1.10	1.10	1.20	1.40	1.23	1.25	1.35	1.75
	%	100.0	100.0	109.1	127.2	111.8	113.6	122.7	159.0
7	cm	1.70	1.10	1.20	1.85	1.38	1.80	2.15	2.45
	%	100.0	64.7	70.6	108.8	81.4	105.9	126.5	144.1
9	cm	1.05	1.60	1.50	1.40	1.50	1.60	1.60	2.00
	%	100.0	152.4	142.9	133.3	142.6	152.4	152.4	190.5
mean	%	100.0	93.6	101.3	124.3	106.3	120.4	133.5	171.6

Table 12.6: Phase 2: Stent diameter within the trachea during the eight week period

Stent type	Dog no	First day		2 Weeks		6 Weeks		8 Weeks	
		cm	%	cm	%	cm	%	cm	%
plain	2	1.65	117.9	2.05	146.4	2.05	146.4	2.05	146.4
	5	1.78	136.9	2.40	184.6	2.25	173.0	2.15	165.4
	6	1.65	117.9	2.00	142.9	2.05	146.4	2.05	146.4
	8	1.90	158.3	2.10	175.0	2.10	175.0	2.35	195.8
	10	1.80	120.0	2.20	146.7	2.10	140.0	2.05	136.7
mean		1.75	130.2	2.15	158.9	2.11	156.2	2.13	158.1
SEM <sup>a</sup>		0.048	7.877	-	8.603	-	7.383	0.058	10.503
hooked	1	1.45	116.0	1.85	148.0	1.90	152.0	1.90	152.0
	3	1.50	150.0	1.90	190.0	1.95	195.0	2.13	213.0
	4	1.35	122.7	1.48	134.5	1.60	145.5	1.75	159.0
	7	2.15	126.5	2.40	141.2	2.40	141.2	2.45	144.1
	9	1.60	152.4	2.15	204.8	1.98	188.6	2.00	190.5
mean		1.61	133.5	1.96	163.7	1.97	164.5	2.05	171.7
SEM		0.140	7.420	-	14.117	-	11.330	0.118	12.981

<sup>a</sup>Standard error of the mean.

Table 12.7: Phase 2: Displacement measurements of the stents

Type of stent	Dog no.	0-2 Weeks (cm)	3-6 Weeks (cm)
plain	2	- <sup>a</sup> 0.9	- 0.3
	5	-1.6	0.0
	6	-1.5	0.0
	8	-1.0	0.0
	10	0.0	0.0
mean		1.0	0.06
SEM <sup>b</sup>		0.284	0.328
hooked	1	+ <sup>c</sup> 0.8	0.0
	3	-1.0	0.0
	4	0.0	0.0
	7	-1.0	0.0
	9	0.0	0.0
mean		0.56	0.0
SEM		0.231	0.199

<sup>a</sup>Caudal displacement.

<sup>b</sup>Standard error of the mean.

<sup>c</sup>Cranial displacement.

Table 12.8: Phase 2: Microscopic reaction of the trachea in the plain stent group after eight weeks

Dog no.	Mucosal thickness/ Nodularity	Tracheal rings/ Trachealis muscle	Lamina propria				
			Necrosis	Edema	Exudate composition	Lymphoid response	Fibrosis
2	1.4 mm one nodule 3 mm size	normal	no	no	focal: N <sup>a</sup> , M <sup>b</sup>	few, one is large	diffuse and around wires
5	1.5 mm	focal cartilage necrosis	around wires	no	moderate M, Pc <sup>c</sup>	sparse, small in lamina propria	mild nodular
6	0.6 mm 2 nodules 1-3 mm size	mild, focal cartilage necrosis	no	no	focal around spaces, M, N, L <sup>d</sup>	moderate	mild focal
8	4 mm irregular mucosa	chronic infl. extends into adventicia through ring fracture	around wires	no	pyogranulomatous with lymphoid nodules	numerous nodules	extreme
10	0.5 mm	normal	no	no	M with lymphoid nodules	moderate number	mild concentric

<sup>a</sup>Neutrophils.

<sup>b</sup>Macrophages.

<sup>c</sup>Plasma cells.

<sup>d</sup>Lymphocytes.

Table 12.9: Phase 2: Microscopic reaction of the trachea in the hooked stent group at eight weeks

Dog no.	Mucosal thickness/ Nodularity	Tracheal rings/ Trachealis muscle	Lamina propria				
			Necrosis	Edema	Exudate composition	Lymphoid response	Fibrosis
1	1.5 mm nodule 3 mm	normal	minimal	mild	moderate; N <sup>a</sup> , M <sup>b</sup>	small, well demarcated	mature
3	1.4 mm	ring fracture with fibrosis extending into adventicia	no	no	N, M, L <sup>c</sup> , E <sup>d</sup> and globule leukocytes	moderate	severe
4	0.5 mm	normal	no	no	none	none	mild diffuse
7	4 mm irregular	chronic infla. extending into	around wires	mild	severe pyogranulomatous	few	severe nodular
9	0.6 mm	minimal	no	no	M, L	small numbers	moderate

<sup>a</sup>Neutrophils.

<sup>b</sup>Macrophages.

<sup>c</sup>Lymphocytes.

<sup>d</sup>Eosinophils.

Table 12.10: Phase 2: Microorganisms cultured from the trachea at the stent level, at necropsy

Microorganisms cultured in the trachea	Dogs with plain stents					Dogs with hooked stents				
	2	5	6	8	10	1	3	4	7	9
<i>Bordetella bronchoseptica</i>			+++ <sup>a</sup>	+ <sup>b</sup>	+++		++ <sup>c</sup>			+++
<i>Pseudomonas</i> spp						+++			+	
Micrococci	+	+								
<i>Staphylococcus intermedius</i>				+					+	
$\alpha$ -Haemolytic streptococcus									+	
Mixed growth							++	+++		

<sup>a</sup>abundant.

<sup>b</sup>few.

<sup>c</sup>heavy infection.

### 13 ACKNOWLEDGEMENT

I would like to express my appreciation to my major professor, Dr. Dean H. Riedesel for giving me the opportunity to conduct this research, and for his support and guidance throughout this work. I would like to thank Dr. Larry Arp for his services and guidance towards this research. Also I would like to thank Dr. Mary Helen Greer for the financial support and guidance, and Dr. Raymond T. Greer for his suggestions regarding the stent coating. In addition, I would like to thank Dr. Robert W. Carithers and Dr. F. Hembrough for serving on my program of study committee, Dr. Elizabeth A. Riedesel for the valuable suggestions and guidance regarding the radiographs, Dr. C. Charmsangavej for his suggestion regarding the stent design, Mr. Ivan C. Alexander for making the stents, and the surgery room staff, at the Small Animal Hospital, ISU, for their assistance.

Finally, I would like to thank my parents-in-law for their understanding and patience while I was writing the thesis and my husband for the support and encouragement. I like to dedicate this work to my daughter Raathai and my husband Molian.