Oesophageal Cancer in rural South Africa:

Challenges in diagnosis and an alternate technique of stent placement for timely palliation in a resource-constrained environment

By

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Submitted in fulfillment of the academic requirements

for the degree of MMedSc

in the Department of Surgery

School of Clinical Medicine

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Durban

2016

As the candidate's supervisors we have approved this thesis for submission.

Signed: _____ Name: _____ Date: _____

Signed: _____ Name: _____ Date: _____

Dedication

To my parents and family who stood by me through thick and thin and never wavered in their belief in me. Thank you for being my biggest supporters.

Thank you for understanding those many years where work and studying came first.

Your sacrifices and faith in me do not go unappreciated. You are the reason I got where I am in life and I am forever in your debt.

Thank you.

Declaration

I , Morganayagi Govender declare that

(i) The research reported in this dissertation, except where otherwise indicated, is my original work.

(ii) This dissertation has not been submitted for any degree or examination at any other university.

(iii) This dissertation does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledged as being sourced from other persons.

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Acknowledgements

Many thanks to my supervisors, Damian Clarke and Colleen Aldous for their guidance and support through the often murky waters of writing an MMed Sci thesis. Your never-ending patience with this fledging researcher was most appreciated. I got there eventually…but I could not have done it without your experience and words of support to guide me. The effort you put into helping me achieve this goal is most appreciated. Thank you.

A special mention goes to Mr V Govindasamy for his IT assistance. And a big thank you to my colleagues at Greys hospital, Mr V Nair and Mr L Ferndale, who helped with proofreading and constructive criticism and allowed me the time off from clinical duties to achieve my deadlines. It's an honour to be part of this team.

Executive Summary

The incidence of oesophageal cancer in KwaZulu-Natal is high and despite advances in management, it remains a disease with dismal outcomes. Most patients in the public health sector present with advanced tumours and can only be offered palliation.

The research project reviewed our current experience with the disease and highlighted long delays in presentation and lack of access to appropriate palliative therapies. In light of this we then reviewed our processes of care to see if we could improve access to palliative care.

One of the strategies identified was to increase access to self-expanding metal stent (SEMS) insertion by refining the process of placing these stents. Once this process had been refined and streamlined we audited our experience with it to show that our approach is safe and effective and then we costed it to show that it is associated with marked cost savings in comparison to others techniques.

The first paper in this thesis observed that there were long delays in the diagnosis and management of oesophageal cancer. This study attempted to quantify the delay as well as identify factors behind it. A cohort of patients with oesophageal cancer was analysed and a timeline plotted from first symptom, to presentation at base hospital, all the way through to definitive management at a tertiary centre. Points of delay were defined and reasons behind it were explored. It was postulated that by understanding the reasons behind the delay, we could identify points of impact and encourage earlier presentation. Only by significantly reducing delays can we hope to impact on the management and long term outcomes of this cancer.

The second paper of this thesis focused on the use of SEMS for palliation of dysphagia in inoperable oesophageal cancer in our setting. In most institutions this procedure is performed under fluoroscopy, a resource that is not readily available at our institution. To obviate the delays that this meant for our patients, we have been using a direct-vision approach which does not require fluoroscopy. This paper documented our experience with this alternative technique and showed that it is both safe and effective

It audited our extensive experience with this modified technique at the Gastrointestinal Unit at Greys hospital over a period of five years. We described our pure endoscopic technique and compared our experience with other large studies using similar and alternate techniques.

The final paper in this thesis describes a cost analysis of both techniques. It goes on to show that the pure endoscopic technique is safe and effective and is associated with significant cost savings in comparison to the standard fluoroscopy-driven technique performed at another tertiary centre in our province.

It is hoped that by showing that our direct vision technique is safe, effective and cost efficient, we can pave the way for this procedure to become the standard practice in a resource constrained health system. This would allow the procedure to be performed at many regional centres and not be restricted to tertiary centres only, ultimately improving access and delivering more timely palliation.

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Chapter 1 : Introduction

Oesophageal cancer is a devastating disease. It is one of the least studied and most lethal cancers worldwide and ranks sixth among all cancers globally in terms of mortality[1]. Despite advances in its management, the overall 5-year survival is still low (17%)[5]. At the time of presentation, more than 50% of patients have metastatic disease, nearly 30% have a tumour that is locally advanced and less than 20% have an early lesion that can be cured [5]

The burden of oesophageal cancer in South Africa is equally devastating, with the number of cancer-related deaths second only to cervical cancer.[1] In Sub-Saharan Africa, the annual mortality from oesophageal cancer is close to the number of new cases diagnosed each year[1].

In contrast to the situation seen in developed countries, adenocarcinoma of the oesophagus is not common in South Africa, and is not often seen in the public health care setting[2].

The subtype of squamous cell carcinoma of the oesophagus is the most prevalent type with an incidence of 46.7/100000 for males and 19.2/100000 for females. These figures are for the Eastern Cape [2,3] which has traditionally been seen as the epicentre for oesophageal cancer in South Africa. While the exact incidence in Gauteng and KwaZulu-Natal are unknown due to lack of official statistics, there seems to be a significant number of cases based on hospital reporting[4,7].

The curative management of oesophageal cancer involves complete surgical and/or endoscopic resection together with multimodal oncological therapy[6]. Sadly, most patients in South Africa present with locally advanced or metastatic disease amenable only to palliation[2,4]. In spite of the burden of oesophageal cancer in South Africa and its attendant morbidity and mortality, there has been little focus on research into this condition locally[7]. Loots et al published a good historical overview of this disease in South Africa and described the current research on the topic as being in a state of crisis. It is hoped that this study will address this crisis by developing research themes which will help South African investigators refine the clinical algorithms for this disease.

Background

The seed for this study was first planted when I arrived as a consultant in the department of surgery at Greys hospital in Pietermaritzburg in 2010. I noted at the time that there were a high number of patients with oesophageal cancer being palliated with the use of self-expanding metal stents (SEMS). What intrigued me was that these were being inserted routinely without the use of fluoroscopy with seeming efficacy and safety. While this technique had been described in world literature in resource-constrained countries, there was no South African study describing its use and certainly no large-volume centre in South Africa routinely utilizing this method.

At this time, I consulted with the GI subspecialist surgeon at Greys, Mr L Ferndale, to perform a departmental audit on this technique. As the sheer number of patients became apparent, we realized that this data could be shared through scientific publication and the idea of an MMedSc was conceived with supervisors Prof DL Clarke and Prof C Aldous. A formal concept sheet and study protocol was developed. Ethics approval was granted through direct application to the Biomedical Research Ethics Committee(BREC) at the University of KwaZulu-Natal (UKZN).

Although the initial concept was to look at the novel stent deployment technique and its effectiveness, it soon emerged that there were other research questions that could be answered. It was noted that most patients presented late with advanced disease and that there seemed to be delays in the diagnosis and management of oesophageal cancer in general in the Pietermaritzburg drainage area. Although this delay was “common knowledge” within the medical fraternity involved, it seemed prudent to delve deeper into this dilemma and obtain information that was more than just anecdotal. Investigation and assessment of these delays or so-called ‘timelines” would form another significant part of this MMed thesis.

Study setting

Pietermaritzburg is the capital city of KwaZulu-Natal and is the largest city in the western part of the province which is also known as Area 2 as per the Department of Health designation.

Figure 1 : MAP OF HEALTH DISTRICTS IN KWAZULU NATAL

Area 2 is a predominantly rural community comprising 4 health districts and servicing a patient population of approximately 2 million. Greys hospital is the only tertiary level hospital servicing this area. As such it is the only centre in Area 2 to practice advanced interventional endoscopy techniques (like stent insertion) and provides the only Oncology service to Area 2 as well.

The bulk of the data collection for this MMed Sci was obtained from Greys hospital.

The following aspects of the thesis were confined to Greys hospital :

- Retrospective chart audit for the stent technique and efficacy arm
- Patient interviews to explore the timelines in diagnosis and delay

In the comparative arm of this study (ie. fluoroscopy versus stenting under direct vision only), Inkosi Albert Luthuli Central Hospital (IALCH) in Durban formed the setting for the fluoroscopic arm of the study. IALCH is a large specialized centre and the only quarternary hospital in KwaZulu-Natal. The GI unit there has ready access to fluoroscopy and thus routinely performs stent insertion under fluoroscopy. It thus provided the perfect setting for comparison between the two techniques.

Study aims

The aims of this research project were :

- To provide an overview on oesophageal cancer in Area 2, and highlight the need for timely and effective palliation
- To quantify the timeline from symptoms to diagnosis and management, with specific emphasis on delays
- To provide a detailed description of an alternative technique of stent placement for palliation which utilizes only endoscopy as opposed to routine usage of fluoroscopy
- To assess safety and efficacy of this technique by retrospectively reviewing its usage over a five year period
- To compare the cost effectiveness of using a pure endoscopic technique versus traditional routine fluoroscopy to insert SEMS

Structure of the thesis

This is a thesis by publication and consists of three parts. Each part corresponds to a paper which is either published or currently under review.

- Chapter two introduces us to the problem of oesophageal cancer in South Africa. It sets the background for the sheer magnitude of the problem and provides an overview of the timeline from first symptom to definitive management, with specific focus on the delays encountered. It also attempts to objectively define reasons behind these delays.

- Chapter three reviews the use of SEMS for palliation of dysphagia in oesophageal cancer with specific emphasis on the technique sans fluoroscopy which is used at Greys hospital. This purely

endoscopic technique was borne out of an institutional need and this section details the technique and provides a five-year review of the peri-procedural outcome.[9, 10, 11, 12]

- Chapter four compares the pure endoscopic technique (used at Greys hospital, Pietermaritzburg) with the standard fluoroscopic technique used at IALCH, Durban. It analyses differences and provides a comparison of cost, time and radiation exposure between the two techniques. It further examines the financial implications in a resource-constrained environment with a high burden of disease taking example from a local costing study.[8]

- The final chapter includes conclusions and recommendations and provides a summary of the thesis. It suggests future developments to improve the management of oesophageal cancer and ultimately improve outcomes.

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Chapter 2 : Oesophageal Cancer in South Africa : An introduction to the burden of disease and analysis of deficiencies in management

Chapter two introduces us to the sheer magnitude of oesophageal cancer in rural South Africa. It highlights that most patients present with advanced disease and emphasises the need for timely and effective palliation. This paper also underscores deficiencies within the health care system, pre-hospital and in-hospital with specific focus on delays in seeking medical attention, and delays in timely diagnosis and management of oesophageal cancer.

It is hoped that by defining these barriers to timely presentation and management, quality improvement interventions may be implemented to help impact favourably on outcomes in the long-term.

Oesophageal cancer in South Africa: The shocking timeline from onset of symptoms to definitive management. Govender M, Ferndale L, Clarke DL

(Submitted and currently under review with SA Family Practice Journal)

Abstract

Background

In rural South Africa most patients with oesophageal cancer have delayed presentations with debilitating symptoms and inoperable disease. This study was undertaken to quantify the delay between onset of symptoms and definitive treatment in rural South Africa. It also sought to establish reasons for delays in seeking medical attention and identify ways to encourage earlier presentation.

Patients and Methods:

It was a two-armed study of patients with oesophageal cancer seen at Greys Hospital in Pietermaritzburg. One was a retrospective chart review establishing a timeline. The second part was a prospective study between June and November 2012 where data was collected by means of patient interviews.

Results:

One hundred and thirteen charts were reviewed. The timelines from first symptoms to definitive management was two to 14 months (average seven months). Forty-six patients were interviewed. All experienced dysphagia but 83 % were only prompted to seek help after weight loss. The duration of symptoms prior to first clinic/hospital attendance was 0 – 12 months (average three months). The reasons for the delay included the following: 41 % of patients didn't consider dysphagia a significant symptom, 24 % had no money, 19 % sought the help of traditional healers first, 15% said the hospital was too far away.

Conclusion:

There are long delays in the management of oesophageal cancer in our setting. The delays are prehospital as well as within the healthcare system. Targeted quality improvement interventions are necessary. The most significant reasons patients defer seeking medical attention are lack of knowledge about oesophageal cancer symptoms and limited access to healthcare. Patient education and improved referral systems are vital in encouraging earlier presentation.

Introduction

There is evidence to suggest that the referral system for acute surgical illness in South Africa is inefficient and this translates into poor outcomes for diseases such as acute appendicitis[1]. There has not been much research done on the situation with regards surgical oncology. Oesophageal cancer in South Africa is the commonest malignancy in African males and the prognosis remain dismal[2-5]. Most patients present late with inoperable disease and therapeutic interventions are directed at palliation rather than at cure. The objective of this study was to quantify the delay between the onset of symptoms and definitive treatment in our environment and to identify the reasons behind these delays. This study attempts to provide a timeline from the onset of symptoms of oesophageal cancer through to definitive care.

Patients and Methods

This study was conducted at Greys Hospital in Pietermaritzburg in 2012. It was a two-pronged study and both quantitative and qualitative methodologies were used. The first arm was a retrospective chart review of all patients with oesophageal cancer diagnosed between January and November 2012. Patients were identified from combined records of the Oncology clinic, the Surgical outpatients department (SOPD) and the Gastrointestinal Unit. These charts were then retrieved and analysed and a timeline plotted. This documented the time elapsed between onset of symptoms, presentation at a health facility, time to diagnosis and to definitive/palliative care. The overall timeline from first symptom to definitive care was also plotted, and overall standardisation of management for oesophageal cancer in these patients was also assessed.

The second aspect was a detailed qualitative interview of patients with oesophageal cancer to assess their experience with the health system during the management of their tumour. This was undertaken between June – November 2012 and consisted of 46 consecutive patients seen with oesophageal cancer at the SOPD during this time period. A single interviewer was used to eliminate bias. Each interview followed a standard format that sought detailed information on the onset of symptoms and the time to the first presentation to hospital. Specific questions were also asked to understand what prompted them to come to hospital and identify reasons for delayed presentation.

Results

Prospective qualitative assessment

Forty-six consecutive patients with oesophageal cancer who were treated at Greys Hospital, Pietermaritzburg between June and November 2012 were interviewed by the primary author. The commonest symptoms were dysphagia (100%), loss of weight (91 %), weakness (50%) and abdominal pain (13%). The symptoms that prompted presentation were weight loss (83 %) and dysphagia (17%). This group experienced symptoms for an average of three months (range 1 -12 months) before seeking attention. The following reasons were given for not seeking help earlier: lack of funds (24%), need to seek traditional advice first (19%), distance to health care facility (15%). Forty-one percent did not consider dysphagia to be a significant problem.

Chart review

A total of 113 charts were, reviewed from January to December 2012. Of the 113 patients, 25 % had been referred primarily to Oncology and 75% to surgical outpatients. A total of three underwent resectional surgery, six underwent radiotherapy and one hundred received a self-expanding metal stent for palliation. The average time from onset of symptoms to presentation was five months, from presentation to diagnosis two months, from diagnosis to definitive management one month. The average delay from onset of symptoms to definitive care was seven months. This is summarized in Table 1.

	RANGE	**AVERAGE**
First symptoms	0 – 12 months	5 months
Time to diagnose	0 – 8 months	2 months
Definitive Mx	0 – 7 months	1 month
Overall	**2 – 14 mnths**	**7 mnths**

Table 1 : Timeline of delay

Table 2 summarizes the delays from presentation to the various investigations obtained and emphasizes the non-standardised care ie. Not every patient was investigated fully.

Investigation	% of Patients	Average time to obtain
Barium Swallow	18.5	2 mnths
Histology	54.8	1.5 mnths
CT scan	9.7	2.9 mnths
Oncology Clinic Review	24.7	4.4 mnths

Table 2 : Delay to individual investigations and non-standardised treatment

Discussion

There is a growing body of work looking at inequalities in outcome of surgical diseases and there is good evidence that economic status determines both health seeking behavior and clinical outcome. This has been clearly demonstrated in acute surgical conditions in South Africa.[1] The situation with surgical oncology is under-reported on but there is evidence to suggest that rural African patients with malignancy present late and have more advanced disease than other groups with similar disease processes. [6-8] In this small cohort we have identified a significant delay from onset of symptoms to definitive care.

There are two distinct areas in which these delays occurred. These are the pre-health system domain and the health system domain and it appears that both of these contribute to the overall delay to definitive care. This is a significant finding since strategies and avenues of research to address these deficits may be guided accordingly. The majority of patients in our series did not make contact with the healthcare system until long after the onset of oesophageal symptoms. Seeking medical attention is influenced by a multitude of factors, such as educational levels, awareness, inadequate infrastructure, endemic poverty, gender inequalities and cultural factors[8]. Factors that deter health-seeking behaviour are collectively referred to as barriers to care and have been divided into cultural (acceptability),

financial (affordability) and structural (accessibility) issues and all of these barriers have been demonstrated in our study.

Our data suggests that rural patients tolerate dysphagia and unduly ignore its significance. Loss of weight was far more likely to precipitate health-seeking behaviour than dysphagia with only 17 % presenting with dysphagia. This is a patient factor and should inform educational programs aimed at raising awareness around oesophageal cancer. Another source of delay which has been documented in similar work from our institution on delays in acute appendicitis is the need to attend a traditional healer first. This once again raises a potential point of intervention and it may well be possible to develop targeted educational initiatives for traditional healers to teach them about so-called alarm symptoms. This simple strategy to redirect these patients into mainstream healthcare may prove invaluable. The lack of funds and the long distances cited by our patients are termed barriers to health and reflect structural inequalities in the society. As such these are difficult for clinicians to address.

Of concern are the delays within the health system and this reflects lack of formal algorithms for the investigation of oesophageal symptoms. The long timeline is even more shocking when one compares it to similar studies done in other parts of the world. Table 3 compares our series with one each from India and Japan. The glaring difference is evident.

	Our series	INDIA 2010 [6]	JAPAN 2008 [7]
First Presentation	5		1.2
To diagnosis	2		1.4
Definitive Mx	1		0.25
OVERALL	7	3.7	2.1

Table 3 : Comparison to other parts of the world (in months)

The haphazard management approach shown in our series for investigating oesophageal symptoms is problematic. In addition the delays associated with each individual investigation contribute to the long delay to definitive treatment. It would seem that clinicians too require a raised awareness on alarm symptoms and the need to expedite referral and diagnosis. A multi-disciplinary team is vital to facilitate

a standardized efficient approach to the management of oesophageal cancer. An enhanced investigative pathway could be developed in conjunction with radiology, oncology and surgery and this may well reduce the health care associated delays.

Conclusion

Patients with oesophageal cancer experience significant delays between the onset of symptoms and definitive surgical treatment. The reasons for this situation are multifactorial and include barriers to healthcare, delays in assessment, and logistical problems with healthcare resources. Understanding these reasons may help in developing targeted quality improvement interventions. Interventions need to be directed at pre-hospital delays and delays within the health system. To this end, educational programs around oesophageal alarm symptoms are necessary and multi-disciplinary algorithms need to be formalized as a matter of urgency. Only by fostering awareness amongst patients and clinicians and encouraging earlier presentation can we hope to impact favourably on outcomes.

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Chapter 3 : Placement of SEMS for oesophageal cancer without fluoroscopy : A description of the technique and overview of its safety and efficacy

Following on from Chapter 2, we see the high number of patients requiring palliation for advanced oesophageal cancer in a resource constrained setting. The technique of utilizing endoscopy alone at our institution was borne out of a need to offer timely palliation, in an environment where fluoroscopy was a scarce resource.

The following paper focusses on inserting self-expanding metal stents as palliation for dysphagia in oesophageal cancer without the use of fluoroscopy. It provides a detailed description of the technique, as well as a five year overview of its usage at our hospital, showing it to be a safe and reproducible technique which may prove invaluable in similarly resource-constrained environments.

Self-expanding metal stent placement for oesophageal cancer without fluoroscopy is safe and effective

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Background. Self-expanding metal stents (SEMS) are widely used to palliate patients with oesophageal cancer. Placement is usually done under endoscopic and fluoroscopic guidance. We have developed an exclusively endoscopic technique to deploy these stents. This article documents the technique and periprocedural experience.

Patients and methods. All patients who had SEMS placement for oesophageal cancer at Grey's Hospital, Pietermaritzburg, South Africa, over a 5-year period (2007 - 2011) were reviewed. Stenting was performed without radiological guidance using the technique documented in this article. At endoscopy, the oesophageal lesion was identified, dilated over a guidewire if necessary, and a partially covered stent was passed over the wire and positioned and deployed under direct vision. Data were captured from completed procedure forms and included demographics, tumour length, the presence of fistulas, stent size and immediate complications.

Results. A total of 480 SEMS were inserted, involving 453 patients, of whom 43 required repeat stenting. There were 185 female patients (40.8%) and 268 male patients (59.2%). The mean age was 60 years (range 38 - 101). There were 432 black patients (95.4%), 15 white patients (3.3%) and 6 Indian patients (1.3%). The reasons for palliative stenting were distributed as follows: age >70 years n=95 patients, tumour >8 cm n=142, tracheo-oesophageal fistula (TOF) n=29, and unspecified n=170. One patient refused surgery, and one stent was placed for a post-oesophagectomy leak. Repeat stenting was for stent migration (n=15), tumour overgrowth (n=26) and a blocked stent and a stricture (n=1 each). Complications were recorded in six cases (1.3%): iatrogenic TOF (n=2), false tracts (n=3) and perforation (n=1). All six were nevertheless successfully stented. There was no periprocedural mortality.

Conclusion. The endoscopic placement technique described is a viable and safe option with a low periprocedural complication rate. It is of particular use in situations of restricted access to fluoroscopic guidance.

S Afr Med J 2015;105(10):858-861. DOI:10.7196/SAMJnew.8329

Although the 5-year survival rate for oesophageal cancer has improved from 5% to 19% over the past 4 decades, the prognosis remains poor.[1-3] This is especially so in rural South Africa (SA), where patients present with advanced disease and therapy is typically directed at alleviating dysphagia, overflow of saliva, pulmonary aspiration and tracheo-oesophageal fistula. Over the past decade self-expanding metal stents (SEMS) have replaced surgical bypass and rigid plastic stents as the gold standard for mechanical palliation of this disease. Studies have shown good relief of dysphagia with SEMS insertion, with minimal risk.[4,5] In SA and in other countries, SEMS insertion is currently usually performed under fluoroscopic guidance, which requires access to a fluoroscopic suite. At Grey's Hospital in Pietermaritzburg, KwaZulu-Natal Province, SA, fluoroscopy is under great demand. We are also faced with a significant burden of inoperable oesophageal cancer. In response to this high demand for a limited resource, we developed an alternative direct-vision approach that does not require fluoroscopy. This technique, first described in the literature in 2001,[6] has been validated with several small studies in equally resource-constrained environments.[7-9] This study at Grey's Hospital was undertaken to describe the technique of stent placement using endoscopy alone and to document our periprocedural experience over a 5-year period (2007 - 2011). We hope that this alternative direct-vision approach will gain acceptance in the SA context, leading to more centres providing the service and ultimately improving patient access.

Methods

This was a retrospective analysis of all patients stented for oesophageal cancer at Grey's Hospital over the 5-year period 2007 - 2011. Data were analysed from completed gastrointestinal procedure reports and included patient demographics, tumour length, presence of a fistula, stent size used and immediate complications. Other variables included the indication for stenting, as well as the need and indication for repeat stenting during the study period.

Technique

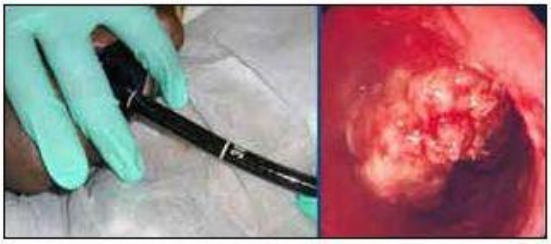
All patients gave consent for the endoscopy, dilatation and stenting using a standard hospital consent form. Patients were counselled in the appropriate language before the procedure regarding the dietary modifications that the stent would mandate. All stenting was performed in the gastrointestinal unit, under sedation using midazolam and fentanyl. The stents used were nitinol partially covered ones with a proximal release mechanism (Ultraflex; Boston Scientific, USA). An initial gastroscopy was performed and the oesophageal tumour identified. If the endoscope could be passed beyond the tumour, proximal and distal measurements of the tumour were taken. If the scope could not initially traverse the

Initial gastroscopy

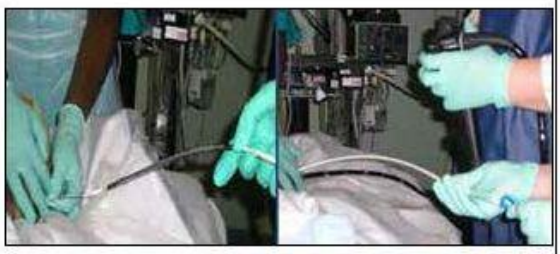
Insertion of guidewire beyond tumour

Scope removed

Dilatation performed if required up to 12/14 mm



Patient rescoped
Proximal and distal measurements obtained to select stent size
Guidewire reinserted



Stent delivery system passed
Positioned above proximal tumour

Scope reinserted parallel to stent

Stent slowly deployed under direct vision

Fig. 1. A photo montage of the technique of deployment.

lesion, a guidewire was passed and the lesion dilated using Savary-Gilliard dilators up to 12 mm diameter. The scope was then reintroduced and tumour measurements obtained. These were then used to select the stent size. Optimal stent size is at least 4 cm longer than tumour length in order to achieve adequate proximal and distal coverage (of 2 cm on either side of the lesion). The guidewire was then inserted under vision beyond the tumour into the stomach, and the scope was removed.

The stent delivery system, which has markings in centimetres, was then passed over the guidewire and positioned using the proximal tumour measurement as a guide. The scope was then reinserted alongside the stent delivery system and the SEMS carefully deployed under direct vision, allowing for adjustment of its position. Following the procedure, the patient recovered in the day ward unless a complication occurred. Once the patient was awake, advice regarding dietary modification was repeated. The patient was discharged with analgesia and a diet sheet back to his/her referral hospital or, in the case of inpatients, back to the ward. Fig. 1 is a photo montage of the technique of SEMS deployment.

Results

A total of 506 stents were placed in 453 patients between 2007 and 2011. Fig. 2 shows a breakdown of the numbers of procedures per year. There were 436 treatment-naive patients and 43 in whom a pre-existing SEMS had become obstructed and who required a salvage procedure. The mean age was 60 years, with the youngest patient being 38 and the oldest 101. There were 185 female patients (40.8%) and 268 male patients (59.2%). In terms of racial distribution (Fig. 3), black patients overwhelmingly predominated. The reasons for stenting were refusal of surgery (n=1), post-oesophagectomy leak (n=1), and inoperable cancer in the remainder. Six percent of patients presented with a tracheo-oesophageal fistula (TOF). Twenty-two percent of patients were older than 70 years, 32.7% had tumours that were >8 cm in length, and 39.4% (170/453) were deemed inoperable owing to comorbidities, locally advanced tumours and the presence of metastases. The reasons for irresectability are depicted in Fig. 4.

Repeat procedures

A total of 43 patients required a repeat procedure, 15 for stent migration, 26 for tumour overgrowth, 1 for a blocked stent and 1 for a stricture. Of the 436 new patients, 26 required restenting, giving a restent rate of 5.9%; an analysis of this subset is shown in Table 1. Restenting in all patients was uneventful. Six periprocedural complications (1.3%) occurred and included iatrogenic TOF (n=2), false tracts created through long tumour (n=3) and a single tumour perforation. All were successfully restented without the use of fluoroscopy, and there was no periprocedural mortality.

Discussion

The burden of disease due to oesophageal cancer in SA is large. This 5-year study reveals a significant number of patients with advanced oesophageal cancer who required palliation. In keeping with available epidemiological data, there was a male predominance and older patients were in the majority, although 15.3% of the patients were <50 years of age. Oesophageal stent placement is usually performed under fluoroscopic guidance in most centres in SA. We set out to show that the purely endoscopic technique of SEMS placement is a safe and effective alternative in the palliation of malignant dysphagia. Oesophageal SEMS

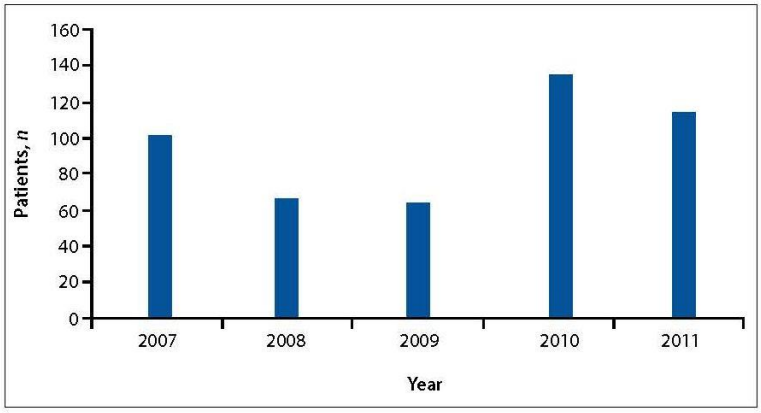


Fig. 2. SEMS deployment per year at Grey's Hospital.

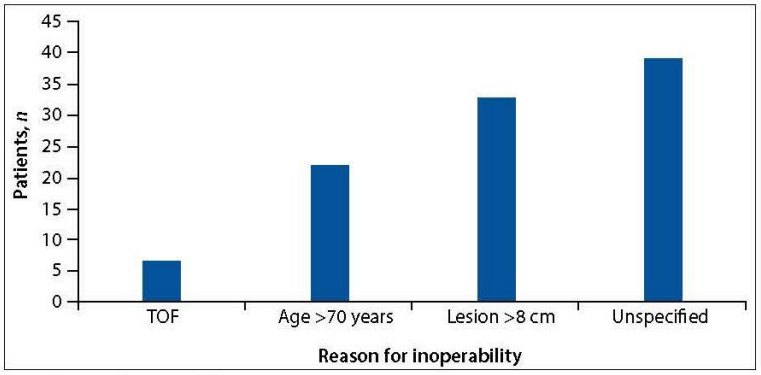


Fig. 4. Reasons for inoperability.

Table 1. Analysis of restenting

Reason	Patients, *n*	Time from initial stent
Stent migration	11	21 days - 7 months (mean 2.1)
Proximal overgrowth	7	2 - 17 months (mean 7.3)
Distal overgrowth	6	2 - 9 months (mean 5.6)
Blocked stent	1	10 months
Stricture	1	2 months

Table 2. Comparison with other series using the direct-vison approach

	N	Perforation, %	Mortality, %	Migration, %	Restent, %
Our series	436	1.4*	0	2.5	5.9
Wilkes *et al.*, 2007[7]	98	0	0	3.1	8.9
Ben Soussan *et al.*, 2005[13]	33	0	3	0	18
White and Mungatana, 2001[14]	70	2.8	0	-	4.2

*False tract and TOF included in our series.

insertion forms the core of palliation in patients in whom curative resection is not possible because they are too old or frail or because lesions are too advanced or extensive. In our series, 21.9% of patients were >70 years old (a local cut-off for oesophagectomy), and the rest had locally advanced or metastatic disease or were

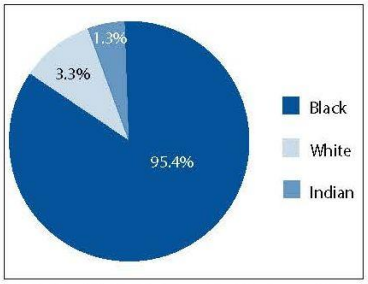


Fig. 3. Racial distribution of patients requiring a SEMS for oeosphageal cancer.

generally in a poor cachetic condition. Delays in seeking medical attention, as well as the lack of awareness of oesophageal cancer in our communities, probably contribute significantly to the advanced stage of disease at presentation.

This study suggests that an exclusively endoscopic technique is a safe and effective alternative to fluroscopically guided placement in a resource-limited setting. Accurate placement of stents was confirmed in 100% of our patients with endoscopic evaluation at the time of stent deployment. This was true for palliating dysphagia as well as for stenting over malignant TOF. Our recorded complication rates with respect to perforation, need for a salvage procedure due to stent migration and/or tumour overgrowth compare favourably with other published series utilising both the fluoroscopically guided and purely endoscopic technique.[7,10-14] Tables 2 and 3 compare our outcomes with those reported in the literature.

Currently we reserve fluoroscopic placement for a select group of patients. These include patients in whom complete luminal obstruction makes safe passage of either the endoscope or the guidewire impossible. Such patients comprise about 15 - 20% of cases at our institution. The direct-vision approach allows for the majority of patients to be stented at a regional level and selects out those for whom fluoroscopy would be necessary. Use of routine fluoroscopy for all patients therefore appears to be a waste of a valuable resource, as well as contributing to an unnecessary delay in patient management.

Conclusion

We have developed a safe technique to accurately deploy SEMS under direct vision, thus obviating the need for fluoroscopy. Our study shows that the periprocedural complication rate is low and reaffirms that the exclusively endoscopic technique of stent insertion is a safe and effective option,

Table 3. Comparison with series using fluoroscopy

	N	Perforation, %	Mortality, %	Migration, %	Restent, %
Our series	436	1.4*	0	2.5	5.9
Dobrucali and Caglar, 2010[10]	90	0	0	4.0	11
Christie *et al.*, 2001[11]	100	1	0	8.7	5.1
Cwiekiel *et al.*, 1998[12]	100	1	0	3.0	7.5

*False tract and TOF included in our series.

especially in units with limited or no access to fluoroscopy. This technique is also applicable to patients with recurrent dysphagia (whether due to stent migration or tumour overgrowth) and to the management of malignant TOF.

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Accepted 13 July 2015.

Chapter 4 : Comparing the routine use of fluoroscopy for stent insertion with the endoscopy alone technique : Financial and other implications

We had set out to document our experience with the pure endoscopic approach of SEMS insertion for palliation in oesophageal cancer.

Chapter 3 showed it to be a safe and effective technique and certainly on par with the routine use of fluoroscopy.Our next thought was thus : we have shown our technique to be equivalent, can we show it to have advantages over the standard technique?

The following paper explored this question with specific focus on costs involved, time taken to perform each procedure as well as radiation exposure.In a country where healthcare and cost-cutting go hand-in-hand, we felt this question of cost was a vital one to be answered.

Self-Expanding Metal Stent (SEMS) insertion: Fluoroscopy versus pure endoscopic technique – A cost comparison

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Background: Oesophageal cancer is a disease with significant morbidity and mortality, and in South Africa most patients present with advanced disease.[1] Self-expanding metal stents (SEMS) are now widely used in the palliation of oesophageal cancer, and in most institutions SEMS are deployed under fluoroscopic guidance. In our institution, we use an exclusive endoscopic deployment technique which is comparable to the traditional fluoroscopic technique in terms of safety and efficacy.[2-4] We undertook a study to compare the two techniques with respect to their time- and cost-effectiveness.

S Afr J Surg 2016;54(3)

Method

This cross-sectional study compared two groups. One group from Greys Hospital in Pietermaritzburg underwent SEMS insertion under direct vision. The second group from Inkosi Albert Luthuli Central Hospital in Durban underwent SEMS deployment using the routine fluoroscopic technique. An average cost analysis was then performed. Following consultation with a statistician, the minimum number per group to achieve significance was calculated to be eleven. Twenty consecutive patients were therefore observed in each arm. A single observer documented the procedures at both institutions to standardise data collection. Each procedure was timed, and staff present, equipment required and drugs used were documented.

When evaluating the additional costs involved for stenting under fluoroscopy, use of the screening suite, fluoroscopy and contrast usage was assessed. As most state hospitals do not utilise an itemised billing service, average costing was estimated using protocols from Greys Hospital revenue department and private institutions. Two private radiology practices provided billing estimates for use in this study. Basic out-patient hospital charges, the use of endoscopy, hospital staff and items that were used as standard in both techniques were excluded from the costing analysis.

Radiation levels were indirectly assessed in the fluoroscopy arm at IALCH. The length of screening per procedure was documented and radiation exposure to the health-care worker was calculated using published data on dispersed radiation during screening.[4] These values were then evaluated against existing occupational health and safety guidelines.

Results

Both groups underwent SEMS insertion as outpatient procedures. This was performed under conscious sedation at both hospitals. The stent delivery system used at both hospitals was identical (partially- covered proximal-release Ultraflex stent manufactured by Boston Scientific). The drugs used in both techniques were Midazolam and Fentanyl. The time range for the pure endoscopic technique was 4–11 minutes (average of five minutes). SEMS insertion under fluoroscopy took between 5–24 minutes to perform (average of 17.5 minutes). The average time difference between the two techniques was 12.5 minutes (statistically significant $p < 0.01$).

Cost estimates were calculated using an average of three prices from the quotes obtained. The estimate for use of the screening suite was R2 056 per patient, fluoroscopy was R259 per 30 minute session, and contrast cost R270 per 300 ml. The range for screening time during fluoroscopic insertion was 1–4.5 minutes (mean of 3.5 minutes). The total amount of contrast used in the fluoroscopy arm was 278 ml. This equated to an average of 13.9 ml of contrast used per patient in this group. Using this information, the total additional cost in the fluoroscopic arm could then be calculated. The total additional cost per procedure done under fluoroscopy was therefore R2 099.

Radiation exposure during stent insertion was estimated at 0.3 micro-Sieverts (mSv) per minute. The average screening time per procedure was 3.5 minutes giving an average estimated radiation exposure to each health-care worker of 1.05 mSv per procedure. The fluoroscopic method was the more expensive technique at an additional R 2099 per patient. When evaluating the time taken for both procedures, the

Table 1: Cost estimates

Variable	Greys Revenue Quote	Private Practice 1 Quote	Private Practice 2 Quote	Average Cost Incurred
Screening Suite Cost (per event)	ZAR2002	ZAR2140	ZAR2025	ZAR2056
Charge on Fluoroscopy (per 30 minutes)	ZAR239	ZAR250	ZAR273	ZAR259
Contrast (per 300mls)	ZAR270	ZAR270	ZAR270	ZAR270

Table 2: Total additional cost associated with fluoroscopy

Variable	Average Unit Cost	Usage	Total Cost
Screening Suite	ZAR2056	per patient	ZAR2056
Fluoroscopy	ZAR259 / 30 mins	3.5 mins	ZAR30.22
Contrast	ZAR270 / 300 mls	13.9 mls	ZAR12.51
			ZAR2099

Table 3: Annual Saving in Perspective

	Per Procedure	Procedures per year	Annual Saving at Greys
Cost	ZAR2099	96	ZAR 201 504
Time	12.5 minutes	96	1200 minutes
Radiation exposure	1.05mSv	96	100.8mSv

exclusive endoscopic technique was 12.5 minutes shorter than the conventional fluoroscopic technique. This was statistically significant. The radiation exposure to the health-care worker per fluoroscopic procedure was estimated at 1.05 mSv.

The number of patients stented at Greys Hospital between 2007 and 2011 was 480. The average annual number of SEMS inserted at our institution over the past five years has been 96 patients. The annual savings from performing this technique at Greys can therefore be extrapolated to be R201 504, 1 200 minutes and 100.8 mSv of radiation exposure.

Conclusion

The exclusive endoscopic technique can be performed at any regional or district level hospital equipped with standard endoscopy. The annual saving of R201 504 could also be translated into the purchase of an additional seventy stent delivery systems, making SEMS available to more patients. The total annual time saved by performing the pure endoscopic procedure is 1 200 minutes. The annual radiation exposure estimated from the fluoroscopy group was 100.8 mSv. The exclusive endoscopic technique spares the health-care workers this exposure. Our data suggests that an exclusive endoscopic approach saves on time, time as money, and radiation and should be considered for all high volume units where the savings would be considerable.

Table 4: OSHA Guidelines

Body part	Radiation level
Whole body	20mSv
Skin, hands, feet, head	500mSv

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Chapter 5: General Discussion

Conclusion and Recommendations

This research project was undertaken to address two major issues involving oesophageal cancer. One was palliation in a resource-constrained environment, looking specifically at self-expanding metal stent (SEMS) insertion. The other was to investigate the deficiencies in the diagnosis and management of this disease, with focus on delays.

It can be concluded that there are statistically significant delays in the diagnosis and management of oesophageal cancer. Points of delay can be defined as being both pre-hospital as well as within the hospital system itself. These various points of delay may form the key in implementing programs to effect change in health-seeking behaviour.

Our data suggests that rural patients ignore the significance of dysphagia as a symptom. This is an important patient factor that could be influenced by educational programs aimed at raising awareness around oesophageal cancer. Another delay is the need to attend a traditional healer first. This once again raises a potential point of intervention. Educational initiatives for traditional healers have been proposed for various chronic health conditions like HIV and TB. Perhaps extending these initiatives to include alarm symptoms like dysphagia may redirect patients sooner into mainstream healthcare. The lack of money and the long distances to access healthcare reflect structural inequalities. As such these are difficult for clinicians to address. Documenting them and citing them as legitimate reasons for failure to implement timely treatment is however still important, and it can only be hoped that those in a position to implement change can reflect upon these challenges.

Delays noted within the health system are concerning. This reflects lack of formal algorithms and multi-disciplinary team for the investigation and management of oesophageal symptoms. Since the commencement of this study, a formal algorithm has been implemented at Greys hospital for referral and management of oesophageal symptoms. A multidisciplinary team approach is also currently in place, but it is too soon to evaluate the impact of these measures. These may well provide the basis of a follow-up study to assess any positive impact.

The other aspects of the study focussed on the use of SEMS for palliation of dysphagia in inoperable oesophageal cancer. In most institutions this procedure was performed under fluoroscopy, a resource

that was not readily available at our institution. To obviate the delays that this meant for our patients, we used a direct-vision approach which did not require fluoroscopy.

Our experience with this alternative technique showed it to be as safe and effective as the standard fluoroscopy technique. In addition, our comparative data showed it to be a viable option with respect to cost and time-saved. In a resource-limited setting with a high volume of advanced oesophageal cancer, time and cost are significant variables. Radiation exposure is also coming to the fore nowadays as an important occupational safety hazard. Our publication showed that our pure endoscopic technique of SEMS insertion is more cost and time-efficient compared to the routine use of fluoroscopy. It also has the additional benefit of sparing the health care worker from unnecessary radiation exposure.

The findings of this study add further validity to the pure endoscopic technique of SEMS placement and may pave the way for this procedure to be performed at many regional centres and not be restricted to tertiary centres only.

Appendices

Appendix 1: The Study Protocol

Type of study : Clinical, Observational – Descriptive

Title :

An alternative technique for the placement of self-expanding metal stents(SEMS) for oesophageal cancer in a resource-limited setting – Description and cost-comparison

Aim :

To evaluate the safety, efficacy and cost-effectiveness of utilising a pure endoscopic technique of SEMS placement for the palliation of oesophageal cancer at a tertiary hospital in South Africa.

Specific Objectives:

1. To provide a detailed description of an alternative technique of stent placement which utilises only endoscopy, as opposed to routine use of fluoroscopic guidance. To also assess safety and efficacy of this technique by retrospectively reviewing its usage at the GI Unit at Greys hospital, Pmb over a 5 year period.

2. To assess the effectiveness of our SEMS placement technique with respect to relief of malignant dysphagia and also assess immediate and short-term complications, by performing a prospective audit at Greys hospital. The audit will analyse data from a 2-hour and 1-week follow-up.

3. To compare the cost-effectiveness of using a pure endoscopic technique of SEMS insertion vs traditional route of SEMS insertion under routine fluoroscopy. The former technique is employed at Greys hospital while the latter is utilised at IALCH, Dbn. This study will provide a costing analysis of both techniques.

Background and Literature

SEMS is widely used for palliation of dysphagia in those patients with inoperable oesophageal cancer. In most institutions (locally and worldwide), it is performed under fluoroscopic guidance. At Greys hospital in Pmb, fluoroscopy is a resource under great demand. Our limited access means long delays before patients can be stented. We have therefore been using a direct-vision approach which does not require fluoroscopy. This study was undertaken to document our peri-procedural experience with this pure endoscopic technique.(NB. There is, as yet, no published South African series utilising this approach)

This study will be a retrospective analysis of patients stented at the GI unit at Greys hospital over a period of 5 years(2007 – 2011). Data will be analysed from completed procedure forms and will include demographics, tumour length, presence of fistulae, stent size and complications. It will include a description of our pure endoscopic technique and will draw comparisons to other large studies using similar and alternate techniques.

A prospective arm of this study will formally evaluate our technique wrt dysphagia relief and complication rates. This audit will analyse data from a two-hour evaluation post-procedure, assessing clinical variables for evidence of immediate complications. The audit will also evaluate outcomes at a 1-week telephonic follow-up. Pain, dysphagia scores and haematemesis will be among the variables analysed.

In a busy state hospital with a limited budget, cost is unfortunately always a factor. Institutional data from Greys hospital shows a high burden of inoperable oesophageal cancer for which the treatment is palliation of the dysphagia. This can be achieved by the insertion of SEMS. As described in objective 1, this is performed under direct vision in our unit while SEMS insertion at IALCH in Durban is performed under fluoroscopic guidance. This study will provide a cost analysis of both techniques. Costing analysis will be extrapolated from a recent model described by Allorto NL and Clarke DL (see reference 1 below). Individual cost drivers will include cost of endoscopy(ies), cost of stents; use of fluoroscopy unit; cost of radiographer; use of contrast and drugs and overall time of procedure.

Key References

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Appendix 2: Ethical approvals

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25 July 2014

Dr. M Govender
Department of Surgery
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PROTOCOL: An alternative technique for the placement of self-expanding metal stents (SEMS) for oesophageal cancer in a resource-limited setting-Description and cost-comparison. REF: BE258/12.

PROVISIONAL APPROVAL

A sub-committee of the Biomedical Research Ethics Committee has considered your response dated 21 July 2014 to BREC letter dated 31 January 2013.

The study is given **PROVISIONAL APPROVAL** pending receipt of:

1. Query 7: SA (2004) Research ethics guidance requires informed consent for prospective record reviews. Please provide a motivated request for a waiver of such consent. Response given to date is not relevant.
2. Query 8: KZN PHRC permission is also required as requested by IALCH CEO.

Only when full ethical approval is given, may the study begin. **Full ethics approval has not been given at this stage.**

PLEASE NOTE: Provisional approval is valid for 6 months only - should we not hear from you during this time - the study will be closed and reapplication will need to be made.
Your acceptance of this provisional approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

Yours sincerely

Mrs A Marimuthu
Senior Administrator: Biomedical Research Ethics

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

22 October 2014

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PROTOCOL: An alternative technique for the placement of self-expanding metal stents (SEMS) for oesophageal cancer in a resource-limited setting-Description and cost-comparison. REF: BE258/12.

EXPEDITED APPLICATION

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 07 September 2012.

The study was provisionally approved pending appropriate responses to queries raised. Your responses received on 26 September 2014 to queries raised on 25 September 2014 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given full ethics approval.

This approval is valid for one year from **22 October 2014.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **RATIFIED** by a full Committee at its meeting taking place on 11 **November 2014.**

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Professor D.R Wassenaar
Chair: Biomedical Research Ethics Committee

XXX

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26 September 2016

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PROTOCOL: An alternative technique for the placement of self-expanding metal stents (SEMS) for oesophageal cancer in a resource-limited setting-Description and cost-comparison. REF: BE258/12.

NEW TITLE OF STUDY: Oesophageal cancer in rural South Africa: Challenges in diagnosis and an alternate technique of stent placement for timely palliation in a resource-constrained environment".

We wish to advise that your application for Amendments received on 08 September 2016 for the above mentioned study has been noted and approved by the sub-committee of the Biomedical Research Ethics Committee (BREC).

The following have been noted and approved:

- Change of Title
- Change of objectives and addition of new objective.

The approval will be **ratified** by a full Committee at a meeting to be held on **11 October 2016.**

Yours sincerely

Mrs A Marimuthu
Senior Administrator: Biomedical Research Ethics

cc: Postgraduate Office

health

Department:
Health
PROVINCE OF KWAZULU-NATAL

Inkosi Albert Luthuli Central Hospital
Ethekwini Health District
Office of the Medical Manager
Private Bag X 03, Mayville, 4058
800 Bellair Road, Mayville, 4058
Tel.: 031 240 1059,
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www.kznhealth.gov.za

Reference: BE258/12
Enquiries: Medical Management

2 October 2013

Dr M Govender
Department of Surgery
IALCH

Dear Dr Govender

RE: PERMISSION TO CONDUCT RESEARCH AT IALCH

I have pleasure in informing you that permission has been granted to you by the Medical Manager to conduct research on: **An alternative technique for the placement of self-expanding metal stents (SEMS) for oesophageal cancer in a resource-limited setting- Description and cost-comparison.**

Kindly take note of the following information before you continue:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Kindly ensure that this office is informed before you commence your research.
4. The hospital will not provide any resources for this research.
5. You will be expected to provide feedback once your research is complete to the Medical Manager.

Yours faithfully

P.D.Ramdas

Dr P D Ramdas
Acting Medical Manager

Appendix 3: Data collection tools

Data Capture 1 – Greys SEMS (Retrospective)

FIRST NAME	
SURNAME	
DATE OF BIRTH	
HOSPITAL NO.	
AGE	
SEX	
RACE	
SITE OF LESION (cm)	
LENGTH OF LESION (cm)	
REASON FOR STENT	
STENT SIZE	
DILATATION PERFORMED	
CALIBRE DILATED TO	
COMPLICATIONS	
ENDOSCOPIST	

Data Capture 2 – SEMS Cost Comparison

Hospital : Greys / IALCH

Stent No.: _____

Staff present : Doctor _____

Nurse_____

Radiographer_____

Time commenced : _____

Time completed : _____

Drugs used : _____

_____

Equipment used : Guidewire _____

Stent _____

Scope_____

Dilator_____

Other_____

Contrast used : Yes / No

Volume : _____

Complications : Yes / No _____

_____

Screening time : _____

CA OES INTERVIEW FORM

NAME : _____

HOSP NO : _____

ONC NO : _____

SEX : _____

AGE : _____

REGION : _____

FIRST SYMPTOM – WHEN : _____

WHAT : _____

FIRST CONTACT WITH HEALTH CARE – WHEN : _____

WHERE : _____

SYMPTOM : _____

_____

REASON FOR DELAY (if any)

- Money
- Distance
- Traditional healer first
- Other _____
- _____
- _____
- _____