

Feracrylum in Reduction of Seroma after Mastectomy

Joseph Gordon Gatura Wambui, MB.ChB (U.O.N)

**A Dissertation to be Submitted as Partial Fulfilment for the Requirements for
the Award of Masters of Medicine Degree (MMED) in General Surgery,
University of Nairobi**

University of NAIROBI Library



0407820 0

2011

UNIVERSITY OF NAIROBI
MEDICAL LIBRARY

USE IN THE LIBRARY ONLY

DECLARATION

RESEARCHER

Apart from where citations are made, this dissertation is my original work and has not been presented in any other institution of higher learning.

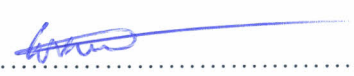
Dr Joseph Gatura

Signed  Date 18/08/11

SUPERVISORS

1) Signature  Date 22/08/2011

Dr Joseph W. Githaiga,
MB.ChB, M.Med. Surg. (U.O.N.), VLS (MUNICH), GVS (TEL AVIV),
Lecturer,
Department of Surgery,
University Of Nairobi

2) Signature  Date 19/08/11

Dr Wickliffe Kaisha Otsianyi,
MB.ChB, M.Med (general Surgery) U.O.N.,
Lecturer,
Department of Human Anatomy,
University Of Nairobi

ACKNOWLEDGEMENT

I hereby acknowledge the following for their support and the role they played in making this dissertation a success.

1. The almighty God for making His grace sufficient
2. My lecturers and especially my supervisors Dr. Joseph Githaiga and Dr. Wickliffe Kaisha for their guidance and support.
3. *My colleagues for their cooperation and help.*
4. The K.N.H administration and the patients who took part in the study.
5. Dr. Benjamin Mbiyu for his assistance in data analysis
6. For my family for their undying support and patience.

ABBREVIATIONS

KNH	-----	Kenyatta national Hospital
MRM	-----	Modified Radical Mastectomy
RCT	-----	Randomised Clinical Trial
SPSS	-----	-Statistical Package For Social Sciences
UON	-----	University Of Nairobi
VEGF	-----	Vascular Endothelial Growth Factor

TABLE OF CONTENTS

DECLARATION	II
ACKNOWLEDGEMENT	III
ABBREVIATIONS	IV
TABLE OF CONTENTS.....	V
LIST OF TABLES	VII
LIST OF FIGURES	VIII
LIST OF APPENDICES	IX
ABSTRACT	X
1 INTRODUCTION	1
1.1 BACKGROUND.....	1
1.2 JUSTIFICATION OF THE STUDY.....	1
1.3 STUDY OBJECTIVES.....	2
1.3.1 MAIN OBJECTIVE.....	2
1.3.2 SPECIFIC OBJECTIVES	2
1.4 HYPOTHESES	2
1.4.1 NULL HYPOTHESIS.....	2
2 LITERATURE REVIEW	3
2.1 PATHOPHYSIOLOGY OF SEROMA	3
2.2 RISK FACTORS IN SEROMA FORMATION	4
2.3 PREVENTION OF SEROMA FORMATION	6
2.4 COMPLICATIONS OF SEROMA AFTER MASTECTOMY	8
2.5 FERACRYLUM	9
2.5.1 PHARMACOLOGY.....	9
2.5.2 USES.....	9
3 RESEARCH METHODOLOGY	10
3.1 STUDY DESIGN.....	10
3.2 STUDY POPULATION	10
3.3 INCLUSION CRITERIA	11
3.4 EXCLUSION CRITERIA.....	11
3.5 SAMPLE SIZE DETERMINATION	11
3.6 SAMPLING METHOD	12
3.7 THE SURGICAL PROCEDURE	12
3.7.1 Details of the surgery.....	13
3.8 DATA PRESENTION AND ANALYSIS	14
3.9 ETHICAL CONSIDERATION	15
4 RESULTS	16
4.1 SEROMA ASSESSMENT.....	20

5	DISCUSSION	25
5.1	CONCLUSION.....	26
5.2	RECOMMENDATION	27
5.3	STUDY LIMITATIONS.....	27
	REFERENCES	28
	APPENDICES	I

LIST OF TABLES

Table 1:descriptive statistics for both treatment and control groups.....	17
Table 2: Result of drain retention, total volume, seroma and complications.....	21
Table 3: Reg total volume, treatment, age, weight, sbp, t-stage, t-size (cm), surgeon.....	23
Table 4: Reg sday – treatment, age, weight, sbp, t-stage, t-size (cm), surgeon.....	24

LIST OF FIGURES

Figure 1: Age distribution among the groups.....	17
Figure 2: Weight distribution among the groups.....	18
Figure 3: Tumor size distribution among the groups.....	18
Figure 4: Systolic BP distribution among the groups.....	19
Figure 5: Surgeons' Experience among the groups.....	19
Figure 6: Node status distribution among the groups.....	20
Figure 7: average no. of days of drain retention among the groups.....	21
Figure 8: total drainage volume among the groups.....	22
Figure 9: seroma formation at day 14 nd 21 among the groups.....	22
Figure 10: total no. of complications among the groups.....	22
Figure 11: average no. of aspirations among the groups.....	23

LIST OF APPENDICES

APPENDIX 1: DATA SHEET	I
APPENDIX 2: CONSENT FORM.....	III

ABSTRACT

Background:

Seroma formation is a common problem after mastectomy. The incidence varies between 2.5% to 51%. It is often an ongoing problem after removal of the drain, and repeated skin puncture is sometimes necessary to remove the seroma. In addition to many ambulatory visits, this also leads to an increased risk of infection and adjuvant treatment can be delayed for several weeks.

Different procedures have been tried to avoid seroma formation including immobilization of the arm and shoulder after mastectomy, different drain regimens, closing of the dead space of the cavity, different chemical substances such as tranexamic acid, thrombin and fibrin. However, none of these has been successful.

The aim of the study: To find out whether Feracrylum can reduce the seroma formation after mastectomy.

Study design: A prospective randomized controlled study, with 2 groups of 24 patients each. 50ml of 1% aqueous solution of Feracrylum was applied over the raw areas intra operatively in 24 patients, and the other 24 patients were the control group.

Inclusion criteria: Women with primary breast cancer, undergoing modified radical mastectomy.

Results: Data for 48 patients was available for the final analysis. 24 underwent mastectomy feracrylum infiltration and tube drainage while 24 had routine drainage. Seroma rate was 88% in the Feracrylum group while it was 38% in the control group ($p \leq 0.0001$). The mean volume of drainage was less with Feracrylum 695ml vs. 1486ml ($p \leq 0.0001$). There was significant reduction

in the days of drain retention 5.9 vs. 12.8($p \leq 0.0001$), and the rate of wound related complications 8% vs. 71% in the Feracrylum group ($p \leq 0.0001$).

Conclusion: Feracrylum does not reduce the incidence of seroma after mastectomy but it reduces the total volume of drainage, the number of days necessary for drain retention and the rate of wound complications.

1 INTRODUCTION

1.1 BACKGROUND

Breast cancer is the most common malignancy in women worldwide (1) and surgery is an important aspect of treatment. Modified radical mastectomy with or without reconstruction or breast preservation in addition to axillary lymph node dissection are common surgical procedures in breast cancer. Surgery of the breast and axilla is associated with numerous complications, including infection, lymphedema of the ipsilateral upper extremity and seroma (1). Seroma is an accumulation of serous fluid that develops following the formation of skin flaps during mastectomy or in the axillary dead space in the immediate or acute post operative period (2). It is the most common complication after breast cancer surgery (3). Although it usually resolves within a few weeks, excessive fluid accumulation will stretch the skin and cause it to sag, resulting in patient discomfort, infection and prolongation of hospital stay. In addition, patients may be troubled by the need for multiple visits to the physician for aspiration (4). The exact aetiology of seroma formation remains controversial. Incidence of seroma formation after breast surgery varies between 2.5% and 51% depending on the method of detection (5,6,7).

1.2 JUSTIFICATION OF THE STUDY

Seroma is the commonest complication after breast surgery. It is a nuisance and its occurrence may lead to delayed wound healing, infections and delay in adjuvant therapy (52). It also leads to economic losses due to prolonged hospital stay and adds to psychological trauma. It also adds to the embarrassment of the operating surgeon as his/her experience does not influence the incidence of seroma after mastectomy (53).

Many methods have been tried to control seroma formation after mastectomy. Among them is shoulder immobilization, use of fibrin sealant, different drain regimens and dead space obliteration with no success as seroma after mastectomy still remains a common problem.

Feracrylum, a coagulant has not been used to control seroma after mastectomy though it has been proved to reduce post-operative fluid collection following dental, orthopedic and laparoscopic procedures.

1.3 STUDY OBJECTIVES

1.3.1 MAIN OBJECTIVE

To determine the effect of Feracrylum in reduction of the incidence of seroma after mastectomy.

1.3.2 SPECIFIC OBJECTIVES

1. To determine whether feracrylum reduces the daily drainage after mastectomy.
2. To determine whether feracrylum reduces the time necessary for drain retention after MRM.
3. To determine whether feracrylum reduces the volume of fluid accumulation after drain removal.
4. To determine whether feracrylum reduces the overall complications of seroma after mastectomy

1.4 HYPOTHESES

1.4.1 NULL HYPOTHESIS

Feracrylum is not effective in reduction of seroma formation after mastectomy

2 LITERATURE REVIEW

2.1 PATHOPHYSIOLOGY OF SEROMA

Aitken *et al* noted that several characteristics of breast surgery such as large dead space, irregularity of chest wall, consistent chest wall movements appear to make fluid accumulation likely (3).

Tadych *et al* in laboratory analysis of seroma of seroma fluid noted that protein and cell count had the characteristics of lymph. Traditionally lymph leakage from the upper extremity through transected lymph trunks is believed to be an important factor in fluid secretion and seroma formation, and post operative arm use is thought to act as a pump that forces large quantities of fluid into the empty axillary fossa (8).

Bonnema *et al* investigated the chemical and cellular nature of axillary seroma. On the 1st post operative day, it contained blood components but on day 2, it changed to a peripheral lymph like fluid that contained cells different from those of lymph, more protein and no fibrinogen, making coagulation impossible (9).

In association with these findings, Oertli *et al* postulated that fibrinolytic activity of the plasmin system in seroma and lymph may contribute to fluid accumulation and that fibrin complexes that have already formed within and around vessels may become degraded resulting in further leakage of fluid. However, their RCT failed to show any significant benefit of tranexamic acid, an antifibrinolytic agent against seroma formation (10).

In contrast, Watt-Boolsen *et al*, demonstrated that seroma is not merely an accumulation of serum, but an exudate resulting from an acute inflammatory reaction. They concluded that

seroma formation reflects an increased intensity and prolongation of the first phase of wound repair (11).

Wu et al, (12) reported an increase of vascular endothelial growth factor (VEGF) and decrease in endostatin in drainage fluid immediately after surgery. VEGF is a known mediator of angiogenesis, vascular proliferation and permeability. Endostatin is a potent inhibitor of angiogenesis (13, 14). These changes reflect induction of angiogenesis as a physiologic response to operative trauma and enhanced fluid accumulation.

2.2 RISK FACTORS IN SEROMA FORMATION

Although the pathophysiology of seroma remains uncertain, several factors make fluid accumulation likely after breast surgery (15). Several studies have been performed to investigate factors related to post-surgical seroma.

Say et al in a retrospective study of 1551 patients, demonstrated that old age increased the risk of seroma after mastectomy (16). Their findings were reproduced by Tejler et al (1985) in a study of 385 patients (17 and Kumar et al in a prospective study of 69 patients (18). However, a study by Chilson et al with a sample size of 351 did not show age as a factor that influenced seroma formation (19)

Tumor stage and grade would be thought to influence seroma formation. Gonzalez et al in 2003 in a study of 359 patients showed no association between tumor size and lymphnode status with seroma formation (20). Lumach in a study of 92 patients showed that tumor size was a principle factor influencing the incidence of seroma formation with T₃ tumors associated with increased incidence of seroma formation (21). No studies have found significant association with other patient and tumor characteristics such as presence of anemia, diabetes, smoking, breast size,

tumor grade, histological type, pathological tumor size, tumor side, specimen weight or size and tumor location (16, 21, 19 and 22).

A retrospective study of 204 patients by Aitken et al showed an increase in seroma formation with radical mastectomy compared with modified radical and simple mastectomy (3). This was also noted by Say et al (16). Gonzalez et al demonstrated that patients who underwent modified radical mastectomy had a greater incidence of seroma formation than those who underwent breast preservation surgery (20). These studies demonstrate that if the dissection is extensive, it will result in a large dead space beneath the flaps hence increasing the risk of seroma formation.

A randomized clinical trial by Purshotham et al (2005), showed a significant reduction of seroma formation with sentinel node biopsy compared with axillary lymph node dissection (23).

The use of electrocautery was significantly associated with increased seroma formation in an RCT by Porter et al (24). In this study, the flap and fascia were dissected either by electrocautery or by scalpel.

Several factors such as previous biopsy, blood loss, blood transfusion, operation time, skin incision, skin graft, surgeon and the type of anesthesia have been assessed, and individual study has demonstrated that a longer operation time and diagonal skin incision as compared to vertical skin incision increase seroma formation (25,16). On the other hand, no association was found for previous biopsy, type of anesthesia (local or general) or blood transfusion (26,27,17,18).

Available evidence was inconclusive for whether or not skill or experience of the surgeon influences seroma formation (17,25,28).

2.3 PREVENTION OF SEROMA FORMATION

Several prophylactic measures have been tried in reducing the incidence of seroma formation. Tranexamic acid was employed by Oertli et al, peri and post operatively in a dose of 1g three times daily in a randomized double-blind trial of 160 patients. No significant difference was observed between the groups (10). The concept of the use of fibrinolysis inhibitor was based on the hypothesis that, fibrinolytic activity of the plasmin system in serum and lymph might contribute to fluid accumulation.

The use of fibrin glue was studied by Uden et al (1993), in an RCT of 68 patients. Though there was a reduction in the incidence of seroma formation in the study group as compared to the control group, the difference was not statistically significant (28). These findings were reproduced by seven other studies (29, 30,31,32,33,34,35). An RCT by Vaxman et al even revealed that the use of fibrin glue increased seroma formation (36). Burak et al, in an RCT of 101 patients studied the use of bovine thrombin. 37 patients in the study group developed seroma compared to 40 in the control group. This difference was not significant (37).

Retention of drain in situ for a longer period seems to be a logical measure as formed seroma usually subsides with aspiration (38), however, drains are associated with a longer postoperative hospital stay, cause more pain after surgery, interfere with mobility and serve as potential routes for infection when drainage is prolonged (39). It has been observed that drains often fell off requiring reinsertion under local or general anaesthesia. This not only increases the risks for infection but also increases hospital costs and adds to the psychological trauma.

The intensity of negative suction pressure, no drainage, number of drains, types of drainage (closed suction versus passive drainage), type of drainage unit (evacuated bottle type versus bellow type) and type of drainage tube (multiple hole versus multiple channel type) have been

assessed. Cameron et al (1988), in an RCT of 40 patients observed that no drainage increased the incidence of seroma formation (40). This was confirmed by Somers, et al (1992), in an RCT of 227 patients (27). The intensity of negative suction pressure was studied by Van Heurn in an RCT of 78 patients. He showed that there was no difference in seroma formation with use of a low(150g/cm²), versus high(700g/cm²) pressure drains (41). His findings were duplicated by Bonnema, in an RCT of 141 patients (42). The efficacy of single drain or multiple drains, as studied by Petrek showed no difference in the number of drains used (26). Morris et al, found no difference in seroma formation between suction drainage versus passive drainage(43). There was still no significant difference in seroma formation with use of suction versus corrugated drainage and high vacuum evacuated bottle type versus low vacuum bellows type as suction unit as demonstrated by Bourke et al and Britton et al respectively (44,45). In contrast, in a study by Porter et al, a flat type drain with multiple channels running the length of the drain reduced seroma formation as compared with a flat type drain with multiple holes (24). It was speculated that the holes might clog more easily than channels which could lead to premature removal of the drains.

Suture flap fixation is a surgical technique for securing flaps to underlying tissue to close the dead space with sutures. Although this technique is not commonly performed, it is interesting that an RCT by Coveney et al demonstrated that this technique reduces seroma formation in patients undergoing mastectomy(46). In association with this, an RCT, by Purushotham et al demonstrated that mastectomy without drainage does not increase seroma formation when this technique is applied (23) also a prospective study by Schuijtvlot et al has demonstrated that seroma formation is reduced by the use of this technique in patients undergoing breast conservation surgery without axillary drainage (47).

The efficacy of shoulder immobilization has been investigated by Flew et al, who used a triangular bandage for 7 days in the study group and shoulder exercise from the second postoperative day in the control group. He noted no difference in the incidence of seroma formation in the two groups(48). These findings were reproduced by Browse et al, who used collar and cuff for 10 days in an RCT of 67 patients (49).

O'Hea et al (1999), investigated the utility of external compressive dressing. In an RCT of 135 patients,he noted that compressive dressing increased rather than reduced the incidence of seroma formation as compared to conventional dressing(50).

A study to determine the effect of single dose steroid injection in the reduction of seroma after mastectomy is ongoing(51).

2.4 COMPLICATIONS OF SEROMA AFTER MASTECTOMY

Although seroma formation is considered a trivial complication after mastectomy, it is the commonest complication and may be a nuisance. Seroma may lead to delayed wound healing, infection and delays adjuvant therapy (52). Besides the economic loss due to prolonged hospital stay and delay in rehabilitation, seroma formation also adds to psychological trauma. This is, in addition, often to the embarrassment of the operating Surgeon whose experience in surgery does not influence the incidence of seroma after mastectomy (53).

Although it usually vanishes within a few weeks, some patients may require repeated aspirations even for a period of months. Prolonged accumulation of post mastectomy seroma and repeated aspirations, predisposes to sepsis and wound related complications.

Seroma formation is also associated with serious morbidity such as flap necrosis, wound dehiscence and multiple outpatient visits.

Bonnema et al reported that low concentrations of albumin and transferrin in the seromas may contribute to the inability of the fluid to support lymphocyte blastogenesis and the wound healing process (9).

2.5 FERACRYLUM

2.5.1 PHARMACOLOGY

Feracrylum is an incomplete iron salt of poly acrylic acid. Within a pH range of 2.9 – 4, it forms water insoluble complexes with proteins of various origins including those contained in blood plasma. It is available as 1% aqueous solution which is transparent, pinkish, odour less with a sour taste. It can be sterilized at 120°C and 1.5 atm. It is stable in this form for 2 years or more. It has been found to be safe in animal studies and the only contraindication for its use, is in patients receiving S-Amino-Caproic Acid. It is safe in children and can be used in patients with blood clotting disorders such as afibrinogenaemia and hemophilia. Due to its high molecular weight it is not absorbed into the systemic circulation and hence does not affect the functioning of any organ such as liver or kidney. It does not display rebound bleeding or affect the healing process (54).

2.5.2 USES

Since it has antibacterial properties over both gram negative and gram positive and haemostatic activity, it has been widely used in external injuries and minor procedures (54). Its use in dental surgery has been studied by Kohli et al. It was shown to reduce post extraction bleeding period with an average time of 5.7 minutes over a control of 15.5 minutes. Vashnav et al demonstrated

that the use of Feracrylum as a haemostatic reduced bleeding from capillaries and venules, giving a clean field of surgery in neurosurgical procedures. He also showed that Feracrylum reduced the frequency of cauterization and post operative drainage collection. A 50ml dose of 1% solution of Feracrylum kept in contact with post operative wound for 2 – 3 minutes was shown to significantly reduce the overall post operative collection in orthopaedic surgical procedure. It has also been proposed for use throughout the procedure whenever any difficult ooze is encountered, as it will lead to a cleaner field without the use of electrocautery or other systemically acting chemical haemostatic agents (55).

The effect of Feracrylum in reduction of post operative oozing from the gall bladder fossa after successful completion of laparoscopic cholecystectomy has been investigated by Hemant Bhonsali et al. A 10ml dose of 1% Feracrylum introduced to the gall bladder fossa by a laparoscopic needle was shown to be effective (56).

In K.N.H feracrylum is extensively used by the cardiothoracic surgeons to control oozing during open heart procedures. It is also used to control oozing in many general surgical procedures.

RESEARCH METHODOLOGY

2.6 STUDY DESIGN

This is a Prospective Randomized Trial

2.7 STUDY POPULATION

All Breast Cancer patients undergoing MRM in Kenyatta National Hospital (K.N.H) Kenya.

2.8 INCLUSION CRITERIA

- All breast cancer patients undergoing MRM.
- All patients who consent to participate in the study.
- Aged over 18 years.

2.9 EXCLUSION CRITERIA

- Patients booked for toilet mastectomy.
- Patients booked for breast conservation.
- Patients with severe co-morbid conditions.

2.10 SAMPLE SIZE DETERMINATION

Sample size calculation was done to detect a 40% reduction in the number of patients developing seroma after mastectomy with Feracrylum compared to those without use of Feracrylum, with a α of 0.05 and a power of 80%. This is because; it has been established in previous studies that with use of drains alone there is a 25% reduction of seroma formation (39). It is of clinical relevance if a 40% reduction for those in the study group (65% of the subjects will have a successful outcome). A sample size of 42 patients was arrived at using the following formula.

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \sigma^2}{\delta^2}$$

Where $\alpha = 0.05$ (i.e. $Z_{1-\alpha/2}$ is 1.960)

$1-\beta$ is the power of 80% (i.e. $Z_{1-\beta}$ is 1.282)

σ is standard deviation (estimated as 2.8 derived from previous similar study)39.

δ is the desired reduction of seroma (by a factor of 2).

$$n = \frac{(1.96 + 1.282)^2 * (2.8)^2}{4} = 82.4$$

This gives 21 patients per group bringing the total to 42.

2.11 METHOD SAMPLING

Eligible persons who filled in a consent form were randomly assigned to two groups by using a computer generated code. The group assignment was not known to both patients and investigators, but known only to a research assistant did not take part in the final data collection and analysis on the effect of Feracrylum on seroma reduction.

2.12 THE SURGICAL PROCEDURE

Surgery and evaluation was performed by Consultants and Registrars in K.N.H. The primary surgeons experience (whether a Consultant or a Registrar) was noted and recorded. Modified Radical Mastectomy (MRM) was performed according to the standard procedure. A research assistant assigned the patients to either group A or B. Dissection of cutaneous flaps and breast was performed by scissors and scalpel and electrocautery was used to control small bleeding vessels. Axillary lymph node dissection was performed up to level two nodes. Group 'A' underwent MRM plus tube drainage. Group 'B' underwent MRM plus tube drainage plus Feracrylum. Drains were of equal calibre and had the same number of holes. No suction pressure was applied. The drains were placed in the chest and axillary flaps. For group B, 50ml of 1% aqueous solution of Feracrylum was applied over the raw areas intra operatively. It was maintained in contact with the raw areas for 5 minutes. The closure of the wound was done as per the standard procedure and conventional dressing applied. There was no shoulder immobilization in both groups. Dissected breast and axillary lymph nodes were taken to a pathologist for assessment of tumour size and node status.

2.12.1 Details of the surgery

An oblique elliptical incision was made to include the tumour and the nipple-areola complex of the involved breast after standard skin preparation. The skin flaps were elevated by scissors and scalpel with control of bleeding with electrocautery as dissection progressed. The flaps were raised superiorly to the clavicle, medially to the edge of the sternum, inferiorly to the rectus sheath and the coastal margins, and laterally to the edge of the latissimus dorsi muscle.

Subcutaneous fat of the axilla was removed as much as possible. The fascia over the pectoralis major muscle as well as the breast was resected as a subfascial dissection starting near the clavicle and extending downward over the mid-portion of the sternum. Perforating intercostals arteries and veins near the sternal margins were carefully clamped and ligated. Axillary flap was retracted upward and fascia over the pectoralis major muscle incised exposing the pectoralis minor beneath and the junction of the coracobrachialis and pectoralis minor origins superiorly at the coracoids process. The loose tissue over the axillary vein was incised and the vein wall exposed for a short distance beyond the subscapular vessels.

Level 1 and 2 lymph nodes were removed in the axillary node dissection that began by incising the clavi-pectoral fascia along the lateral edge of pectoralis minor muscle.

The specimen was freed from the latissimus dorsi muscle and finally from the suspensory ligaments in the axilla, where large veins and lymphatics were carefully ligated.

Operation field was inspected repeatedly for any bleeding points which were ligated. The wound was irrigated with saline and final inspection made for haemostasis. Two closed system perforated suction catheters were inserted for drainage. They were introduced through separate stab incisions made in the lower flap posteriorly. One was directed to the axilla. The other was

secured anterior to pectoralis major for drainage from under the skin flaps. The catheters were secured to the skin with non absorbable suture and attached to a urine bag.

For the feracrylum group, 50mls of 1% aqueous solution of feracrylum was instilled in the wound and remained in contact for five minutes before introduction of the drains.

Skin flaps in the axilla and elsewhere were compressed into place as the skin was finally closed. The choice of skin closure and wound dressing was performed according to the surgeon's preference.

Post operatively, volume drained was recorded daily for the two groups. Drain removal was performed when drainage was less than 30ml per day for two consecutive days. The day of drain removal was recorded and the total volume of the drainage was also be noted. Patients were free for discharge after drain removal unless seroma was detected before discharge.

Patients were reviewed on day 14 and 21 after discharge. The diagnosis of seroma was made clinically when a collection was detected beneath the skin flaps. In those with evident collection, aspiration was performed under sterile conditions both for diagnosis and treatment. The volume of each aspirate was noted. Repeat aspirations were performed weekly until no collection was detected.

2.13 DATA PRESENTION AND ANALYSIS

Data was collected by the principal investigator using a pre-designed data sheet. Coded data was entered into Microsoft Excel© and data cleaning performed before final data analysis. Data was then exported to STATA™ version 10 (College Station, Texas, USA) for analysis. The descriptive

statistics of age, weight, surgeons experience, tumour size, node status, total volume, day of drain removal, seroma, number of aspirations, and any complication of seroma formation were analyzed and presented in charts and tables. The total volume, the day of drain removal, the proportion of patients forming seroma and the complications of seroma were compared in both groups. Student's t-test was used for comparing the continuous variables and chi-square or Fisher's exact test for categorical variables. P value of 0.05 or less was considered significant.

2.14 ETHICAL CONSIDERATION

The study was commenced after approval by K.N.H/U.O.N Ethical Committee and an informed consent obtained from the patients.

3 RESULTS

Between May and September 2010, 48 breast cancer females undergoing MRM at KNH were enrolled in our study. They were randomized in two groups of 24 patients each. One group had Feracrylum infiltrated in the raw surfaces after MRM while the other one was the control group.

The ages of the patients ranged from 25 years to 84 years with a mean age of 51.3 years in the treatment group and 47.8 years in the control group (figure1). The weight ranged from 30kg to 86kg with a mean of 65.5kg in the treatment and 64.9kg in the control group (figure2). The mean systolic blood pressure was 127.9 mmHg in the treatment and 127.4 mmHg in the control group (figure4). The tumour size ranged from 3cm to 7cm with a mean size of 4.7cm in the treatment and 5.1cm in the control group (figure3). Different surgeons operated on patients in the study.

They were classified as either consultants or registrars depending on whether the surgeon was a qualified or a trainee surgeon. 13(54%) patients in the treatment group were operated on by consultant surgeons while 11(46%) in the control group were operated on consultant surgeons (figure 5). There was no significant difference in the surgeons experience among the two groups.

The mean tumour size in the control treatment group was 4.7cm (range 3cm to 7cm) while in the control group with a it was 5.1cm (range 3cm to7cm) (figure 3) the difference was not significant (p 0.15). 13(54%) patients in the treatment group had tumour positive nodes compared to 14(58%) (figure 6). This difference was not significant. There was no significant difference in the treatment and control groups in terms of age, weight, blood pressure, surgeon experience, node status and tumour size as shown in table 1

Table 1: descriptive statistic for both the treatment and control groups

Description	Treatment Group	Control Group	P value
Age (mean) (years)	51.3	47.8	0.25
Weight (mean) (kg)	65.5	64.9	0.90
Systolic Blood Pressure	128	127	0.88
Surgeon's experience			
- Consultant (%)	13(54)	11(46)	0.76
- Registrar	11(46)	13(54)	0.81
Node positive(%)	13(54)	14(48)	
Tumour Size	4.7	5.1	0.15

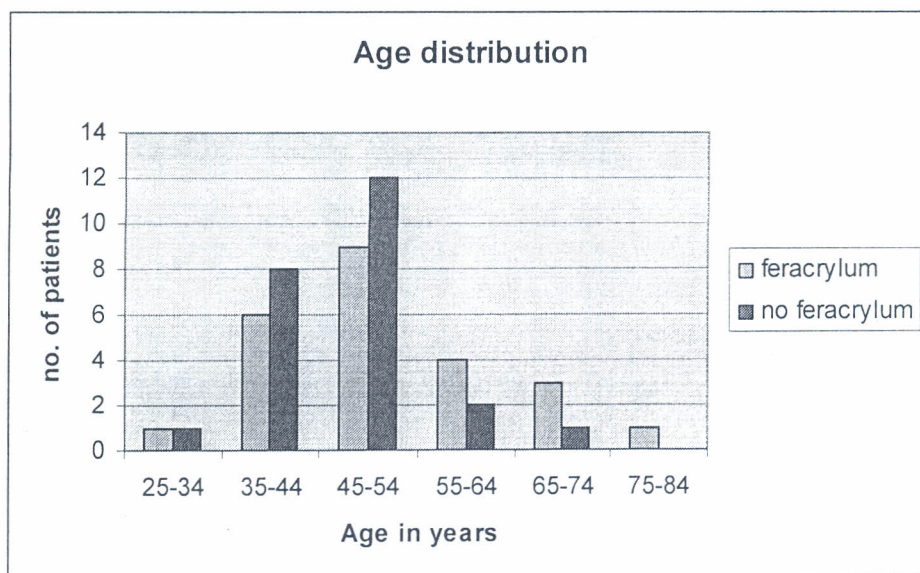


Figure 1: Age distribution among the groups

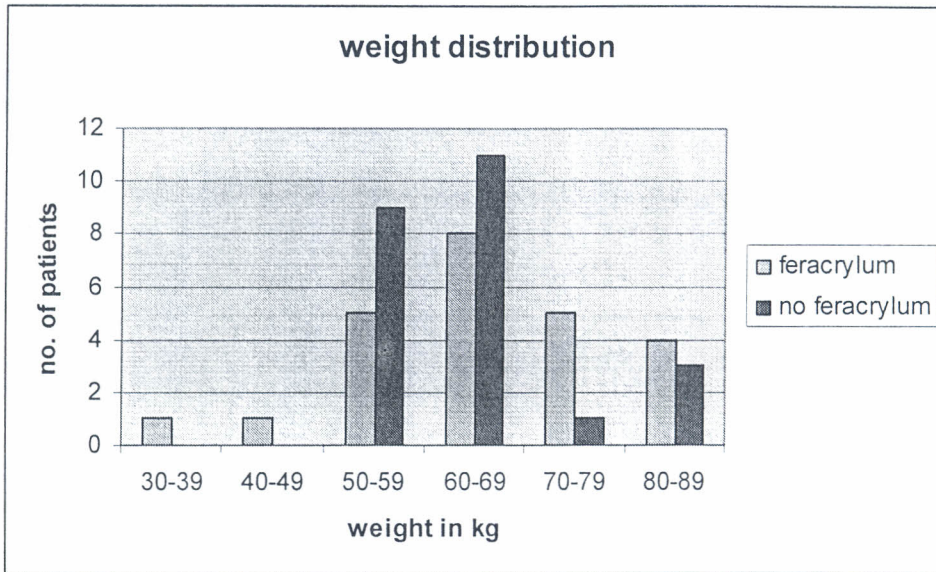


Figure 2: Weight distribution among the groups

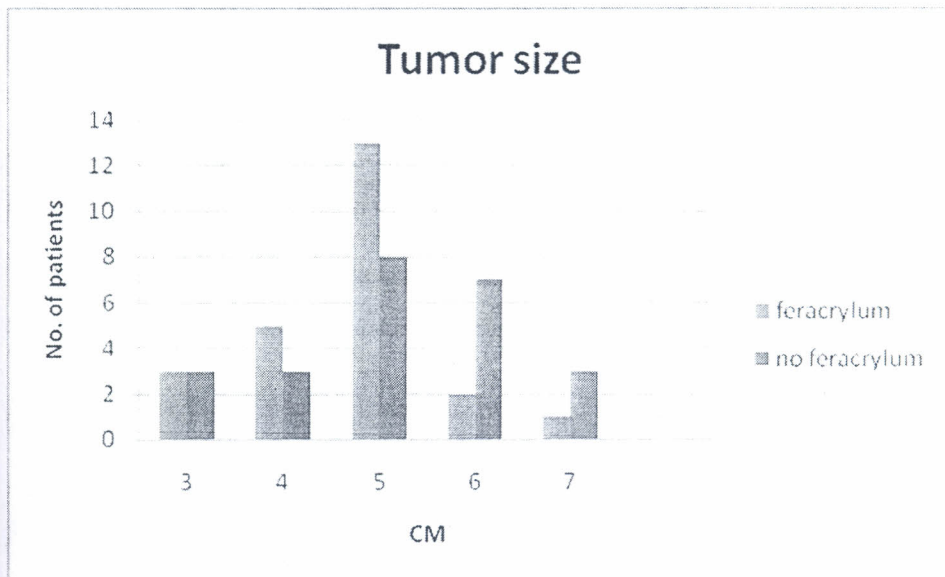


Figure 3: Tumor size distribution among the groups

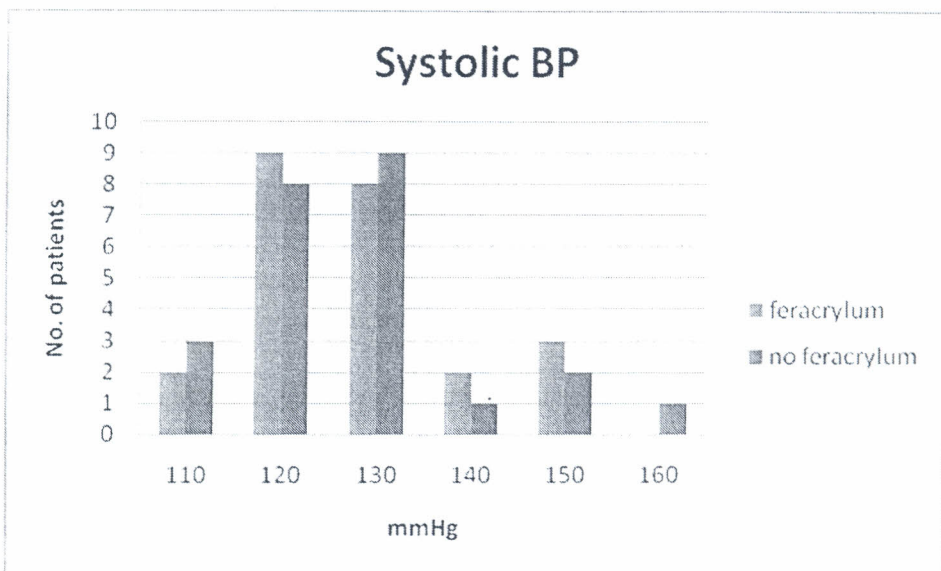


Figure 4: Systolic BP distribution among the groups

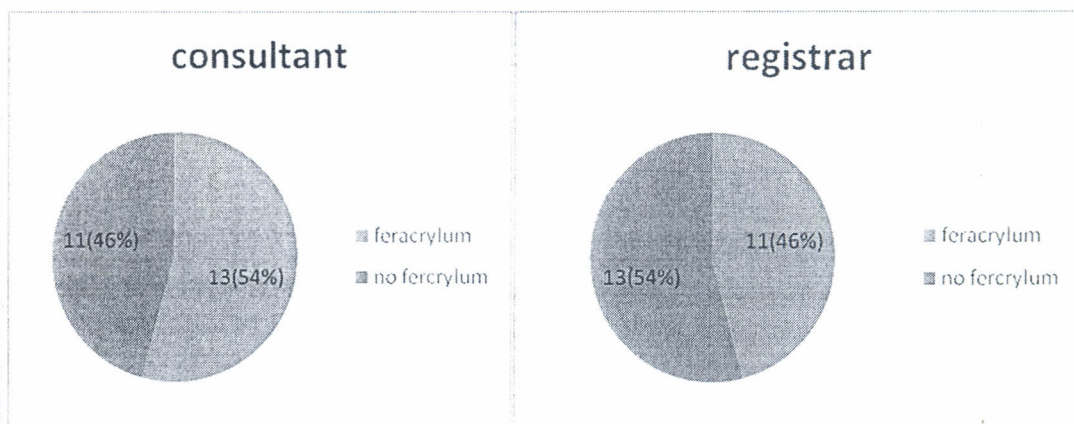


Figure 5: Surgeons' Experience among the groups

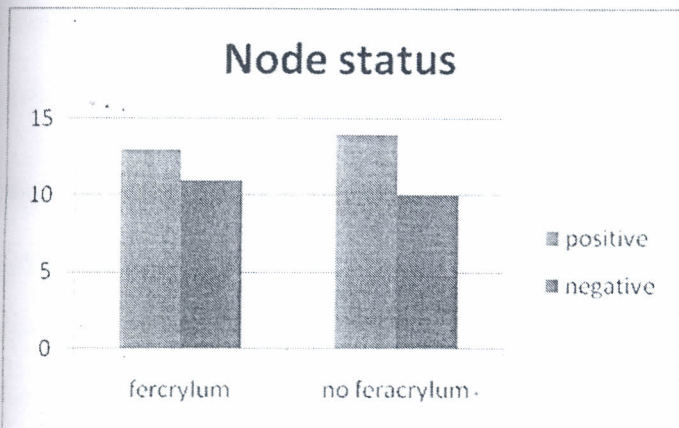


Figure 6: Node status distribution among the groups

3.1 Seroma assessment

The average number of days drains were retained was 5.9 in the treatment group while it was 12.8 in the control group (figure 7). This difference was significant (p less than 0.0001). On average the total volume of drainage was 695ml in the treatment group while it was 1486ml in the control group (figure 8) again this was a significant difference (p less than 0.0001). By the 14th post operative day 11(46%) patients had developed seroma in the treatment group while none (0) had developed in the control group. By the 21st day, 21(88%) patients in the treatment group had developed seroma but only 9(38%) in the control group had seroma (figure 9). The difference was significant (p less than 0.0001). Those patients in the treatment group who developed seroma required an average of 4 aspirations to drain the seroma while in the control group they required one aspiration (figure 10). (p less than 0.0001). No patient in the study developed major complication like flap necrosis. 2(8%) of patients in the treatment group developed wound infection requiring outpatient antibiotic treatment while the control group had 15(71%) patients with infection mainly at the drain site (figure 11). The difference was

significant, thus feracrylum was associated with reduced volume of drainage, reduced days of drain retention and reduced complication rates (Table 2).

Table 2: Result of drain retention, total volume, seroma and complications.

Description	Treatment Group	Control Group	P Value
Number of days drain retained	5.9	12.8	< 0.0001
Total Volume of drainage	695	1486	< 0.0001
Seroma formation (day 14) (N)	11 (46%)	0 (0%)	< 0.001
Seroma formation (day 21) (N)	21 (88%)	9 (38%)	< 0.001
Complication(s)	2 (8%)	15 (71%)	< 0.001
No. of Aspirations	3.6	0.7	< 0.0001

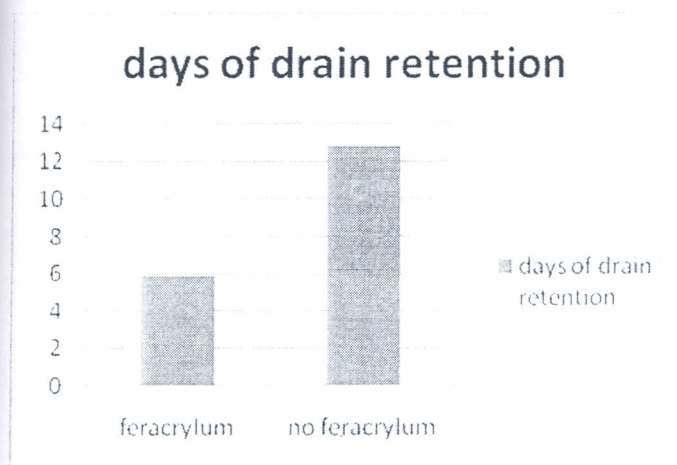


Figure 7: average no. of days of drain retention among the groups

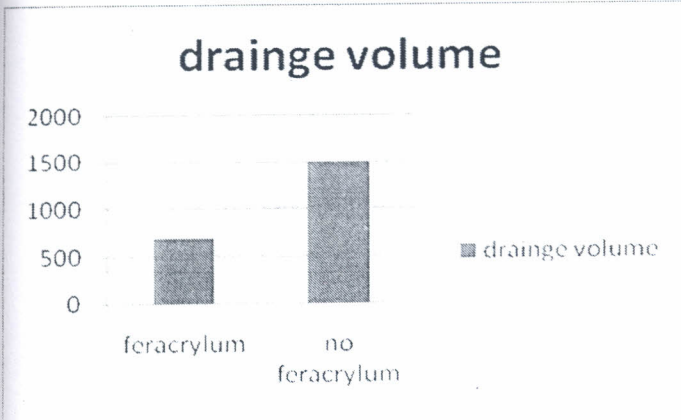


Figure 8: total drainage volume among the groups

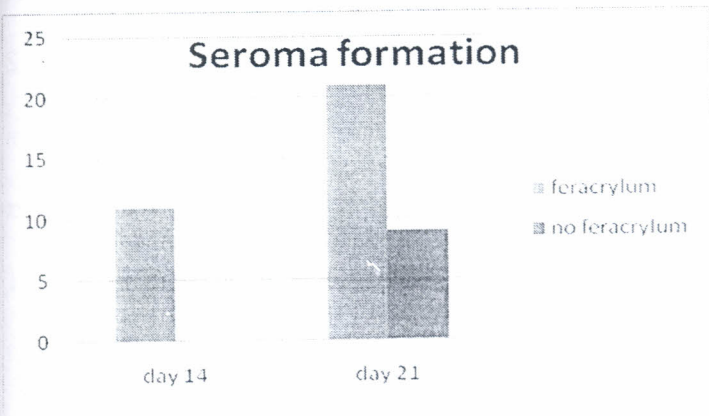


Figure 9: seroma formation at day 14 nd 21 among the groups

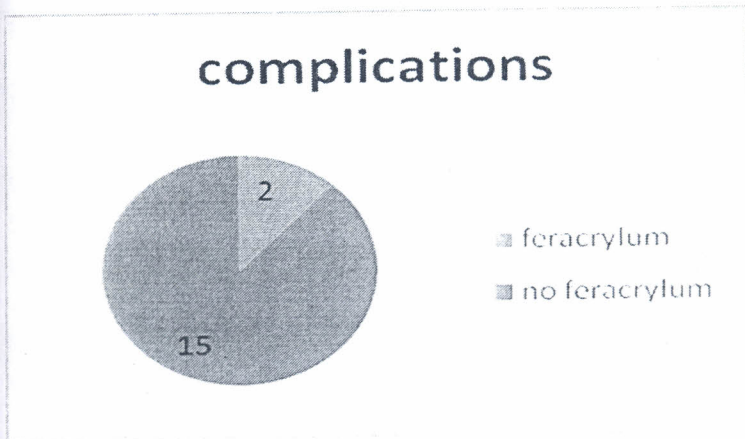


Figure 10: total no. of complications among the groups

no. of spirations

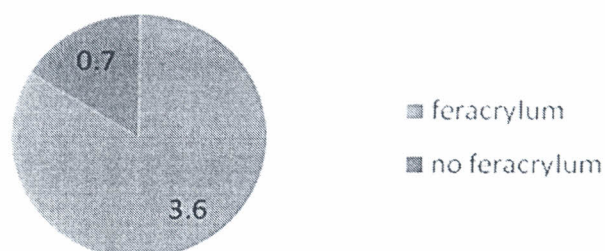


Figure 11: average no. of aspirations among the groups

Since there was a significant difference observed between the feracrylum and the control group, in terms of total volume of drainage a multivariate analysis was performed to evaluate the association between the various clinic-pathological factors and the total volume of drainage.

There was no association between the age, the weight, systolic blood pressure, tumour size, tumour stage, surgeon's experience and the total volume of drainage (table 3).

Table 3: Regression total volume, treatment, age, weight, systolic bp, tumour-stage, tumour-size (cm), surgeon

Total volume	Coefficient	Std Error	T	p> t	95% Confidence Interval	
Treatment	-741.003	130.596	-5.67	0	1005.159	-476.847
Age	11.39	8.337	1.37	0.18	-5.466	28.247
Weight	-1.876	7.124	-0.26	0.794	-16.286	12.533
Sbp	-5.277	8.07	-0.65	0.517	-21.6	11.045
t-stage	-107.471	83.857	-1.28	0.208	-277.09	62.149
t-size (cm)	68.474	63.1	1.09	0.285	-59.158	196.106
Surgeon	181.689	115.397	1.57	0.123	-51.725	415.102
Constant	1340.812	721.269	1.86	0.071	-118.09	2799714

Multivariate analysis was also performed to evaluate the association between the significant difference in seroma formation at day 21 observed in the feracrylum and the control group with respect to the various clinico-pathological factors. There was no association between the age, weight, systolic blood pressure, tumour size, tumour stage, surgeon's experience and the incidence of seroma (table 4).

Table 4: Regression seroma day21 – treatment, age, weight, systolic bp, tumour-stage, tumour-size (cm), surgeon

sday 21	Coefficient	Std Error	T	p> t	95% Confidence. Interval	
Treatment	0.57	0.14	4.19	0	0.29	0.84
Age	-0.01	0.01	-0.77	0.45	-0.02	0.01
Weight	0.01	0.01	0.72	0.49	-0.01	0.02
Sbp	0.01	0.01	0.62	0.54	-0.01	0.02
t-stage	-0.09	0.09	-1.07	0.29	-0.27	0.08
t-size	0.05	0.07	0.82	0.41	-0.08	0.19
Surgeon	0.06	0.12	0.47	0.64	-0.19	0.3
_cons	-0.48	0.75	-0.64	0.53	-2	1.04

4 DISCUSSION

The main aim of this RCT was to determine the effect of feracrylum on seroma after modified radical mastectomy. The randomization was success in the two groups with the distribution of patents being balanced in terms of age, tumour size, lymph node status and systolic blood pressure. There was also no difference in terms of surgeons experience among the two groups.

The incidence of seroma was 38% in the control group while it was 88% in the study group. This is in keeping with other studies that give seroma incidence in the range of 30% to 92%. A study by Barwell et al found the incidence as 51% after drain retention for one week and concluded that drain retention for a longer time did not protect against seroma formation(5). However in our study, early drain removal as in the feracrylum group (5.9 vs12.8 days) was associated with significant increase in the incidence ($p<0.0001$).

This study showed that patients' age and weight do not affect the incidence of seroma after mastectomy. This is in keeping with a study by chilson et al (19). Also in this study no relationship was observed between the incidence of seroma and tumour size, lymph node status, blood pressure, and surgeon's experience. This agrees with studies by Gonzalez et al in 2003(20), and another study by Tegler et al, though it contradicts the findings of Lumachi et al in 2004 which showed tumour size as the principle factor influencing seroma formation (21).

Feracrylum was associated with a significant reduction in the total volume of drainage (695ml and 1486ml in the control group). This is in keeping with observation by Kohli et al who showed reduced bleeding with feracrylum following dental extraction (54). It also agrees with the findings of Vaishnav who used feracrylum to arrest bleeding from small veins and capillaries in neurosurgical and orthopaedic procedures (55).

Feracrylum use was associated with a significant reduction in the number of days necessary for drain retention (5.9 vs 12.8). This could be because of its ability to coagulate plasma proteins leading to reduced post operative drainage. While this was an advantage in that it reduced the days of hospital stay and overall hospital bill, as patients were discharged home after drain removal, it was associated with a high incidence of seroma formation. Probably because feracrylum coagulates serum proteins it led to obstruction of drain holes leading to reduced drain output and hence early removal. This was associated with several outpatient visits, and multiple skin punctures (3.6 vs 0.7) to drain the seroma. Our findings correspond with other studies performed to investigate other chemical agents and seroma. Vexman in his study showed that fibrin glue increased the incidence of seroma while Burac using bovine thrombin did not show a difference in seroma rates following mastectomy (36, 37).

Our study demonstrates that drain retention for a long time was associated with significant reduction in the incidence of seroma (38% vs. 88%), but did not abolish seroma completely. On the other hand it was associated with a higher frequency of wound related complications (71% vs. 8%). This corresponds with other studies that have showed drain retention for long to be associated with longer post operative hospital stay, cause more pain after surgery, interfere with mobility and serve as potential routes for infection (36).

4.1 CONCLUSION

Although feracrylum did not reduce the incidence of seroma after modified radical mastectomy, it was associated with significant reduction in the total volume of drainage, reduced number of days necessary for post operative retention of drains and wound related complications. This translated to early discharge from hospital, reduced hospital costs, reduced post operative pain, and reduced psychological trauma.

REFERENCES

1. Harris JR, Lippman ME, Morrow M, Osborne C: Disease of the breast. 2nd Edition Philadelphia: Lippincott, Williams and Wilkins, 2000.
2. Pogson CJ, Adwani A, Ebbs SR. seroma following breast cancer surgery. *European journal of Surgical oncology*. 2003; 29: 711-17.
3. Aitken DR, Minton JP. Complications associated with mastectomy. *Surg Clin North AM* 1983; 63:1331-52.
4. Halsted WS : Developments in the skin grafting operations for cancer of the breast. *JAMA* 60:416 – 452, 1913.
5. Barwell J, Campell L, Watkins RM, Teasdale C: How long should drains stay in after breast surgery with axillary dissection? *Ann R coll surg Eng* 1997; 99:435-437.
6. Woodworth PA, McBoyle MF, Helmer SD, Beamer RL. Seroma formation after breast cancer surgery; incidence and predicting factors. *AM Surg* 2000; 66: 444 – 450.
7. Brayant M, Baum M: Post operative seroma following mastectomy and axillary dissection.
8. Tadych K. Donegan WL. Postmastectomy seromas and wound drainage. *Surg Gynecol Obstet*. 165:483 – 487, 1987.
9. Bonnema J, Van Geel AN, Ligtenstein DA, Wiggers T: The composition of serous fluid after axillary dissection. *Eur J Surg* 165:9 – 13, 1999.
10. Oertli D. Laffer U. Habertuer F. Kreuter U. Harder F. Perioperative tranexamic acid reduces the local wound complication rate after surgery for Breast cancer. *Br J Surg*. 1995;130:99-101.

11. Watt – Boolsen S, Nielsen VB, Jensen J, Bak S: Postmastectomy seroma. A study of the nature and origin of seroma after mastectomy. *Da Med Bull*, 36:487 – 489, 1989.
12. Wu FP, Hoekman K, Meijer S, Cuesta MA: VEGF and endostatin levels in wound fluid and plasma after breast surgery. *Angiogenesis* 6:255 – 257, 2003.
13. Toi M, Matsumoto T, Bando H: vascular endothelial growth factor: Its prognostic, predictive and therapeutic implications. *Lancet Oncol* 2:667 – 673, 2003.
14. Folkman J: Endogenous angiogenesis inhibitor. *Apmis* 112:496 – 507, 2004.
15. Kuroi K, Shimozuma K, Taguchi T, Imai H, Yamashiro H, Ohsumi S, Saito S. Evidence based risk factors for seroma formation in breast surgery. *Jpn J Clin Oncol*. 2006;36:197 – 206.
16. Say CC, Donegan W. A bio-statistical evaluation of complications from mastectomy, *Surg Gynecol Obstet* 1974; 138: 370 – 6.
17. Tejler G, Aspegren K: Complications and hospital stay after surgery for breast cancer. A prospective study of 384 patients. *Br J Surg* 1985; 72: 542 – 4.
18. Kumar S, Lal B, Misra MC. Post mastectomy seroma: A new look into the etiology of an old problem. *JR Coll Surg Edinb* 1995; 40: 292 – 4.
19. Chilson TR, Chan FD, Lonser RR, Wu TM, Aitken DR. Seroma formation after MRM. *American J Surg* 1992; 58: 704.
20. Gonzalez EA, Saltzstein EC, Reidner CS, Nelson BK. Seroma formation following breast cancer surgery. *Breast J* 2003, 9: 385 – 388.
21. Lumachi F, Brandes AA, Burelli P, Basso SM, Iacobone M, Ermani M. seroma prevention following axillary dissection in patients with breast cancer by using

- Ultrasound scissors. A Prospective Clinical study. *Eur J Surg Oncol* 2004; 30: 526 – 530.
22. Woodworth PA, McBoyle MF, Helmer SD, Beamer RL. Seroma formation after breast cancer surgery; incidence and predicting factors. *AM Surg* 2000; 66:444 – 450.
23. Purushotham AD, Upponi S, Klevesath MB, Bobrow L, Millar K, Myles JP et al. Morbidity after sentinel node biopsy in primary breast cancer: results from RCT. *J clin Onco* 2005; 23: 4312-21.
24. Porter KA, O'connor S, Rimm E, Lopez M: Electrocautery as a factor in seroma formation following mastectomy. *AM J Surg* 1998; 176: 8 – 11.
25. Schultz I, Barholm M, Grondal S. Delayed shoulder exercises in reducing seroma frequency after MRM. A prospective randomized study. *Ann Surg Onco* 1997; 4: 293 – 7.
26. Petrek JA, Peters MM, Cirrincione C, Thaler HT. A progressive trial of single versus multiple drains in the axilla after lymphadenectomy. *Surg Gynaecol Obstet* 1992; 51: 266 – 9.
27. Somers RG, Jablon LK, Kaplan MJ, Sandler GL, Roosenblatt: The use of closed suction drainage after lymphectomy and axillary node dissection for breast cancer. A prospective randomized trial. *Ann Surg* 1992; 215: 146 – 9.
28. Uden P, Aspegren K, Balldin G, Game JP, Larsson SA. Fibrin adhesive in radical mastectomy. *Eur J Surg* 1993; 159: 263 – 5.

29. Gilly FN, Francois Y, Sayag –Beaujard AC, Glehen O, Brachet A, Vignal J.
Prevention of lymphorrhoea by means of fibrin glue after axillary lymphadenectomy in breast cancer: Prospective Randomized trial. *Eur Surg res*: 1998;30:439-443.
30. Berger A, Tempfer C, Hartmann B, Kornprat P, Rossmann A, Neuwirth G et al. sealing of postoperative axillary leakage after axillary lymphadenectomy using a fibrin glue coated collagen patch: A prospective randomized study. *Breast cancer Res Treat* 2001; 67: 9 – 14.
31. Moore M, Burak WE Jr, Nelson E, Kearney T, Simmons R, Mayers L et al. Fibrin sealant reduces the duration and amount of fluid drainage after axillary dissection: A randomized prospective clinical trial. *J AM Coll Surg* 2001; 172; 591 – 9.
32. Langer S, Guenther JM, Di Fronzo LA: Does fibrin sealant reduce drain output and allow earlier removal of drainage catheters in women undergoing operation for breast cancer? *AM Surg* 2003; 69: 77 – 81.
33. Ulusoy AN, Polat C, Alvur M, Kandermir B, Bulut F. Effect of fibrin glue on lymphatic drainage and on drain removal time after MRM for breast cancer. *Eur J Surg Onco* 2004; 30: 602 – 9.
34. Mustonen PK, Harma MA, Eskelinen MJ. The effect of fibrin sealant combined with fibrinolysis inhibitor on reducing the amount of lymphatic leakage after axillary evacuation in breast cancer. A prospective randomized clinical trial. *Scand J Surg* 2004; 93: 209 – 12.
35. Medl M, Mayerhofer K et al. The application of fibrin glue after axillary lymphadenectomy in the surgical treatment of human breast cancer. *Anticancer Res* 1995; 15: 2843 – 5.

36. Vaxman F, Kolbe A, Stricher F, Zund D, Volkman P, Gros D, et al. Does fibrin glue improve drainage after axillary lymph node dissection? Prospective and randomized study in humans. *Eur Surg Res* 1995; 27:346 – 52.
37. Burak WE Jr, Goodman PS, Young DC, Farrar WB. Seroma formation following axillary dissection for breast cancer: Risk factors and lack of influence of bovine thrombin. *J Surg Oncol* 1997; 64: 27 – 31.
38. Collins JP, Simpson JS. Guidelines for the surgical management of breast cancer. *Aust NZ J surg suppl* 1988; 68: 17-18.
39. Jain PK, Sowdi R, Anderson AD, Mac Fie J. Randomized clinical trial investigating the use of drains and fibrin sealant following surgery for breast cancer. *Br Surg* 2004; 91:54-60.
40. Cameron AE, Ebbs SR, Wylie F, Baum M. Suction drainage of the axilla: a prospective randomized trial. *Br J Surg* 1988;75:1211.
41. Van Heurn LW, Brink PR. Prospective randomized trial of high versus low drainage after axillary lymphadenectomy. *Br J Surg* 1995;82:931–2.
42. Bonnema J, Van Geel AN, Ligtenstein DA, Schmitz PI, Wiggers T. A prospective randomized trial of high versus low vacuum drainage after axillary dissection for breast cancer. *Am J Surg* 1997;173:76–9.
43. Morris AM. A controlled trial of closed wound suction. *Br J Surg* 1973;60:357–9.
44. Bourke JB, Balfour Tw, Hardcastle JD, Wilkins JL. A comparison between suction and corrugated drainage after simple mastectomy: a report of a controlled trial. *Br J Surg* 1976;63:67–9.

45. Britton BJ, Gilmore OJ, Lumley JS, Castleden WM. A comparison between disposable and non-disposable suction drainage units: a report of a controlled trial. *Br J Surg* 1979; 66: 279- 80.
46. Coveney EC, O'Dwyer PJ, Geraghty JG, O'Higgins NJ. Effect of closing dead space on seroma formation after mastectomy. A prospective randomized clinical trial. *Eur J Surg Oncol* 1993;19:143–6.
47. Schuijtvlot M, Sahu AK, Cawthorn SJ. A prospective audit of the use of a buttress suture to reduce seroma formation following axillary node dissection without drains. *Breast* 2002;11:94–6.
48. Flew TJ. Wound drainage following mastectomy: The effect of restriction of shoulder movement. *Br Surg* 1979;66:302–5.
49. Browse DJ, Goble D, Jones PA. Axillary node clearance: Who wants to immobilize the shoulder? *Eur J Surg Oncol* 1996;22:569–70.
50. O'Hea BJ, Ho MN, Petrek JA: External compression dressing versus standard dressing after axillary lymphadenectomy. *Am J Surg* 1999;177:450–3.
51. [Clinicaltrials.gov/show/ NCT00307606](https://clinicaltrials.gov/show/study/NCT00307606).
52. De-Feiter PW, Stockmann HB, Wereldsma JC, Van-Putten WL, Van-Assendelft PJ. Wound infection after mastectomy or lymphectomy for breast cancer. *Breast J* 1997; 6: 1 – 11.
53. Funnel IC, Crowe PJ, Dent DM. Does surgical experience influence mastectomy complication? *Ann R Coll Surg Engl* 1992; 74: 178 – 180.

54. AM Bhagwat, S Save, S Burli SG Karki: A study to evaluate the antimicrobial activity of feracrylum and its comparison with povidone iodine. *Indian J Pathol Microbiol* 44 (4): 431-433, 2003.
55. Vaishnav MC: Controlled trial of a new locally hemostatic agent in major orthopaedic surgery. Paper read at the all India orthopaedic conference. Lucknow 18th November 1992.
56. Bhonsali H: Effect of feracrylum on laparoscopic cholecystectomy. Proceedings from the 39th World congress on surgery. International college of surgeons. London, p35, 1994.
57. Melinda M Mortenson, Yan Xing, Storm W, et al. Fibrin sealant does not decrease seroma output or time to drain removal following inguino-femoral lymph node dissection in melanoma patients: A randomized controlled trial. *World J Surg Oncol*. 2008; 6:63

APPENDICES

APPENDIX 1: DATA SHEET

PERSONAL INFORMATION

NAME OF THE PATIENT

IP. NO

SEROMA RISK FACTORS

AGE

WEIGHT

TUMOR STAGE

B.P

TYPE OF SURGERY

Surgeon experience

Tumor size

Node status

SEROMA ASSESSMENT

Total volume of drainage

Day of drain removal

Seroma presence

Day 14

Day 21

Duration of seroma

Complications of seroma

Infection

Wound dehiscence

Flap necrosis

APPENDIX 2: CONSENT FORM

CONSENT EXPLANATION

Study objective

Results obtained from the study will provide baseline information for the prevention of seroma after mastectomy.

RISKS

The study will involve puncturing of the skin and numerous visits to the hospital.

BENEFITS

The test drugs will be free of charge.

COST AND PAYMENT

Participation is voluntary and patients will meet all the hospital and theatre expenses.

WITHDRAWAL PRIVILEGE

Patients will be free to withdraw from the study at any time

CONSENT FORM

I-----from----- do agree to be part of the study the risks and benefits of which have been fully explained as by Dr Gatura.

My participation is voluntary and I do not expect any financial benefit.

I will bear the cost of multiple visits to the hospital and will withstand the many skin punctures required for aspiration of the seroma

Full name-----

Sign-----

Date-----

Dr's signature-----

swahili version

Mimi-----kutoka-----nimekubali kuhushishwa kwa utafiti wa feracrylum ambao unaendelea.madhara ya utafiti huu yameelezwa vyema kabisa na daktari Gatura. Naelewa kwamba kuhusika kwangu ni kwa kujitolea na sitarajii kulipwa. Pia nitagharamia mahitaji yote ya hospitali na upasuaji. Ni tavumilia kundungwandungwa iwapo maji itaonekana kwa mwili wangu pahali pa upsauji.

Sahihi-----

Tarehe-----

Sahihi ya daktari-----.



KENYATTA NATIONAL HOSPITAL

Hospital Rd. along, Ngong Rd.

P.O. Box 20723, Nairobi.

Tel: 726300-9

Fax: 725272

Telegrams: MEDSUP", Nairobi.

Email: KNHplan@Ken.Healthnet.org

17th May 2010

Ref: KNH-ERC/ A/486

Dr. Joseph Gordon Gatura Wambua
Dept. of Surgery
School of Medicine
University of Nairobi

Dear Dr. Gatura

RESEARCH PROPOSAL: "FERACRYLUM IN REDUCTION OF SEROMA AFTER MASTECTOMY" (P5/1/2010)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and **approved** your above revised research proposal for the period 17th May, 2010 to 16th May, 2011.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF. A. N. GUANTAI
SECRETARY, KNH/UON-ERC

c. Prof. K. M. Bhatt, Chairperson, KNH/UON-ERC
The Deputy Director CS, KNH
The Dean, School of Medicine, UON
The Chairman, Dept. of Surgery, UON
The HOD, Records, KNH
Supervisors: Dr. Joseph W. Githaiga, Dept. of Surgery, UON
Dr. W.K. Otsianyi, Dept. of Human Anatomy, UON

UNIVERSITY OF NAIROBI
MEDICAL LIBRARY