CASE SERIES OF SUBTOTAL EXENTERATION WITH BUCCAL MUCOSAL GRAFT FOR ORBITAL SQUAMOUS CELL CARCINOMA

by

Sharisha Surajballi

Submitted in partial fulfilment of the academic requirements for the degree of MMed in the Department of Ophthalmology School of Clinical Medicine College of Health Sciences University of KwaZulu-Natal Durban 2016
Declaration

I Sharisha Surajballi 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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Signed: ___________________________  Date: 21 March 2017
Acknowledgements

Acknowledgement is given to Dr Carl-Heinz Kruse for his guidance in this study.
Overview of Thesis

The aim of the study was to look for a safe alternative to a disfiguring total orbital exenteration for orbital squamous cell carcinoma, so that a standard hospital issue inexpensive stock ocular prosthesis can be fitted with improved aesthetic results, rather than an expensive custom made prosthesis for the patient’s own cost.

The subjects and methods involved a retrospective case review which was performed of patients from St Aidan’s Missionary Hospital initially, which was later amalgamated into the McCords Provincial Eye Hospital, Durban, KwaZulu-Natal, South Africa. Ten consecutive patients who underwent an ‘extended’ lid-sparing subtotal exenteration with minimally preserved healthy conjunctiva and a buccal mucosal graft were identified over a 3 year period from 1 January 2011 to 31 December 2013. Patients’ clinical records were reviewed.

Results included all of the ten patients having a good aesthetic outcome at 4 weeks and six months with a standard hospital issue stock ocular prosthesis. One patient had a repeat buccal mucosal graft after forniceal shortening. Three patients had local recurrences within one year but all recurrences were identified easily and total exenteration was successfully performed. The survival rate at 3 years was ninety percent as one patient was lost to follow-up.

A subtotal orbital exenteration with minimally preserved healthy conjunctiva and a buccal mucosal graft is cost effective, safe and cosmetically acceptable with a standard ocular prosthesis.
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PART 1: INTRODUCTION

The purpose of this retrospective study was to look for a safe alternative to a disfiguring total orbital exenteration for orbital squamous cell carcinoma, so that a standard hospital issue inexpensive stock ocular prosthesis can be fitted with improved aesthetic results, rather than an expensive custom made prosthesis for the patient’s own cost. Records were reviewed from 1 January 2011 to 31 December 2013 from the McCords Provincial Eye Hospital, KwaZulu-Natal, South Africa.

SQUAMOUS CELL CARCINOMA OF THE EYE:
“Understanding the disease and therapeutic options”

Ocular squamous cell carcinoma of the cornea and conjunctiva was first described in the 19th century [1]. Ocular surface squamous neoplasia (OSSN) was later used to describe intraepithelial and invasive squamous cell carcinoma of the cornea and conjunctiva [2]. This is further broken down into:

A) Conjunctival intraepithelial neoplasia (CIN/ conjunctival dysplasia). CIN involves replacement of the normal conjunctival epithelium by atypical squamous cells. Mild dysplasia involves less than fifty percent thickness of the epithelial layer, whereas severe dysplasia involves more than fifty percent.

B) Carcinoma in situ (CIS) is the replacement of full thickness epithelium by dysplastic cells, however the basement membrane remains intact.

C) Invasive squamous cell carcinoma (SCC) represents malignant cells which have broken through the epithelial basement membrane.
Presenting symptoms may be asymptomatic, or a conjunctival lump, ocular surface redness, irritation, pain, blurred vision, etc. Clinical appearance includes any of the following: no specific lesion seen, leukoplakia (white keratinization), fibrotic, gelatinous, fleshy, papillomatous, papillary, vascular, nodular, diffuse or pigmented. Size and distribution is varied.

Risk factors for OSSN include: male gender, advanced age, ultraviolet light exposure, xeroderma pigmentosum, blonde hair, light complexion, cigarette smoking, human papillomavirus, and atopic disease. There is a higher occurrence in patients with HIV.

Investigations range from histopathological confirmation of the disease either with an incisional or excisional biopsy. Impression cytology when available has a positive predictive accuracy of 97.4% when compared to tissue histology.

Radiological imaging with Computerized Tomography (CT) scan for extent of surgical planes, bone involvement and brain metastasis. Ideally, a MRI is best suited for clearer tissue involvement, however access to this is limited. General abdominal ultrasound imaging and chest x-rays for metastatic assessment is included. Haematological workup is part of this workup too. A general physical examination must include lymph node assessments with palpation and ideally fine needle biopsies performed on suspiciously enlarged lymph nodes.

Treatment is aimed at complete eradication of the tumour mass with the primary goal of saving the patient’s life and saving the vision as the secondary goal. Treatment modalities range from medical non-invasive methods, simple excision to exenteration. Management plans are individualized, however this is guided by the size of the lesion (basal area and thickness), lesion location, invasiveness of the lesion, the fellow eye status and the general health and age of the patient.

Discrete non-invasive masses of the cornea or conjunctiva can be treated with mitomycin C or 5-fluorouracil topical chemotherapeutic agents, topical and or intralesional immunotherapy with Interferon alpha-2b or simple excision. With a simple excision, frozen section technique is preferred to obtain clear surgical margins or modified Moh’s micrographic technique. However many of the above modalities are not widely available.
Further to this would be other globe preserving treatment options for invasive OSSN, which can include varied combinations of topical chemoreduction, topical and or intralesional Interferon alpha, surgical excision, cryotherapy or brachytherapy\(^{[18-22]}\). When a lesion invades the anterior orbit or if there is a recurrence of the tumour which is not amenable to medical treatment or combination therapy, then an exenteration is the treatment of choice\(^{[23]}\).

Understanding what options are available for an orbital exenteration and which patients are suitable for such options are very important. An orbital exenteration can be either a total, subtotal or extensive exenteration. A total exenteration involves the removal of the eyelids, conjunctiva, globe, entire orbital contents including the periorbita\(^{[24]}\). A subtotal exenteration may spare the eyelids and periorbita, but removes the globe, and extraocular muscles\(^{[25]}\). An extended or superexenteration is the most aggressive, involving everything as with a total exenteration, as well as removal of the bony orbital walls, surrounding paranasal sinus tissues and/or intracranial tissue.

The following classification by Goldberg et al\(^{[9]}\) was utilized for this study: “Orbital exenteration was either total or subtotal based on the following criteria: Total exenteration procedures involved removal of the entire orbital contents including the periorbita, whereas subtotal exenterations preserved at least a quadrant of the orbit or the apical orbital tissues posterior to the globe. Exenteration procedures were then subclassified as eyelid-sparing, conjunctival-sparing and globe-sparing procedures. Eyelid-sparing and conjunctival-sparing procedures were defined as those in which 50% or more of the patient’s pretarsal eyelid or bulbar conjunctiva was preserved.”

The above methods are tailored to individual patients based on their disease process (eyelid or orbital malignancy or infection); the extent of tissue involvement; the health status of the patient as well as the patient’s desires. Treatment is either lifesaving, for disease control, palliative or cosmetic.

A subtotal exenteration is recommended where tumour free margins can be obtained and is more successful if this is achieved before distant metastasis occurs\(^{[26]}\). A total exenteration is
aimed at extensive anterior or posterior orbital involvement with or without bony involvement. It can take months to fully heal, frequent wound dressing changes and follow-ups are required and complications are often encountered. Complications include: fistula or sinus formation, infection, orbital abscesses, tissue necrosis or eschar formation, non-healing ulcer or implant exposure. A subtotal exenteration as in this study was aimed at less extensive anterior orbital involvement since preservation of some orbital tissues facilitates completion of the primary reconstruction. Healing is much faster and complications are infrequent.

Rehabilitation of an exenterated socket can be either by primary granulation and secondary skin flaps or muscle to cover the defect. Prosthetic implants can be titanium osseointergrated implants attached with magnetic clips or prosthesis attached to the frame of spectacles. Goldberg et al, found that in their series of patients, many patients resort to just wearing an eye patch.

**BACKGROUND TO THE STUDY**

In KwaZulu-Natal, and more specifically at the study hospital, patients are of very poor socio-economic standing. Many patients cannot afford basic transportation for medical assistance. Whilst priority is given to the curative process, cosmetic rehabilitation can be very difficult and expensive for the patient as institutional budgets do not cover the expenses of custom made prostheses for every patient.

Patients that have had a subtotal exenteration heal faster with fewer complications and thus require fewer postoperative wound management follow-ups which can also be quite expensive for the individual patient.

The patients identified in this study were less than 50 years old and all were HIV positive. Previously reported studies have shown a relationship between patients less than 50 years old with conjunctival squamous cell carcinoma and the presence of HIV[27]. A higher grade of malignancy is more common in HIV positive patients as opposed to HIV negative patients[28].
Patients whose HIV status was unknown at diagnosis were also tested for HIV as it has been suggested that underlying HIV may have OSSN as one of the first manifestations\textsuperscript{[29]}.

Immunocompromised patients heal slower than their Immunocompetent counterparts, and thus also brings forth the need for a therapeutic option with a shorter recovery period.

**SUBJECTS AND METHODS**

A retrospective case review was performed of patients from St Aidan’s Missionary Hospital initially, which was later amalgamated into the McCords Provincial Eye Hospital, Durban South Africa. Ten consecutive patients who underwent a lid-sparing subtotal exenteration with buccal mucosal graft were identified over a 3 year period from 1 January 2011 to 31 December 2013. Patients’ clinical records were reviewed.

The following information was obtained from each patients’ records: Age, gender, involvement of which eye (laterality); whether or not the diagnosis was made on incisional biopsy, duration of symptoms before presentation, radiological extent of the tumour, Human Immunodeficiency Virus (HIV) status, type of primary surgery, histopathological clearance of surgical margins, aesthetic follow-ups at 1 week, 1 month, 2 months and 6 months and standard cancer follow ups at 1 year to 3 years; outcome and any surgical revisions.

The inclusion criteria included all patients that had subtotal orbital exenteration with buccal mucosal graft for histologically confirmed squamous cell carcinoma. Exclusion criteria were that of tumours that involved the bony orbit, the posterior 1/3 of orbital contents or that had metastatic spread at the time of diagnosis.

No patients with medial canthal or caruncle involvement were considered for this procedure, as these have been found to have a high rate of recurrence\textsuperscript{[30, 31]}. 
The minimally preserved healthy conjunctiva in this study was twenty percent, which is markedly reduced from the technique described by Goldberg et al, in 2003, in which a minimum of fifty percent of healthy conjunctiva was preserved.

All surgeries were performed by the same surgeon. The first step of the procedure under general anaesthesia involved the Shields “No-Touch Technique” [15] enucleation and tumour excision with 4mm clearance margins from macroscopically affected conjunctiva (Fig 1 & 2). This achieved preservation of approximately twenty percent of the lateral bulbar conjunctiva, and approximately forty percent of orbital fat and soft tissue laterally. The surgical plane for a temporal mass extended to the bony orbital wall with removal of periosteum, muscles, orbital fat and other orbital soft tissue (Fig 3). A 3 cm × 2 cm buccal mucosal graft was harvested from the left cheek of the patient [32]. The prepared mucosa was sutured directly to the remaining lateral bulbar conjunctiva and fornical conjunctiva nasally with 8/0 silk interrupted sutures (Fig 4 & 5). Forniceal deepening sutures were placed, chloramphenicol ointment instilled, and a conformer was positioned which was removed after 4 weeks and a standard issue hospital prosthetic shell was fitted (Fig 6). Using identical surgical principles all ten patients had very similar surgeries. (Data results Appendix 4)

**SUMMARY**

This method highlights that for even larger masses, the patient does not have to undergo a total exenteration, but rather have this form of ‘extended’ subtotal exenteration with an acceptable cosmetic outcome. Whilst cure of the disease process is pivotal, rehabilitation and cosmesis of the survivor has to be considered in the primary management plan.

The use of a buccal mucosal graft for a subtotal exenteration can be performed at the primary surgery with faster rehabilitation using an inexpensive artificial eye. This is especially feasible in patients who cannot afford the custom made prosthesis.
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Part 2: A submission ready manuscript.
CASE SERIES OF SUBTOTAL EXENTERATION WITH BUCCAL MUCOSAL GRAFT FOR ORBITAL SQUAMOUS CELL CARCINOMA: A study of 10 consecutive cases

S. Surajballi¹, MB ChB, FC Ophth(SA); C-H Kruse², MB ChB, FC Ophth(SA), MMed(Ophth)

¹Department of Ophthalmology, McCords Eye Hospital, Durban, and Department of Ophthalmology, Faculty of Health Sciences, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, South Africa
²Department of Ophthalmology, Pietermaritzburg Hospital Complex, Pietermaritzburg, and Department of Ophthalmology, Faculty of Health Sciences, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, South Africa

Corresponding author: S. Surajballi (sharishas@hotmail.com)

Aim: To look for a safe alternative to a disfiguring total orbital exenteration, so that an inexpensive stock ocular prosthesis can be fitted with improved aesthetic results, rather than expensive onlay prosthesis.

Methods: Retrospective case series of ten consecutive patients that had a subtotal lid-sparing exenteration with preservation of minimal conjunctiva, and buccal mucosal graft for orbital squamous cell carcinoma. Records were reviewed from 1 January 2011 to 31 December 2013 from the McCords Provincial Eye Hospital, South Africa.

Results: Of the ten patients all had good aesthetic results at 4 weeks as well as at six months. One patient had a repeat buccal mucosal graft after fornical shortening. Three patients had recurrences within one year and total exenterations were successfully performed. The survival rate at 3 years was ninety percent.

Conclusions: A subtotal orbital exenteration, preserving minimal conjunctiva, with a buccal mucosal graft and standard ocular prosthesis can be cost effective, safe and cosmetically acceptable.

Synopsis: A subtotal exenteration, for anterior orbital squamous cell carcinoma, with minimally preserved conjunctiva and a buccal mucosal graft, can be cost effective, safe and cosmetically acceptable with a standard ocular prosthesis.

Keywords: Subtotal exenteration.
INTRODUCTION

An orbital exenteration can be classified as Total, Subtotal (or Lid Sparing) or Extensive (which may involve removal of paranasal sinuses)\(^1\). An exenteration is indicated for either curative, including inflammation or infection considered to be life threatening or palliative therapy, and as in the case of advanced or metastatic disease, for debulking with or without radiotherapy.

No matter what type of exenteration is performed, it is physically and psychologically disfiguring for every patient to some degree.

Goldberg et al, in 2003, described a subtotal exenteration with preservation of at least a quadrant of the orbit or apical tissues\(^2\). With their technique, a minimum of 50% of conjunctiva needed preservation to maintain an ocular prosthesis. In this study a minimum of 20% of residual conjunctiva was found to be equally efficacious in maintaining an ocular prosthesis with the use of a buccal mucosal graft. The mucosal graft forms a stable base, and can be removed, re-sited or re-grafted if needed for recurrences, dehiscence or infection.

In KwaZulu-Natal, South Africa, many patients are of very poor socio-economic standing. Whilst priority is given to the curative process, cosmetic rehabilitation can be very difficult and expensive for the patient as institutional budgets do not cover the expenses of custom made prostheses for every patient.

Patients that have had a subtotal exenteration heal faster with fewer complications and thus require fewer postoperative wound management follow-ups which can also be quite expensive for the individual patient.

The purpose of this study was to identify a safe alternative to a disfiguring total exenteration so that improved cosmesis can be achieved with an inexpensive stock ocular prosthesis.

MATERIALS AND METHODS

A retrospective case review was performed of patients from St Aidan’s Missionary Hospital initially, which was later amalgamated into the McCords Provincial Eye Hospital, Durban South Africa. Ten consecutive patients who underwent a lid-sparing subtotal exenteration with buccal mucosal graft were identified over a 3 year period from 1 January 2011 to 31 December 2013. Patients’ clinical records were reviewed.

The following information was obtained from each patients’ records: Age, gender, involvement of which eye (laterality); whether or not the diagnosis was made on incisional biopsy, duration of symptoms before presentation, radiological extent of the tumour, Human Immunodeficiency Virus (HIV) status, type of primary surgery, histopathological clearance of
surgical margins, aesthetic follow-ups at 1 week, 1 month, 2 months and 6 months and standard cancer follow ups at 1 year to 3 years; outcome and any surgical revisions.

The inclusion criteria included all patients that had subtotal orbital exenteration with buccal mucosal graft for histologically confirmed squamous cell carcinoma. Exclusion criteria were that of tumours that involved the bony orbit, the posterior 1/3 of orbital contents or that had metastatic spread at the time of diagnosis.

No patients with medial canthal or caruncle involvement were considered for this procedure, as these have been found to have a high rate of recurrence \[3,4\].

The preoperative assessment included patient counselling, incisional biopsy and histological confirmation of squamous cell carcinoma, radiological imaging to delineate the extent of localised tumour margins, bony involvement and the presence of metastases. A general systemic review and examination including lymph node assessments were performed for possible metastasis. Haematological investigations, chest x-ray, abdominal ultrasound or CT imaging also formed part of the metastatic workup. A tailored management plan involved patient counselling, available surgical options, including a lid sparing subtotal exenteration or a subtotal exenteration with a buccal mucosal graft, and post-operative management and rehabilitation for the above. A total exenteration was also part of the counselling process as either primary surgery or as secondary surgery, if surgical margins were not clear from the tumour, or other complications like severe infection, etc.

Surgical technique: All surgeries were performed by the same surgeon. Clinical and radiological surgical planes were identified, as in the case of patient “A” a nasal mass, 10 mm diameter, eight limbal clock hour mass involving conjunctiva, sclera and cornea while sparing the caruncle, palpebral conjunctiva and fornices (Fig 1). The first step of the procedure under general anaesthesia involved a “No-Touch Technique” \[5\] enucleation and tumour excision with 4mm clearance margins from macroscopically affected conjunctiva (Fig 2). This achieved preservation of approximately twenty percent of the lateral bulbar conjunctiva, and approximately forty percent of orbital fat and soft tissue laterally. The surgical plane for a temporal mass extended to the bony orbital wall with removal of periosteum, muscles, orbital fat and other orbital soft tissue (Fig 3).

After removal of the main tumour block, marked additional specimens were taken for histology to confirm completeness of the tumour excision. Haemostasis was achieved.

A 3 cm × 2 cm buccal mucosal graft was harvested from the left cheek of the patient \[6\]. The prepared mucosa was sutured directly to the remaining lateral bulbar conjunctiva and fornical conjunctiva nasally with 8.0 silk interrupted sutures (Fig 4).

Forniceal deepening sutures were placed, chloramphenicol ointment instilled, and a conformer was positioned which was removed after 4 weeks. All patients were sent home with paracetamol oral analgesia, chloramphenicol ointment and an antiseptic mouthwash.

Using identical surgical principles all ten patients had very similar surgeries.
RESULTS

Ten eyes of ten patients were identified for inclusion in the study. Patient ages ranged from 34 to 49 years old, with a mean age of 41.5 years. There were 6 female and 4 male patients. Of the ten eyes, three were left eyes and seven were right eyes. The duration of symptoms for each patient varied between three months to seven months with a mean of five months. All tumours were confirmed histopathologically as invasive squamous cell carcinoma on initial incisional biopsy.

Patient “A” initially refused primary surgical treatment after counselling. A trial of 6 cycles of Mitomycin C was offered for the duration of further patient counselling. The patient subsequently agreed to a subtotal exenteration. Patient “C” defaulted primary surgery, but returned 6 months later, was re-evaluated and underwent a subtotal exenteration. Patient “G” refused all forms of treatment, but returned 6 months later and had a subtotal exenteration (Table 1). Of the 3 patients that refused initial surgery, Patient “G” had a recurrence of the primary tumour at 9 months after primary surgery and went on to have a total exenteration.

All patients had Computerized Tomography (CT) scan radiological imaging as part of the preoperative assessment for surgical planes and as part of their metastatic workup. Six patients had anterior scleral involvement. Four patients had anterior sclera with either anterior medial rectus muscle or lateral rectus muscle involved. No patients had clinical metastasis noted by either systemic examination, including lymph node assessment by palpation, haematological tests and chest x-ray, CT or abdominal ultrasound imaging.

All ten patients were HIV positive, either previously known or diagnosed at presentation. The primary surgery after definitive diagnosis for all patients was a lid-sparing subtotal exenteration with a buccal mucosal graft. All surgical margins were reported clear of tumour on histological examination.

At four weeks follow-up all ten patients had healthy and viable mucosal graft tissue in their orbits (Fig 5). The harvest site of the buccal graft had healed well in all patients. All ten patients had a successful stock prosthetic eye fitting at this time (Fig 6). The choice of prosthesis was restricted to the institutional budget and the patients’ financial constraints. The sizes, shapes and colour variants of the prosthetic shells were standard issue as this was limited by the institutional budget.

Patient “E” had a repeat buccal mucosal graft and fornical deepening five months after the primary surgery due to fornical shortening and inability to readily retain a prosthesis. At six month follow-up all ten patients had aesthetically pleasing results and a stable fitting stock prosthesis.
Patients “I”, “G” and “F” had recurrence of the primary carcinoma on routine follow up at six months, nine months and one year respectively, and all went on to have a total orbital exenteration. These patients used a standard eye patch for final cosmesis. All three patients are tumour-free at the 3 year cancer follow-up. Patient “J” defaulted the routine one year follow-up and all contact attempts were in vain (Table 2). All other patients were cancer free at their 3 year routine cancer follow up. The survival rate at 3 years was ninety percent, as patient “J” was lost to follow up and presumed deceased.

**DISCUSSION**

Patients presented relatively late, as they had already surpassed the more conservative treatment options, such as is the case in non-invasive Ocular Surface Squamous Neoplasia (OSSN) with mitomycin C or 5-fluorouracil topical chemotherapeutic agents\[^{7-9}\], or simple excision. Further to this would be other globe preserving treatment options for invasive OSSN, which can include varied combinations of topical chemoreduction, topical and or intralesional Interferon alpha, surgical excision, cryotherapy or brachytherapy\[^{10-14}\]. Treatment options at the study hospital were limited to mitomycin C, 5-fluorouracil and surgical management.

Ideally, an MRI would have also been preferred for better imaging and delineation of preoperative tissue planes, however this was not readily available. Other useful imaging options, that were also not available to these patients for anterior segment involvement, especially angle involvement if not clear on gonioscopy, is the use of ultrasound biomicroscopy and ultra-high resolution optical coherence tomography (UHR-OCT), which is also beneficial to identify any anterior scleral/ciliary body masses\[^{15,16}\].

The patients identified in this study were less than 50 years old and all were HIV positive. Previously reported studies have shown a relationship between patients less than 50 years old with conjunctival squamous cell carcinoma and the presence of HIV\[^{17}\]. A higher grade of malignancy is more common in HIV positive patients as opposed to HIV negative patients\[^{18,19}\]. Patients whose HIV status was unknown at diagnosis were also tested for HIV as it has been suggested that underlying HIV may have OSSN as one of the first manifestations\[^{20}\].

A total exenteration is aimed at extensive anterior or posterior orbital involvement with or without bony involvement. It can take months to fully heal, frequent wound dressing changes and follow-ups are required and complications are often encountered. Deep exposed sockets are psychologically disturbing to the patient\[^{21}\]. A subtotal exenteration as in this study is aimed at less extensive anterior orbital involvement since preservation of some orbital tissues facilitates completion of the primary reconstruction. Healing is much faster and complications are infrequent. The outcome is considered aesthetically acceptable.
With both techniques a biopsy can be easily accessed if recurrences are suspected. In the case of a subtotal exenteration with a buccal mucosal graft, the graft can easily be detached or removed, a biopsy taken, and the graft re-sited. In the event of possible complications such as wound sepsis, graft dehiscence, late socket bleed, etc., the mucosal graft can be removed, the wound managed and once stable, the patient can undergo a repeat buccal mucosal graft. The use of the prosthetic shell lends for ease of removal, disinfection and reinsertion by the patient, as well as self-monitoring of the graft integrity. Patients need to be counselled about preventing micro trauma to the graft after the initial 4 week convalescent phase, as this may be a nidus for infection and graft dehiscence.

For better orbital volume, a dermis fat graft can be incorporated into the primary surgery\(^{[22]}\). Placing a ball implant for orbital volume may also be an option, however extrusion would be a risk factor as the non-vascularized buccal mucosal graft may be inadequate to maintain the implant in situ.

Whilst all patients had clear surgical margins on histolological examination, which included no tumour cells found at the free margins of all biopsied specimens, 3 patients (30 %) had a recurrence of the primary tumour. There is controversy surrounding subtotal exenterations and local control or metastasis\(^{[23]}\), as surgical marginal clearance is not always indicative of a cure since micro-metastasis may be a culprit\(^{[24]}\). Also to consider is a higher recurrence occurs in HIV individuals, as described by Makupa et al. The relationship between a patient’s CD4 count (a low CD4 count) and recurrence rate may provide future predictive outcomes, however a larger prospective study might be of value.

Patients with carcinoma of the eye and or adnexa need an exclusive management plan which involves patient counselling, histological confirmation, radiological imaging to delineate the extent of localised tumour margins, bony involvement and the presence of metastases. Of critical importance is that patients be involved in this plan as post-surgical follow-ups are life-long. Financial constraints of the patient and institutional resources are also of paramount importance.

A limitation of this study is that this procedure is limited to non-extensive anterior involvement of tumour, in which surgical clearance of the primary tumour is anticipated with the primary surgery. Due to the rarity, variance of invasiveness of tissue planes and debilitating nature of the disease it is difficult to do prospective randomisation or get numbers large enough to be statistically significant.

In conclusion, all patients had histological surgical clearance with the minimally preserved conjunctiva and with cosmetic rehabilitation within four weeks. The study achieved the primary goals of being cost effective and cosmetically acceptable for the study subjects. There was a thirty percent recurrence rate but recurrences were easily identified and managed.

Surgical clearance and immediate cosmetic rehabilitation is a possibility in one surgical procedure.
IMAGES:

Fig 1: A large nasal mass, not involving the caruncle.

Fig 2: Nasal mass: Enucleation nasally, removing muscles, orbital tissue and periosteum.

Fig 3: Temporal mass: Periosteum removed temporally, with clean bone. Nasal orbital tissue remaining.

Fig 4: Buccal mucosal graft sutured to conjunctiva and fornix.

Fig 5: Buccal mucosa nasal 3/4 and temporal ¼ with remnant conjunctiva.

Fig 6: Stock ocular prosthesis fitting at 1 month follow up. Inset: Standard stock ocular prosthetic shells.
Table 1: Patient demographics and presentation

<table>
<thead>
<tr>
<th>PATIENT STUDY NUMBER</th>
<th>AGE</th>
<th>SEX</th>
<th>EYE</th>
<th>Duration of Symptoms</th>
<th>Diagnosis on incisional biopsy</th>
<th>Radiological extent</th>
<th>Immune Status and CD4 count</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>47</td>
<td>F</td>
<td>R</td>
<td>6 months. Trial of Mitomycin C 6 cycles</td>
<td>Yes</td>
<td>Anterior cornea &amp; sclera</td>
<td>HIV + 175</td>
</tr>
<tr>
<td>B</td>
<td>34</td>
<td>F</td>
<td>L</td>
<td>4 months</td>
<td>Yes</td>
<td>Anterior sclera</td>
<td>HIV + 430</td>
</tr>
<tr>
<td>C</td>
<td>40</td>
<td>F</td>
<td>L</td>
<td>1 year, defaulted. Returned 6 months later</td>
<td>Yes</td>
<td>Anterior sclera</td>
<td>HIV + 385</td>
</tr>
<tr>
<td>D</td>
<td>36</td>
<td>F</td>
<td>R</td>
<td>8 months</td>
<td>Yes</td>
<td>Anterior sclera + anterior lateral rectus muscle</td>
<td>HIV + Not noted</td>
</tr>
<tr>
<td>E</td>
<td>49</td>
<td>F</td>
<td>R</td>
<td>6 months</td>
<td>Yes</td>
<td>Anterior sclera</td>
<td>HIV + 118</td>
</tr>
<tr>
<td>F</td>
<td>45</td>
<td>F</td>
<td>R</td>
<td>9 months</td>
<td>Yes</td>
<td>Anterior sclera and anterior medial rectus muscle</td>
<td>HIV + 180</td>
</tr>
<tr>
<td>G</td>
<td>43</td>
<td>M</td>
<td>L</td>
<td>6 months Refused treatment. Returned 6 months later</td>
<td>Yes</td>
<td>Anterior sclera + anterior lateral rectus muscle</td>
<td>HIV + 149</td>
</tr>
<tr>
<td>H</td>
<td>47</td>
<td>M</td>
<td>R</td>
<td>3 months</td>
<td>Yes</td>
<td>Anterior sclera + anterior lateral rectus muscle</td>
<td>HIV + 541</td>
</tr>
<tr>
<td>I</td>
<td>36</td>
<td>M</td>
<td>R</td>
<td>6 months</td>
<td>Yes</td>
<td>Anterior sclera</td>
<td>HIV + 435</td>
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<tr>
<td>J</td>
<td>39</td>
<td>M</td>
<td>R</td>
<td>6 months</td>
<td>Yes</td>
<td>Anterior sclera</td>
<td>HIV + 156</td>
</tr>
</tbody>
</table>
### Table 2: Patient follow up results

<table>
<thead>
<tr>
<th>PATIENT STUDY NUMBER</th>
<th>Followup aesthetics 1/52</th>
<th>Followup aesthetics 1/12</th>
<th>Followup aesthetics 2/12</th>
<th>Followup aesthetics 6/12</th>
<th>Surgical revision</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>None</td>
</tr>
<tr>
<td>C</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>None</td>
</tr>
<tr>
<td>D</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>None</td>
</tr>
<tr>
<td>E</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>Forniceal deepening and repeat buccal mucosa at 5 months</td>
</tr>
<tr>
<td>F</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>Recurrence at 9 months. Total exenteration</td>
</tr>
<tr>
<td>G</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>Recurrence at 9 months. Total exenteration</td>
</tr>
<tr>
<td>H</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>None</td>
</tr>
<tr>
<td>I</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>Recurrence at 1 year. Total exenteration</td>
</tr>
<tr>
<td>J</td>
<td>Buccal mucosa healthy</td>
<td>Stock eye inserted</td>
<td>Stock eye placement stable</td>
<td>Patient satisfied</td>
<td>Defaulted 1 year follow up</td>
</tr>
</tbody>
</table>
REFERENCES

Part 3: Appendices
Appendix 1: The final Study Protocol

Subtotal exenteration with buccal mucosal graft for orbital squamous cell carcinoma.

Principal Investigator: Dr. Shariha Surajbelli
Department of Ophthalmology
University of KZN
Umhlo Road
0835657567

Co-Investigator: None
Supervisor: Dr. Carl-Heinz Kruse

Protocol Date: 10/04/2014

Purpose
To look for a safe alternative to a total exenteration, so that an inexpensive stock ocular prosthesis can be fitted with improved aesthetic results, rather than an expensive onlay prosthesis.

Objectives
Primary Objective: Complete excision of ocular squamous cell carcinoma
Secondary Objectives: Successful buccal mucosal graft able to hold a stock ocular prosthesis.

Background and Rationale
Traditionally orbital exenteration involved the removal of the entire orbital contents including the peri-orbita, with or without the removal of the eyelid skin. The modification of an eyelid sparing exenteration technique, by Shields et al. reduced healing time and had better cosmetic results. Yeats et al. went on to describe a total and subtotal exenteration category, with subtotal involving sacrificing the eye and the partial removal of orbital tissue. Many other authors have attempted conservative modifications in order to preserve uninvolved eyelids, conjunctiva, peri-orbita, and/or posterior apical orbital tissues. However many still adhere to converting to a total exenteration if there is less than fifty percent of healthy tissue with reconstruction taking weeks to months to complete.

With the subtotal technique as described, reconstruction can be done at the same time as the primary surgery. However this can only be executed successfully if a good preoperative evaluation is carried out.

This involves, firstly, deciding upon available surgical planes based on clinical examination and relevant radiographic studies. A surgical plane could be at the level of the bony orbital wall or other tissue planes such as the globe itself, orbital septum, lower eyelid retractor and extraocular muscles.

Secondly, the pre-operative process includes the planned reconstruction and rehabilitation of the proposed exenterated socket, including assessment of the host buccal mucosa.

Thirdly, the patient's financial situation must be considered, especially with regards to the rehabilitation process. This involves the type of ocular prosthesis available or affordable, and the ability to carry out good postoperative wound management and routine clinic follow ups. Although subtotal exenteration with a buccal
graft has significantly fewer post-operative complications, the patient still requires regular (but shorter) follow 
up until the tissues have healed. The standard cancer follow up of more than five years must be adhered to.

For an enucleated socket to retain an ocular prosthesis, there needs to be support for the ocular prosthesis 
in the form of orbital tissue volume and adequate fornices. The buccal graft, even with the wider excision 
margins, performs both of these functions. For further support, a ball implant may be attempted.

Apart from the stigma of being labelled with cancer, patients should not be doomed to a life-time of deformity 
based on their financial constraints.

Study Design and Methods
Retrospective case series of patients that have had subtotal exenteration with buccal mucosal graft for 
squamous cell carcinoma from St. Aedans Hospital.

Inclusion criteria
# Confirmed squamous cell carcinoma (SCC) on biopsy
# Patients that have had subtotal orbital exenteration with buccal mucosal graft for squamous cell carcinoma.

Exclusion criteria:
# Subjects aged 17 and under
# Involvement of the bony orbit or the posterior 1/3 of orbital contents
# Metastatic disease

Patient study sample:
We aim to review 10 patients

References:
Appendix 2: The Guidelines for Authorship

British Journal of Ophthalmology

A peer review journal for health professionals and researchers in ophthalmology

Home > About the journal > Instructions for authors

Instructions for Authors

For guidelines on policy and submission across our journals, please click on the links below:

Editorial Policy

British Journal of Ophthalmology is committed to disseminating ongoing advances in ophthalmology across the whole range of sub-specialties and globally. Clearly the requirements of clinicians vary within different settings and in different countries. This is an essential principle that underlies the future planning of the journal and guides the editorial board and reviewers in making their judgements on whether papers submitted to British Journal of Ophthalmology should be accepted or rejected.

Our policy is to provide a broad mix of articles that will be of professional and educational value to specialist, visual scientists and trainees. Our priorities are to:

- Publish up-to-date advances on diagnosis, management and pathogenesis of ocular disease.
- Continue to develop specialist areas of publication that deal with health service delivery globally.
- Publish contentious issues that are of educational importance.
- Ensure that a fair, independent peer review system is in place.
- Adhere to the highest ethical standards concerning research conduct.

Authors should use the American Joint Commission on Cancer classification scheme when describing patients with ophthalmic malignancies; see American Joint Committee on Cancer. ACC Cancer Staging Manual, Seventh Edition, Springer, New York.

Submission to British Journal of Ophthalmology implies that the work described has not been accepted for publication elsewhere, that it is not under consideration for publication elsewhere and does not duplicate material already published.

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The word count excludes the title page, abstract, tables, acknowledgements and contributions and the references. For guidance on how to improve your graphs and tables

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**Editorials**

Timely succinct commentary on any aspect of clinical or laboratory ophthalmology, usually in relation to the subject matter of a paper to be published in the same issue. All editorials are commissioned.

1500 words, up to 2 images and tables, 25 references.

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2. **Laboratory Science**: up to 2500 words, 5 images and tables, 25 references

Editors may request authors to shorten a submitted manuscript when in the opinion of the Editorial Board, the content does not justify the length.

All types of original article should include the following:

- Title
- Sub-title
- Keywords (up to four)
- Addresses and which author address for correspondence
- Structured abstract: (250 words, headings, "Background/aims", "Methods", "Results", and "Conclusion")
- Introduction
- Materials and methods
- Results
- Discussion
- References and acknowledgements
- Legends for display items (Figures and Tables)

All original articles are subject to peer review and editorial approval.
Appendix 3: Hospital approval; Department of Health approval; Ethical approval.

4 May 2016

TO WHOM IT MAY CONCERN

RETROSPECTIVE CASE STUDY: SUBTOTAL EXENTERATION WITH BUCCAL MUCOSAL GRAFT FOR SQUAMOUS CELL CARCINOMA
REFERENCE NO: BE 318/14

Permission is hereby granted for Dr Sharisha Surajbali to conduct a retrospective case study of Subtotal Exenteration with Buccal Mucosal Graft for Squamous Cell Carcinoma.

Kind Regards

DR. JAY MANNIE
ACTING CEO
McCord Hospital

E-mail: jay.mannie@kznhealth.gov.za
Tel: 031 2685701
Cell: 0836414382
Date: 9 June 2016

Dear Dr. S. Surajbally
University of KwaZulu Natal/ McCord Eye Hospital

Approval of research

1. The research proposal titled ‘Subtotal exenteration with buccal mucosal graft for orbital squamous cell carcinoma’ was reviewed by the KwaZulu-Natal Department of Health.

The proposal is hereby approved for research to be undertaken at McCord Eye Hospital.

2. You are requested to take note of the following:
   a. Make the necessary arrangement with the identified facility before commencing with your research project.
   b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.

3. Your final report must be posted to HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200 and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mr. X. Xaba on 033-395 2805.

Yours Sincerely

[Signature]

Dr. E. Lutge
Chairperson, Health Research Committee

Date: 13/07/16

Fighting Disease, Fighting Poverty, Giving Hope
11 July 2016

Dr Shariha Suraajbally
133 Crescent Road
Riddells, Phoenix
4068
sharihas@hotmail.com

PROTOCOL: Case study of subtotal exenteration with buccal mucosal graft for orbital squamous cell carcinoma. Degree Purposes: School of Ophthalmology: Medicine (WHE)

BREC REF: RE313/14.

EXPEDITED APPLICATION

The Biomedical Research Ethics Committee has considered and noted your application received on 20 June 2016.

The study was provisionally approved pending appropriate responses to queries raised. Your response received on 06 July 2016 to queries raised on 09 June 2016 have been noted and approved 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 11 July 2016. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for re-certification 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.


BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRR) Federal-wide Assurance (FAA 670).

The sub-committee’s decision will be RATIFIED by a full Committee at its meeting taking place on 16 August 2016.

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

Yours sincerely,

Professor J Tekwa-Gwegwe
Chair: Biomedical Research Ethics Committee

Postgraduate Office

Biomedical Research Ethics Committee
Professor J Tekwa-Gwegwe (Chair)
Westville Campus, Governor Malibongwe Building
Postal Address: Private Bag X5502, Durban 4000
Telephone: +27 (0) 31 260 4266 Fax: +27 (0) 31 260 4444 Email: biorecg@ukzn.ac.za
Website: http://research.ukzn.ac.za/research-ethics/biomedical-research-ethics.aspx

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## Appendix 4: Data collection tools

**Appendix 4: DATA COLLECTION SHEET: A CASE STUDY OF SUBTOTAL EXENTERATION WITH BUCCAL MUCOSAL GRAFT FOR ORBITAL SQUAMOUS CELL CARCINOMA**

| PATIENT STUDY NUMBER | AGE | SEX | R/L | EYE | Duration of Symptoms | Diagnosis on incisonal biopsy | Radiological extent | Immune Status and CD4 count | Primary Surgery | Followup aesthetics 1/52 | Followup aesthetics 1/12 | Followup aesthetics 2/12 | Followup aesthetics 6/12 | Surgical revision |
|----------------------|-----|-----|-----|-----|----------------------|-----------------------------|-------------------|-----------------------------|-----------------|-------------------------|--------------------|-------------------------|-------------------------|-----------------|------------------|
| A                    | 47  | F   | R   |     | 6 months. Trial of Mitomycin C 6 cycles | Yes | Anterior cornea & sclera | HIV + 175 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | None |
| B                    | 34  | F   | L   |     | 4 months | Yes | Anterior sclera | HIV + 430 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | None |
| C                    | 40  | F   | L   |     | 1 year, defaulted. Returned 6 months later | Yes | Anterior sclera | HIV + 385 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | None |
| D                    | 36  | F   | R   |     | 8 months | Yes | Anterior sclera + anterior lateral rectus muscle | HIV + Not noted | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | None |
| E                    | 49  | F   | R   |     | 6 months | Yes | Anterior sclera | HIV + 118 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | None |
| F                    | 45  | F   | R   |     | 9 months | Yes | Anterior sclera and anterior medial rectus muscle | HIV + 180 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | Recurrence at 1 year. Total exenteration |
| G                    | 43  | M   | L   |     | 6 months Refused treatment. Returned 6 months later | Yes | Anterior sclera + anterior lateral rectus muscle | HIV + 149 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | Recurrence at 9 months. Total exenteration |
| H                    | 47  | M   | R   |     | 3 months | Yes | Anterior sclera + anterior lateral rectus muscle | HIV + 541 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | None |
| I                    | 36  | M   | R   |     | 6 months | Yes | Anterior sclera | HIV + 435 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | Recurrence at 1 year. Total exenteration |
| J                    | 39  | M   | R   |     | 6 months | Yes | Anterior sclera | HIV + 156 | Subtotal exenteration | Completely excised | Buccal mucosa healthy | Stock eye inserted | Stock eye placement stable | | Patient satisfied | Defaulted 1 year follow up |
Appendix 5: Images

Fig 1: A large nasal mass, not involving the caruncle.

Fig 2: Nasal mass: Enucleation nasally, removing muscles, orbital tissue and periosteum.

Fig 3: Temporal mass: Periosteum removed temporally, with clean bone. Nasal orbital tissue remaining.

Fig 4: Buccal mucosal graft sutured to conjunctiva and fornix

Fig 5: Buccal mucosa nasal ¾ and temporal ¼ with remnant conjunctiva

Fig 6: Stock ocular prosthesis fitting at 1 month follow up. Inset: Standard stock ocular prosthetic shell