

**SIMULTANEOUS THREE OR FOUR HORIZONTAL RECTUS
MUSCLE SURGERY VERSUS TWO-STAGED SURGERY FOR
LARGE ANGLE CONGENITAL ESOTROPIA IN CHILDREN: A
RANDOMIZED CONTROLLED TRIAL**

By

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As the candidate's supervisor I have/have not approved this thesis for submission.

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I, Magritha du Bruyn, declare that

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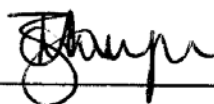
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Overview

Large angle congenital esotropia is commonly seen in South Africa. The optimal surgical approach for angles larger than 50 prism dioptres (PD) esotropia is controversial. Conventional bilateral medial rectus muscle recessions used for smaller angles is not sufficient to achieve and maintain alignment in large angles. Large esotropias therefore either require very large medial rectus muscle recessions, or surgery on the medial rectus as well as one or both lateral rectus muscles. In the past supramaximal medial rectus recessions have been associated with late consecutive exotropia and other long term complications. Three or four horizontal rectus muscle surgery can be performed as one procedure or as staged surgery. In staged surgery the medial rectus muscles of both eyes are recessed, the residual angle measured and the lateral rectus muscles resected for the remaining deviation during a second procedure. One would expect the two procedure surgery to have greater accuracy with lateral rectus resections once the effect of the initial medial rectus recession surgery has been established. I could find no data comparing the outcome between one and two procedure surgery.

KwaZulu-Natal is one of the largest provinces in South Africa and patients in rural areas need to travel long distances to the hospital. Financial resources are limited. I wanted to know how the outcome between a single three or four muscle procedure compares to a staged procedure. If the results are similar, a single procedure would save patients time and money, avoid exposure of the child to a second general anaesthetic and save valuable theatre time and resources.

The purpose of this comparative study was to compare the outcome of a single three or four horizontal rectus muscle surgery to a staged procedure in children aged 9 months to 16 years with large angle congenital esotropia presenting to the Eye Clinic at Inkosi Albert Luthuli Central Hospital from March 2011 to July 2014.

All children with congenital esotropia and angles larger than 50PD within the required age group who had not had previous strabismus surgery, significant refractive errors, amblyopia, eye pathology leading to poor vision or neurological problems were recruited for the study. Each child was randomly assigned to one of two treatment groups (one procedure or two procedure staged surgery 6 to 12 weeks apart). The surgery was performed by a single surgeon. The amount of rectus muscle surgery was based on standard of care surgical tables. Alignment in the two groups was compared 6 weeks after the final procedure.

I hope that the results of this study would assist in optimizing the management of children with large angle congenital esotropia.

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Chapter 1:

Introduction

Congenital (infantile, essential) esotropia is an idiopathic condition of misalignment of the eyes noticed within the first six months of life in an otherwise normal infant with no neurological abnormality and no significant refractive error.^{1,2} Episodes of convergence are often noticed in babies younger than 4 months of age, but any ocular misalignment after 4 months of age is abnormal.^{1,3}

Literature review

Epidemiology and pathogenesis

The incidence of congenital esotropia is 1% in healthy children and higher in children with neurological problems.⁴ Sex distribution is equal. In South Africa congenital esotropia is substantially more common in African patients than accommodative esotropia.⁵

Associated ocular features

Inferior oblique overaction is present in up to 75% of patients with congenital esotropia. It may be present at the time of diagnosis, but mostly manifests in the second year of life.⁶

Dissociated vertical deviation (DVD) is a slow upward drifting with abduction and excyclotorsion of the non-fixating eye. It is usually bilateral but asymmetrical and can be manifest or latent. It occurs in 48%-92% of patients with infantile esotropia.^{7,8,9,10,11}

Nystagmus is sometimes present and may be latent or manifest.³

Anatomy

The six voluntary extraocular muscles of the orbit are responsible for the eye movements.

The horizontal movements of the eye are produced by the medial rectus and lateral rectus muscles that move the eye horizontally along the vertical axis in the primary position. The superior rectus and inferior rectus muscles move the eye up and down along the horizontal axis.

The four rectus muscles originate from the annulus of Zinn which is a periosteal thickening at the apex of the orbit. They pass forward and insert into the sclera of the eye. The medial rectus muscle inserts 5.5mm from the nasal limbus and the lateral rectus 6.9mm from the temporal limbus. The medial rectus is responsible for adduction in the primary position and receives its nerve supply from the inferior division of the oculomotor nerve. The lateral rectus muscle abducts the eye in the primary position and is supplied by the abducent nerve.^{1,12}

The oblique muscles are inserted behind the equator of the eye and their main actions are intorsion and extorsion. The superior oblique muscle arises from the body of the sphenoid bone supero-medial to the optic foramen, passes through the trochlea between the superior and medial orbital walls and insert into the sclera in the posterior upper temporal quadrant of the globe. It primarily intorts the eye but also has secondary functions of depression and abduction. The superior oblique is supplied by the trochlear nerve.^{1,12}

The inferior oblique muscle originates from the floor of the orbit just posterior to the orbital rim, passes laterally and posteriorly along the globe and inserts into the sclera at the postero-lateral aspect of the eyeball. It primarily extorts the eye but is also able to elevate and abduct the eye. Its nerve supply comes from the inferior division of the oculomotor nerve.^{1,12}

Diagnosis

The diagnosis of esotropia is made by the Cover test where the fixing eye is covered and the examiner looks for an outward movement of the uncovered eye to take up fixation. The angle of the deviation is measured by using base out prisms in front of the eyes until any movement to take up fixation has been neutralized.¹

The onset of congenital esotropia is usually before the age of 6 months. The angle of deviation is usually large, from 30 Prism Dioptres (PD) to 100PD and usually more than 30PD esotropia. The refractive error is normal for age (less than +2.00 dioptre hypermetropia). Cross-fixation is common.^{1,3}

Differential diagnosis

Congenital esotropia must be differentiated from accommodative esotropia which has a later onset of presentation and is associated with significant hypermetropia.

It must also be distinguished from esotropia with a high accommodative convergence/accommodation ratio(AC/A), which occurs either with and without a hypermetropic element. This is frequently regarded as non-refractive accommodative esotropia.¹³

In nystagmus blockage syndrome convergence dampens a horizontal nystagmus and this may be confused with a congenital esotropia.¹

Congenital cranial dysinnervation disorders such as Duane retraction syndrome and congenital fibrosis of the extraocular muscles may present with early onset esotropia. In Duane retraction syndrome there is an anomalous innervation of the lateral rectus muscle by the third nerve as the sixth nerve is absent or abnormal. These patients may have limited abduction and/or adduction, and globe retraction is present on adduction. Congenital fibrosis of the extraocular muscles syndrome is characterized by bilateral ptosis and restrictive external ophthalmoplegia.¹

Mobius syndrome is characterized by cranial nerve palsies of the 6th, 7th, 9th and 12th nerves. These patients present with bilateral abduction deficits and may have an esotropia.^{1,3}

Cyclic esotropia is a rare condition with onset between 3 and 4 years of age. It is characterized by episodes of esotropia lasting 12 to 36 hours. It may become constant.¹

Congenital unilateral or bilateral sixth nerve palsies may present as an esotropia at birth.

Esotropia is often associated with neurological impairment. Esotropia may also be present in patients with unilateral defective vision.

Treatment and outcome

The aims of treatment is to obtain good vision in each eye with as much binocularity as possible, and to have a good psycho-social result.

Amblyopia is present in 25% to 40% of patients with congenital esotropia.¹⁴ It is treated by occluding the better eye with an eye patch, or by blurring its vision (penalizing) with atropine eye drops. It should be treated prior to surgery as compliance is better and response to treatment is quicker at a younger age.

The mainstay of treatment in congenital esotropia is horizontal muscle surgery. Ideally children with congenital esotropia should be aligned as early as possible. In a study by Ing⁴ in 1981 93% of patients developed peripheral fusion when surgical alignment was achieved before 24 months of age. Thereafter peripheral fusion was only seen in 31% of patients. More recent studies showed that correcting alignment before 1 year of age, or 1 year of duration of misalignment increased the percentage of patients that develop stereopsis.^{15,16} However, the duration of misalignment and not the age at surgery is significant in determining the quality of stereopsis.^{16,17} Wright et al¹⁸ performed surgery for infantile esotropia on children aged 13 to 19 weeks and proved that high-grade stereopsis is possible when alignment is achieved at a very early age.

The development of DVD's are also affected by the timing of surgery. When surgery is done prior to 24 months more latent DVD's were observed compared to more manifest DVD's in children who had surgery after 24 months. This put them at higher risk for repeat surgery.^{8,9,10,11,17,19}

The surgical management of large angle congenital esotropia in children is controversial. Large angle esotropias of greater than 50PD tend to require on average more strabismus procedures than smaller angled esotropias to achieve and maintain horizontal alignment.²⁰ The optimal surgical approach to these patients has not been established.

Conventional bilateral medial rectus muscle recession has a low success rate in children with large angle esotropia with a less than 50% rate of adequate ocular alignment.^{13,21,22,23}

Bilateral supramaximal medial rectus muscle recessions greater than 6.0mm have been performed for angles larger than 50PD. This procedure has been favoured as it is quicker to perform than three or four muscle surgery and leaves the lateral rectus muscles untouched.^{24,25,26} With this approach short-term ocular alignment is achieved in between 60%-91% of patients.^{24,25,26,27,28} Supramaximal medial rectus muscle recessions are however associated with adduction deficits due to medial rectus muscle underaction resulting in impairment of convergence and a tendency towards late exotropic drift and incomitance.^{13,21,27,29,30,31,32,33}

Several medium and long-term studies on three and four muscle surgery for large angle congenital esotropia have shown good results at long-term follow-up.^{21,34,35,36,37} Chatzistefanou *et al* compared long-term outcomes (median 54 months) with 8-week outcomes after three muscle surgery in 194 patients with esotropia.³⁵ They found more late overcorrections than undercorrections which were more marked in angles of less than 70PD. Bayramlar and associates looked at the medium term outcomes (median 32 months) in 18 patients after three muscle surgery and showed an increase in residual esotropia.³⁶ In a study by Scott *et al* they found that patients who were initially

overcorrected after three and four muscle procedures tend to drift in towards orthotropia over time.²¹

It has been shown that the magnitude of the pre-op angle adversely affects the outcome in terms of alignment.^{20,35,38} Children with large angle esotropia therefore have worse results than smaller angles.

Other factors that affect the outcome negatively are: amblyopia,^{20,39} inferior oblique overaction,³⁵ lateral rectus muscle underaction,³⁸ and surgery prior to 16 months of age.²⁰ Nevertheless early surgery may potentiate more successful sensory results.^{15,16,17,18,40,41}

The presence of DVD, A and V patterns, gender, family history, parental age, refractive error and nystagmus made no difference in the outcome.^{20,35,38}

Problem statement:

Three- and four horizontal rectus muscle surgery can be performed as a single procedure (bilateral medial rectus recession and unilateral or bilateral lateral rectus resection), as a staged procedure (bilateral medial rectus recessions followed by unilateral or bilateral lateral rectus resections), or as a sequential recess/resect procedure (medial rectus recession and lateral rectus resection in one eye followed by medial rectus recession with or without lateral rectus resection in the other eye). Staged surgery may be more accurate than simultaneous three or four muscle surgery in that the angle of the residual esotropia after the initial bilateral medial rectus recessions can be established and a second surgery can be planned based on the residual angle.

The aims of this study are to determine the outcome of squint surgery in children with congenital esotropia larger than 50PD, and to compare a single three or four horizontal rectus muscle procedure to a two-stage procedure consisting of maximal bilateral medial rectus muscle recessions followed by bilateral lateral rectus muscle resections 6 to 12 weeks later.

Research question

Hypothesis to be tested:

Two-stage horizontal muscle surgery for large angle congenital esotropia in children has a better post-operative outcome than single three or four horizontal muscle surgery.

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Chapter 2: A submission ready manuscript.

Title of the manuscript:

Simultaneous three or four horizontal rectus muscle surgery versus two-staged surgery for large angle congenital esotropia in children: a randomized controlled trial

1 Abstract:

2

3 Purpose: To compare the outcome of simultaneous three or four horizontal rectus muscle
4 surgery to two-staged surgery for large angle congenital esotropia in children.

5 Methods: A prospective, randomized trial was performed involving 34 patients (17 in each
6 group) between the ages of 9 months and 16 years with congenital esotropia and angles larger
7 than 50 prism diopters (PD). Patients in group 1 received a single three or four horizontal
8 muscle surgery and those in group 2 a staged approach consisting of maximal medial rectus
9 muscle recessions followed by the appropriate lateral rectus muscle resection 6 to 12 weeks
10 later. Post-operative angles in the two groups were compared 6 weeks after the final surgery.

11 Results: Two patients from group 2 were lost to follow-up. 14 of 17 patients (82%) in Group
12 1 and 12 of 15 patients (80%) in Group 2 were successfully aligned with no significant
13 difference between groups ($p=0.34$). When comparing smaller angles (<70 PD) and larger
14 angles (≥ 70 PD) across both groups, smaller angles were more likely to be successful
15 ($p=0.056$). The presence of a dissociated vertical deviation ($p=0.51$) and inferior oblique
16 overaction ($p=0.31$) had no effect on success.

17 Conclusions: Single three or four horizontal rectus muscle surgery for large angle congenital
18 esotropia has the same rate of success as a two-staged surgical approach. In both surgical
19 strategies, surgery for smaller angle esotropia was more likely to be successful than that for

20 larger angle esotropia. The presence of a dissociated vertical deviation or inferior oblique
21 overaction did not affect rates of success.

22

23 **Text:**

24

25 **Introduction:**

26 The optimal surgical approach in children with congenital (infantile) esotropia with angles
27 larger than 50 prism diopters (PD) is controversial. Large esotropias tend to require on average
28 more strabismus procedures than smaller angles to achieve and maintain alignment.^{1,2,3}

29 Conventional bilateral medial rectus muscle recession has a rate of adequate ocular alignment
30 of less than 50% in angles greater than 50PD.^{2,3} Supramaximal medial rectus recessions (more
31 than 6mm from the insertion) have a short-term success rate of 70% to 91%, but are associated
32 with adduction deficits, convergence impairment, late exotropic drift and incomitance.^{2,4,5,6,7}

33 By distributing the surgery among multiple muscles in three-and four horizontal rectus muscle
34 surgery, incomitance is reduced, greater stability ensured and better long-term outcomes
35 achieved.^{2,4,8,9,10}

36 The best approach for three and four horizontal rectus muscle surgery has not been established.
37 Surgery may be performed as a single three to four muscle procedure or as a staged procedure
38 where maximal recessions of the medial rectus muscles are followed several weeks later by
39 lateral rectus resections based on the residual angle. The rationale to a staged approach is firstly
40 that some patients may be adequately aligned with medial rectus surgery alone, thereby
41 preserving the lateral rectus muscles, and secondly that one might expect greater accuracy with
42 lateral rectus resections once the effect of the initial medial rectus recession surgery has been

43 established. The staged approach would however be more costly and inconvenient involving
44 two surgeries as well as subjecting patients to two general anesthetics.

45 The objective of this study was to determine which surgical approach was superior in terms of
46 achieving ocular alignment.

47

48 **Materials and methods:**

49 A prospective, randomized controlled trial was performed on 34 children with congenital
50 esotropia larger than 50PD, comparing the outcome after a single three or four horizontal
51 muscle procedure to a staged procedure consisting of bilateral medial rectus recessions
52 followed by the appropriate bilateral lateral rectus resections 6 to 12 weeks later. Congenital
53 esotropia was defined as a misalignment of the eyes present within the first six months of life
54 in a healthy baby with no neurological abnormality and no significant refractive error. The term
55 "Congenital esotropia" is historically frequently used in the literature when defining this
56 condition. However its use is somewhat controversial as the esotropia is not present at birth
57 but develops early in life. For this reason "Infantile esotropia" is preferred by many. For the
58 purpose of this study the historical term "Congenital esotropia" is used.

59 The study was performed at XXX Hospital in XXX, South Africa, between March 2011 and
60 September 2014. Ethics approval was obtained from the XXX School of Medicine Ethics
61 Committee. Consent for inclusion in the study was obtained from a parent or guardian for each
62 patient at the first visit.

63 We included children with congenital esotropia measuring more than 50PD aged 9 months to
64 16 years in the study.

65 Exclusion criteria were patients with untreated amblyopia (a difference in best corrected visual
66 acuity of two Snellen lines or more between eyes), uncorrected significant refractive error
67 (hypermetropia of more than +2.00 diopter or astigmatism of more than -1.00 diopter or myopia
68 of -5.00 diopter in children under the age of 2 years, -3.00 diopter from 2 years to 4 years or
69 any myopia in older children), accommodative and partially accommodative esotropia,
70 significant patterns (A and V patterns), previous strabismus surgery, concomitant eye
71 pathology leading to poor vision or any neurological problems.

72 A full clinical history and examination was performed. The history included age, gender,
73 history of strabismus (age of onset, age of first presentation, previous treatment, previous
74 occlusion therapy or penalization and spectacle history), birth history, developmental history,
75 medical history and family history. In the examination we documented visual acuity, abnormal
76 head posture, ductions and versions, A and V patterns, the presence of dissociated vertical
77 deviation (DVD) and dissociated horizontal deviation (DHD), prism cover test on
78 accommodative targets (with and without spectacle correction for near (33 cm) and for the
79 distance in older patients (6 meters)) or Modified Krimsky where prism cover test is not
80 possible, slit lamp examination where possible, dilated fundoscopy and cycloplegic refraction
81 with atropine (for three days prior to refraction).

82 Eligible patients were randomly assigned to 1 of 2 experimental groups. Randomization was
83 performed by using 34 sealed envelopes, 17 assigned to each group.

84 Patients in group 1 were treated with a single three or four horizontal rectus muscle procedure
85 based on Scott's surgical tables (table 1)¹¹. Patients in group 2 were treated with a two-stage
86 procedure consisting of bilateral medial rectus muscle recessions 11mm from the limbus,
87 followed by the appropriate bilateral lateral rectus muscle resections 6 to 12 weeks later for the

88 residual angle, based on the lateral rectus resection schedule in Wright's surgical dosing tables
 89 (table 2)¹².

90 **Table 1: Table for 1 procedure surgery (Group 1)**
 91
 92
 93

Pre-operative deviation (PD)	Bimedial rectus recession (mm from limbus)	Unilateral lateral rectus resection (mm)	Bilateral lateral rectus resection (mm)
55 PD	11mm	4-5mm	
60 PD	11mm	6mm	
65 PD	11mm	7mm	
70 PD	11mm		4mm
75 PD	11mm		5mm
80 PD	11mm		6mm
90 PD – 100 PD	11mm		7mm

94 Extracted from: Scott WE. Concomitant strabismus: esotropias. In: Taylor D, Hoyt C, eds. PEDIATRIC
 95 OPHTHALMOLOGY AND STRABISMUS. 3rd ed. Elsevier Saunders; 2005:885.¹¹

96 PD = prism diopter
 97
 98

99 **Table 2: Table for 2 procedure surgery (Group 2)**
 100
 101

Bilateral lateral rectus resection (mm)
15PD – 3.5mm
20PD – 4.5mm
25PD – 5.5mm
30PD – 6.0mm
35PD – 6.5mm
40PD – 7.0mm
50PD – 8.0mm

102

106 All surgeries were performed by a single surgeon. The technique of medial rectus recession
107 consisted of a nasal limbal conjunctival incision. The medial rectus muscle was isolated, tagged
108 with a 6/0 absorbable suture on double-armed needles, disinserted from the globe and sutured
109 to the sclera 11mm from the limbus using a Helveston scleral marker for measurement. The
110 conjunctiva was closed with an 8/0 silk suture. The technique of lateral rectus resection was
111 similarly done through a temporal limbal conjunctival incision. The muscle was isolated,
112 tagged with a 6/0 absorbable suture on double-armed needles, placed such as to permit
113 resection of the appropriate of amount of muscle,as measured with a caliper. It was then sutured
114 to the sclera at the original insertion. The conjunctiva was closed with 8/0 silk.

115 Post-operative evaluation took place on day 1 and week 3 in both groups. Patients were
116 assessed for residual angle of strabismus for distance and near. Patients in group 1 were
117 reassessed at week 6 post-operatively. Patients in group 2 proceeded to bilateral lateral rectus
118 muscle resection surgery 6 to 12 weeks later if there was a residual esotropia of 15PD or more.
119 The surgical outcomes in the 2 groups were compared 6 weeks after the final surgery.

120

121 **Results:**

122 Surgical outcomes were evaluated in 32 patients - 17 patients in group 1 and 15 patients in
123 group 2. Two patients in group 2 failed to present for the second procedure and were excluded.
124 A successful outcome was defined as alignment within 10PD of orthotropia (including
125 esotropia and exotropia) for near and distance. An esotropia of more than 10PD was considered
126 an undercorrection and an exotropia greater than 10PD an overcorrection. Results for the two

127 groups are shown in Table 3 and the results for individuals in each group are shown in Tables
128 4 and 5.

129 **Table 3: Comparison of results between the 2 groups**

130
131
132

	GROUP 1	GROUP 2
PATIENTS	17	15
GENDER	8 male 9 female	5 male 10 female
AGE (years)	Median: 5 Range: 3-8	Median: 5 Range: 2-15
PRE-OP ANGLE (PD)	Mean: 77 Range: 55-100	Mean: 82 Range: 60-100
DVD	7 (41%)	9 (60%)
IOOA	5 (29%)	8 (53%)
SOOA	5 (29%)	1 (7%)
SUCCESS	14 (82%)	12 (80%)

133

134 PD = prism diopter
135 DVD = dissociated vertical deviation
136 IOOA = inferior oblique overaction
137 SOOA = superior oblique overaction
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143 **Table 4: Individual results of patients in Group 1**

Patient	Age (years)	Gender	Pre-op angle ET (PD)		Post-op angle (PD)		DVD present	Oblique overaction	Outcome
			Near	Distance	Near	Distance			
1	7	M	90	90	5 ET	0	no	no	successful
2	7	M	60	55	3 XT	3 XT	no	SOOA	successful
3	7	M	100	60	5 ET	3 ET	yes	no	successful
4	4	M	90	60	5 ET	3 ET	no	SOOA	successful
5	4	F	90	95	0	3 XT	no	no	successful
6	4	F	100	95	6 XT	10 XT	yes	IOOA	successful
7	4	F	80	100	20 ET	5 ET	yes	IOOA	unsuccessful
8	6	F	75	70	12 XT	16 XT	yes	SOOA	unsuccessful
9	4	M	60	60	0	0	no	no	successful
10	5	M	75	100	0	0	yes	no	successful
11	7	F	75	75	4 XT	10 XT	no	SOOA	successful
12	3	F	60	65	5 ET	5 ET	yes	IOOA	successful
13	6	F	100	95	14 ET	14 ET	no	IOOA	unsuccessful
14	5	F	60	70	10 ET	10 ET	no	no	successful
15	7	M	65	75	0	4 XT	yes	SOOA	successful
16	8	F	100	70	0	0	no	IOOA	successful
17	4	M	100	70	8 ET	8 ET	no	no	successful

144
 145 ET= esotropia, PD= prism diopter, DVD= dissociated vertical deviation, XT= exotropia, SOOA= superior oblique
 146 overaction, IOOA= inferior oblique overaction
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158 **Table 5: Individual results of patients in Group 2**

Patient	Age (years)	Gender	Pre-op angle ET (PD)		Post-op angle (PD)		DVD present	Oblique overaction	Outcome
			Near	Distance	Near	Distance			
1	3	M	90	90	defaulted	defaulted	yes	no	defaulted
2	15	M	60	60	0	0	yes	SOOA	successful
3	10	F	100	100	0	0	no	IIOOA	successful
4	7	F	90	80	0	3 XT	yes	no	successful
5	5	F	90	85	8 XT	18 XT	yes	IIOOA	unsuccessful
6	3	F	100	95	0	0	no	IIOOA	successful
7	9	F	80	70	8 ET	4 ET	yes	no	successful
8	4	M	75	70	6 XT	6 XT	yes	IIOOA	successful
9	4	F	60	60	defaulted	defaulted	no	no	defaulted
10	4	F	75	75	10 ET	10 ET	no	IIOOA	successful
11	3	F	75	75	4 ET	4 ET	yes	no	successful
12	5	M	60	60	10 XT	10 XT	no	IIOOA	successful
13	3	F	100	100	14 ET	14 ET	yes	no	unsuccessful
14	5	F	60	50	0	0	yes	IIOOA	successful
15	2	M	65	65	0	0	no	IIOOA	successful
16	8	M	100	95	18 ET	8 ET	yes	no	unsuccessful
17	10	F	100	100	8 ET	6 ET	no	no	successful

159

160 ET= esotropia, PD= prism diopter, DVD= dissociated vertical deviation, SOOA= superior oblique overaction, IIOOA=
 161 inferior oblique overaction, XT= exotropia

162

163 The Fischer exact test was used to analyze data. There was no statistically significant difference
 164 in the outcomes between groups 1 and 2 (p=0.34). Several previous studies^{1,13,14} have looked
 165 at whether the presence of DVD, inferior oblique overaction (IIOOA) and superior oblique
 166 overaction (SOOA) has an effect on surgical outcomes. In this study the presence of a DVD
 167 (p=0.51) and IIOOA (p=0.31) did not affect successful outcomes. There were not enough
 168 patients with SOOA to make an assessment. Of the unsuccessful patients, in both groups 2
 169 patients were undercorrected and 1 patient overcorrected.

170

171 When combining the patients in both treatment groups and dividing them according to the size
172 of the pre-operative angle into smaller angles (less than 70PD esotropia) and larger angles
173 (70PD esotropia and more), we found that 9 of 9 patients (100%) in the smaller angle group
174 had a successful outcome and 17 of 23 patients (74%) in the larger angle group had a successful
175 outcome. By comparing these two groups we showed strong statistical evidence that angles
176 smaller than 70PD esotropia are more likely to be successful than angles of 70PD and larger
177 ($p=0.056$).

178

179 **Discussion:**

180 Large angle congenital esotropia is commonly seen in South Africa and is substantially more
181 prevalent than accommodative esotropia in African patients.¹⁵ The mean pre-operative angle
182 of esotropia in our study was 77PD for group 1 and 82PD for group 2 which is much more than
183 the average of 60PD to 68PD found in most other studies on large angle esotropia.^{2,8,9,13,16,17}
184 XXX Hospital is a state referral hospital and many strabismus patients are late presenters for
185 various reasons. Distances to hospital are often far and transport facilities are inadequate.
186 Poverty is common, especially in the rural areas, and the costs involved with transport and
187 multiple hospital visits are not affordable. The tribal culture and influence of traditional healers
188 prevent parents from seeking medical attention. Patients are often unaware of the treatment
189 options. Concerns about the risks of surgery also play an important role. As a result, surgery in
190 this study was performed on children older than those in studies from developed countries. As
191 the children were older, the probability of robust binocularity was significantly reduced,
192 increasing the risk of consecutive exotropia if they were surgically aligned within 10 PD of
193 orthotropia.

194 In previous studies the outcome of surgery after a three or four horizontal rectus muscle
195 procedure in large angle esotropia varied from 64.5% to 100%.^{2,8,9,10,13} The success rate in our
196 study was 82% (Group 1) and 80% (Group 2) at 6 weeks follow-up. The outcome after
197 simultaneous surgery was no different to that after a staged surgical approach. This has
198 important clinical implications: a single surgery has less anesthetic risks, saves costs and
199 valuable theatre time and is more convenient for patients.

200 Several studies have indicated that the magnitude of the pre-operative angle adversely affects
201 that those with the outcome.^{1,13,14} When we divided our patients into smaller and larger angle
202 groups, we also found smaller angles were more likely to have a successful result. Additional
203 factors that were found to adversely affect the outcome of surgery in other studies were:
204 amblyopia^{1,18}, IOOA, lateral rectus underaction¹⁴ and surgery prior to 16 months of age^{1,10}. The
205 presence of IOOA had no effect on the outcome in our study which was in keeping with the
206 findings of Trigler and Siatkowski.¹ Of patients with infantile esotropia 48%-92% of patients
207 with infantile esotropia have DVD's.^{19,20,21} We looked at the presence of a DVD as an adverse
208 risk factor for surgical outcome but found no significance in our study, confirming the findings
209 of Trigler and Siatkowski¹ and Rajavi and associates.¹⁴ A limitation of our study is the small
210 patients numbers, so these DVD and IOOA findings should be interpreted with caution as the
211 subset size was small.

212 Three of 17 patients (18%) in the staged surgical group (group 2) achieved success with the
213 maximal medial rectus surgery alone and did not need further surgery (patients 1, 14 and 17)
214 Patient 1 had a residual angle of 35PD esotropia 3 weeks after the initial surgery, but failed to
215 return for the second procedure. He presented 9 months later and by then was successfully
216 aligned. One may assume that 3 to 4 muscle surgery would have resulted in an overcorrection
217 in these patients and that a staged approach has preserved the lateral rectus muscles and
218 probably a second surgery for the potential overcorrection. The clinical significance of this

219 favorable outcome in 18% of patients is a point for debate. The pre-operative angles in these
220 patients were 90PD esotropia (patient 1), 60PD esotropia (patient 14) and 100PD esotropia
221 (patient 17) and they were 3 years, 5 years and 10 years old respectively. Stereopsis was tested
222 with the Titmus fly, but all of them failed to display fine stereopsis. The reason for a successful
223 outcome after only one procedure in these patients is unclear but does pose the question: if the
224 second surgery was delayed for longer than the 6 to 12 weeks prescribed in this study, could
225 there have been more patients who ultimately achieved success with maximal medial rectus
226 recessions alone? This may indicate that a longer interval before repeat surgery is required in
227 some patients. However which patients this applies to has yet to be determined

228 The follow-up period in this study was relatively short and we did not study long-term results.
229 A larger study with long term follow up may be required. It is well known that the size of
230 angles change with time.^{2,8,9,13,22} Several medium and long-term studies on three and four
231 muscle surgery for large angle congenital esotropia have shown good results at long-term
232 follow-up.^{2,8,9,13,22} Chatzistefanou et al compared long-term outcomes (median 54 months)
233 with 8-week outcomes after three muscle surgery in 194 patients with esotropia.¹³ They found
234 more late overcorrections than undercorrections which were more marked in angles of less than
235 70PD. The median age of patients at the time of surgery in their study was 31 months (20
236 months to 432 months) which was older than the median age of 22 months (range 10 months
237 to 168 months) in a study by Bayramlar.²² Bayramlar and associates looked at the medium term
238 outcomes (median 32 months) in 18 patients after three muscle surgery and showed an increase
239 in residual esotropia.²² Forrest *et al*⁹ also showed an increase in residual esotropia at medium
240 term in patients who had surgery at a younger age. In this study 49 patients underwent three
241 horizontal muscle surgery for large angle infantile esotropia. The mean age of the children at
242 the time of surgery was 12.9 months and the mean follow-up period 32.9 months post-
243 operative. This may suggest that one would need to consider reducing the surgical numbers in

244 patients presenting late as their eyes behave different from patients who have surgery at an
245 early age. In a study by Scott et al² they found that patients who were initially overcorrected
246 after three and four muscle procedures tend to drift in towards orthotropia over time.

247

248 **Conclusion:**

249 Single three or four horizontal rectus muscle surgery for large angle congenital esotropia has a
250 similar success rate to a two-staged procedure when the second procedure took place 6 to 12
251 weeks after the first. The presence of a DVD or inferior oblique overaction did not affect
252 outcomes in this study.

253

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Appendices

Appendix 1: The final Study Protocol



UNIVERSITY OF
KWAZULU-NATAL

RESEARCH OFFICE

BIOMEDICAL RESEARCH ETHICS COMMITTEE

APPLICATION FOR ETHICS APPROVAL
For research on human participants (Medical)

PART 1

SECTION 1: ADMINISTRATIVE DETAILS (PLEASE TYPE)

NAME: PI - Prof/Dr/Mr/Mrs/Miss/Ms	Dr Magritha du Bruyn
NAME: Co-investigator- Prof/Dr/Mr/Mrs/Miss/Ms	Dr Anthony Zaborowski Dr Dharmesh Parbhoo
Professional status (if student, year of study)	Registrar ^{4th} year of study in July 2010
UKZN Department	Ophthalmology
Hospital / Institution where employed	King Edward VIII Hospital, Durban
Full Postal address	27 Templeton Green, 60 Bellevue Rd, Musgrave, Durban, 4001
Contact telephone and fax numbers	Cell phone 0827829329 Fax 0866607399
Email Address	aritha2@gmail.com
Full time/part time employment	Full time
Current HPCSA Number	MP 0484393

1.1 TITLE OF PROJECT in full:

Simultaneous three or four horizontal rectus muscle surgery versus staged surgery for large angle congenital esotropia in children: a randomized controlled trial.

1.2 WHERE WILL THE RESEARCH BE CARRIED OUT? (*interaction with participants*)

Inkosi Albert Luthuli Central Hospital, Ophthalmology Department

1.3 PURPOSE OF RESEARCH:

Postgraduate Degree: (*circle applicable*) **Masters degree: MMed (Ophth)**

(SUBMIT A COPY OF THE APPROVAL LETTER FROM THE POSTGRADUATE EDUCATION COMMITTEE).

1.4 IF STUDENT: YES STUDENT NO: 207529573

1.5 PRINCIPAL INVESTIGATOR/CO-INVESTIGATOR/S (state exact role/s in the study):

Name/Dept	Role	Signature
M Du Bruyn (Ophthalmology)	Designing of study; preparing of protocol; examination of patients pre-operative and post-operative; evaluation of study results	
A Zaborowski (Ophthalmology)	Assisting in study design and protocol; assisting in evaluation of study results; overseeing study	
D Parbhoo (Ophthalmology)	Performing all surgical procedures; pre-operative and post-operative examination of patients	

1.6 FUNDING

Has funding been secured? **No**

Source of funding (full details): Not applicable

Can this project proceed without funding? Yes

Give a brief explanation: All procedures done will form part of normal clinical work.

SECTION 2: DISCLOSURES

2.1 Has this study been, or is it likely to be, submitted to any other ethics review committee? No

2.2 If yes, please name the Committee/s and give outcome - i.e. approved/rejected/pending/not applicable? Not applicable

- 2.3 Have you been previously/are you presently being investigated in regard to alleged misconduct relating to research-related activities? No
- 2.4 Are any of your intended research participants in other research studies and/or trials? If so, please provide details. No
- 2.5 Are you presently involved in other research and/or clinical trial activities? If so, please provide details. No
- 2.6 If tissues are to be stored, give details of storage facilities. No tissues to be stored
- 2.7 If tissues are to be exported, please attach a copy of export and import permits and International Aviation Clearance. No tissues to be exported

2.8 Conflict of Interest:

Investigators should have no undisclosed conflict of interest with their study collaborators, sponsors or participants. Conflicts can arise, for example, when a commercial or other sponsor may not wish research results detrimental to their corporate image / interest to be disclosed, especially when the investigator is being remunerated by the sponsor for the research in question; when research subjects are being rewarded for their participation in the research; or when an investigator has a vested interest in, or is an employee / shareholder / director in the sponsor's corporate entity. Investigators should note that the duty to disclose a conflict of interest to the ethics review committee begins during application for ethical approval and continues until the research in question is complete and the research results are submitted to the sponsor / published (if applicable).

If the investigator(s) has / have / foresees any such conflict of interest, please provide details here:
None foreseen

SECTION 3: THE PROTOCOL

Type of Study: Interventional Randomized Controlled Trial

3.1 THE PROJECT:

3.1.1 Aims:

- To determine the outcome of squint surgery in children with congenital esotropia larger than 50 prism dioptres (PD).
- To compare a single three or four horizontal rectus muscle procedure to a two-stage procedure consisting of maximal bilateral medial rectus recessions followed by a bilateral lateral rectus muscle resection 6 to 12 weeks later.
- To investigate an appropriate surgical dosing protocol for residual esotropia following maximal medial rectus muscle recession.
- To perform a sub analysis to evaluate the treatment success between patients of 2 years and younger (where monofixation is expected) and patients older than 2 years.

3.1.2 Hypothesis to be tested:

- Two-stage horizontal muscle surgery for large angle congenital esotropia in children has a better post-operative outcome than single three or four horizontal muscle surgery.

3.1.3 Summary of the proposed research: (restrict to 100 words)

A randomized controlled trial to determine the outcome of surgery for large angle congenital esotropia in children. A single three or four horizontal muscle strabismus correction procedure based on standard of care surgical dosing tables will be compared with a two-stage strabismus procedure. The two-stage procedure will consist of bilateral maximal medial rectus recessions followed by appropriate bilateral lateral rectus resections 6 to 12 weeks later. The surgical outcomes between the two groups will be compared 6 weeks after the final surgery.

3.1.4 Keywords: strabismus; squint; infantile esotropia; large angle; maximal medial rectus recession; lateral rectus resection; outcome; randomized controlled trial.

3.1.5 Background and Literature:

Congenital (infantile, essential) esotropia is an idiopathic condition of misalignment of the eyes noticed within the first six months of life in an otherwise normal infant with no neurological abnormality and no significant refractive error.^{1,2}

The surgical management of large angle congenital esotropia in children is controversial. Large angle squints of greater than 50 PD tend to require on average more squint procedures than smaller angle squints to achieve and maintain horizontal alignment.³ The optimal surgical approach to these patients has not been established.

Conventional bilateral medial rectus muscle recession has a low success rate in children with large angle esotropia (angles greater than 50 PD) with a less than 50% rate of adequate ocular alignment.^{4,5,6,7} Three or four horizontal rectus muscle surgery is associated with better outcomes.^{4,8}

Bilateral supramaximal medial rectus muscle recessions greater than 6.0mm have been performed for angles bigger than 50 PD. This procedure has been favored as it is quicker to perform than three or four muscle surgery and leaves the lateral rectus muscles untouched.^{9,10,11} Success rates in achieving ocular alignment varies between 60%-91% with this approach.^{9,10,11,12,13} Supramaximal medial rectus muscle recessions are however associated with adduction deficits due to medial rectus muscle underaction resulting in impairment of convergence and a tendency towards late exotropic drift and incomitance.^{4,7,12,14,15,16,17,18}

Three- and four horizontal muscle surgery can be performed as a single procedure (bilateral medial rectus recession and unilateral or bilateral lateral rectus resection) or as a staged procedure (bilateral medial rectus recessions followed by unilateral or bilateral lateral rectus resections). Staged surgery may be more accurate than simultaneous three or four muscle surgery in that the angle of the residual esotropia after the initial bilateral medial rectus recessions can be established and a second surgery can be planned based on this residual angle. Outcomes might be more predictable than a single three or four muscle procedure.¹⁹

A literature search on Pubmed using the words “large angle squint”, “infantile esotropia”, “squint surgery”, “strabismus”, “maximum medial rectus recession” and “lateral rectus resection” has found no study comparing simultaneous three or four muscle surgery to a staged approach.

The medial rectus muscle insertion is normally found at 5.5mm from the limbus, but several studies have shown that this distance varies among patients.^{20,21,22} The insertion distance also alters once the medial rectus muscle is disinserted. It is therefore more accurate to measure from the limbus and not the medial rectus insertion when adjusting the muscles during strabismus surgery.

3.1.6 Key References:

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3.2 PLAN OF INVESTIGATION:

3.2.1 Design and/or experimental procedures :

In the case of Higher Degrees, please state name and department of person consulted regarding the design.

People consulted are Dr A Zaborowski (Department of Ophthalmology, University of KwaZulu Natal) and Dr D Parbhoo (Department of Ophthalmology, University of KwaZulu Natal)

An interventional randomized controlled trial to determine the outcome of surgery for large angle congenital esotropia in children.

Eligible patients will be assigned randomly to 1 of 2 experimental groups:

(Randomization will be performed as follows: 34 sealed envelopes will be used – 17 will be assigned to group 1 and 17 to group 2. Prior to surgery the ophthalmologist performing the surgery will draw one envelope and perform the surgery as planned for patients in group 1 or group 2.)

- Group 1 will be treated with a single three or four horizontal muscle procedure. Surgical dosing will be based on Scott's surgical tables¹ in the treatment of congenital esotropia. (Appendix 1)
- Group 2 will be treated with a two-stage procedure consisting of bilateral medial rectus recessions 11mm from the limbus, followed by the appropriate bilateral lateral rectus resections 6 to 12 weeks later, based on the lateral rectus resection schedule in Wright's surgical dosing tables² (derived from Parks' surgical dosing tables³) for the residual angle. (Appendix 2)

The surgical outcomes in the two groups will be compared 6 weeks after the final surgery. The surgical outcomes in group 2 will be specifically evaluated with a view to establishing an appropriate surgical dosing schedule for lateral rectus muscle resection to treat residual esotropia following maximal medial rectus recession residual in large angle strabismus.

Secondly the distance of the insertion of the medial rectus muscle from the limbus will be measured before the surgery in each patient using a Helveston scleral marker.

Inclusion criteria:

- Constant esotropia measuring >50 PD
- Children aged between 9 months and 16 years

Exclusion criteria:

- Untreated amblyopia (a difference in best corrected visual acuity of two Snellen lines or more between the two eyes⁴)

- Uncorrected significant hypermetropia (a hypermetropic refractive error of more than +2.00 dioptres)
- Accommodative and partially accommodative esotropia
- Previous strabismus surgery
- Any concomitant eye pathology resulting in poor vision
- Neurological problems

Consent will be obtained from the parent/guardian for entry into the study and for surgical intervention. Once informed consent is obtained the following assessment will be recorded:

Clinical history:

Age

Gender

History of strabismus

- age of onset
- age of first presentation
- previous treatment
- previous occlusion therapy or penalization
- spectacle history

Birth history

Developmental history

Medical history

Family history

Examination:

Visual Acuity

- Snellen chart acuity testing – letters or tumbling E's
- Lea cards for children unable to read the E-chart
- Preferential looking using acuity cards with gratings in varying widths for very young children unable to use Lea cards

Appearance

- Abnormal head posture: head turn, head tilt or chin lift

Movements

- Ductions, versions, convergence, A and V patterns
- Muscle overaction and underaction
- Presence of DVD and/or DHD

Cover Tests

- Prism cover test
- With and without available spectacle correction
- Near and distance
- Primary position, 30 degrees left and right, 30 degrees up and down

Slit lamp examination (if the child allows) and dilated funduscopy

Stereopsis will not be tested for as only large angle squints are included in this study and stereopsis is very poor in large angle strabismus.

Cycloplegic refraction

- Atropine 1% twice a day x 3 days prior to refraction

Children with hypermetropic refractive errors of more than +2.00 dioptres or astigmatism of more than -1.00 dioptre or myopia of -5.00 dioptre in children under the age of 2 years or myopia of -3.00 dioptre in children from 2 years to 4 years or any myopia in older children will receive full correction.

All surgeries will be performed by a single ophthalmologist (Dr Dharmesh Parbhoo). Prior to commencing the surgery a forced duction test will be performed. The technique for the medial rectus recession is as follows: A limbal double wing incision is made through the conjunctiva and Tenon's capsule. Westcott scissors are used to undermine the anterior conjunctiva and Tenon's capsule. The inferior border of the medial rectus is identified and a Steven's hook passed behind the muscle. A Jameson hook is passed behind the muscle parallel to the muscle insertion line. The intermuscular septum is opened with Westcott scissors and the anterior Tenon's capsule removed. Light cautery is applied to the anterior ciliary arteries overlying the muscle tendon. The distance of the medial rectus insertion from the limbus is measured with a Helveston scleral marker and documented. A 6-0 Vicryl (Polyglactin 910, Ethicon) suture on double-armed needles is passed through half-thickness tendon, through half of the tendon width, then passed through full-thickness tendon, a quarter of the muscle width and again passed a third of the width. The suture is locked after each pass. The same procedure is followed with the other edge. Once the muscle is secured with locking sutures at both edges, the insertion of the muscle is removed with Westcott scissors. The 11mm recession is measured from the limbus with a Helveston scleral marker. The needles are passed superficially through the sclera, parallel to the insertion line with the needles exiting in a crossed-sword configuration. The muscle is tied in place, widely splayed out to the same width as the scleral insertion line. The conjunctiva is sutured back in place with an 8-0 silk suture.

The lateral rectus resection (when indicated) is performed through a temporal limbal incision that is made through the conjunctiva and Tenon's capsule. Westcott scissors are used to undermine the anterior conjunctiva and Tenon's capsule. A posterior dissection is performed to approximately 3mm posterior to the planned muscle resection. The anterior Tenon's capsule is removed in front of the muscle. Two large Jameson hooks are inserted below the muscle. The amount of resection from the tendon insertion is measured in millimetres by using a Helveston scleral marker. A 6-0 vicryl suture on double-armed needles is passed through half muscle thickness (approximately 0.5mm behind the desired resection point) through half of the tendon width, then passed through full-thickness tendon, a quarter of the muscle width and again passed a third of the width. The suture is locked after each pass. The same procedure is followed for the other edge of the muscle. The muscle is then clamped with a Hartman clamp (to maintain haemostasis after the muscle has been resected) and muscle is excised anterior to the clamp. The muscle stump is removed close to the sclera so that the scleral insertion can be visualized. The muscle is secured to the original insertion by passing the needles through superficial sclera at the insertion line. The muscle is advanced to the scleral insertion and the sutures tied. The conjunctiva is then closed with 8-0 silk sutures.

Post-operative assessment will take place at day 1 and week 3 in both groups. Patients in both groups will be assessed for residual angle of strabismus for distance and near. A successful outcome will be defined as alignment within 10PD of orthotropia (including esotropia and exotropia).³ A second measure for success will be personal judgement (see below). These two groups will be statistically evaluated separately at the end of the study.

Patients in group 1 will be reassessed at week 6 post-operatively. Patients in group 2 will proceed to bilateral lateral rectus resection surgery after 6 to 12 weeks if there is a residual esotropia of equal to or greater than 15PD and deemed to be significant by the patient's parents/caregivers. A residual angle of 12PD esotropia will be rounded off to 10PD and be considered successful. An angle of 14PD will be rounded off to 15PD and these patients will proceed to bilateral lateral rectus muscle resection. If the caregiver is happy with a residual angle of esotropia of more than 10PD after the initial surgery and refuses the second procedure, this will also be considered successful based on personal judgment. There will therefore be two measures of success: anatomical (an angle within 10PD of orthophoria – esotropia or exotropia) and personal (a result deemed acceptable by the caregiver and refusal of further surgery based on a psychosocially acceptable result).

1. Scott WE. Concomitant strabismus: esotropias, in Taylor D, Hoyt C (ed): *Pediatric Ophthalmology and Strabismus*, 3rd ed. Elsevier Saunders; 2005, chap 80. p885-886.
2. Wright KW. *Colour Atlas of Ophthalmic Surgery: Strabismus*. Philadelphia: JB Lippincott Company;1991.p241-242.
3. Parks MM, Mitchell PR, Wheeler MB. Concomitant esodeviations, in Tasman W (ed): *Duane's Clinical Ophthalmology*, revised ed. Philadelphia:Lippincott Williams and Wilkins; 2004, vol 1, chap 12. p12-13.
4. Kanski JJ. *Clinical Ophthalmology*. 6th ed. Edinburgh: Elsevier Butterworth- Heinemann; 2007.p746.

3.2.2 Statistical Planning:

Has this project been discussed with:
a professional statistician?

Yes

If yes, (a) Name of statistician: Mrs T Esterhuizen
(b) Give details - outline statistical considerations such as randomization, size of groups, exclusions etc.

The following assumptions have been made:

- An estimated difference of 5PD in the residual angle between the two groups at the final assessment.
- An estimated standard deviation of 5.0 in each group.

The following confounders will need to be looked at:

- Population and social status: Patients will be taken from the same hospital for both surgical procedure groups
- Gender and age will be statistically assessed at the end of the trial.
- Single surgeon factor: The surgeon routinely performs both procedures and is therefore equally competent in both procedures.

The total number of patients needed is therefore 34 (17 in each group).

Randomisation will be performed as follows: 34 sealed envelopes will be used – 17 will be assigned to group 1 and 17 to group 2. Prior to surgery the ophthalmologist performing the surgery will draw one envelope and perform the surgery as planned for patients in group 1 or group 2.

If no, specify why statistical consultation was not obtained and motivate the design adopted. Not applicable

3.2.3 Participants:

Clinical data:

Source: Patients from the Eye Clinic at Inkosi Albert Luthuli Central Hospital (Outpatients)

Age: Patients between the ages of 9 months and 16 years

Numbers: 34 patients

Will you have control groups? no

Detail inclusion and exclusion criteria:

Inclusion:

- Patients from 9 months to 16 years with infantile esotropia of more than 50PD without any previous eye muscle surgery who fit the inclusion criteria as discussed below

Exclusion:

- No consent to the surgery after being counselled or refusing to be included in the study.
- Patients who do not fit the inclusion criteria as discussed below

Inclusion criteria:

- Constant esotropia measuring >50 PD
- Children aged between 9 months and 16 years

Exclusion criteria:

- Untreated amblyopia (a difference in best corrected visual acuity of two Snellen lines or more between the two eyes)
- Uncorrected significant hypermetropia (a hypermetropic refractive error of more than +2.00 dioptries)
- Accommodative and partially accommodative esotropia
- Previous strabismus surgery
- Any concomitant eye pathology resulting in poor vision
- Neurological problems

Describe recruitment process for all groups:

Patients attending the Eye Clinic at Inkosi Albert Luthuli Central Hospital who fit the inclusion criteria will be asked to join the study.

3.2.4 The Environment:

3.2.4.1 Is this a multi-national study? **No.**

If yes, state collaborating countries. Not applicable

3.2.4.2 List all sites in South Africa in which the project will be carried out.

Inkosi Albert Luthuli Central Hospital, Durban

3.2.4.3 Can the project have any negative consequences on participants, members of the public, researchers, field staff or the physical environment (incl. the laboratory)?

No

3.2.4.4 How many hours/week will the PI devote to this project?

10 hours per week

3.3 ETHICAL ASPECTS:

3.3.1 Responsibility: *In respect of any litigation which may result from this research:*

3.3.1.1 Are the pharmaceutical manufacturers prepared to take responsibility?

Not applicable

3.3.1.2 Have you ensured that reimbursement for participants and investigators is in accordance with 1) *Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa – Department of Health (2006) – and 2) Ethics in Health Research: Principles, Structures and Processes – (2004)?*

No compensation to be given

3.3.1.3 If this project is to be conducted at another institution, is additional ethical clearance approval required?

Project is to be conducted at one institution only which forms part of the training facilities for Ophthalmology for the University of KwaZulu Natal

3.3.2 Incentives / Reimbursement

3.3.2.1 List any incentives, explicit and implicit, that have or will be offered to study participants, either to recruit or to retain within the study.

None

3.3.2.2 List reimbursement / compensation for participation in the study (e.g. travel costs, out of pocket expenses, etc.).

None

3.3.3 Potential risks or discomfort:

Compared to persons or patients with similar conditions indicate, for each study group, the potential additional

- Risk – None. Treatment interventions are accepted standards of care for congenital esotropia.
- Discomfort – None. Treatment interventions are accepted standards of care for congenital esotropia.

3.3.4 Health Service Utilization:

Compared with persons or participants with similar conditions indicate, for each study group, the likely additional:

Duration of hospital stay (days): 0
Outpatient attendances (number): 0
Laboratory services used: 0
Samples to be drawn: 0
Extent of nursing involvement: Translation and discussing consent for the study

Have the nursing team who will be involved in the study been informed of the study and the nursing involvement which will be required? Yes

Other (specify): none

3.3.5 Management:

In the case of participants drawn from patient populations, indicate, in respect of each sub-group, how management differs from that usually offered to patients with similar conditions.

Identical (Both single and multiple surgical procedures are standard practice in the care of patients with large angle esotropia.)

3.3.6 Community Consultation:

In the case of community based studies, explain what consultation is planned within the community

Not applicable

3.3.7 State the expected benefits arising from this study under the following headings:

3.3.7.1. Possible direct benefits to study participants: No direct benefits to the study participants, but the study may improve standards of care in future.

3.3.7.2 Clinical care: Knowledge about the best surgical management for patients with large angle infantile esotropia. This can optimize care for the patients and prevent unnecessary additional surgical procedures for residual esotropia.

3.3.7.3 Public health: Improvement in service delivery for large angle squint surgery.

3.3.7.4 Financial: Optimizing the management of patients with large angle congenital esotropia will minimize unnecessary surgery and thus financial costs due to suboptimal initial treatment.

3.3.7.5 Prospects of tested intervention being available to the study population if proven effective: Once the best surgical option has been determined, it will be discussed with the study population during future visits (patients with strabismus require long term follow-up and will still be seen at the Eye Clinic after the study has been completed).

3.3.7.6 Other (Specify): None

SECTION 4: INFORMATION DOCUMENT

Study title:

Simultaneous three or four horizontal rectus muscle surgery versus staged surgery for large angle congenital esotropia in children: a randomized controlled trial

Hello and welcome to our clinic.

Dr. M du Bruyn is doing research for a Masters degree (MMed(Ophth)) on children with squint eyes. Squint eyes are a common problem and many children develop squint eyes before the age of six months. There are different ways to treat the squints depending on the kind of squint. Often, especially when the squint is very big, it is necessary to do one or more operations to make the eyes straight.

Research is the process to learn the answer to a question. In this study we want to learn which kind of operation gives better results by comparing two different procedures. The aim is to get the eyes as straight as possible with as few as possible operations. Both procedures are used and both work well, but we want to see if one gives a better outcome than the other. Maybe one is better and maybe they are both the same.

We are asking you to participate in this research study. If your child has squint eyes that was noticed before the age of six months and that would need to be operated to make it straight, we would like you to participate in this study. We are looking for 34 patients to do this research on. Seventeen of these patients will undergo the one procedure and seventeen patients will undergo the other procedure. The first procedure consists of one operation, but we will operate on two muscles in the one eye and one or two muscles in the other eye at the same time. The second procedure will consist of two operations (6 to 12 weeks apart), but we only operate on one muscle in each eye during the first operation and then on one muscle in each eye during the second operation.

The risks and benefits to your child are not higher if you are in this study because the operations and treatment are exactly the same as what are normally used. You will be told about the results of the study and if there are any problems.

You can also choose not to be part of this study if you want to. In this case we will still give you all the correct treatment to help you. If you want to be in the study now you are allowed to stop at any other time without a problem.

All your personal information will be kept secret as well as possible. The only people allowed to see your information are the people involved in the study, people that do checks on the study (e.g. the Research Ethics Committee and the Medicines Control Council) and if required by law. If the results are published your personal details will not be mentioned.

If you have any problems or questions please phone Dr M Du Bruyn at 031 240 1262 at Inkosi Albert Luthuli Central Hospital.

To report complaints please contact

Biomedical Research Ethics Committee, Research Office, Private Bag X54001, Durban 4000

Telephone: +27 (0) 31 260 4769

Fax: +27 (0) 31 260 4609

F-mail: BRFC@ukzn.ac.za/marimuthu@ukzn.ac.za

SECTION 5: INFORMED CONSENT

Consent to Participate in Research

Simultaneous three or four horizontal rectus muscle surgery versus staged surgery for large angle congenital esotropia in children: a randomized controlled trial

You have been asked to participate in this research study.

You have been informed about the study by _____

You may contact **Dr. M Du Bruyn** at **031 2401262** any time if you have questions about the research or if you are injured as a result of the research.

You may contact the **Biomedical Research Ethics Office** on **031 260-4769** if you have questions about your rights as a research participant.

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to stop.

If you agree to participate, you will be given a signed copy of this document and the participant information sheet, which is a written summary of the research.

The research study, including the above information, has been described to me orally. I understand what my involvement in the study means and I voluntarily agree to participate. I have been given an opportunity to ask any questions that I might have about participation in the study.

Signature of Parent or Legal guardian

Date

Signature of Witness

Date

(Where applicable)

Signature of Translator

Date

(Where applicable)

SECTION 6: APPENDIX

Appendix 1:

Preoperative deviation (Prism Diopters)	Bimedial rectus recession (mm from limbus)	Unilateral lateral rectus resection (mm)	Bilateral lateral rectus resection (mm)
30 PD	10mm		
35 PD	10.5mm		
40 PD	11mm		
45 PD - 50 PD	11.5mm		
55 PD	11mm	4-5mm	
60 PD	11mm	6mm	
65 PD	11mm	7mm	
70 PD	11mm		4mm
75 PD	11mm		5mm
80 PD	11mm		6mm
90 PD – 100 PD	11mm		7mm

Scott WE. Concomitant strabismus: esotropias, in Taylor D, Hoyt C (ed): *Pediatric Ophthalmology and Strabismus*, 3rd ed. Elsevier Saunders; 2005, chap 80. p885.

Appendix 2:

<i>BINOCULAR SURGERY</i>
<i>Esotropia</i>
LR OU Resection:
15 ^Δ –3.5 mm
20 ^Δ –4.5 mm
25 ^Δ –5.5 mm
30 ^Δ –6.0 mm
35 ^Δ –6.5 mm
40 ^Δ –7.0 mm
50 ^Δ –8.0 mm

Extracted from Wright KW. *Colour atlas of Ophthalmic Surgery: Strabismus*. Philadelphia: JB Lippincott Company;1991.p241-242.

SECTION 7: DECLARATION

CONFLICT OF INTEREST:

Investigators should have no undisclosed conflict of interest with their study collaborators, sponsors or participants. Conflicts can arise, for example, when a commercial or other sponsor may not wish research results detrimental to their corporate image / interest to be disclosed, especially when the investigator is being remunerated by the sponsor for the research in question; when research subjects are being rewarded for their participation in the research; or when an investigator has a vested interest in, or is an employee / shareholder / director in the sponsor's corporate entity. Investigators should note that the duty to disclose a conflict of interest to the ethics review committee begins with application for ethical approval and continues until the research in question is complete and the research results are submitted to the sponsor / published (if applicable).

If the investigator(s) has / have / foresees any such conflict of interest, please provide details. None foreseen

Is there any conflict of interest – financial or otherwise - to your involvement in this study? No

Oversight of study: Will this study be overseen by a professional Clinical Research Organisation or study sponsor? Please give details: **Yes.** UKZN Research Ethics Committee

I understand and accept that I will be required to submit half-yearly progress reports for pharmaceutical studies and annual reports for other studies. Where applicable, all reports from the Data Safety Monitoring Boards (or similar committees) will be provided to the Biomedical Research Ethics Committee within 7 days.

I agree to provide monitoring data if and when required.

I expect the project to be completed by (*Date*): June 2011

I agree to abide by the guidance contained in the SA Department of Health (2004) *Ethics in Health Research: Principles, structures and processes* and the (2006) *South African Good Clinical Practice Guidelines* and the UKZN Terms of Reference and Standard Operating Procedures of the UKZN Biomedical Research Ethics Committee. All are available at <http://research.ukzn.ac.za/ResearchEthics11415.aspx>

I understand and accept that all information pertaining to this application is a true reflection of the project proposed and I take full responsibility should there be any transgression.

SIGNATURE OF PRINCIPAL INVESTIGATOR:

DATE:

Appendix 2: The Guidelines for Authorship for the Journal selected for submission of the manuscript



JOURNAL OF AAPOS

Official publication of the [American Association for Pediatric Ophthalmology and Strabismus](#)

Submission

Submission to this journal proceeds totally online and you will be guided stepwise through the creation and uploading of your files. The system automatically converts source files to a single PDF file of the article, which is used in the peer review process. Please note that even though manuscript source files are converted to PDF files at submission for the review process, these source files are needed for further processing after acceptance. All correspondence, including notification of the Editor's decision and requests for revision, takes place by email.

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All new manuscripts must be submitted in digital form through the *Journal of AAPOS* online submission and review Web site <https://www.elsevier.com/elsevier/jrn/jaaapos>.

Submission items include (as separate files), in the following order: Cover letter (for specific content of which, see below, "Authors' Responsibility") Signed release forms for identifiable patients Response to reviews (revised manuscripts only) Title page (as a separate file for initial review but integrated into manuscript with revisions) Manuscript (abstract, text, references, and figure legends), including continuous marginal line numbers, or "clean" revised manuscript (with all changes accepted) Highlighted revision, with changes tracked and including continuous marginal line numbers (revised manuscripts only) Tables Figures. Clinical, radiological, and histopathological images should be cropped closely to the point(s) of interest, which may be further indicated by arrows and the like. Video clips or e-supplements

Each page of the manuscript must include continuous line numbers in the margin. Files should be labeled with appropriate and descriptive file names (eg, Text.doc, Fig1.eps, Table3.doc). Upload text, tables, and graphics as separate files. A ".zip" file combining all files may also be used. Do not import figures or tables into the text document, and do not upload your text as a PDF file.

For initial review, a "masked" manuscript is required. Manuscript files, tables, figures, and electronic media should not contain the author's identities in the contents, header/footer, or file names.

Revised manuscripts must be submitted in two versions: a "clean" version, without highlighting or marginal callouts, and a second, "highlighted" version, with substantive changes tracked. Author name(s), institution(s), or the geographic location of the study masked for initial review may be unmasked in revision. Revised manuscripts must be accompanied by a separate file (distinct from the cover letter) with point-by-point responses to reviewers' comments and indications of line numbers in the highlighted revision where changed text may be found. *Note, it is not acceptable to simply reply to reviewers without also modifying the text accordingly; authors who decline to make a suggested revision must explain their reasoning.*

The publisher and editors regret that they are not able to consider submissions that do not follow these procedures. Authors who are unable to provide electronic files or have other circumstances that prevent online submission may contact the editorial office prior to submission to discuss alternate options.

Referees

Please submit, with the manuscript, the names, addresses and email addresses of at least 2 potential referees. Note that the editor retains the sole right to decide whether or not the suggested reviewers are used.

If a manuscript is returned to the author for revision, the revised version should be received by the Journal within 2 months. Otherwise, it will be considered a new submission.

PREPARATION

In general, manuscripts should follow *AMA Manual of Style* (9th ed.) guidelines; technical terminology should reflect *Dorland's Illustrated Medical Dictionary* (30th ed.). Spelling must conform to U.S. English. Word processing software can assist with this task; in MS Word, for example, choose Tools, then Language, and Set Language: select English (U.S.). See also the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (<http://www.icmje.org/>).

Limit the use of abbreviations to those that are commonly understood without explanation (eg, mm Hg). Do not abbreviate a syndrome or term merely because it appears frequently in the manuscript. Pharmaceuticals should be referred to by the generic name. When brand names of equipment or other products are specified, the manufacturer and city and state of manufacture must be included in parentheses following first mention. Patients should be referred to by case number rather than by name or initials.

To mask author identity from reviewers, references to the author(s), institution(s), or geographic location(s) by name or initial should be masked from the manuscript until after initial peer review. If authors refer to their own previously published work, they may forgo masking that material. In such cases, authors should identify the issue in question in the cover letter. The editorial office can make a decision about whether or not to mask the material.

To enable the publisher to use your text files, please follow these instructions carefully. Do not justify the right margin or use centering tabs for text or headers. Be sure to key the letter O, the number 0, the letter l, and the number 1 correctly. Use only one space after colons or periods. Use the default hyphenation of your word processor. Use two hyphens for long dashes. Key in the reference list at the end of the text. Software designed to create references that is used as an adjunct to word processing software (eg, Endnote) may be used, but do not use your word processor's footnote or endnote feature to create such references. When preparing tables, use the table format or use only tabs, not spaces, to align columns. Text to be italicized or set in boldface in print may be keyboarded thus (italics may also be indicated by underlining). Do not input special typesetting codes. The publisher will handle all design considerations for typefaces and page layout.

Authors should make every effort to present Major Articles as concisely as possible. The Introduction generally need not exceed 2 paragraphs. Methods that require extensive detail may be supplemented with e-components. Discussions should focus on interpretation of the most salient features of the results. There is no need for a summary at the end of the manuscript.

Literature search

When making a statement such as "this is, to our knowledge, the first/only report of...", or providing a review of the published literature in a field, authors must demonstrate that they have conducted a comprehensive and systematic review of the literature. Methods of literature search and criteria for including/excluding articles must be stated directly in the manuscript in these cases. This paragraph, which should be placed at the end of the manuscript, before the reference list, under the heading "Literature Search," should state the databases and search terms used, years covered, and additional sources. (eg, articles cited in the reference lists of other articles). It should also indicate how the foreign literature was treated. Other databases such as Excerpta Medica/EMBASE (1947- present), Ophthalmic Literature (1947-1988), and Zentralblatt für die gesamte Ophthalmologie und ihre Grenzgebiete may include key articles that are not cited in MEDLINE.

Double-masked review

This journal uses double-masked review, which means that both the reviewer and author name(s) are not allowed to be revealed to one another for a manuscript under review. The identities of the authors are concealed from the reviewers and vice versa. For more information please refer to <http://www.elsevier.com/reviewers/peer-review>. To facilitate this, please include the following separately:

Title page (with author details): This should include the title, authors' names and affiliations, and a complete address for the corresponding author including telephone and email address.

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Use of word processing software

It is important that the file be saved in the native format of the word processor used. The text should be in single-column format. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. In particular, do not use the word processor's options to justify text or to hyphenate words. However, do use bold face, italics, subscripts, superscripts etc. When preparing tables, if you are using a table grid, use only one grid for each individual table and not a grid for each row. If no grid is used, use tabs, not spaces, to align columns. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the [Guide to Publishing with Elsevier](#)). Note that source files of figures, tables and text graphics will be required whether or not you embed your figures in the text. See also the section on Electronic artwork.

To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

MAJOR ARTICLES

Structure

Major Articles may not exceed 3,000 words in length, not including references. Most manuscripts submitted to the journal do not require encyclopedic referencing; please provide justification in the cover letter during the submission process if more than 25 references are cited. This limitation does not apply to Review articles or AAPOS Workshops.

Subdivision - unnumbered sections

Divide your article into clearly defined sections. Each subsection is given a brief heading. Each heading should appear on its own separate line. Subsections should be used as much as possible when cross-referencing text: refer to the subsection by heading as opposed to simply 'the text'.

Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Materials and Methods

Provide sufficient detail to allow the work to be reproduced. Methods already published should be indicated by a reference: only relevant modifications should be described.

Results

Results should be clear and concise.

Discussion

This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

Conclusions

The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Essential title page information

Title page. The title page should include the following elements: Title of the manuscript Each author's name and two highest academic degrees only Author affiliations Corresponding author Institution at which the study was conducted Word count for entire manuscript, including abstract Word count for abstract alone

The word count for the entire manuscript should include the words in the abstract and body of the manuscript but not the acknowledgments, legends, and references. It should not include the words on the title page itself. The corresponding author's address, telephone number, fax number, and email address should be listed. Authors wishing to receive email communication from readers may have their email addresses printed with the published manuscript. Authors should indicate on the title page whether material was presented at the AAPOS annual meeting or any other national meeting. Any author's financial conflict of interest regarding the subject matter in the manuscript should be disclosed on the title page.

Abstract

The abstract must be in the "structured" format and less than 250 words in length. Where appropriate, abstract headings should read: background or purpose; methods; results; and conclusions. See Ann Intern Med 1997;126:36-47 (<http://www.annals.org/cgi/content/full/126/1/36>) for more information on structured abstracts. Short reports should not have an abstract but should have an introductory paragraph (in boldface) that summarizes the article.

Clinical implications

When you upload your Major Article, you will be required to highlight the clinical implications of your study in fewer than 150 words.

Abbreviations

Ensure consistency of abbreviations throughout the article.

Acknowledgments

Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (eg, providing language help, writing assistance or proof reading the article, etc).

Presentation of data

Correlation coefficient. When interpreting correlation coefficients, avoid using the terms "significant correlation" or "correlated significantly." A correlation coefficient is concerned with the strength of the relationship between two variables, not merely whether the correlation observed differs significantly from zero. (It is possible, given enough data points, to have a "significant" correlation coefficient of 0.1, which represents a very weak relationship between variables, where one variable influences the other by less than 1%.) Authors are encouraged to calculate and present 95% confidence intervals on the observed and reported correlations (instead of using *P* values) and to comment on the strength of the correlation as, for example, "strong," "moderate," or "weak."

Multiple comparisons. Statistical comparisons are generally considered statistically significant when the *P* value is <0.05, that is, when there is less than a 5% chance that the observed differences are not due to a chance sampling error. When just one test is performed, this is correct; however, when 100 comparisons are performed, we expect that 5% of those (5 comparisons) will falsely appear to be "significantly different." Therefore, when making more than a few statistical comparisons, it is important to perform an additional analysis (for example, the Bonferroni analysis) to refine the desired *P* value. Statistical consultation may be necessary. For more information, see http://en.wikipedia.org/wiki/Multiple_comparisons.

Mean visual acuity. When calculating the mean visual acuity, it is not correct to determine the mathematical average of the decimal equivalent of Snellen acuity. In general, it is important to convert to LogMAR acuity prior to statistical manipulations; it is then possible to convert back to Snellen equivalents after the calculations have been performed. For more information consult the following article: Holladay JT. Visual acuity measurements. *J Cataract Refract Surg* 2004;30:287-90 (<http://www.ascrs.org/publications/jcrs/guestfeb04.html>).

Numeric precision. For numeric results, avoid reporting too many digits the precision of a reported value should not exceed what can be justified by the data. For example, a study might report a quotient of 30/93 as 0.3225, implying that the number is known with greater precision and accuracy than is possible with this sample size. In general, the number of digits in the reported value should not exceed the number of digits in the quantity of measurements (eg, for 8 subjects, report one digit of precision, for 80 report two digits of precision, for 800 subjects report three digits of precision). In the example above, the quotient may be reported as 0.32. There are three exceptions to this guideline. First, at least two

digits may be reported for percentages (eg, 2 of 6 subjects would be reported as 33%.) Second, when the first digit of a value is 1, an extra digit of precision may be warranted (eg, when reporting the mean refraction of 80 patients, 1.23 D may be preferable to 1.2 D.) Third, it does not make sense to report a value to its true precision if such precision exceeds its clinical significance or measurability (eg, while it may be technically correct to report the mean esotropia of 4,300 patients as 23.59 PD, this degree of precision is neither measurable nor important.)

Safe and effective. In the U.S. context, the term *safe* and *effective* has a specific meaning, having been adopted by the U.S. Food and Drug Administration to indicate that a device or drug has met that agency's standards and may be sold and marketed in the United States. (For details, consult Albrecht J and Bigby M. The meaning of "safe and effective." J Am Acad Dermatol 2003;48:144-7.) Published case reports and case series generally cannot establish either safety or effectiveness and the term is thus rarely appropriate. Authors may of course use either term in, say, discussions of complication rates, noting how effectively a procedure met specified goals; furthermore, they may compare this procedure to the complication and effectiveness rates of others. Likewise, statements concerning the relative safety of a procedure in particular contexts may be appropriate. However, general statements concerning a procedure's "safety" or "effectiveness," while perhaps desirable for rhetorical effect, are in fact meaningless and should be avoided.

Present simple formulae in the line of normal text where possible and use the solidus (/) instead of a horizontal line for small fractional terms, eg, X/Y. In principle, variables are to be presented in italics. Powers of e are often more conveniently denoted by exp. Number consecutively any equations that have to be displayed separately from the text (if referred to explicitly in the text).

Footnotes

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Tables

Number tables consecutively in accordance with their appearance in the text. Place footnotes to tables below the table body and indicate them with superscript lowercase letters. Abbreviations should be resolved in a note. Avoid vertical rules. Be sparing in the use of tables and ensure that the data presented in tables do not duplicate results described elsewhere in the article. Very large tables documenting extensive clinical details are discouraged and will be printed at the discretion of the editor in chief; authors are encouraged to analyze and summarize these data in a concise format. Submit each table as a separate file.

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For publications by more than six authors, list only the first three, followed by "et al." Titles of books and journals are capitalized but not italicized. Journal titles are abbreviated as in Cumulated Index Medicus. Do not include issue number or month of publication for continuously paginated journals.

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Phillips SJ, Wisnant JP, Norman IJ, et al. Hypertension and stroke. In: Laragh JH, Brenner BM, eds. Hypertension: Pathophysiology, Diagnosis, and Management. Vol 2. 2nd ed. Albany, NY: Raven Press; 1995:465-78.

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Unpublished material

(Child CS, Dawson E, Adams GGW, Lee JP. Pediatric ocular myasthenia gravis. J AAPOS 2009; 13: Abstract 046)

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Appendix 3: Ethical approvals



Health Research & Knowledge Management sub-component
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3200
Tel.: 033 – 3953189
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Email.: hrkm@kznhealth.gov.za
www.kznhealth.gov.za

Reference : HRKM04/11
Enquiries : Mrs G Khumalo
Telephone : 033 – 3953189

18 January 2011

Dear Dr M du Bruyn

Subject: Approval of a Research Proposal

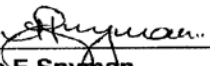
1. The research proposal titled **'Simultaneous three or four horizontal rectus muscle surgery versus staged surgery for large angle congenital esotropia in children: a randomized controlled trial'** was reviewed by the KwaZulu-Natal Department of Health.

The proposal is hereby **approved** for research to be undertaken at **Inkosi Albert Luthuli Central 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 Mrs G Khumalo on 033-3953189.

Yours Sincerely


Mrs E Snyman

Interim Chairperson, Health Research Committee
KwaZulu-Natal Department of Health

Date: 21/01/2011

uMnyango Wezempilo . Departement van Gesondheid

Fighting Disease, Fighting Poverty, Giving Hope



RESEARCH OFFICE
BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Westville Campus
Govan Mbeki Building
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4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za
Website: <http://research.ukzn.ac.za/ResearchEthics/BiomedicalResearchEthics.aspx>

21 December 2010

Dr. M du Bruyn
c/o Dept. of Ophthalmology
Nelson R. Mandela School of Medicine
University of KwaZulu-Natal

Dear Mr du Bruyn

PROTOCOL: Three or four horizontal rectus muscle surgery versus staged surgery for large angle congenital esotropia in children. REF: BFC142/010.

The Biomedical Research Ethics Committee (BREC) has considered the abovementioned application.

The study was provisionally approved by a quorate meeting of BREC on **10 August 2010** pending appropriate responses to queries raised. Your responses dated 18 December 2010 to queries raised on 02 September 2010 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given full ethics approval and may begin as from 21 December 2010.

This approval is valid for one year from **21 December 2010**. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

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

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at <http://research.ukzn.ac.za/ResearchEthics11415.aspx>.

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

The following Committee members were present at the meeting that took place on 10 August 2010:

Professor V Rambiritch	Pharmacology (ACTING CHAIR)
Professor D J Pudifin	Medicine
Mrs P Naidoo	External
Dr Z Khumalo	KZN Health (External)
Dr U Govind	Private Pract. - Gen. Practitioner
Ms J Hadingham	External
Mr R Moore	IPO - Research Office
Prof Puckree	Physiotherapy
Dr M A Sathar	Medicine
Professor S Collings	Psychology
Prof R Bhimma	Paediatrics and Child Health
Dr S Paruk	Psychiatry
Ms T Esterhuizen	Family Medicine
Professor T E Madiba	General Surgery
Dr T Hardcastle	Surgery - Trauma

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

Yours sincerely


PROFESSOR D R WASSENAAR
Chair: Biomedical Research Ethics Committee



DEPARTMENT OF HEALTH

PROVINCE OF KWAZULU-NATAL

INKOSI ALBERT LUTHULI CENTRAL HOSPITAL

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Email. ursulanun@ialch.co.za

Reference: BFC142/010
Enquiries: Dr M E L Joshua

8 December 2010

Dr M du Bruyn
Department of Ophthalmology
IALCH

Dear Dr du Bruyn

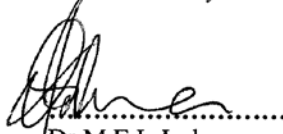
RE: PERMISSION TO CONDUCT RESEARCH AT IALCH

I have pleasure in informing you that permission has been granted to you by the Medical Manager to conduct research on **Three or four horizontal rectus muscle surgery versus staged surgery for large angle congenital esotropia in children**

Kindly take note of the following information before you continue:

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

Yours faithfully


.....
Dr M E L Joshua
Medical Manager



Appendix 4: Data collection tools

NAME OF PATIENT:

HOSPITAL NR: KZ

DATE:

1. Clinical history:

Age

Gender

Main complaint

History of strabismus

- age of onset
- age of first presentation
- previous treatment
- previous occlusion therapy or penalization
- spectacle history

Birth and peri-natal history

Developmental history

Medical history

Family history

2. Examination:

Visual Acuity (Snellen / Lea cards / Preferential looking) - unaided and BCVA:

Cycloplegic refraction (atropine 1% bd x 3 days prior to refraction):

General appearance (Abnormal head posture: head turn, head tilt or chin lift):

Pupils:

Ocular motility:

- Ductions, versions, vergence, A and V patterns, saccades and pursuit
- Muscle overaction and underaction
- Presence of DVD or DVHD
- Nystagmus
- Fixation preference

Measurement:

- Krimsky

Prism cover tests:

- Near and distance
- Primary position, 30 degrees left and right, 30 degrees up and down
- With and without spectacles

Slit lamp examination (if the child allows):

Dilated funduscopy:

3. Assessment:

4. Plan:

5. Surgery date:

6. Follow-up date:

Group 1 (simultaneous surgery)

Intra-op:

Surgery done:

Distance of medial rectus from limbus:

Post-op assessments:

	DAY 1	WEEK 3	WEEK 6
<p>Visual Acuity - unaided and BCVA:</p> <p>Ocular motility:</p> <ul style="list-style-type: none"> • Ductions, versions, vergence, A and V patterns • Muscle overaction and underaction • Presence of DVD or DVHD <p>Measurement:</p> <ul style="list-style-type: none"> • Krimsky <p>Prism cover tests:</p> <ul style="list-style-type: none"> • Near and distance • Primary position, 30 degrees left and right, 30 degrees up and down • With and without spectacles <p>Slit lamp examination (if the child allows):</p> <p><u>Assessment: Residual angle for near and distance in primary position:</u></p> <p><u>Plan:</u></p> <p><u>Follow-up date:</u></p>			

Group 2 (staged surgery)

Intra-op:

Surgery done:

Distance of medial rectus from limbus:

Post-op assessments:

	DAY 1	WEEK 3		DAY 1	WEEK 3	WEEK 6
<p>Visual Acuity - unaided and BCVA:</p> <p>Ocular motility:</p> <ul style="list-style-type: none"> • Ductions, versions, vergence, A and V patterns • Muscle overaction and underaction • Presence of DVD or DVHD <p>Measurement:</p> <ul style="list-style-type: none"> • Krimsky <p>Prism cover tests:</p> <ul style="list-style-type: none"> • Near and distance • Primary position, 30 degrees left and right, 30 degrees up and down • With and without spectacles <p>Slit lamp examination (if the child allows):</p> <p><u>Assessment: Residual angle for near and distance in primary position:</u></p> <p><u>Plan:</u></p> <p><u>Follow-up date:</u></p> <p><u>Second surgery date (6 - 12 weeks post surgery):</u></p>						