Continuous Irrigation as Dead Space Management For Fracture Related Type 1 Intramedullary Chronic Osteomyelitis

by

Dr Jan-Petrus Grey

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Department of Surgical Sciences

Faculty of Medicine & Health Sciences

Stellenbosch University

Clinical Supervisor(s): Professor Nando Ferreira

Research Supervisor(s): Doctor Marilize Burger; Professor Leonard Charles Marais

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DECLARATION

I, Jan-Petrus Grey, hereby declare that the work, on which this dissertation is based upon, is my original work (except where acknowledgements indicate otherwise). The complete work or any part of it has not been or is to be submitted at this or any other university. I empower the university to reproduce this work for the purpose of furthering research, either in its entirety or in any specific portion selected out of the contents.

DATE: 17/01/2022

LIST OF ABBREVIATIONS

IQR	-	Interquartile range
PMMA	-	Polymethyl-methacrylate
GSW	-	Gunshot wound
MRSA	-	Methicillin-resistant *Staphylococcus aureus*
CT	-	Computerized tomography

RESEARCH MANUSCRIPT

Manuscript based dissertation assignment

The following MMed dissertation is prepared in accordance with a **new format** which requires the candidate to submit said dissertation to a scientific journal of choice.

The following dissertation was written in preparation for submission to the Indian Journal of Orthopaedics.

The candidate is required to fulfil all requirements, as requested by **the Indian Journal of Orthopaedics** and outlined in the author's guidelines (**Appendix III**). These instructions prescribe, for example, the length of the abstract and the total manuscript as well as the referencing style to be used.

Continuous Irrigation as Dead Space Management For Fracture Related Type 1 Intramedullary Chronic Osteomyelitis

Jan-Petrus Grey[1]**,** MBChB (UFS)
Marilize Burger[1]**,** BSc, B(Med)Sc, M(Med)Sc, PhD
Leonard Charles Marais[2], MBChB, FC Orth SA, MMed (Ortho), PhD
Nando Ferreira[1]*****, BSc, MBChB, FC Orth (SA), MMed (Orth), PhD

[1]Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg Hospital, Cape Town, 7505, South Africa
[2]Department of Orthopaedics, School of Clinical Medicine, University of KwaZulu-Natal, 719 Umbilo Road, Durban, 4001, South Africa

ORCID

Jan-Petrus Grey	0000-0001-5073-0173
Marilize Burger	0000-0003-2831-4960
Leonard Charles Marais	0000-0002-1120-8419
Nando Ferreira	0000-0002-0567-3373

***Corresponding author:**

Nando Ferreira	0000-0002-0567-3373

Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Tygerberg hospital, Stellenbosch University, Cape Town, 7505, South Africa
Tel: +27 (21) 938 5456
Email: ********@sun.ac.za

ABSTRACT

Introduction: Dead space management following intramedullary debridement and reaming can be challenging and several alternatives have been described. The main objective of this study was to investigate the clinical outcome and resolution rate in patients treated for fracture related Cierny and Mader anatomical type 1 intramedullary chronic osteomyelitis by means of continuous irrigation (modified Lautenbach system) as dead space management following intramedullary reaming.

Material and Method: A consecutive series of thirty patients with Cierny and Mader type 1 chronic osteomyelitis, treated between May 2016 and September 2019, were evaluated retrospectively. Patient history and clinical information, including imaging and laboratory results, were reviewed. Treatment procedures and antibiotic profiles were also recorded.

Results: The initial cohort included 30 cases with 18 tibias, 11 femurs and one humerus. Seven patients were excluded; three patients did not return for follow up and four patients had less than six months follow up. Of the remaining 23 patients, 91% (21/23) achieved resolution of infection over a median follow up period of 16 months (Interquartile range, IQR 7-21 months). Infecting organisms where isolated in 65% (15/23). The median duration of hospital stay was 6 days (IQR 4-7 days). Post-operative complications were noted in two cases and involved a tibial and femoral refracture, respectively. Both patients however achieved union without recurrence of infection following surgical intervention.

Conclusion: Continuous irrigation is a cost-effective single-stage surgical option for dead space management during the treatment of intramedullary chronic osteomyelitis. It provides the advantage of instilling high dose intramedullary antibiotics and negates the need for a second surgical procedure while achieving similar outcomes than other dead space management techniques.

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Level of evidence: IV, single-center retrospective study

Keywords

Chronic osteomyelitis, Dead space management, Continuous irrigation, Fracture-related infection, Lautenbach method

INTRODUCTION

Chronic osteomyelitis remains one of the most challenging problems in orthopaedic surgery [1,2]. It is a major cause of morbidity with considerable socio-economic and health implications including extended antibiotic usage, as well as multiple hospital admissions and theatre visits [3,4].

Intramedullary nailing remains the preferred method of fixation in tibia and femur shaft fractures [36]. With a steady increase in trauma volumes resulting from road traffic accidents as well as gunshot victims, low- and medium-income countries will face a proportionate increase in fracture-related infection following intramedullary fixation [5–7]. Open fractures on average have a 3.2 times increased risk of overall infection compared to closed fractures following intramedullary fixation [5,8].

In established chronic osteomyelitis, a local environment of poorly perfused tissue, sequestrum and biofilm limit the efficacy of systemic antibiotic therapy [3,9]. The commonly used classification system for chronic osteomyelitis was described by Cierny and Mader in 2003 [10]. This classification system distinguishes chronic osteomyelitis cases according to four anatomical types and three physiological host classes, to define the 12 clinical stages [9–12]. Fracture-related infection following intramedullary nailing typically results in anatomical type 1 infections, if the fracture has united, where the infection is limited to the medullary canal.

The principles in surgical management of chronic osteomyelitis include judicious bone and soft tissue debridement with collection of deep tissue specimens, management of the dead space, followed by soft tissue cover and bone reconstruction as required [13–18]. Surgical debridement is augmented with adjunctive local antimicrobial therapy to increase the clinical cure rate [17]. Currently there is a lack of evidence regarding the optimal method of intramedullary dead space management [16,18,19]. Debridement without adequate dead space management is associated with higher recurrence rates [20]. We hypothesize that the resolution rate with continuous irrigation as dead space management in type 1 intramedullary chronic osteomyelitis may be comparable to other described techniques for intramedullary dead space management.

Dead space management following removal of infected nails and intramedullary reaming (so-called indirect unroofing) is challenging. Surgical options include custom-made antibiotic-impregnated polymethyl-methacrylate (PMMA) nails and biodegradable calcium sulphate pellets with 4% tobramycin have been described [9,21,22]. The use of wound irrigation in the management of chronic osteomyelitis was initially described in the early 1900's [23]. Intramedullary irrigation was later introduced by Weber and Lautenbach for infected total hip arthroplasties as well as pan diaphyseal chronic osteomyelitis [24]. Lautenbach et al. achieved an 80% resolution rate with the technique of using a closed double-lumen suction irrigation system [24]. Despite promising early results, a paucity of studies has been published on the potential use of continuous irrigation as dead space management following intramedullary reaming of type 1 chronic osteomyelitis of the appendicular skeleton [1-3].

The main aim of the present single-center retrospective study was to investigate the clinical outcomes and resolution rates in patients treated for Cierny and Mader anatomical type 1 intramedullary chronic osteomyelitis by means of continuous irrigation (modified Lautenbach system) as dead space management following intramedullary reaming. The secondary objective was to compare the resolution and complication rates of the modified Lautenbach system to other techniques of intramedullary dead space management described in the current literature.

Patients and study design

A single-center retrospective review of a prospectively collected database, of all consecutive patients treated between May 2016 and September 2019 for Cierny and Mader anatomical type 1 intramedullary chronic osteomyelitis with continuous irrigation as dead space management following intramedullary reaming, was conducted. Ethical approval as well as hospital board approval was obtained prior to data collection. Patients were excluded if they did not meet the criteria of type 1 chronic osteomyelitis, if they had less than six months follow up or if they required further surgical fixation due to fracture non-union, malunion or deformity correction. To be considered eligible for the procedure the fracture had to be deemed united by x-rays at a minimum of six months following definitive fracture fixation. The collected data included patient demographics, comorbidities, smoking history, fracture related history, duration and details of hospital stay and the microbiological results.

Defining chronic osteomyelitis and recurrence of infection

Chronic osteomyelitis was defined as a fracture related infection present, where the causative organisms were thought to have persisted either intracellularly or in interactive biofilm-based colonies [25]. Recurrence of infection was defined as clinical, biochemical or radiological evidence of ongoing infection following the initial definitive eradication surgery.

Surgical technique and assessment

The beginning of treatment was regarded as the day of surgical intervention, when deep tissue specimens was obtained, and empiric antibiotic therapy was started. Standard surgical technique involved removal of all implants, deep tissue sampling, intramedullary reaming and irrigation, followed by the insertion of a continuous irrigation system. After removal of the screws, the distal locking holes were enlarged to an oblong aperture using a high-speed burr. The distal metaphyseal region was then curetted through this window to remove any biofilm. Sequential intramedullary reaming was then performed over a guidewire until the maximum passable reamer size was reached. During reaming suction was applied at the distal window to remove debris and biofilm. Biofilm obtained at all sites, including the nail entry point, screw holes and reaming contents were sent for microscopy, culture and sensitivity.

Following reaming, the canal was irrigated with saline using a pulse lavage system. Our modification to the original Lautenbach technique included a single lumen 6mm perforated tube, from a standard closed suction system, that was passed along the length of the intramedullary canal. Distally the tube was connected to a continuous infusion of 0.9% normal saline with gentamycin. Proximally the tube was secured to a urinary catheter collection bag to allow free drainage by gravity and monitoring of the effluent. [Figure 1]

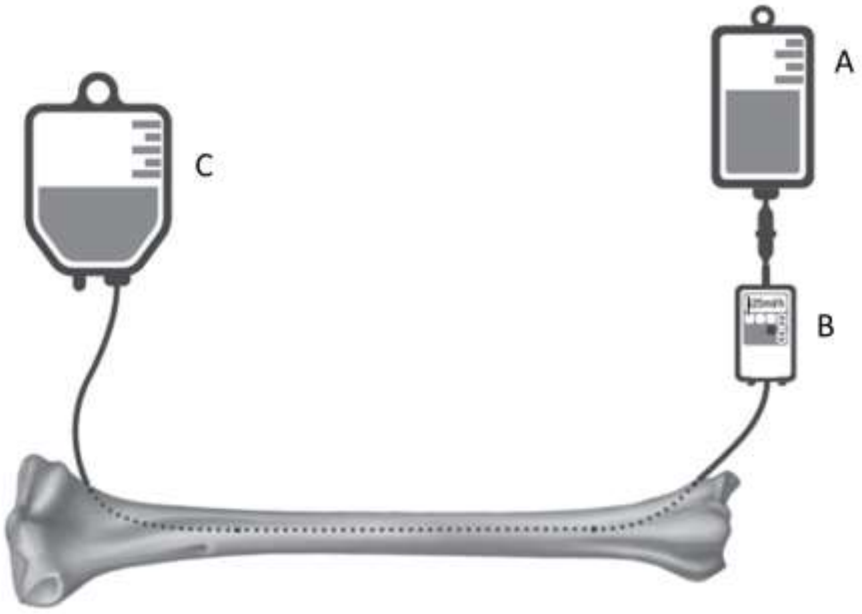

Fig. 1 A: Continuous infusion of 0.9% normal saline with 80mg Gentamycin. B: Infusion set at a rate of 125ml per hour. C: Collection bag to allow free drainage by gravity and monitoring of the effluent.

Irrigation consisted of 1000ml 0.9% normal saline with 80mg Gentamycin at a rate of 125ml per hour. The limb was elevated in the ward so that the distal segment (inlet) was higher than the proximal segment (outlet) to facilitate gravity-assisted drainage. Once the blood-stained effluent became clear in colour the irrigation tube was removed in the ward and dry dressings applied. Effluent volume was monitored but it was not cultured, and routine serum antibiotic levels was not performed. All operations were performed by a single surgeon. Protected weight bearing with the use of crutches was prescribed following removal of the irrigation system.

All pre-operative antibiotics was stopped at least seven days prior to surgery. Empiric post-operative broad spectrum intravenous antibiotic therapy consisted of meropenem and vancomycin until culture and sensitivity results became available. The antibiotic regime was subsequently adjusted to directed oral preparations according to the culture and sensitivity profile. This consisted of dual therapy including at least one agent with anti-biofilm activity. In cases where no growth was observed the intravenous therapy was changed to oral co-trimoxazole and rifampicin. Antibiotic therapy was then continued for a total duration of six weeks.

Standard outpatient follow-up consisted of 2-week, 6-week, 3-month, 6-month and 12-month post-operative reviews.

Statistical analysis

Data was analyzed using Statistica v13 (Tibco Software) and is reported as means ± standard deviations or medians (interquartile ranges, IQR) for parametric and non-parametric data, respectively. Categorical variables are reported as frequencies and counts.

RESULTS

Patient characteristics

Thirty patients were managed with continuous irrigation following medullary reaming during the study period. Seven patients were excluded; four patients had less than six months follow up and three patients were lost to follow up. The final cohort comprised 16 men and seven women with a mean age of 34.7 ± 10.5 years (range 16 to 55). (Table 1). All cases were classified as Cierny and Mader anatomical type 1 chronic osteomyelitis. The anatomical segment of infection included 13 tibias, 9 femurs and one humerus (Table 1). A history of open fractures was noted in thirteen (13/23, 57%) of cases. All cases had prior insertion of intramedullary devices. All fractures were deemed to be united prior to surgery. Twenty-one (21/23, 91%) patients presented with a chronic draining sinus. Two (2/23, 9%) presented with abscess formation that required initial debridement. Seven (7/23, 30%) patients were noted to be active smokers.

Table 1. Participant demographic information

		N=23
Age		34.7 ± 10.5
Sex		
	Male	69.9 (16)
	Female	31.4 (7)
Smoker		
	Yes	31.4 (7)
	No	69.6 (16)
Segment involved		
	Tibia	56.5 (13)
	Femur	39.1 (9)
	Humerus	4.4 (1)
Fracture type		
	Open	56.5 (13)
	Closed	17.4 (4)
	GSW	21.7 (5)
	Other	4.4 (1)

Data is presented as mean ± standard deviation or as frequencies with counts indicated in parentheses. GSW, gunshot wound.

Follow up

The follow up period for the cohort ranged from 6-25 months, with median follow up of 16 months (interquartile range, IQR 7-21 months) (Table 2).

Clinical outcome

An overall resolution rate of 91% (21/23) was achieved following removal of the intra-medullary device, intramedullary reaming and continuous irrigation as dead space management (Table 2). The median length of hospital stay was 6.0 days (IQR 5.0-6.0 days). Post-operative recurrence of infection was noted in two cases (2/23, 9%). The first had recurrence after non-compliance with antibiotic treatment following incarceration and was still awaiting re-operation at the time of writing this manuscript. The second patient was a known smoker with recurrence of femoral osteomyelitis. After subsequent sequestrectomy this patient achieved resolution of infection.

Table 2. Follow up and clinical outcome

	N=23
Follow up (months)	16.0 (7.0 – 21.00)
Hospital stay (days)	6.0 (5.0-6.0)
Continuous irrigation duration (days)	5.0 (4.0-6.0)
Outcome	
Resolution	91.0 (21)
Recurrence	9.0 (2)

Data is presented as median (interquartile range) or as frequencies with counts indicated in parentheses

Organisms

Infecting organisms where isolated in 65% (n=15) of the thirty cases (Table 3). *Staphylococcus aureus* isolates were the most common gram-positive bacteria and *Proteus* *mirabilis* and *Pseudomonas aeruginosa* were the most common gram-negative bacteria cultured.

Table 3. Bacterial isolates.

Culture information	% (n)
Organism cultured	
No growth	34.8 (8)
Single organism	30.4 (7)
Multiple organisms	34.8 (8)
Gram-positive bacteria	
Methicillin-sensitive *Staphylococcus aureus*	21.7 (5)
Methicillin-resistant *Staphylococcus aureus*	4.3 (1)
Enterococcus faecalis	4.3 (1)
Enterobacter cloacae	8.6 (2)
Streptococcus species	4.3 (1)
Gram-negative bacteria	
Proteus mirabilis	34.8 (8)
Pseudomonas aeruginosa	8.6 (2)
Providencia stuartii	4.3 (1)
Morganella morganii	4.3 (1)
Citrobacter freundii	4.3 (1)

Data is presented as frequencies with counts indicated in parentheses.

Complications

Post-operative complications, other than recurrence of infection, were observed in two cases (2/23, 9%) in the present study. Both patients sustained a long bone refracture following treatment. The first patient sustained a femoral refracture four months after treatment. This patient was noted to have full resolution of infection at the time of fracture. After intramedullary fixation the patient progressed to union without recurrence of infection. The second patient sustained a tibial refracture early after treatment and union was achieved after application of a circular fixator and the patient was noted to be infection free at the 12 months follow up. On retrospective review of the patient records we believe that adequate strength at the union site was not achieved as thought peri-operatively.

DISCUSSION

Lautenbach et al. introduced the intramedullary closed double-lumen suction irrigation model as dead space management for pan diaphyseal chronic osteomyelitis in 1975. They reported an 80% resolution rate over a seven-year period [24]. This technique was affordable, reproducible and allowed for a single surgical intervention. Additionally, local antibiotic instillation could be achieved without accompanying systemic toxic effects [1,26,27]. We have modified the original Lautenbach irrigation system as to maintain the dead space management properties as well as local antibiotic instillation but decreasing reported complications such as lumen blockage, wound leakage, local skin problems, prolonged bed occupancy and the need for frequent adjustments to the irrigation system. [1,3,24]

The main objective of the present study was to investigate the clinical outcomes and resolution rates in patients treated for Cierny and Mader anatomical type 1 intramedullary chronic osteomyelitis following fracture fixation by means of continuous irrigation as dead space management following intramedullary reaming.

The main finding of the study was an infection resolution rate of 91% (21/23), observed after a median follow-up period of 16 months. This finding agrees with that reported by Hashmi et al. in their series of 17 patients with fracture related infection treated using the Lautenbach method where they reported a resolution rate of 94.4% after a mean follow up of 75 months [1]. In a different study, using a modified irrigation system that was based on that of Lautenbach, Caesar et al. reported a resolution rate of 85.3% at a mean follow-up of 101 months [3]. The lower resolution rate may be attributed to their longer follow up period. Late recurrence of infection has been noted years after clinical resolution as reported by McNally et al. with their review of 344 cases [21]. At two year follow up the authors reported a resolution of infection in 98.5% of cases, whilst after four years a resolution of infection in 92% of cases and at five years 90% of those cases remained infection-free [21].

In comparison to the modified Lautenbach method, the antibiotic-impregnated cement rod is a well described alternative for intramedullary dead space management. Kanakaris et al. reviewed 24 patients treated with intramedullary reaming and antibiotic cement rod placement as dead space management and reported a resolution rate of 96% after a mean follow up of 21 months. Although their reported resolution rate is comparable to our study, it is important to keep in mind that a second operation was required to remove the cement rod after a mean of 2.6 months following the initial operation [7]. The requirement for cement rod removal, which includes the additional cost of re-admission and the second operation as well as the inherent risk of removal and occasional failure of removal. These are the most important criticism against this method and have resulted to further research to find an alternative, single stage surgical solution including the use of biodegradable products [18,22].

Another option for dead space management includes the use of biodegradable calcium-sulphate pellets containing 4% tobramycin, following debridement. Ferguson et al. reported on 195 patients, falling within all four Cierny and Mader anatomical subtypes [22]. Although the authors reported a 100% resolution rate in the Cierny and Mader anatomic type 1 subgroup (n=12) over a mean follow up period of 44.4 months, they observed prolonged wound drainage in 15.4% of cases [22]. Calcium sulphate pellets may provide the opportunity for a single stage treatment solution, although its increased cost might not be feasible in a resource constrained environment. This is illustrated in the limited data on the use of biodegradable products as dead space management from low- and medium-income countries, where the burden of disease is high, but the resources available for treatment is limited [18].

The second finding of this study was a positive microbiological culture result in 65% (15/23) of the cohort. The low culture positive yields in the current study could be explained by the presence of fastidious pathogens that have lost viability prior to culture, or exposure to antibiotics, including those given pre-operatively. Bacterial isolate findings from the present study are similar to those from a recent systematic review which included 13 studies that reported *S. aureus* to be the most common organism isolated [18]. Where methicillin-resistant *Staphylococcus aureus* (MRSA) accounted for 28.4% of isolates in the Pincher et al. review, we only encountered this resistant strain in 4.3% of isolates [18]. The predominant gram-negative organisms included Pseudomonas species. Similar outcomes were also reported by Mthethwa et al. in 2017, after reviewing cultures on sixty patients with chronic osteomyelitis treated curatively in a South African study [28]. The authors reported that in fracture-related infections, which comprised 55% (n=33) of the cohort, the most common organisms cultured included methicillin-sensitive *Staphylococcus aureus*, *Serratia marcescens* and *Pseudomonas aeruginosa* [28]. Similarly, Caesar et al. also reported a comparable positive microbiological diagnosis on 62.9% of cases with *Staphylococcus aureus* and Pseudomonas the most cultured organisms [3].

Two patients (2/23, 9%) experienced recurrence of infection in the present study. Following CT scan, one patient proved to have residual sequestrum at the previous fracture site. It is important to note that cortical sequestra might not be adequately addressed following medullary during reaming. Refracture was observed in two patients. Similar complications have been reported in a retrospective study which included 11 patients with intramedullary osteomyelitis, the authors noted a post-operative complication in one case with a distal tibia refracture four months after intermedullary debridement [29]. It is important to note that the technique of reaming the infected intramedullary canal may lead to temporary decreased biomechanical properties of the long bone to withstand physiological load. Although fractures following intramedullary reaming are rare, protected weight bearing should be advised to err on the side of caution.

The study is not without limitations. The relatively small sample size and short follow-up period of this study is the first limitation because osteomyelitis may recur months after treatment, even after initial quiescence was achieved [21]. Tice et al. showed the 78% of recurrences occur within six months after surgery while 95% of all recurrences manifest within one year of surgery [30]. Although we do accept that the shorter follow up period may result in an overestimation of the efficacy of the treatment technique it is important to note that, at present, our outcomes are in keeping with the international described resolution rates. This provides an ideal opportunity for future research, to investigate the long term follow up outcomes of intramedullary osteomyelitis treated with continuous irrigation as dead space management. Another limiting factor of the present study is the high number of cases that defaulted follow up. Loss to follow up is not unique in the South African setting, and this has been reported in several previous studies, specifically in the context of orthopaedic surgery [31-33]. This may possibly be attributed to the long travel distances and the poor socio-economic factors in the South African setting [34,35].

CONCLUSION

Continuous irrigation is a cost-effective single-stage option for dead space management during the treatment of intramedullary chronic osteomyelitis. It provides the advantage of instilling high dose intramedullary antibiotics and negates the need for a second surgical procedure while achieving similar outcomes than other dead space management techniques.

DISCLOSURE OF INTEREST STATEMENT

The authors declare that they have no competing interest.

AUTHOR CONTRIBUTIONS

JP Grey: Research question development, Research design, Data collection, article writing and revision.

M Burger: Research question development, Research design, Statistical analysis, article writing and revision.

L Marais: Article writing and revision.

N Ferreira: Research question development, Data collection, article writing and revision.

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APPENDIX I: HEALTH RESEARCH ETHICS COMMITTEE APPROVAL

UNIVERSITEIT
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Approval Letter
Progress Report

31/01/2020

Project ID: 8743

Ethics Reference No: S19/01/002

Project Title: Continuous irrigation as dead space management following indirect unroofing of intramedullary chronic osteomyelitis

Dear Dr Jan-Petrus Grey

We refer to your request for an extension/annual renewal of ethics approval received 26/01/2020.

The Health Research Ethics Committee reviewed and approved the annual progress report through an expedited review process.

The approval of this project is extended for a further year.

Approval date: 19 March 2020

Expiry date: 18 March 2021

Kindly be reminded to submit progress reports two (2) months before expiry date.

Where to submit any documentation

Kindly note that the HREC uses an electronic ethics review management system, *Infonetica*, to manage ethics applications and ethics review process. To submit any documentation to HREC, please click on the following link: https://applyethics.sun.ac.za.

Please remember to use your Project Id 8743 and ethics reference number S19/01/002 on any documents or correspondence with the HREC concerning your research protocol.

Yours sincerely,

Mrs. Melody Shana

Coordinator

Health Research Ethics Committee 1

National Health Research Ethics Council (NHREC) Registration Number:
REC-130408-012 (HREC1)•REC-230208-010 (HREC2)

Federal Wide Assurance Number: 00001372
Office of Human Research Protections (OHRP) Institutional Review Board (IRB) Number:
IRB0005240 (HREC1)•IRB0005239 (HREC2)

The Health Research Ethics Committee (HREC) complies with the SA National Health Act No. 61 of 2003 as it pertains to health research. The HREC abides by the ethical norms and principles for research, established by the World Medical Association (2013). Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects; the South African Department of Health (2006).Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa (2nd edition); as well as the Department of Health (2015). Ethics in Health Research: Principles, Processes and Structures (2nd edition).

The Health Research Ethics Committee reviews research involving human subjects conducted or supported by the Department of Health and Human Services, or other federal departments or agencies that apply the Federal Policy for the Protection of Human Subjects to such research (United States Code of Federal Regulations Title 45 Part 46); and/or clinical investigations regulated by the Food and Drug Administration (FDA) of the Department of Health and Human Services.

APPENDIX II: HOSPITAL CLEARANCE

UNIVERSITEIT
STELLENBOSCH
UNIVERSITY

Approval Letter
Progress Report

31/01/2020

Project ID: 8743

Ethics Reference No: S19/01/002

Project Title: Continuous irrigation as dead space management following indirect unroofing of intramedullary chronic osteomyelitis

Dear Dr Jan-Petrus Grey

We refer to your request for an extension/annual renewal of ethics approval received 26/01/2020.

The Health Research Ethics Committee reviewed and approved the annual progress report through an expedited review process.

The approval of this project is extended for a further year.

Approval date: 19 March 2020

Expiry date: 18 March 2021

Kindly be reminded to submit progress reports two (2) months before expiry date.

Where to submit any documentation

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Yours sincerely,

Mrs. Melody Shana

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APPENDIX III: INDIAN JOURNAL OF ORTHOPAEDICS GUIDE FOR AUTHORS

https://www.springer.com/journal/43465/submission-guidelines

APPENDIX IV: TURN-IT-IN REPORT

Kindly note that the saoa.org.za source indicates the study abstract, which was published as part of the South African Orthopaedic Congress, held in 2021: https://saoa.org.za/wp-content/uploads/2021/08/5.-SAOA-2021-Abstract-Book-26-Aug-2021.pdf

JP Grey

ORIGINALITY REPORT

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1	saoa.org.za Internet Source	6%
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3	Willem Oosthuysen, Rudolph Venter, Yashwant Tanwar, Nando Ferreira. "Bioactive glass as dead space management following debridement of type 3 chronic osteomyelitis", International Orthopaedics, 2019 Publication	2%
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