Thermal Analysis of Cementing in Hip Arthroplasty

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Medicine

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Presentations arising from the research project

Ajodha T., Frey C. & Milner B. Thermal Analysis of Cementing in Hip Arthroplasty

- Podium presentation for South African Orthopaedic Association - Biennial Congress of the South African Arthroplasty Society. 16-18 March 2022, Cape Town.

Declaration

I Dr Tapeshwar Ajodha declare that this research report in the format of a “submissible” paper is my own, unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Orthopaedic Surgery at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

……
(Signature of candidate)

30th day of August 2022 in Johannesburg, South Africa

Dedication

Through your grace, seemingly insurmountable mountains were climbed.

I am eternally grateful for all those whose love I have been blessed with.

And for all those whom I have been blessed to love.

“Baba Nam Kevalam”

“Submissible” format of a paper

Thermal Analysis of Cementing in Hip Arthroplasty

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Nomenclature

ASTM	American Society for Testing and Materials
BCIS	Bone Cement Implantation Syndrome
CEO	Chief Executive Officer
CHBAH	Chris Hani Baragwanath Academic Hospital
°C	Degrees Celsius
EU MDD	European Union Medical Devices Directive
FDA	Food and Drug Administration
MAC	Medical Advisory Committee
PMMA	Polymethyl methacrylate
THA	Total Hip Arthroplasty
THR	Total Hip Replacement

Declarations

Authorship

The authors confirm that all authors have made substantial contributions to all of the following:

- The conception and design of the study, or acquisition of data, or analysis and interpretation of data.
- The drafting of the article or its critical revision for important intellectual content.
- Final approval of the version to be submitted.

Sound scientific research practice

The authors further confirm that:

- The manuscript, including related data, figures and tables, has not been previously published and is not under consideration elsewhere.
- No data have been fabricated or manipulated (including images) to support conclusions.
- This submission does not represent part of a single study that has been split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (e.g. ‘salami-publishing’).

Plagiarism

The authors confirm that the work submitted is original and does not transgress the plagiarism policy of the journal.

- No data, text or theories by others are presented as if they were the authors’ own.

- Proper acknowledgements of others' work have been given (this includes material that is closely copied, summarised and/or paraphrased); quotation marks are used for verbatim copying of material.
- Permissions have been secured for copyrighted material.

Conflict of interest statement

Tapeshwar Ajodha, Chris Frey and Brenda Milner declare that they have no conflict of interest.

Funding sources

No funding was received for the purposes of performing this study.

Compliance with ethical guidelines

The author/s declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.

Prior to the commencement of the study ethical approval was obtained from the following ethical review board: Human Research Ethics Committee (HREC) (Medical), University of the Witwatersrand. Reference M210412.

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed written consent was obtained from all patients for being included in the study.

Consent was obtained from patients for the use of clinical photographs and these images were adequately anonymised.

Abstract

Background:

Since the advent of hip replacement surgery in the late 1800's, the procedure has evolved into one of the most successful and commonly performed elective operations in the world. The use of Polymethyl methacrylate, otherwise known as bone cement, in hip arthroplasty was first described in 1958. Polymethyl methacrylate polymerises through an exothermic reaction, yielding temperatures that exceed the threshold for thermal osteonecrosis. A paucity of *in vivo* data exists, describing the thermal effects of this exothermic reaction. This study aimed to analyse the thermal changes that occur during cementing in hip arthroplasty.

Methods:

Temperature trends were evaluated over a twelve-minute period in patients undergoing primary total hip arthroplasty.

Infrared thermometry was used to measure the temperatures at the femoral stem and the bone-cement interface or the bone-implant interface in cemented and uncemented hip arthroplasty respectively.

Confounding variables were controlled as cemented and uncemented hip arthroplasty thermal dynamics were compared, to isolate the thermal effects of cementing in hip arthroplasty.

Results

During uncemented hip arthroplasty, the highest bone temperatures were at the time of implant insertion. In contrast, during cemented hip arthroplasty, the lowest bone temperatures were recorded at the time of implant insertion, as this subsequently increased. Bone

temperature in the cemented group was persistently and significantly higher than the uncemented counterparts for 8 minutes during the observed period.

In cemented hip arthroplasty, implant temperature raised by 19.7°C and bone temperature raised by 10.9°C and from their respective initial temperatures. The maximum recorded implant temperature was 46.8°C in the cemented group and 33.4°C in the uncemented group. The maximum recorded bone temperature was 41.1°C in the cemented group and 34.4°C in the uncemented group. The median peak temperature difference between cemented and uncemented hip arthroplasty was 14.5°C at the implant and 8.6°C at the bone interface.

Conclusion

Thermal dynamics *in vivo* differ from those described in literature, *ex vivo*. The exothermic reaction of bone cement causes significant increases in temperature of both the bone and implant. During cemented hip arthroplasty, bone is exposed to temperatures of sufficient intensity and duration to cause thermal osteonecrosis. The clinical significance of these findings is yet to be determined. Further research is needed to enhance our understanding of cementing in hip arthroplasty and to explore measures of modulating heat energy during the procedure.

Keywords

Hip arthroplasty, Hip replacement, Polymethyl methacrylate (PMMA), Bone cement, Exothermic, Thermal, Osteonecrosis

Level of evidence

- Level 2c

Introduction

Background and literature review

Background of Hip Arthroplasty

Arthroplasty is the process of surgically refashioning a joint. Total hip arthroplasty (THA), also known as total hip replacement (THR), refers to the replacement of the femoral, as well as acetabular components of the hip joint.

The first hip replacement was presented in 1891 by Professor Glück, who used ivory to replace the femoral heads of patients whose hip joints were diseased by tuberculosis. Through advancements in technology and surgical technique, this procedure has subsequently developed into one of the most successful operations in medicine (1). Recent years have shown staggering increases in the number of hip replacement surgeries as it evolves into one of the most common elective surgeries performed, and this is projected to continue to rise (2).

Hip replacement surgery is performed for a wide spectrum of disease. The main indications for surgery are pain, functional limitation and joint stiffness as this procedure dependably offers pain relief and appreciably improves function and quality of life (3).

Current hip replacement prosthesis designs pivot on the fundamental principles that were established in the early 1960's, which have remained largely unchanged because of the reproducible success experienced (4). The implant components may or may not be augmented with bone cement.

Bone Cement

Bone cement, as it is commonly known, is Polymethyl methacrylate (PMMA). The concept of cementing an orthopaedic prosthesis was described as early as 1870. The evolution to the

era of PMMA began in 1943, with its first use in hip replacement surgery in 1958 by Sir John Charnley (5).

PMMA has no innate properties to bind substances as an adhesive, instead it is used as a space filler, so it is essentially applied as a grout. In hip arthroplasty surgery, it serves to tightly compact the space between the femoral stem and surrounding bone, thereby aiding in securing the implant position (5).

No consensus has been established on the optimal fixation when comparing cemented and uncemented THR. Uncemented THR is favoured in the United States - their joint registry shows two thirds of primary THR surgeries performed there are uncemented (6). Scandinavian countries favour cemented THR and report lower revision rates in similar patient groups (6).

In the early post-operative period, cemented hip arthroplasty may provide improved mobilisation and decreased pain as compared to their uncemented counterparts, owing to earlier stability provided by the cement (7). Furthermore, the use of cement in hip arthroplasty surgery is associated with the following advantages: improved implant positioning and fit, fewer peri-implant fractures, and cheaper implant costs (8). It does bear mentioning however, that many of these comparisons were drawn in studies comparing older implant models, and uncemented hip arthroplasty surgery has become increasingly popular in recent times - likely owing to the advancements in implant design (9).

The use of cement in hip arthroplasty surgery is not without its complications, the most significant of which is the phenomenon called Bone Cement Implantation Syndrome (BCIS). No single universally accepted pathophysiological process has been identified for BCIS, it is likely a combination of processes, which manifests with hypoxia, hypotension, arrythmias and may result in cardiac arrest (8). The incidence and severity of BCIS varies, with the mildest form occurring in 21% and the most severe form occurring in 1.7% of patients who undergo cemented hip arthroplasty surgery (10). Consequently, the use of PMMA in hip arthroplasty

surgery has become associated with higher death rates in the early post-operative period. Further disadvantages include: longer surgical operation times and higher overall treatment costs (9).

The mixture of a liquid monomer and a powdered co-polymer forms PMMA as it sets into a hardened, hydrophilic polymer. This polymerisation reaction generates heat, owing to an exothermic reaction, reaching temperatures as high as 86°C (5). It is this fundamental property of heat generation that is of the central focus in this study.

Thermal Injury and Necrosis

Excessive heat can cause structural damage and functional disturbances in cells, as well as disrupt the physiological environment of tissues. The extent of injury to the tissues is related to the temperature of the external heat source; the duration of exposure to the heat source; as well the heat tolerance of the affected tissues (11). Bone exposed to temperatures of 47°C-55°C sustains localised cellular injury (12). The effect of high levels of heat are not confined to the direct cellular death of bone cells. In addition, excessive heat exposure disrupts blood supply to areas of the bone which leads to bone resorption. There are several proposed biological mechanisms for bone resorption. When it is secondary to heat exposure, it is termed thermal osteonecrosis (13). Thermal osteonecrosis is a key concept in this study. The aforementioned loss of bone from cellular death and thermal osteonecrosis may potentially result in loosening of orthopaedic implants and may also contribute to the development of an infection (14).

Revision Arthroplasty

As the number of hip arthroplasty surgeries performed rises, the burden of arthroplasty revision is predicted to increase (15). There is an anticipated fivefold increase in the clinical and economic impact imparted by revision arthroplasty over the next decade (16).

Aseptic loosening is the failure of a joint prosthesis without an overt mechanical cause or infection. Bone resorption, a concept introduced earlier, is commonly associated with aseptic loosening (17). Aseptic loosening, bone resorption and implant instability are the commonest cause of prosthetic implant failure resulting in the need for revision hip surgery (18).

Another indication for revision arthroplasty is deep seeded infection, which is a disastrous complication of joint arthroplasty surgery. While the incidence is uncommon, there is an increasing number of infections being diagnosed in patients who have undergone hip arthroplasty surgery. The underlying cause of this increase is not uniformly identified (19).

Significance of this Study

This study could potentially expose a need for advancements in bone cement and techniques centred around modulating the thermal environment during hip arthroplasty surgery.

Thermal osteonecrosis may play a vital role in the development of bone resorption and infection which are major contributing factors to the burden of revision arthroplasty. This introduces the need for analysing the thermal effects of bone cement, which theoretically may generate sufficient heat to cause thermal osteonecrosis.

In order to address the demand of revision arthroplasty, operative efficiency and implant longevity will need to be refined (15). Enriching our knowledge of the thermal effects of bone cement with this study could contribute towards improving both operative efficiencies, as well as the implant longevity.

As implants develop and the potential toxicity of bone cement becomes better understood, the role for cementing hip arthroplasty is evolving. Research in the field of bone cement is required to improve quality and reduce adverse side effects (5).

There is a paucity of data regarding the temperature dynamics of cemented hip arthroplasty and a noted vacancy of data *in vivo*. This study will strive to fill that void.

Research in the field of temperature changes around the hip, associated with bone cement, was done by Farvadin et al. This study was performed in cadaveric specimens after reviewing work done on artificial models. From this, came an indication that further data is required on the use of bone cement in order to prevent thermal necrosis (20).

Gundapadeni and Goswami investigated the potential of thermal necrosis induced by bone cement by evaluating artificial, constructed 3D hip models. This showed that the maximum temperature during cemented hip arthroplasty surgery could reach 71°C and that this was related to the cement mantle thickness (21).

Kaorapapong et al., Vallo, Maffezzoli et al. and Li et al. used theoretical, mathematical models to describe the thermal changes in cemented hip arthroplasty surgery. Kaorapapong et al. found that the surface of the cement reached 62°C and that the maximum temperature was influenced by the initial temperature before cementing (22). Vallo found that cement mantle thickness as well as initial temperature had an effect on maximum temperature, which could reach levels considerably higher than the heat tolerance of bone (23). Maffezzoli et al. and Li et al. concluded that the use of bone cement may cause thermal necrosis and found that different implant materials also affected the conduction of heat (24, 25).

These studies suggest that there may be a potentially clinically significant increase in temperature owing to the use of bone cement.

However, studies done using cadaveric, artificial, or theoretical models form assessments that are difficult to extrapolate to clinical settings. Living tissue *in vivo* is perfused, and has ongoing nutrient and oxygen metabolism, which results in heterogenous temperature effects. A confounding interaction is PMMA's hydrophilic effect on living tissues and the subsequent effect on heat dispersion and tolerance (26).

Existing literature calls for thermal analysis in clinical settings. Specific mention is given to non-invasive thermometry, which will be used in this study, as a promising measure in making such data more accessible (27).

Study aim and objectives

Study aim and objectives:

Aim: To analyse the thermal changes that occur during cementing in hip arthroplasty.

The objectives of the study are to:

- Describe the temperature levels during hip arthroplasty surgery.
- Compare the temperature changes between cemented and uncemented hip arthroplasty surgery.

Methodology

The management of the patients included in the study followed the established best clinical practices, as planned by the Chris Hani Baragwanath Academic Hospital (CHBAH) Orthopaedic Surgery Arthroplasty Unit, without any alteration inflicted by the study.

Research question

What are the thermal effects of cementing during hip arthroplasty?

Research Design

Observational: Prospective Study

This study had no influence on the process of stratifying nor managing patients. As such, this was an observational study.

The data were captured in real-time during the surgical procedures thus, this was a prospective study.

- The two study groups compared were:
    - Patients undergoing uncemented hip arthroplasty surgery.
    - Patients undergoing cemented hip arthroplasty surgery.
- The clinical decision of cementing was made independently of this study, in accordance with the existing departmental protocol. There was no intervention from this study.

Site of Study

Chris Hani Baragwanath Academic Hospital

- Department of Orthopaedic Surgery: Arthroplasty Unit

Inclusion and Exclusion Criteria

Inclusion criteria:

- Patients 55 years of age and older.
- Patients undergoing primary THR surgery.
- Patients who provide informed consent to participate in this study.

Exclusion criteria:

- Patients who have had any form of surgery in the preceding 24 hours.
- Patients with evidence of active infection locally or systemically.
- Patients with evidence of pyrexia consequent to any aetiology.

The rationale of the selection criteria:

- An age exclusion criterion of patients younger than 55 years old assists with making the study population more uniform to allow for more comparable study groups. In this age group, there were patients in both the cemented and uncemented hip arthroplasty categories as dictated by the existing clinical protocol - with no influence by this study.
- Recent surgery, sepsis and pyrexia are all accompanied by inflammatory responses and alteration in body temperature which is undesirable in this study where the measured variable is temperature.

In the normal Orthopaedic Surgery assessment of patients presenting for hip arthroplasty surgery, there are two groups: those in whom the use of bone cementing is elected by the surgeon, and those in whom it is not. Hence, there was a natural division into the two groups being studied i.e. cemented hip arthroplasty group and uncemented hip arthroplasty group.

Methods and materials

- Patients followed the established assessment procedure as per the Department of Orthopaedic Surgery: Arthroplasty Unit in being planned for hip arthroplasty surgery.
- Once scheduled for hip arthroplasty surgery, informed consent (Appendices A and B) was obtained from patients who elected to participate in this study.
- Patients underwent the routine pre-operative and intra-operative processes according to the current protocol.
- In an effort to limit any confounding variables, the measurements were conducted in the same operating theatre, with the same surgical approach by the same surgeon- who is an experienced, high volume hip arthroplasty surgeon (28). This did not deviate from the current practice nor change the patients' experience.
- The cement used for this study was Palacos®+G. This is the standard cement used at our institution for arthroplasty surgery and it is commonly used throughout the country. This allows for results that could be reasonably extrapolated.
- During surgery, temperature measurements were taken in degrees Celsius (°C) using a non-contact, infrared thermometer - the Beurer Medical FT100. Beurer Medical manufactures thermometers which are Food and Drug Administration (FDA) approved for measuring temperatures in humans. This device is quoted to measure temperatures with an accuracy within a fraction of a degree Celsius (within 0.2°C).

  This device complies with:

  - European Union Medical Devices Directive (EU MDD) 93/42/EEC
  - German Medical Devices Act (Medizinproduktegesetz)
  - American Society for Testing and Materials (ASTM) E 1965 – 98
  - European Standard EN60601-1-2 (in accordance with CISPR11, IEC 61000-4-2, IEC 61000-4-3, IEC 61000-4-8)

Published literature demonstrates that this technology is an established means by which to evaluate bone temperature (29-32). An official declaration of conformity certificate has been issued for this device (Appendix C).

- During this process, the routine surgical sterility protocol was respected.
- Temperature was measured at specified sites (see Figures 1 to 4):
    - Bone-cement interface (for cemented hip arthroplasty).
    - Bone-implant interface (for uncemented hip arthroplasty).
    - Neck of the femoral implant.
- The temperature probe was placed in two surgically sterilised plastic sleeves and the person operating the probe was fully scrubbed and donned in surgically sterilised operating attire. Full surgical field sterility was maintained.
- Temperature measurements were taken at the above sites, at the following time increments:
    - Following femoral canal preparation (neck cuts and broaching), prior to the insertion of any implant or cement material. This was referred to as the index time T^0.
    - At 1-minute intervals subsequent to definitive femoral stem insertion (into the cement mantle for cemented hip arthroplasty; or directly into the femoral canal for uncemented hip arthroplasty). As such, T^1 refers to 1 minute post femoral stem insertion, T^2 refers to 2 minutes post femoral stem insertion and so forth.
    - Manufacturer information (Heraeus Medical) indicates that PMMA sets prior to 11 minutes, thus the measurements were taken up to 12 minutes post femoral stem insertion, referred to as T^{12}.
- Temperatures were documented for analysis.
- The surgical procedure and post-operative routine continued unaffected.

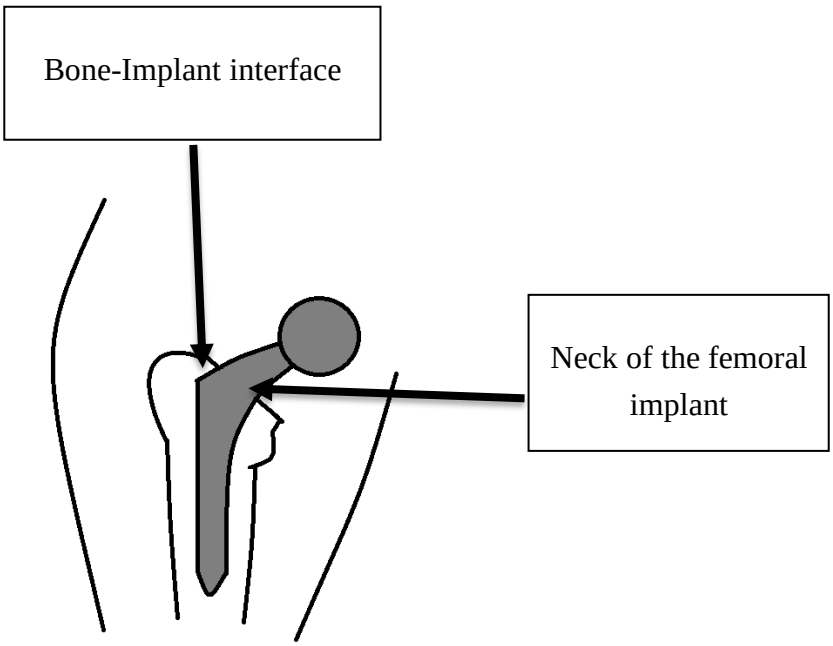

Figure 1: Measurement points in Uncemented Hip Arthroplasty group

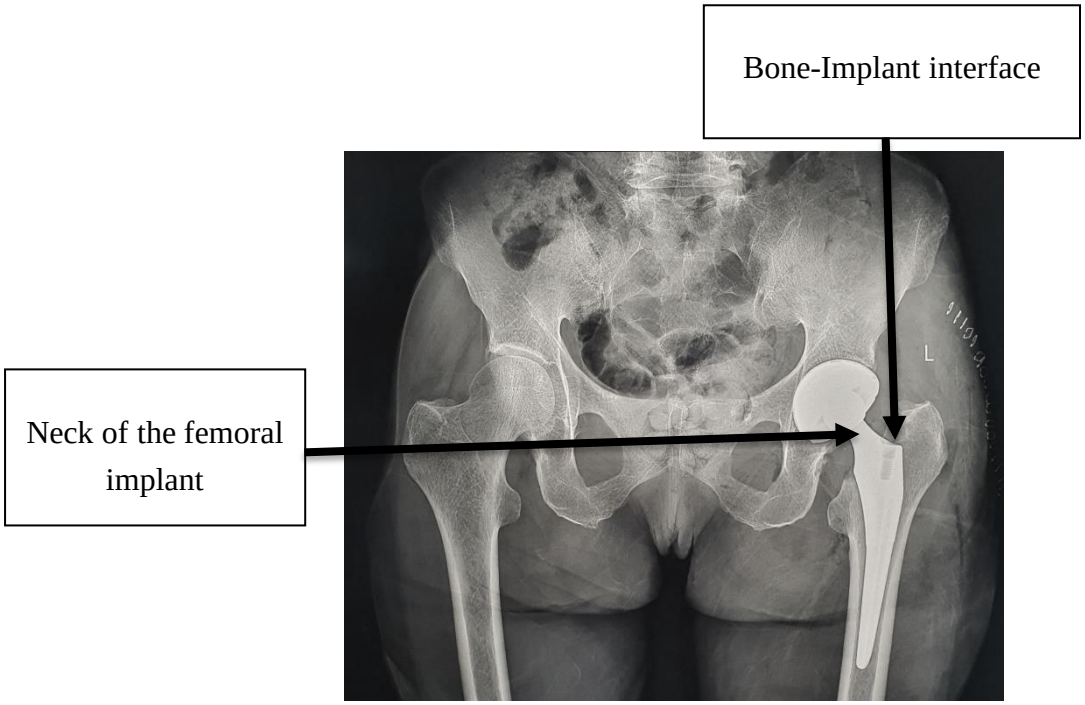

Figure 2: Post operative X-ray of study patient (De-identified to “UC 2”) in the Uncemented Hip Arthroplasty group, demonstrating measurement points

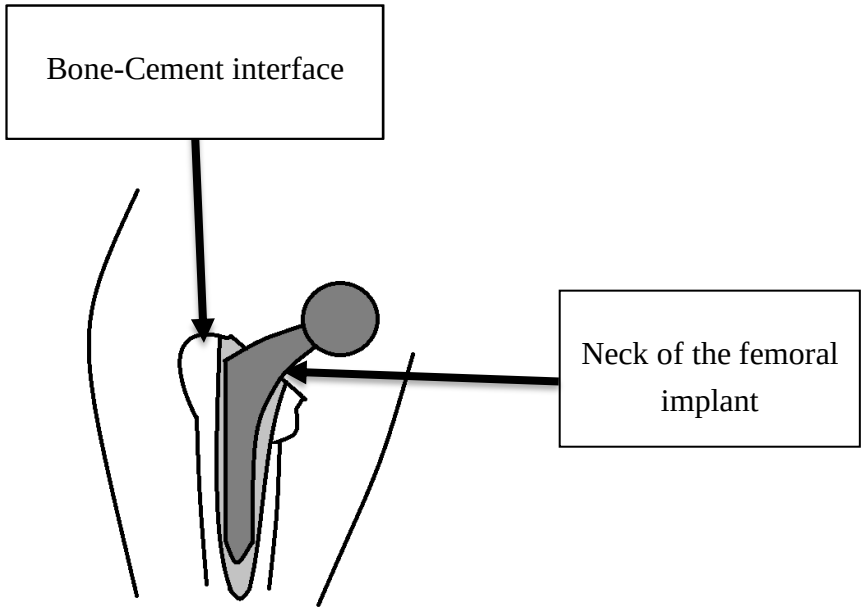

Figure 3: Measurement points in Cemented Hip Arthroplasty group

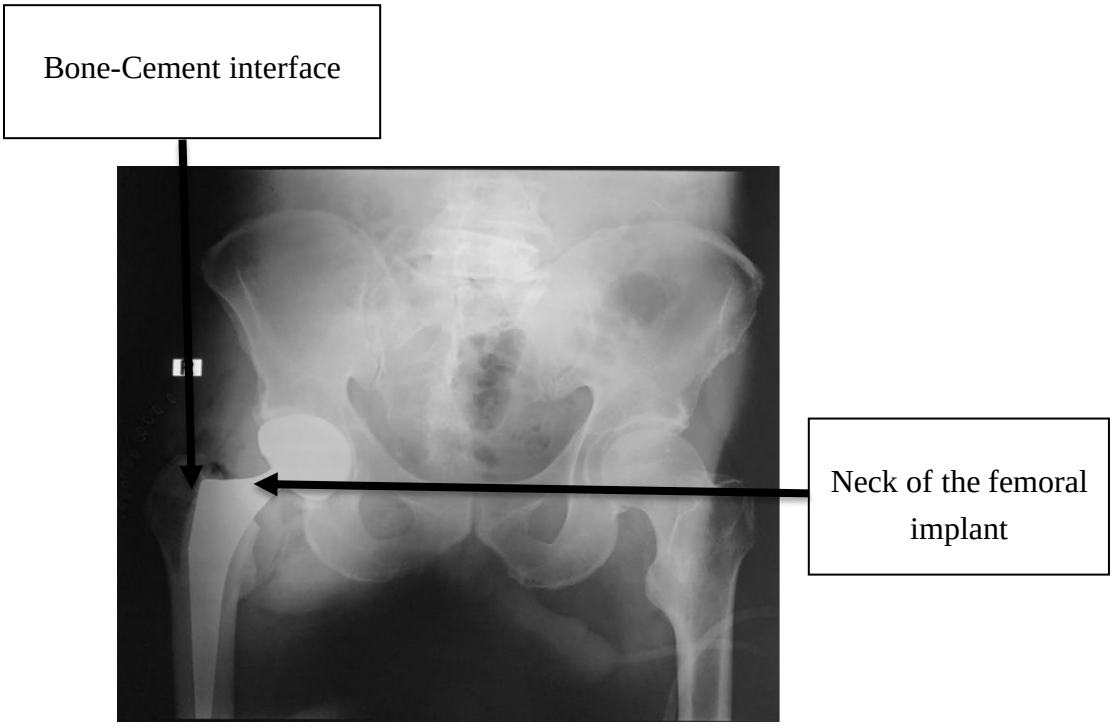

Figure 4: Post operative X-ray of study patient (De-identified to “C 3”) in the Cemented Hip Arthroplasty group, demonstrating measurement points

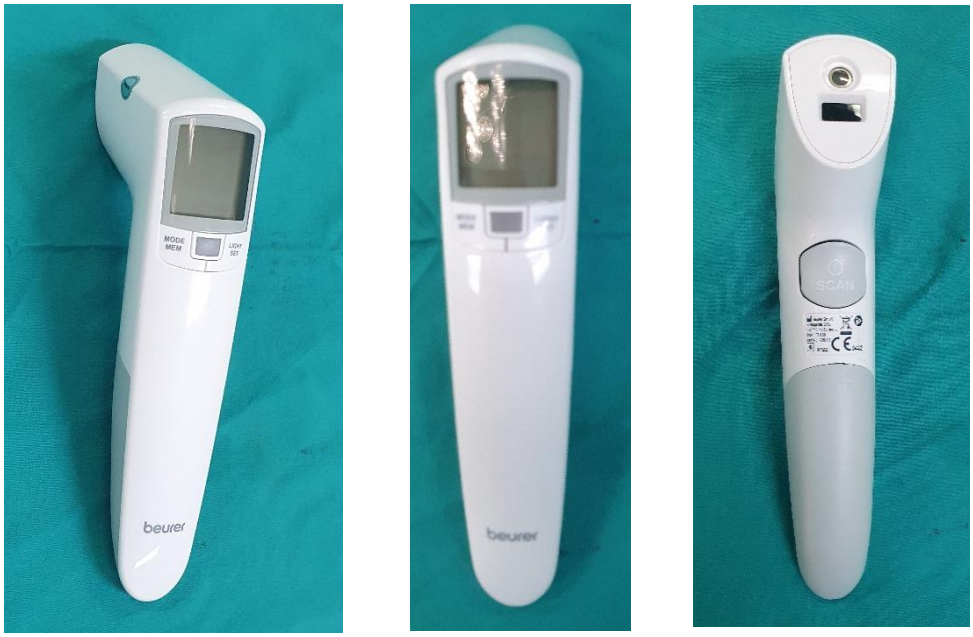

Figure 5: Thermometer used for temperature measurements

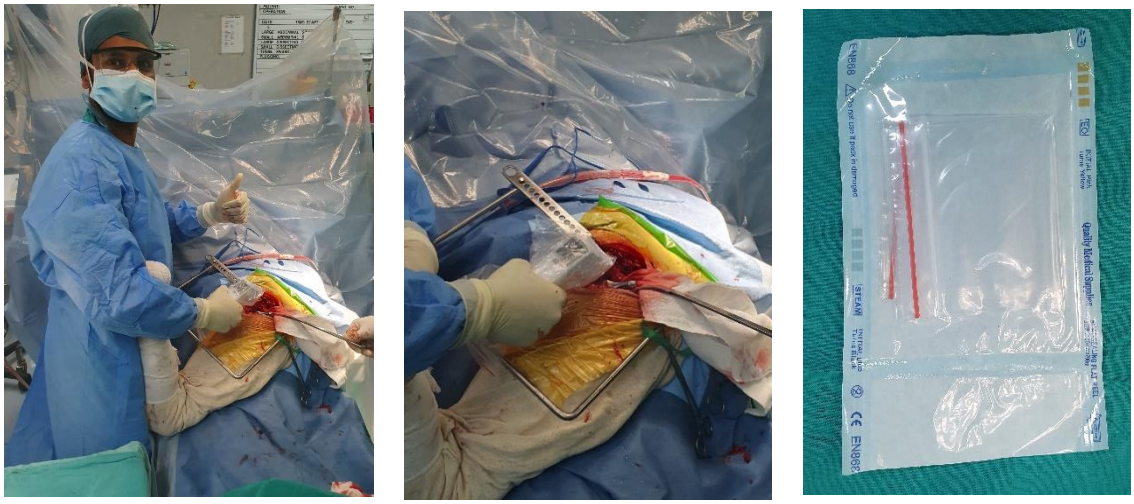

Figure 6: Intra-operative photographs of temperature measurement technique, with sterile sleeves demonstrated (far right)

Study Power and Sample Size

Sample size: N = 8 (four patients per group)

- This study measured temperatures in two distinct independent, unpaired, populations i.e. (i) patients undergoing cemented hip arthroplasty surgery and (ii) patients undergoing uncemented hip arthroplasty surgery.
- Based on the available literature: the mean temperature of uncemented hip arthroplasty was 25°C with a standard deviation of 8°C; and for cemented hip arthroplasty, the mean temperature was 49°C.
- The enrolment rate, being the ratio of patients in each group, was one.
- Regarding Type I errors, which occur when it is concluded that there is a difference between the two groups, but no such difference actually exists (a false positive rate, or incorrectly rejecting a null hypothesis): The standard alpha level with a *p*-value of 0.05 was used.
- Regarding Type II errors, which occur when it is concluded that there is no difference between the two groups, but such difference actually exists (a false negative rate, or incorrectly accepting a null hypothesis): The standard beta of 0.2 with a Power of 80% was used.

Data Analysis

Statistical methods

Collation of the data were done on a Microsoft Excel® Spreadsheet - all devices used were password protected and the data were only made available to the primary investigator, supervisors and relevant statisticians.

All patient details were de-identified and made anonymous prior to presentation or publication of the results. De-identification was done by assigning a study number to each patient.

The data were analysed using the statistical analysis software STATA ® Version 15.1. This process was done in conjunction with a bio-statistician through the Faculty of Health Sciences Research Office at the University of the Witwatersrand.

Frequencies and percentages were used to describe categorical variables (e.g. gender), while median and interquartile range (IQR) were used to describe continuous variables (e.g. age and temperature).

The Wilcoxon rank-sum test was used to compare differences in age and temperature in the cemented and uncemented arthroplasty groups.

The non-parametric equality of medians test was used to compare temperatures of the adjacent bone, neck of implant and the ambient temperature at each time point and *p*-values are reported.

A *p*-value < 0.05 was considered statistically significant.

Line graphs were used to analyse trends in temperature over time.

Results

Table I: Overall description of study participants (N=8)

Characteristic	**Total (N)**	**Cemented**	**Uncemented**	***P*-value**
Age in years, median (IQR)	66 (55.5 – 75.5)	70 (58.5 – 77)	61.5 (55.5 – 71.5)	0.773
Gender	**n (%)**	**n (%)**	**n (%)**	
Male	4 (50%)	1 (25%)	3 (75%)	0.486
Female	4 (50%)	3 (75%)	1 (25%)	

Table I shows a total of 8 patients, 4 males and 4 females were included in the study. The median age was 66 years (IQR 55.5 – 75.5).

Patients who had cemented arthroplasty were older than those who had uncemented arthroplasty, however the difference was not statistically significant (p=0.773).

More males than females received uncemented arthroplasty, whereas more females than males received cemented arthroplasty, although these differences were not statistically significant (p=0.486).

Table II: Overall description of temperature levels during hip arthroplasty

Time (Minutes)	Adjacent bone temperature (°C)	Neck of implant temperature (°C)	Ambient temperature (°C)	*p*-value
0	29.75 (29.45 – 31.15)	26.10 (25.65 – 26.80)	25.65 (25.0 – 25.90)	0.002
1	30.60 (29.70 – 31.40)	27.60 (26.85 – 28.05)	25.25 (24.70 – 26.30)	<0.001
2	30.95 (29.55 – 32.45)	29.0 (28.05 – 31.10)	25.40 (25.05 – 25.50)	<0.001
3	31.35 (30.25 – 33.70)	30.75 (28.60 – 36.55)	25.55 (24.9 – 25.65)	0.006
4	32.20 (30.25 – 34.40)	35.40 (29.50 – 44.30)	25.20 (24.40 – 25.90)	0.002
5	31.65 (30.60 – 35.50)	36.65 (30.50 – 44.85)	25.40 (24.50 – 26.10)	0.002
6	33.95 (30.4 – 38.7)	38.05 (30.45 – 44.35)	25.35 (25.0 – 25.60)	0.002
7	35.30 (30.25 – 39.70)	37.2 (30.60 – 43.70)	25.45 (25.0 - 25.75)	0.002

8	36.10 (30.40 – 42.55)	36.10 (30.4 – 42.55)	25.50 (25.25 – 26.10)	0.002
9	33.65 (29.45 – 38.40)	35.70 (30.15 – 39.35)	25.30 (24.95 – 25.45)	0.002
10	32.85 (29.35 – 37.10)	33.70 (29.30 – 37.30)	25.20 (25.05 – 26.10)	0.002
11	32.60 (29.35 – 36.15)	33.45 (29.10 – 36.15)	25.40 (25.35 – 25.75)	0.002
12	31.30 (29.25 – 34.75)	31.4 (28.85 – 34.75)	25.60 (25.40 – 26.15)	0.002

Table II shows median temperatures and interquartile ranges of the adjacent bone, neck of implant and the ambient temperature from times T^0 to T^{12}. T^0 represents the time of insertion of the definitive femoral implant, following femoral canal preparation. The femoral stem was implanted into the cement mantle in cemented hip arthroplasty and directly into the femoral canal in uncemented hip arthroplasty. T^{12} represents 12 minutes post definitive implant insertion. The time interval between sequential temperature measurements was 1 minute.

The temperatures differences from T^0 to T^{12} in adjacent bone, neck of implant and ambient temperatures were all statistically significant (*p* range <0.001 to 0.006).

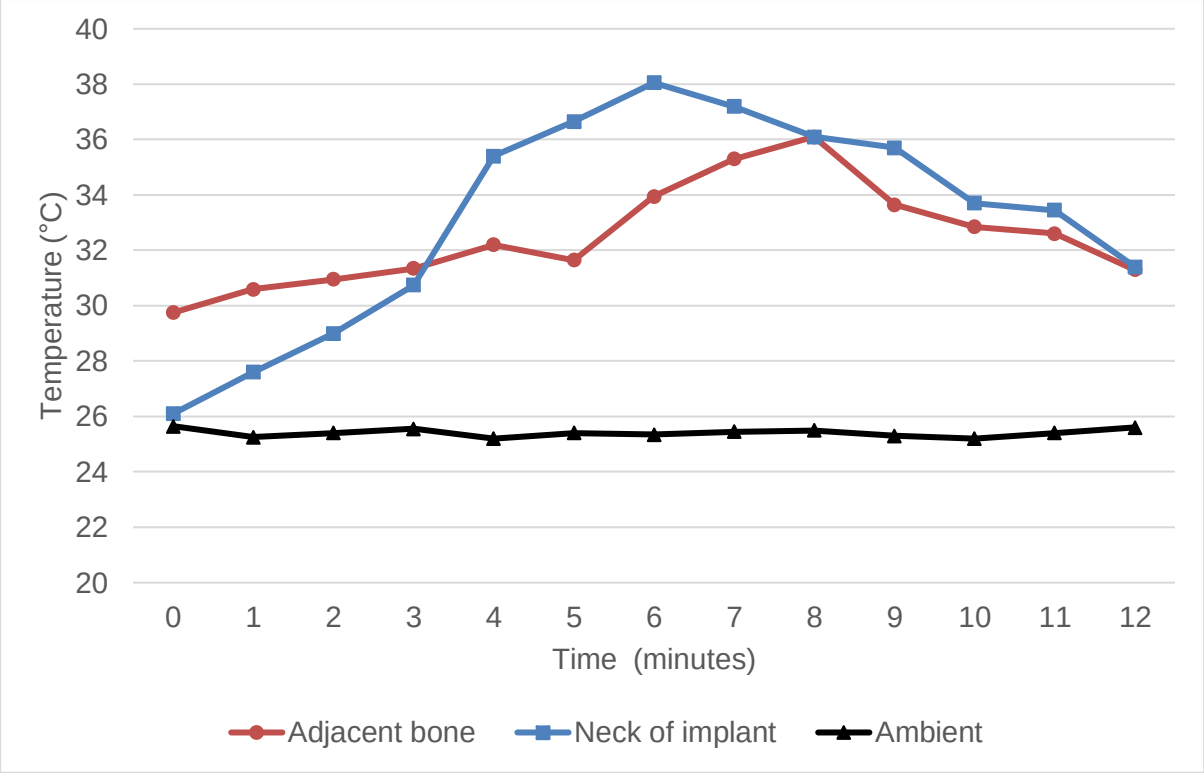

Figure 7: Overall trends of temperatures levels during hip arthroplasty (cemented and uncemented)

Adjacent bone temperature was persistently higher than ambient temperature throughout the 12 minute duration. Neck of implant temperature closely resembled ambient temperature at the time of insertion (T^0) but became persistently and significantly higher from 1 minute post insertion of the implant (T^1).

Peak neck of implant temperature occurred at T^6. Peak adjacent bone temperature followed at T^8.

From T^4 to T^7, and T^9 to T^{11}, the neck of implant temperature was significantly higher than the adjacent bone temperature (p=0.020).

Table III: Ambient temperatures during cemented and uncemented hip arthroplasty

Time (Minutes)	Ambient temperature (°C)		
	Cemented hip arthroplasty	Uncemented hip arthroplasty	*p*-value
0	25.8 (25.65 – 26.8)	25.0 (24.45 – 25.65)	0.110
1	26.3 (25.55 – 26.95)	24.85 (24.0 – 25.25)	0.083
2	25.5 (25.25 – 26.8)	25.25 (24.45 – 25.4)	0.144
3	25.6 (25.55 – 26.65)	24.9 (23.95 – 25.5)	0.146
4	25.9 (25.25 – 26.85)	24.4 (23.9 – 25.15)	**0.043**
5	26.1 (25.4 – 27.25)	24.5 (23.5 – 25.3)	0.059
6	25.6 (25.35 – 26.35)	25.0 (23.8 – 25.35)	0.080
7	25.6 (25.25 – 26.5)	25.2 (24.15 – 25.6)	0.245
8	25.8 (25.45 – 26.65)	25.3 (24.85 – 25.8)	0.242
9	25.45 (25.25 – 26.6)	25.0 (24.65 – 25.3)	0.110

10	25.6 (25.0 – 26.75)	25.2 (25.05 – 25.7)	0.767
11	25.5 (25.4 – 26.55)	25.35 (24.85 – 25.65)	0.237
12	25.55 (25.4 –26.5)	25.7 (25.05 – 26.15)	0.884
Peak temperature	26.55 (26.25 – 27.4)	25.85 (25.75 – 26.2)	0.083
Duration above baseline (mins)	12 (12 – 12)	11.5 (11 – 12)	0.127

Table III shows median temperatures and interquartile ranges of the ambient temperature from times T^0 to T^{12}. Ambient temperatures were compared for cemented and uncemented hip arthroplasties over the described time period and *p*-values are reported.

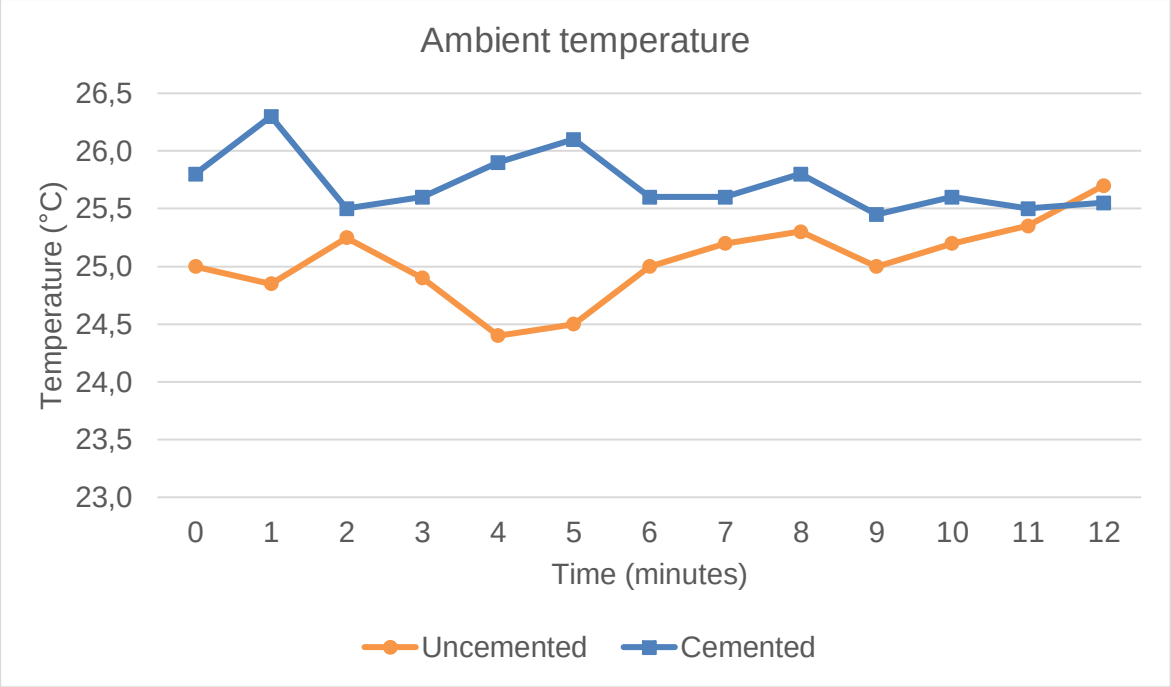

Figure 8: Trends in ambient temperature during uncemented and cemented hip arthroplasty

There were no significant differences in ambient temperature in cemented and uncemented groups except at T^4.

Table IV: Comparison of adjacent bone and neck of implant temperatures during uncemented hip arthroplasty

Time (Minutes)	**Adjacent bone temperature (°C)**	**Neck of implant temperature (°C)**	***p*-value**
0	31.15 (30.1 – 32.85)	26.8 (25.8 – 27.45)	**0.021**
1	31.4 (30.3 – 33.9)	27.15 (26.35 – 27.6)	**0.021**
2	31.45 (30.4 – 32.6)	28.15 (27.35 – 29.0)	**0.021**

3	31.15 (30.25 – 32.65)	28.6 (28.4 – 29.55)	**0.043**
4	31.4 (30.25 – 32.2)	29.5 (28.7 – 30.8)	0.149
5	30.6 (29.65 – 31.5)	30.5 (29.2 – 32.45)	1.000
6	30.4 (29.55 – 31.05)	30.45 (29.35 – 32.3)	0.772
7	30.25 (29.45 – 31.55)	30.6 (29.9 – 31.95)	0.468
8	29.65 (29.35 – 30.45)	30.4 (29.7 – 31.9)	0.386
9	29.45 (29.1 – 29.75)	30.15 (29.55 – 31.65)	0.110
10	29.35 (29.15 – 29.5)	29.3 (29.1 – 30.2)	0.883
11	29.35 (29.25 – 29.5)	29.1 (28.8 – 30.3)	0.245
12	29.25 (29.1 – 29.4)	28.85 (28.15 – 29.55)	0.248

Table IV shows median temperatures and interquartile ranges of the adjacent bone and neck of implant in uncemented hip arthroplasty from times T^0 to T^{12}. Adjacent bone temperatures and neck of implant temperatures were compared over the described time period and *p*-values are reported.

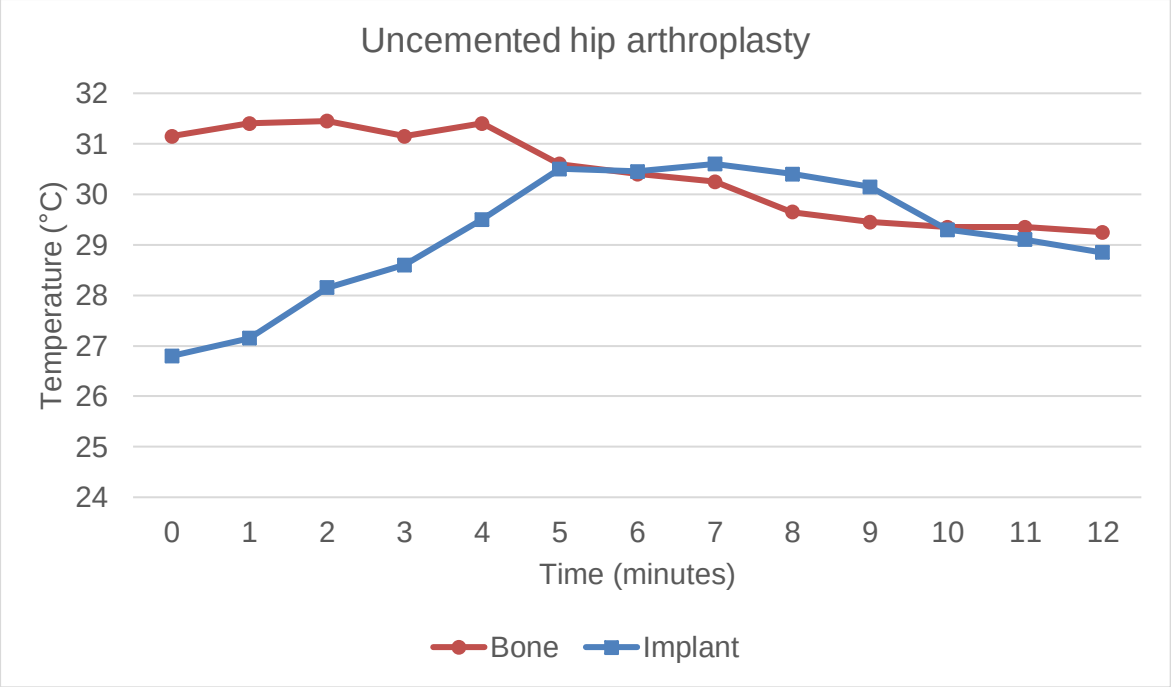

Figure 9: Trends in neck of implant and adjacent bone temperature during uncemented hip arthroplasty

The initial implant temperature was not significantly different form the ambient temperature. The adjacent bone temperature was significantly higher than the implant temperature from T^0 (p=0.021) to T^3 (p=0.043). This difference transitioned from significant to insignificant at T^4 as the implant and adjacent bone temperatures converged. Convergence occurred by T^5 and there continued to be no significant difference between the implant and bone temperatures from T^5 to T^{12}.

Table V: Comparison of adjacent bone and neck of implant temperatures during cemented hip arthroplasty

Time (Minutes)	Adjacent bone temperature (°C)	Neck of implant temperature (°C)	*p*-value
0	29.55 (28.85 – 29.75)	26.0 (25.05 – 26.1)	**0.021**
1	30.1 (29.7 – 30.6)	28.05 (27.35 – 29.1)	0.083
2	30.1 (29.3 – 31.95)	31.1 (29.05 – 33.9)	0.772
3	32.5 (30.55 – 34.6)	36.55 (33.0 – 38.55)	0.248
4	34.4 (31.2 – 37.0)	44.3 (41.5 – 45.8)	**0.021**
5	35.5 (33.0 – 37.25)	44.85 (42.05 – 45.8)	**0.021**
6	38.7 (37.4 – 40.3)	44.35 (43.35 – 45.0)	**0.021**
7	39.7 (38.7 – 40.8)	43.7 (42.3 – 44.5)	**0.021**
8	40.05 (39.6 – 40.4)	42.55 (40.8 – 43.15)	0.248
9	38.4 (37.7 – 39.3)	39.35 (38.7 – 40.05)	0.248
10	37.1 (36.3 – 38.1)	37.3 (36.55 – 38.4)	0.468

11	36.15 (35.85 – 36.65)	36.15 (35.65 – 36.9)	1.000
12	34.75 (33.75 – 35.4)	34.75 (33.4 – 36.3)	1.000

Table V shows median temperatures and interquartile ranges of the adjacent bone and neck of implant in cemented hip replacements from times T^0 to T^{12}. Adjacent bone temperatures and neck of implant temperatures were compared over the described time period and *p*-values are reported.

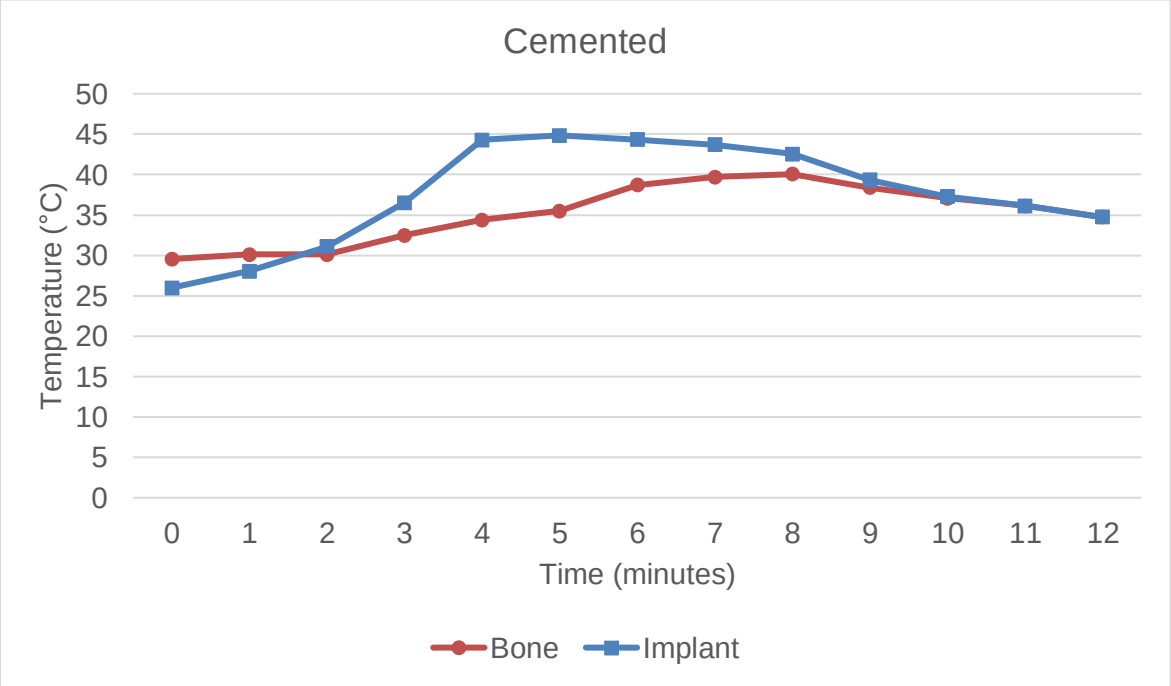

Figure 10: Trends in neck of implant and adjacent bone temperature during cemented hip arthroplasty

The initial implant temperature was not significantly different form the ambient temperature. Adjacent bone temperature was significantly higher than implant temperature at T^0 (p=0.021). There was no significant difference between adjacent bone temperature and implant

temperature between T^1 and T^3. The implant temperature increased to become significantly higher than the adjacent bone from T^4 to T^7 (p=0.021). There was again no significant difference between implant and adjacent bone temperature between T^8 and T^{12}.

Table VI: Comparison of adjacent bone and neck of implant temperatures between cemented and uncemented hip arthroplasty

Time (Minutes)	Adjacent bone temperature (°C)			Neck of implant temperature (°C)		
	Cemented hip arthroplasty	Uncemented hip arthroplasty	*p*-value	Cemented hip arthroplasty	Uncemented hip arthroplasty	*p*-value
0	29.55 (28.85 – 29.75)	31.15 (30.1 – 32.85)	0.083	26.0 (25.05 – 26.1)	26.8 (25.8 – 27.45)	0.146
1	30.1 (29.7 – 30.6)	31.4 (30.3 – 32.85)	0.191	28.05 (27.35 – 29.1)	27.15 (26.35 – 27.6)	0.083
2	30.1 (29.3 – 31.95)	31.45 (30.4 – 32.6)	0.248	31.1 (29.05 – 33.9)	28.15 (27.35 – 29.0)	0.083
3	32.5 (30.55 – 34.6)	31.15 (30.25 – 32.65)	0.663	36.55 (33.0 – 38.55)	28.6 (28.4 – 29.55)	**0.021**

4	34.4 (31.2 – 37.0)	31.4 (30.25 – 32.2)	0.191	44.3 (41.5 – 45.8)	29.5 (28.7 – 30.8)	**0.021**
5	35.5 (33.0 – 37.25)	30.6 (29.65 – 31.5)	**0.043**	44.85 (42.05 – 45.8)	30.5 (29.2 – 32.45)	**0.021**
6	38.7 (37.45 – 40.3)	30.4 (29.55 – 31.05)	**0.021**	44.35 (43.35 – 45.0)	30.45 (29.35 – 32.3)	**0.021**
7	39.7 (38.7 – 40.8)	30.25 (29.45 – 31.55)	**0.021**	43.7 (42.3 – 44.5)	30.6 (29.9 – 31.95)	**0.021**
8	40.05 (39.6 – 40.4)	29.65 (29.35 – 30.45)	**0.021**	42.55 (40.8 – 43.15)	30.4 (29.7 – 31.9)	**0.021**
9	38.4 (37.7 – 39.3)	29.45 (29.1 – 29.75)	**0.021**	39.35 (38.7 – 40.05)	30.15 (29.55 – 31.65)	**0.021**
10	37.1 (36.3 – 38.1)	29.35 (29.15 – 29.5)	**0.020**	37.3 (36.55 – 38.4)	29.3 (29.1 – 30.2)	**0.021**
11	36.15 (35.85 – 36.65)	29.35 (29.25 – 29.5)	**0.021**	36.15 (35.65 – 36.9)	29.1 (28.8 – 30.3)	**0.021**
12	34.75 (33.75 – 35.4)	29.25 (29.1 – 29.4)	**0.021**	34.75 (33.4 – 36.3)	28.85 (28.15 – 29.55)	**0.021**

Baseline	29.55 (28.85 – 29.75)	29.2 (29.05 – 29.35)	0.309	26 (25.05 – 26.1)	26.65 (25.65 – 27.45)	0.465
Peak temperature	40.4 (39.85 – 40.9)	31.8 (30.75 – 32.95)	**0.020**	45.65 (45.0 – 46.45)	31.2 (30.2 – 32.5)	**0.021**
Duration above baseline (mins)	12 (11.5 – 12)	11.5 (10.5 – 12.0)	0.405	11 (11 – 11.5)	12 (11.5 – 12)	0.186

Table VI shows median temperatures and interquartile ranges of the adjacent bone and neck of implant in cemented and uncemented hip replacements from times T^0 to T^{12}. Adjacent bone temperatures of the cemented and uncemented groups are compared over the described time period and *p*-values are reported. Neck of implant temperatures of the cemented and uncemented groups are also compared over the described time period and *p*-values are reported.

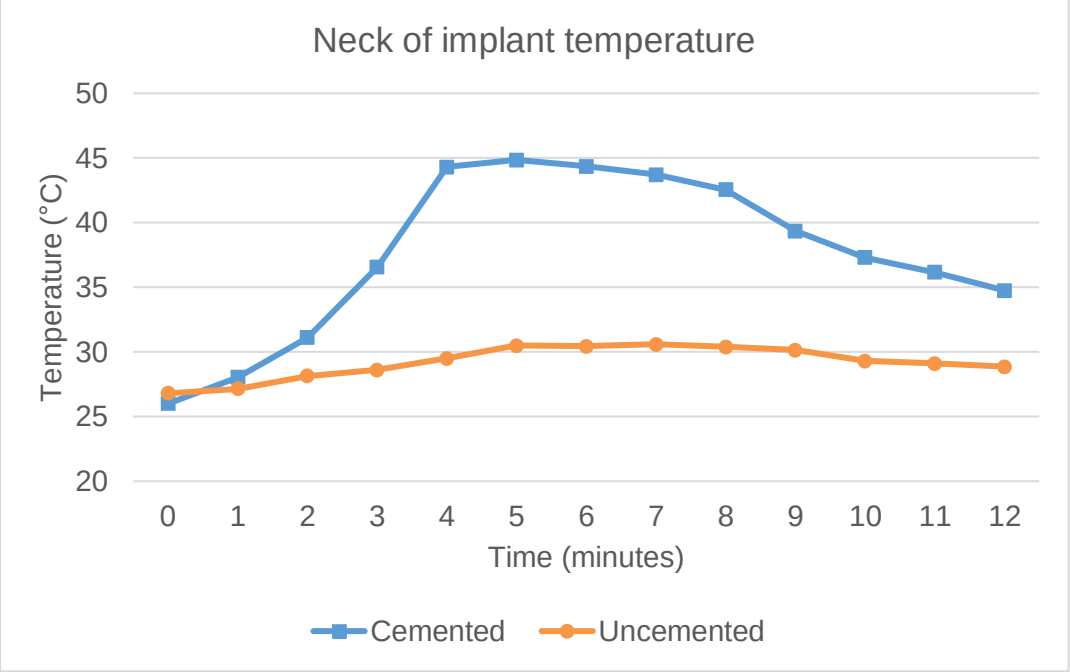

Figure 11: Comparison of trends in neck of implant temperatures between cemented and uncemented hip arthroplasty

From T^3, the neck of implant temperature in the cemented group was persistently and significantly higher than in the uncemented group (p=0.021).

The maximum neck of implant temperature recorded in the cemented group was 46.8°C, whilst the maximum neck of implant temperature recorded in the uncemented group was 33.4°C.

At the neck of the implant, the median peak temperature difference between the cemented hip arthroplasty and uncemented hip arthroplasty groups was 14.5°C and this difference was statistically significant (p=0.021).

In the cemented hip arthroplasty group, the highest neck of implant temperatures were recorded between T^4 and T^8 and the lowest temperatures were recorded at T^0.

In the uncemented hip arthroplasty group, the highest neck of implant temperatures were recorded between T^5 and T^9 and the lowest temperatures were recorded at T^0.

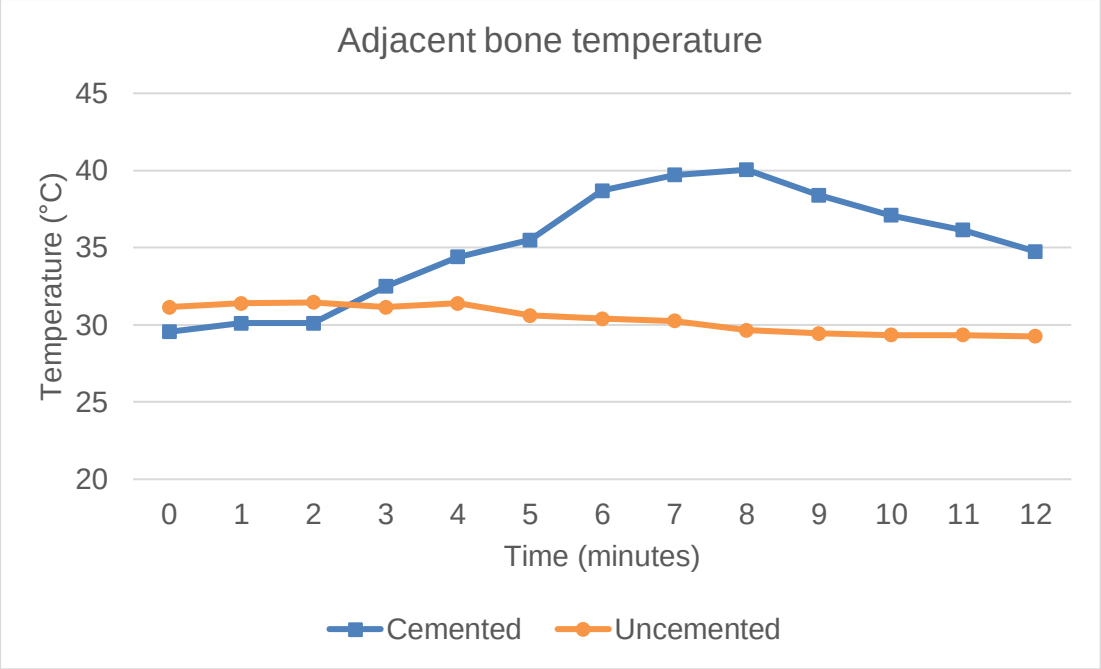

Figure 12: Comparison of trends in adjacent bone temperatures between cemented and uncemented hip arthroplasty

From T^5, adjacent bone temperature in the cemented group was persistently and significantly higher than in the uncemented group.

The maximum adjacent bone temperature recorded in the cemented group was 41.1°C, whilst the maximum adjacent bone temperature recorded in the uncemented group was 34.4°C.

At the adjacent bone, the median peak temperature difference between the cemented hip arthroplasty and the uncemented hip arthroplasty groups was 8.6°C and this difference was statistically significant (p=0.020).

In the uncemented hip arthroplasty group, the highest adjacent bone temperatures were recorded between T^0 and T^4 and the lowest temperatures were recorded at T^{12}.

In the cemented hip arthroplasty group, the highest adjacent bone temperatures were recorded between T^6 and T^9 and the lowest temperatures were recorded at T^0.

Discussion

Patient demographics

Though the tendency to cement in relation to patient demographics was not statistically significant, the overall trends are in keeping with expected physiological changes in bone biology. There is a decrease in bone mineral density associated with advanced age. Female gender is also an independent risk factor for decreased bone mineral density in post-menopausal patients (33). This is likely the reason that more cemented hip arthroplasties were done in females and the median age of patients receiving cemented hip arthroplasty was 8.5 years older than those receiving uncemented hip arthroplasty.

Ambient theatre temperature analysis

Ambient temperature measurements showed no significant difference between the cemented and uncemented hip arthroplasty groups. Temperatures remained constant throughout the procedures. The consistency between the study groups in this report eliminates a potentially confounding variable and aids in drawing accurate conclusions. The average ambient temperature of 25.49°C is also within the ambient temperature range of 24-28°C as reported in the literature (21, 23, 24). Corresponding ambient conditions helps to reasonably compare these findings with those in available literature.

Initial bone temperature

The initial temperature of the bone was significantly higher than the ambient temperature. This finding differs from Gundapaneni and Vallo who used ambient temperature as a surrogate for bone temperature for initial conditions in their 3D and mathematical models, respectively (21, 23). The reasoning cited was that the bone surface was exposed to the environment prior to implantation of cement or a prosthesis. The combination of two factors may explain the higher

starting bone temperature. Firstly, bone is a vitalised structure with thermal regulation - this is supported by Farvadin who, in his cadaveric study report, stated that vitalised bone likely has a higher temperature than non-vitalised substitutes (20). Secondly, due to the broaching procedure used to prepare the femur during the surgical procedure. Broaching uses course surfaced tools that are repeatedly impacted and advanced down the medullary canal. Sequentially larger broaches are used to increase the diameter of the medullary canal and maximise compaction of bone. Broaching inherently creates friction and subsequent heat generation (34). These factors could only be accurately accounted for in an *in vivo* study, such as this one.

Uncemented hip arthroplasty analysis

The overall trend of uncemented hip arthroplasty was that the adjacent bone was at its hottest at the initial measurement and gradually cooled over the 12 minutes. The initial temperature was taken closest to the broaching procedure which, as previously mentioned, generates heat through friction. Some of this heat likely diffused to the implant, whose temperature closely resembled ambient temperature at the time of insertion. This heat diffusion is evidenced by the increase in implant temperature which corresponded temporally with the decrease in adjacent bone temperature. These thermal dynamics in uncemented hip arthroplasty procedures were overlooked in previous literature, thus making it challenging to isolate the thermal effects of cement prior to this study.

Cemented hip arthroplasty analysis and comparison

The adjacent bone temperature in cemented hip arthroplasty was initially similar to that of uncemented hip arthroplasty, which is in keeping with the femoral preparation for both procedures being similar. In contrast to uncemented hip arthroplasty, the adjacent bone temperature in cemented hip arthroplasty rose during the evaluated time frame - becoming significantly higher than the uncemented counterparts five minutes after cement insertion. The

adjacent bone temperature then remained significantly higher in the cemented group until the end of the observed period - a total of eight minutes. The heat generated by the cement during the exothermic reaction appears to diffuse to the implant first, as the significant increase in implant temperature precedes the increase in the adjacent bone temperature by two minutes. Overall, during cementation, implant temperature increased more rapidly than that of the adjacent bone; reached a higher peak and sustained the increased temperature for a longer duration. This, likely owing to metals' enhanced thermal conduction properties when compared to bone (35, 36). This property is exemplified by the convergence of the implant temperature with ambient temperature prior to insertion and convergence with bone temperature post insertion; as well as once the PMMA exothermic reaction subdues. Both the implant and adjacent bone peak temperatures in the cemented group were significantly higher than in the uncemented group - this increase is attributed directly to the PMMA as other variables were regulated. The implant temperature raised by 19.7°C and adjacent bone temperature raised by 10.9°C and from their respective initial temperatures. When compared to uncemented hip replacements, the peak measured temperature differences in cemented hip replacements amount to as much as 14.5°C higher on the implant and 8.6°C higher on the adjacent bone.

Peak temperatures

In uncemented hip arthroplasties, the peak temperature recorded on the implant was 33.4°C (median 31.2°C) and the peak adjacent bone temperature was 34.1°C (median 31.8°C). During cemented hip arthroplasty, the peak temperature recorded on the implant was 46.8°C (median 45.7°C) and the peak adjacent bone temperature was 41.3°C (median 40.4°C), both of which are significantly higher than the corresponding peak temperatures in uncemented hip arthroplasty. The peak measured adjacent bone temperature was significantly lower than the 59.9°C described by Vallo (23), but corroborated Gundapaneni's reported peak temperature of 46.9°C (21) and closely resembled Maffezzoli's reported peak temperature of 49°C (24).

Thermal osteonecrosis is a coefficient of three factors: the peak temperature to which the bone is exposed; the duration of exposure to the external heat source; and the bone's tolerance to heat (11).

The maximum recorded temperature of the implant in the cemented group reached a level at which bone necrosis is described to occur (12, 13).

Regarding duration of exposure, the implant in the cemented group sustained significantly higher temperatures for ten minutes and maintained peak temperatures for three minutes. Whilst adjacent bone sustained peak temperatures for three minutes. Both of which may potentially be long enough to cause necrosis (24).

Bone's tolerance of heat was not explored in this study; however, it may also be affected by PMMA's effect on the local physiological environment and the disruption of blood supply and moisture caused by heat as well as PMMA's hydrophilic properties (11, 13, 26).

Limitations

This study is descriptive of the thermal dynamics around hip arthroplasty and directly compares cemented and uncemented hip arthroplasty in this context. There was no direct clinical impact nor correlations studied.

Temperature measurements taken at the surface of the bone cement/implant interface are not necessarily representative of the entire interface. Of specific note, at the surface measured, the bone is inherently exposed to the ambient temperature whilst the remainder of the interface is not exposed to this. To fully evaluate this interface *in vivo*, invasive thermometry would likely have to be utilised.

The cement mantle thickness was not correlated with the heat generated, though this concept is described in the literature (21, 23). This was not explored in this study as cementing

techniques, mantle thickness and implant designs were kept constant to avoid confounding variables.

These thermal dynamics can only be applied to the specific PMMA and implants used in this study as different material compositions may not interact in the same way.

Although the number of participants included in the study was adequately powered to test for statistical significance, the sample size was relatively small.

Clinical contribution

This study describes *in vivo* that there are significant temperature changes owing to the exothermic reaction resulting from PMMA. This lays a foundation for future work where the clinical significance of these temperature changes can be further explored.

The study also gives merit to discussion around protecting the bone interface from heat transfer by the following techniques:

<u>Directing heat energy preferentially to the implant and thus limiting its transference to the bone</u>

- Early siting of the femoral head, as well as early reduction of the hip joint - this is specifically founded as heat energy was preferentially transferred to the implant. This may increase the surface area for heat distribution.

- Pre-cooling implants and convection based techniques could increase the heat diffusion gradient towards the implant.

- Different implant designs and materials that are more thermo-conductive with lower specific heat properties.

Reducing the overall heat energy

- Exploring different cementing techniques, such as those described by the “French paradox” (37, 38). Reducing the cement mantle thickness may reduce the overall heat produced, with literature recommending a mantle thickness of five to six millimetres or less (21, 23).

- Development of less exothermic or poorer heat conductive PMMA to decrease the total heat energy produced and limit the amount that transfers to the implant and bone.

Managing the heat energy through timing

- Timing the cementation process to allow the initial bone temperature to settle following canal preparation. Thus, separating heat exposures rather than compounding them. Timing adjustments may also allow for reduced time between cement insertion and hip joint reduction - the potential benefits of which as aforementioned.

Conclusion

Thermal dynamics *in vivo* differ from the thermal dynamics described in the literature, which were not based on *in vivo* measurements. Adjacent bone heats up from femoral canal preparation prior to final implantation of any material. The exothermic reaction during polymerisation of bone cement causes significant increases in temperature in the adjacent bone and the implant. The implant is most readily affected by heat diffusion and tends towards a temperature equilibrium with its surrounds over time. This finding may be taken advantage of by modifying techniques to help divert heat away from the adjacent bone. Bone is exposed to temperatures high enough to cause thermal osteonecrosis during cemented hip arthroplasty. Likely owing to its moisture and blood supply, the adjacent bone itself does not reach the same peak temperatures as the implant. This however does not exclude thermal osteonecrosis, as the prolonged duration of heat exposure may render the adjacent bone vulnerable to thermal osteonecrosis. The clinical significance of these findings is yet to be determined. This research report lays a foundation on which further research may be built, to enhance our understanding of cementing in hip arthroplasty.

Ethics statement

- All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.
- Prior to the commencement of the study ethical approval was obtained from the following ethical review board: Human Research Ethics Committee (HREC) (Medical), University of the Witwatersrand. Clearance certificate number: M210412 (Appendix E).
- Permission to perform this study was be obtained from the CHBAH Chief Executive Officer (CEO) and Medical Advisory Committee (MAC) (Appendices F and G).
- Informed written consent was obtained from all patients for being included in the study.
- Consent was obtained from patients for the use of clinical photographs and these images were adequately anonymised.

Author contributions

- T. Ajodha contributed to the study conceptualisation, design, data collection, data analysis and manuscript preparation.
- C. Frey contributed to the study conceptualisation, design, data analysis and manuscript preparation.
- B. Milner contributed to study design, data analysis and manuscript preparation.

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Appendices

Appendix A: Study information sheet

STUDY INFORMATION DOCUMENT

Study title: "Thermal Analysis of Cementing in Hip Arthroplasty"

Good day.

Introduction:

I, Dr T. Ajodha, together with Professor C. Frey and Dr B. Milner, am doing research on temperature changes that happen during hip replacement surgery. Research is a process used in seeking new knowledge. In this study we want to learn about the temperature effects of using bone cement during hip replacement surgery. Bone cementing is a normal part of the procedure for some hip replacements. As the cement sets, it generates heat and, in this study, I am going to look at how this heat spreads in the hip.

Invitation to Participate:

We are asking / inviting you to take part in a research study.

What is involved in the study:

Anyone who chooses to participate:

- Will undergo the normal procedure for hip replacement surgery at Chris Hani Baragwanath Academic Hospital. The same procedures and protocols will be followed, irrespective of the patients choice to participate in or abstain from the study. Temperature changes will be measured during surgery using a non-invasive, medical grade thermometer. The process will respect routine sterile practices.
- Temperatures will be measured during the surgery, and this does not require an additional effort to be made by the patient.
- This will not affect the duration of the operation, recovery or time spent in the hospital.
- Participants will not have any additional blood tests, or any other investigations done for the study.

Risks of being involved in the study:
The study is observing elements of an established procedure and is not altering this procedure. There are no foreseeable risks to being involved in this study.

Benefits of being in the study:

There is no direct benefit to participants who choose to be involved in the study. The study may help us understand the effects of bone cement better and guide us as to whether we need to consider ways to improve the current procedures. This knowledge may help future patients with the longevity of their hip replacements.

Participation is voluntary: refusal to participate will involve no penalty or loss of benefits to your health-care services. You are free to discontinue or withdraw at any time without penalty or loss of benefits and there is no requirement to provide reason/s for withdrawing.

Reimbursement:

There is to be no payment or cost associated with participation.

Confidentiality:

Personal information will be treated in the strictest confidence and will only be made available to the Principal Investigator (PI) and Supervisors- Dr T. Ajodha as PI and Professor C. Frey and Dr B. Milner as supervisors.

The only exceptions would be:

1. personal information may be disclosed if required by law
2. the Human Research Ethics Committees of the University may exceptionally require personal data to respond to a formal complaint, or for a compliance audit
3. the South African Health Products Regulatory Authority (SAHPRA), which is the successor body to the South African Medicines Control Council (SAMCC), might conceivably require access to personal data, if conducting an investigation into a drug trial

If results are published, this may, exceptionally, lead to cohort, or more rarely, individual identification. All data collected in the course of the study will be securely retained for two (2) years, if a scientific publication arises from the study and six (6) years, if there is no publication. Thereafter it will be destroyed accordingly.

Contact details of researcher/s:
To get further information, please contact:
Principle Investigator:
Dr T. Ajodha
Tel: 082 261 9478
Email: purpletakkies@gmail.com

Supervisors:
Dr B. Milner
Tel: 082 468 2145
Email: Brenda.Milner@wits.ac.za

Professor C. Frey
Tel: 082 451 6449
Email: cfrey@iafrica.com

Outputs

The data will be measured temperature values during hip replacement surgery. These results may be shared with participants, should they so wish.

Contact details of HREC administrator and chair – for reporting of complaints / problem

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Study Information Sheet.

Date: February 2021

Appendix B: Participant consent sheet

WITS UNIVERSITY

PARTICIPANT CONSENT SHEET

Project Title: Thermal Analysis of Cementing in Hip Arthroplasty

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached hereto.
2. I was given time to read it, or had it read to me, in the language I best understand.
3. I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory.
4. I believe I fully understand why the study is being conducted and what the intended outcomes will be.
5. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything but my time.
6. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained
7. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study, I am free to speak to any of these contacts.

Contact details:

Principle Investigator:
Dr T. Ajodha
Tel: 082 261 9478
Email: purpletakkies@gmail.com

Supervisors:
Dr B. Milner
Tel: 082 468 2145
Email: Brenda.Milner@wits.ac.za

Professor C. Frey
Tel: 082 451 6449
Email: cfrey@iafrica.com

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.
Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____

Date: _____

Place: _____

Signature or mark _____

Witnessed by:

Name of Witness: _____

Signature: _____

Date: _____

Appendix C: Declaration of conformity certificate

beurer health and well-being	Title	EC Declaration of Conformity
	File	FT 100_EC DoC_Beurer_20200622

Manufacturer:	Beurer GmbH (see address in footer)
Product category:	Infrared thermometer
Product type:	FT 100
The product specified above is in conformity with the provisions of the following Union legislation and harmonized standards.	
93/42/EEC	Medical device directive (MDD)
UMDNS code and name:	17-888 Thermometer, Infrared
Classification/applied rule(s):	Class IIa/rule 10
Conformity assessment procedure:	Annex II - excluding section 4
The notified body mdc medical device certification GmbH, located at Kriegerstr. 6, 70191 Stuttgart, Germany, identification number 0483, issued in the course of the mentioned conformity assessment procedure the following certificate:	
Certificate no. and validity:	D1311700043, valid to 2024-05-26
	EN 60601-1:2006 + A1:2013 EN 60601-1-2:2015 ISO 80601-2-56:2009 ASTM E1965-98
2011/65/EU	Restrictions of the use of certain hazardous substances in electrical and electronic equipment (ROHS)
This declaration of conformity is issued under the sole responsibility of the manufacturer.	
Signed for and on behalf of:	Beurer GmbH
Place, date of issue:	Ulm, 22.06.2020
Name, function, signature, stamp:	Daniel Kammerer, Team Leader RA Beurer GmbH Söflinger Straße 218 · 89077 Ulm

Beurer Document 410-0040-KADA / rev02 / 2019-11-20

Appendix D: Human Research Ethics Committee (Medical) Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr Tapeshwar Ajodha

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M210412

NAME: (Principal Investigator)	Dr Tapeshwar Ajodha
DEPARTMENT:	Orthopaedic Surgery Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Thermal Analysis of Cementing in Hip Arthroplasty
DATE CONSIDERED:	30/04/2021
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof C. Frey and Dr B. Milner
APPROVED BY:	Dr CB Perry, Chairperson, HREC (Medical)
DATE OF APPROVAL:	05/07/2021

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **April** and will therefore be due in the month of **April** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature — Date: 12 July 2021

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix E: Hospital CEO clearance

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 12th March 2021

TITLE OF PROJECT:

Thermal Analysis of Cementing in Hip Arthroplasty

UNIVERSITY: Witwatersrand

Principal Investigator: Dr T Ajodha

Department: Orthopaedics

Supervisor : Prof C Frey

Permission Head Department (where research conducted): Yes

NHRD No.

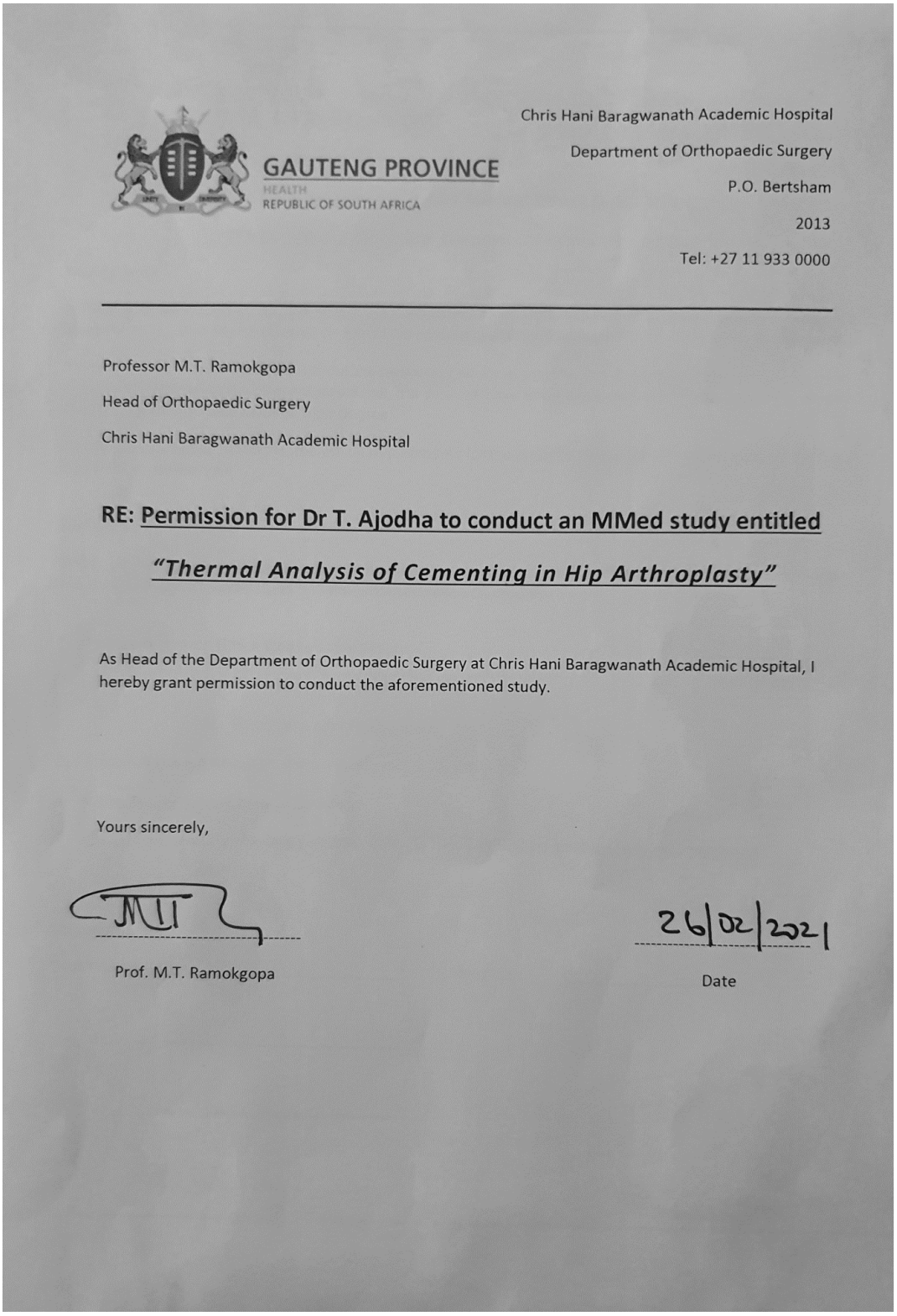
The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- **Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.**
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

Recommended
(On behalf of the MAC)
Date: 12/03/2021

Approved/Not Approved
Hospital Management
Date: 16/03/2021

Appendix F: HOD permission letter



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Chris Hani Baragwanath Academic Hospital
Department of Orthopaedic Surgery
P.O. Bertsham
2013
Tel: +27 11 933 0000

Professor M.T. Ramokgopa
Head of Orthopaedic Surgery
Chris Hani Baragwanath Academic Hospital

RE: Permission for Dr T. Ajodha to conduct an MMed study entitled

"Thermal Analysis of Cementing in Hip Arthroplasty"

As Head of the Department of Orthopaedic Surgery at Chris Hani Baragwanath Academic Hospital, I hereby grant permission to conduct the aforementioned study.

Yours sincerely,

Prof. M.T. Ramokgopa

26/02/2021
Date

Appendix G: South African Orthopaedic Journal Guidelines

Criteria for publication

- The article falls within the scope of the journal.
- Methods, statistics, and other analyses are performed to a high technical standard and are described in sufficient detail.
- Results reported have not been published elsewhere.
- Conclusions are presented appropriately fashion and are supported by the data.
- The article is presented in an intelligible fashion and is written in standard English (British usage).
- The research meets all applicable ethical standards.
- The article adheres to guidelines provided in the instructions for author's section.

Guidelines for authorship

- Each author should participate and is responsible for the content and design of the study, the preparation of the manuscript and its revisions, and final approval.
- In order to qualify for authorship, authors should satisfy all four the criteria for authorship as specified by the ICMJE:
    1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
    2. Drafting the work or revising it critically for important intellectual content; AND
    3. Final approval of the version to be published; AND
    4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Other 'contributors' or 'collaborators' can be acknowledged at the end of the manuscript together with their contribution. Those whose contributions do not justify

authorship may be acknowledged individually or together as a group under a single heading (e.g., “Clinical Investigators” or “Participating Investigators”), and their contributions should be specified (e.g., “served as scientific advisors,” “critically reviewed the study proposal,” “collected data,” “provided and cared for study patients”, “participated in writing or technical editing of the manuscript”.

- The South African Orthopaedic Journal accepts a maximum of 8 authors per article. If there are more than eight authors, the first eight authors must be listed along with the group name at the end. The remaining authors and their affiliations must then be listed in an appendix.
- On submission of your article, the ORCID (Open Researcher and Contributor ID) identifier of at least the corresponding author will be required. ORCID provides a persistent digital identifier that distinguishes you from every other researcher and supports automated linkages between you and your professional activities, ensuring that your work is recognised. To register and find more information, please visit: http://orcid.org

Registration of clinical trials

- A clinical trial is defined as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects of health outcomes. Interventions include drugs, surgical procedures, devices, behavioural treatments, dietary interventions, and process-of-care changes.
- Clinical trials should be registered in a public trials registry in accordance with International Committee of Medical Journal Editors
- Trials must be registered and approved by the relevant authorities before the onset of patient enrolment.

- The Medicines Control Council (MCC) reference number and the SA National Clinical Trial Register (SANCTR) registration number should be included at the end of the abstract of the article.
- Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) do not require registration.

Reporting guidelines

- All articles should be prepared in accordance with the guidelines relevant to the study design, as described in the Equator Network Guidelines (https://www.equator-network.org/reporting-guidelines/)
- Randomised trials should be accompanied by a flow diagram that illustrates the progress of patients through the trial, including recruitment, enrolment, randomisation, withdrawal and completion, and a detailed description of the randomisation procedure.

Reporting of statistics

In terms of the statistical reporting, the Equator Network advises on the use of the SAMPL guideline: https://www.equator-network.org/2013/02/11/sampl-guidelines-for-statistical-reporting/

The SAMPL guidelines provide two guiding principles

1. *"Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results."* When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as *P* values, which fail to convey important information about effect size.
2. *Provide enough detail that the results can be incorporated into other analyses.* This requires reporting the descriptive statistics from which other statistics are derived, such

as the numerators and denominators of percentages, especially in risk, odds, and hazards ratios. Likewise, P-values are not sufficient for re-analysis. Needed instead are descriptive statistics for the variables being compared, including sample size of the groups involved, the estimate (or effect size) associated with the P-value, and a measure of precision for the estimate, usually a 95% confidence interval.

Some specific guidelines applicable to the SAOJ:

- Consistency is one of the most important factors in presenting a well-formatted, professional manuscript.
- The nature of the measurements and variables reported on will often dictate the amount of precision required. Report numbers - especially measurements? with an appropriate degree of precision. For ease of comprehension and simplicity, round to a reasonable extent.
- The recommendation is to report the number of decimals that have both clinical and statistical meaning and consistently reporting all other variables in the same manner.
- Note: Generally, for descriptive purposes, percentages are reported as whole numbers except when dealing with really large sample sizes
- At least for the primary outcomes, report a measure of precision (a confidence interval).
- Although not preferred to confidence intervals, if desired, *p* values should be reported as equalities to three decimal places (e.g., $p = 0.031$ and not as inequalities: e.g., $p < 0.05$). Do NOT report NS; give the actual *P-value*. The smallest *P*-value that needs to be reported is $P < 0.001$.
- Report numerators and denominators for all percentages
- Summarize data that are approximately normally distributed with means and standard deviations (SD). Use the format: mean (SD) not mean?
- Summarize data that are not normally distributed with medians and inter-percentile ranges, ranges, or both.

- Do NOT use the standard error of the mean (SE) to indicate the variability of a data set. Use standard deviations, inter-percentile ranges, or ranges instead.

Formatting examples:

- $p = 0.028$ or $p < 0.001$
- (43% vs 21%; p = 0.002)
- (odds ratio (OR) 0.38; 95% confidence interval (CI) 0.71 to 1.82; $p = 0.822$) or after first use (OR 1.62; 95% CI 1.41 to 1.86; $p < 0.001$)
- *Descriptive stats normal distribution:* mean age 36 years (SD 4 years) or 36 years (SD 4; range 40 to 97 years)
- *Descriptive stats non-normal distribution:* median age 36 years (IQR 44 to 88 years) or 36 years (IQR 44 to 88 years; range 40 to 97 years)
- *Descriptive stats percentage:* (149 of 202; 74%)

Formatting of submissions

Text formatting

- Use Helvetica or Arial font, size 11.
- Use double line spacing throughout the document.
- Number the pages of the blinded manuscript consecutively.
- Use italics for emphasis.
- When referring to an article with multiple authors, please use the following format: Rabinowitz et al. published their retrospective review.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.

- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Headings

- Use no more than three levels of displayed headings.

Abbreviations

- Define abbreviations and acronyms at first mention and use consistently thereafter.

Units

- Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

Figures

- Figures should be numbered consecutively with illustration Arabic numbers 1, 2, 3, etc.
- The figure should be listed in the text as follows: … wound irrigation and splinting (*Figure 1*).
- Figures should be clear and easily understandable with a full descriptive legend stating any areas of interest and explaining any markings, letterings or notations. All figures and figure legends should be understandable as a stand-alone item, without having to read the main body of the text.
- For radiographs, please ensure you state the view used and the time point at which it was taken, as well as the demographic details of the patient if applicable.
- Please submit the original JPEG (300 dpi) or TIFF of all photographs, as well as the figure saved as a Word document. The Word version of the figure should be complete with the legend and any necessary markings such as letters or arrows.

- Figures such as graphs and algorithms should be in Word or PowerPoint in order to be editable.
- Figures should not be imbedded in the text file but should be submitted as separate individual files. Each figure should be a separate file, entitled Figure 1, Figure 2, etc.
- Remove all markings, such as patient identification, from radiographs before photographing. Clinical photos must be adequately anonymised.
- A statement of patient consent for clinical photographs must be provided on the title page.
- In images depicting X-rays of children there should exhibit adequate shielding of radiation.
- All line or original drawings must be done by a professional medical illustrator.
- We accept a maximum of six figures. You may apply to the Editor-in-Chief for permission to include more figures if considered critical to the clarity and completeness of the submission.
- Do not submit any figures, photos, tables, or other works that have been previously copyrighted or contain proprietary data unless you have obtained and can supply written permission from the copyright holder to use that content.

Tables

- Tables should carry uppercase Roman numerals, I, II, III, etc.
- Tables should always be cited in the text in consecutive numerical order.
- The table should be identified in the text as follows: Details of results are listed in *Table I*. Or, alternatively,? high-energy trauma that is often associated with these fractures (*Table II*).
- Tables should be used to present information in a clear and concise manner. All tables should be understandable without the main text.
- For each table, please supply a table heading explaining the components of the table.

- Identify any previously published material by giving the original source in the form of a reference at the end of the table heading.
- Footnotes to tables should be indicated by superscript lower-case letters and included beneath the table body.
- Please submit tables as editable text and not as images. They should be created using the Table tool in Word.
- Do not embed tables in the text file but submit them as separate individual files. Each table should be a separate file, entitled Table I, Table II, etc.
- We accept a maximum of eight tables.
- Do not duplicate information given already in the text.
- Do not submit any figures, photos, tables or other works that have been previously copyrighted or contain proprietary data unless you have obtained and can supply written permission from the copyright holder to use that content.

References

- References should be numbered consecutively in the order that they are first mentioned in the text and listed at the end in numerical order of appearance.
- Identify references in the text by Arabic numerals in superscript after punctuation.
- References should not be a listing of a computerised literature search but should have been read by the authors and have pertinence to the manuscript.
- Accuracy of references is the authors' responsibility, and the author is to verify the references against the original documents.
- Manuscripts in preparation, unpublished data (including articles submitted but not in the press) and personal communications may not be included in the reference listing. They may be listed in the text in parentheses only if absolutely necessary to the contents and meaning of the article.

- The titles of journals should be abbreviated according to the style used in Index Medicus, obtainable through the website http://www.nlm.nih.govshould
- The following format should be used for references:

Journal article:

Sidhu GS, Ghag A, Prokuski V, Vaccaro AR, Radcliff KE. Civilian gunshot injuries of the spinal cord: a systematic review of the current literature. *Clin Orthop Relat Res* 2013;**471**:3945-55.

Ideally, the names of all authors should be provided, but the usage of *et al*. in long author lists (more than six authors) will also be accepted: Fong K, Truong V, Foote CJ, *et al*. Predictors of nonunion and reoperation in patients with fractures of the tibia: an observational study. *BMC Musculoskelet Disord* 2013;**14**:103.

Online journal article:

Caetano-Lopes J, Lopes A, Rodrigues A, *et al*. Upregulation of inflammatory genes and downregulation of sclerostin gene expression are key elements in the early phase of fragility fracture healing. *PLoS One* 2011;**6**:e16947.

Web reference (with authors):

Cierny G, DiPasquale D. Adult osteomyelitis protocol. http://www.osteomyelitis.com/pdf/treatment_protocol.pdf.

(date last accessed 05 March 2013).

Web reference (no authors listed):

No authors listed. International commission on radiological protection. http://www.icrp.org (date last accessed 20 September 2009).

Chapter in a book:

Young W. Neurophysiology of spinal cord injury. In: Errico TJ, Bauer RD, Waugh T (eds). *Spinal Trauma*. 3rd ed. Philadelphia: JB Lippincott; 1991: 377-94.

Dissertation:

Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

Abstract:

Peterson L. Osteochondritis of the knee treated with autologous chondrocyte transplantation [abstract]. ISAKOS Congress, 2001.

Structure and content of submission

- We accept a maximum of 3 500 words, including the abstract and body of the text (excluding references).
- Exceptions to this rule may be made for systematic reviews and meta-analysis at the discretion of the Editor-in-Chief.
- Please follow the following structure when preparing your submission. Each of the following should be submitted as a separate file.
- Title page (title, authors and affiliations, corresponding author and declarations)
- Blinded manuscript (Abstract, keywords, introduction, methods, results, discussion, funding sources, conflict of interest statement, ethics statement, acknowledgements and references)
- Tables (with headings), each table as a separate file.
- Figures (with legends), each figure as a separate file.

<u>Title page</u>

Title

- The title should be concise and informative.

Author names and affiliations

- Please provide the following information for each author:
    - Full names and surname, as well as title
    - Qualifications
    - Designation
    - Affiliation and address
    - ORCID ID (see Article Submission section)
- Please check that all names are accurately spelled.
- Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate affiliation details.
- Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.

Corresponding author

- Clearly indicate who will handle correspondence at all stages of refereeing and publication, including post-publication.
- Ensure that the e-mail address and permanent address is given and that contact details are kept up to date by the corresponding author.
- Please note that the corresponding author's contact details will be provided in the final article.
- Provide the following information for the corresponding author:
    - Full names and title
    - Affiliation

- Physical address
- Postal address
- Telephone number
- E-mail address

Declarations

Authors are to insert a section at the end of the title page entitled declarations (please provide the author's name, signature and date). The following statements are required under the declarations section:

Authorship

The authors confirm that all authors have made substantial contributions to all of the following:

- The conception and design of the study, or acquisition of data, or analysis and interpretation of data.
- The drafting of the article or its critical revision for important intellectual content.
- Final approval of the version to be submitted.

Sound scientific research practice

The authors further confirm that:

- The manuscript, including related data, figures and tables, has not been previously published and is not under consideration elsewhere.
- No data have been fabricated or manipulated (including images) to support conclusions.
- This submission does not represent part of a single study that has been split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (e.g. ‘salami-publishing’).

Plagiarism

The authors confirm that the work submitted is original and does not transgress the plagiarism policy of the journal.

- No data, text or theories by others are presented as if they were the authors' own.
- Proper acknowledgements of others' work have been given (this includes material that is closely copied, summarised and/or paraphrased); quotation marks are used for verbatim copying of material.
- Permissions have been secured for copyrighted material.

Conflict of interest statement

A conflicting interest exists when professional judgment concerning a primary interest (such as the patient's welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It represents a situation in which financial or other personal considerations from authors, reviewers or editors have the potential to compromise or bias professional judgment and objectivity. It may arise for the authors when they have a financial interest that may influence their interpretation of their results or those of others. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, grants or other funding. All potential conflicts of interest need to be declared. The conflict of interest statement should list each author separately by name, e.g.,

'Author A.B. (*use initials of relevant author, not full name in order for the document to remain blinded*) has received research grants from Company A. Author B.C. has received a speaker honorarium from Company X and owns stock in Company Y. Author C.D. is a member of committee Z.'

If no conflicts of interest exist, state this as follows:

‘The authors declare they have no conflicts of interest that are directly or indirectly related to the research.’

Funding sources

All sources of funding should be declared. Also, define the involvement of study sponsors in the study design, collection, analysis and interpretation of data; the writing of the manuscript; and the decision to submit the manuscript for publication.

List all funding sources as follows:

‘This work was supported by the xxxx (grant numbers xxxx, yyyy).’

When funding is from a block grant or other resources available to a university, college or other research institution, submit the name of the institute or organisation that provided the funding.

If no funding was received, state as follows:

‘No funding was received for this study.’

Compliance with ethical guidelines

- For all publications:

‘The author/s declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.’

Available from: http://publicationethics.org/resources/international-standards-for-editors-and-authors

Institutional Review Board (IRB) ethical approval must have been given if the study involves human subjects or animals. Please provide the approval number. IRB documentation should be available upon request.

‘Prior to the commencement of the study ethical approval was obtained from the following ethical review board: *Provide name and reference number’*

- For studies with human subjects include the following:

‘All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.’

‘Informed written consent was or was not obtained from all patients for being included in the study.’

‘Consent was obtained from patients for the use of clinical photographs and these images were adequately anonymized’

- For studies with animals, include the following sentence:

‘All institutional and national guidelines for the care and use of laboratory animals were followed.’

- For articles that do not contain studies with human or animal subjects:

‘This article does not contain any studies with human or animal subjects.’

- If doubt exists whether the research was conducted in accordance with the Helsinki Declaration, the authors must explain the rationale for their approach and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study. If any identifying information about patients is included in the article, the following

sentence should also be included: Additional informed consent was obtained from all patients for which identifying information is included in this article. The Helsinki Declaration 2008 can be found at http://www.wma.net/en/30publications/10policies/b3/

Please provide the names and email addresses of two reviewers.

Title Page Example

Title of Submission

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Declarations:

Authorship

The authors confirm that all authors have made substantial contributions to all of the following:

- The conception and design of the study, or acquisition of data, or analysis and interpretation of data.
- The drafting of the article or its critical revision for important intellectual content.
- Final approval of the version to be submitted.

Sound scientific research practice

The authors further confirm that:

- The manuscript, including related data, figures and tables, has not been previously published and is not under consideration elsewhere.
- No data have been fabricated or manipulated (including images) to support conclusions.
- This submission does not represent part of a single study that has been split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (e.g. 'salami-publishing').

Plagiarism

The authors confirm that the work submitted is original and does not transgress the plagiarism policy of the journal.

- No data, text or theories by others are presented as if they were the authors' own.
- Proper acknowledgements of others' work have been given (this includes material that is closely copied, summarised and/or paraphrased); quotation marks are used for verbatim copying of material.
- Permissions have been secured for copyrighted material.

Conflict of interest statement

John Smith declares that he has no conflict of interest. Paula Taylor has received research grants from Drug Company A.

Funding sources

No funding was received for the purposes of performing this study.

Compliance with ethical guidelines

The author/s declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.

Prior to the commencement of the study ethical approval was obtained from the following ethical review board: *Provide name and reference number.*

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed written consent was or was not obtained from all patients for being included in the study.

Consent was obtained from patients for the use of clinical photographs/ and these images were adequately anonymised.

Author Name	**Signature**	**Date**
J Smith		15/8/2017
P Taylor		16/8/2017

Blinded manuscript

To ensure a blinded review, the main body of the manuscript should not contain any identifying information, including author's names, institutions or affiliations. Please do not include the name of the ethics committee, this information should be provided in the title page.

Abstract

- A structured abstract (maximum of 350 words) summarising the most important points in the article is required.
- The abstract consists of four paragraphs with the subheadings:
    - Background (must include the aim of the study)
    - Patients and methods
    - Results
    - Conclusion
- References should be avoided. Avoid uncommon abbreviations. If essential, they must be defined at their first mention in the abstract itself.

Keywords

- Immediately after the abstract, provide a maximum of six keywords using standard searchable terms. These keywords will be used for indexing purposes.

Level of evidence

- Level 1 to 5.
- Please follow the level of evidence guidelines provided by the Oxford Centre for Evidence-Based Medicine (OCEBM); version 2.1.
- Available from: OCEBM Levels of Evidence Working Group. 'The Oxford Levels of Evidence 2'. Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

Introduction

- The introduction should contextualise the study by providing the background to the research; explain the problem that is to be addressed and provide the rationale for the study.
- Briefly outline the relevance of the study with respect to the current literature. Avoid a detailed literature survey or a summary of the results.
- The last sentence should outline the research question or hypothesis.

Patients (or Materials) and methods

- State the methods, outcome measures, and selection criteria. The following aspects need to be described:
    - The study design and research methodology
    - Whether randomisation (with methods) was applied
    - If case-controlled, how the controls were selected

    - The time period under review
    - Number of patients/subjects under investigation and why this number was chosen
    - Inclusion and exclusion criteria
    - Case and outcome definitions
    - A description of the procedure or intervention, including post-operative protocol
    - The outcome measures or scores used
    - The minimum follow-up period
    - Statistical analysis paragraph. This should be included at the end of this section to detail statistical tests and package used, the reasons why these tests were used, and what p-value was considered statistically significant. A power analysis is recommended for studies comparing two or more groups.
- Provide sufficient detail so that another researcher can replicate the study.
- The reader should understand from this description all potential sources of bias such as referral, diagnosis, exclusion, recall or treatment bias. This includes the manner in which investigators selected the patients. Consecutive inclusion implies all patients with a given diagnosis are included, while selective implies patients with a given diagnosis but selected according to certain explicit criteria (e.g., state of disease, choice of treatment).
- Do not describe standard procedures for common operations. Only include new procedures or adaptations to standard procedures.
- If you name any specific product, it requires the manufacturer's name, city and state/country.
- Present information in the narrative format and use the past tense.
- Where relevant, tables or figures may be included to provide information more clearly.
- Generally, no data should be presented in this section.

Results

- Describe the relevant results and analysis thereof.
- Provide details of the number of patients included and excluded, as well as the reason for exclusion.
- It is important to state the follow-up period (mean and range).
- The results can be broken down into separate sections, e.g. Treatment, Functional outcome, Complications, etc.
- Tables may be used but avoid repeating data reported in the text in the tables.
- All appropriate data should be presented as means with ranges, not with standard deviations (SDs). Medians should only be used when the data is skewed, accompanied by an interquartile range (IQR).
- Avoid using percentages in studies involving well under 100 subjects.
- All results must be backed up with p-values or survivorship analysis. All Kaplan-Meier data should be presented with confidence intervals. Always present exact absolute p-values, whether significant or not, unless $p<0.001$.
- However, *P-values* do not always convey the entire picture and where relevant, the confidence interval will also be required (in addition to the power of the study reported in the methods section).

Discussion

- The question or hypothesis stated at the end of the introduction should be discussed and either supported or rejected.
- The results must be interpreted clearly, and any deficiencies expressed. All possible confounding factors, sources of bias or weaknesses in the study should be identified.
- Explore the significance of the results of the work rather than repeating the results.
- The discussion must point out the relevance of the work described in the paper and its contribution to current knowledge.
- Explain what can be deduced from the results and how will it affect clinical practice.

- Include a review of the relevant literature, placing the results of the study in the context of previous work in this area.
- Discussion of relevant prior research and references must be concise. Avoid extensive citations and discussion of published literature emphasize previous findings that agree (or disagree) with those of the present study.
- Do not repeat the introduction.
- Present the limitations of the study and suggest how the study could have been improved for a future study.
- Avoid making inferences from non-significant trends unless you believe your study is adequately powered to answer the question; in that case, provide a power analysis.

Conclusion

- Provide a summary statement that conveys the conclusions of the findings.
- Do not draw conclusions not supported by the data obtained from the specific study presented.

Ethics statement

- For studies involving human subjects, please include an ethics statement as follows: 'All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.'
- For animal studies, please include the following ethical statement: 'All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.'

- If the study did not involve human or animal subjects, state that: ‘This article does not contain any studies with human participants or animals performed by any of the authors.’
- Please also include an informed consent statement: ‘Informed consent was obtained from all individual participants included in the study.’
- Alternatively, for retrospective studies, please add the following sentence: ‘For this study formal consent was not required.’
- If identifying information about participants is available in the article, the following statement should be included: ‘Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.’

Acknowledgements

- Acknowledgements should be placed at the end of the discussion and before the references.
- In this section, persons who were involved but did not earn authorship can be acknowledged.
- Statements should be brief. A person can be thanked for assistance or comments.
- Do not include contributions by editors or referees.

Author contributions

- Please state the contributions of each author
- For example: ‘A.B contributed to the study conceptualisation, design, data analysis and manuscript preparation. C.D. contributed to data collection and manuscript preparation. E.F. contributed to ....’
- The types of contributions are:
    - Conceptualisation and design
    - Data collection or contribution

- Data analysis
- Manuscript preparation
- Other contributions (please specify)

References

- Please refer to the section on Formatting of submissions.

Tables and figures

- Tables and figures should not be imbedded in the text file but should be submitted as separate individual files. Each table should be a separate file, entitled Table I, Figure 2, etc.
- Each table and figure should be provided with a heading or legend.
- Please refer to the 'Formatting of submission' section for further guidelines.

Case reports

In addition to the preceding guidelines the following applies:

- The following headings need to be adhered to in the body of the manuscript:
  - Abstract
  - Keywords
  - Background
  - Case report
  - Discussion
  - Conclusion
  - Ethics statement
  - References

- Abstract: Minimum 250 words (350 maximum), using the following headings:

    - Background
    - Case report
    - Discussion
    - Conclusion
- Statement of informed consent must be included in the ethics statement.

Current Concepts Review Article (by invitation only)

General Guidelines:

- A narrative review will suffice (and systematic or scoping review not necessary)
- A thorough literature review needs to be done prior to writing the manuscript to ensure that the author is well acquainted with the current concepts related to the topic (with emphasis on the most recent developments)
- A balanced and unbiased view of the current clinical aspects of the topic.
- Focus on clinical aspects like diagnosis and treatment.
- Discuss controversies and state both sides of the argument.
- Avoid extensive discussion of basic science (anatomy/physiology/pathology) aspects, except for some really novel and clinically relevant new developments in the field.
- The topic may be adapted, but only with the permission of the Editor-in-Chief.

Outline of Article:

- Abstract = One paragraph, no headings, ≤350 words.
- Introduction = Brief introduction to the topic
- Contents = Please use headings (in bold) and sub-headings (in italics) to structure the manuscript in a reader-friendly manner
- South African context = Discuss matters which may be particularly relevant or unique to the South African clinical setting.

- Learning points = Make use of tables to summarize important learning points
- Conclusion = Brief evidence-based conclusion and summary
- Conflict of interest statement
- References = As usual