

A review of fluoroscopy guided percutaneous transpedicular spinal biopsies at Charlotte Maxeke Johannesburg Academic Hospital



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Declaration

I, Shivam Bhikha 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)

21st day of July 2023 in Johannesburg

Dedication

I would like to dedicate this work to my beloved Guru, Babaji.

Thank you for your infinite blessings and unconditional love.

Gratitude to my wife Puja and baby daughter Tara, you've been a rock at my side without whom I could not accomplish this. Thank you for your sacrifice.

Thank you to my parents Kishore and Sapna for the constant encouragement and motivation. A special thank you to my siblings Vishal and Reyna, your support and guidance has been invaluable.

Bless you, Love you all infinitely.

“You are the creator of your own destiny”

-Dr Avdoot Shivanand

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Nomenclature

AIDS	Acquired Immune Deficiency Syndrome
ANOVA	Analysis of Variance
AP	Anterio-Posterior
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
CT	Computed Tomography
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
INR	International Normalised Ratio
MRI	Magnetic Resonance Imaging
NHLS	National Health Laboratory Service
OPD	Out-Patient Department
PACS	Picture Archiving and Communication System
PCR	Polymerase Chain Reaction
PI	Primary Investigator
TB	Tuberculosis

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Abstract

Background

When a suspicious spine lesion is identified, an accurate diagnosis based on tissue biopsy is required in order to direct towards the correct treatment protocol. Several studies have demonstrated that the percutaneous fluoroscopy guided biopsy of a vertebral lesion is a safe, effective and accurate diagnostic tool and is preferred over open techniques when possible. Thereby obviating the need for major surgery and expediting appropriate management of patients. Fluoroscopy guided percutaneous transpedicular vertebral biopsies have a varying complication rate from 0 to 10%.

Study Aim

The aim of the study was to review percutaneous fluoroscopy guided transpedicular spinal biopsies at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) over a 6-year period.

Methodology

The research design was a retrospective study of patients who underwent a percutaneous transpedicular spinal biopsy under fluoroscopy guidance. Research site was the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). The time period for the study covered a span of six years i.e. from 1st of January 2016 to the 31st of December 2021.

The CMJAH spine theatre registry and hospital records system were used as the source for data collection. Statistical analysis was conducted to determine the effectiveness of the transpedicular spinal biopsy, compare spinal pathology amongst age and gender and to identify any complications.

Results

The study analysed 180 biopsies, with 120 yielding a positive result (66.67%). Of these 8.9% were pyogenic infection, 18.4% neoplasm, 36.7% Tuberculosis and 2.7% other. There were 75 males and 105 females with an age range between 9 and 86 years and mean age of 43.44. Comparing age and gender distribution showed no statistical significance ($p = 0.778$). Comparing biopsy result and gender showed no statistical significant relationship ($p = 0.970$). Comparison of biopsy result with age showed no statistical significant association ($p = 0.545$). Four complications were identified (2.22%).

Conclusion

The study showed that fluoroscopy guided percutaneous transpedicular biopsy is an effective modality in obtaining thoracic and lumbar vertebrae specimens in all age groups for a wide spectrum of spinal pathological lesions. The study also proves that it is a safe procedure with no long term complications.

Keywords

Spine lesion, Transpedicular, Percutaneous biopsy, Fluoroscopy guided, Spinal Tuberculosis, Spinal Metastases

Level of Evidence: III (retrospective, observational analysis)

INTRODUCTION

Background

Patients referred to the spine unit undergo clinical examination, laboratory tests and non-invasive imaging studies. Radiological investigations such as X-rays, magnetic resonance imaging (MRI) and computed tomography (CT) assist to identify pathological lesions in the spine.^(1,2) These radiological investigations and bone scan tests have an increased sensitivity but are less specific.⁽¹⁾ Hence to arrive at the correct and definitive diagnosis histopathological or microbiological confirmation is needed. This in turn allows the treating physicians to determine the correct treatment protocols and further management of the disease.^(3,4)

Infections, metastatic lesions, and primary malignancies are among the most common pathological lesions of spine.⁽¹⁾ Lee *et al.* (2020) states that early specific diagnosis for spinal infections and tumours has been pertinent in reducing patient mortality and morbidity as well as being cost effective in the long run.⁽⁵⁾ A definitive and specific diagnosis necessitates the obtaining of biopsy samples for histopathological testing and culture studies.⁽⁶⁾ This directs towards the correct treatment regimen such as surgical intervention, radiation therapy, chemotherapy, and/or targeted antibiotic treatment.⁽²⁾ Chamakeri *et al.* (2017) states that the gold standard method (98% of accuracy) of obtaining a biopsy specimen for the diagnosis of bone lesions is *via* an open biopsy, however this is accompanied with the risk of further associated morbidity.^(2,7) An open spinal biopsy requires invasive and extensive surgery leading to possible complications of neural or vascular damage and excessive blood loss. To negate such complications, needle biopsy techniques which are less invasive have been developed.^(4,8)

Percutaneous image-guided spinal biopsy techniques have been developed to accurately diagnose suspected spinal neoplasms or to confirm the diagnosis of infective spondylodiscitis. In addition, indications include the diagnosis of atraumatic vertebral fractures of unknown origin with differentiation between osteoporotic, inflammatory and neoplastic fractures.^(5,9,10) Dave *et al.* (2009) states that a percutaneous transpedicular spinal biopsy has both a high specificity and sensitivity when confirming a diagnosis, due to the sample undergoing specific histopathological and bacteriological tests. This then offers a clear directive in the further management of these patients.^(11,12)

Layton *et al.* (2006) demonstrated that the transpedicular route can be used to take a biopsy specimen from a disc space and both adjacent vertebral endplates by a modified

vertebroplasty approach.^(13,14) Imaging assists the user to safely navigate a biopsy needle *via* a precise route through the vertebral body without injury to neural or vascular structures. Imaging modalities used for guidance during percutaneous biopsy can be CT, MRI or fluoroscopy using an image intensifier.^(15–17)

The “all-through-pedicle” procedure is a concept encompassing a true safe zone, which has several applications including bone biopsy, surgery for bone graft, pedicle screws, vertebroplasty, and kyphoplasty.⁽¹⁸⁾

When performing a percutaneous transpedicular spinal biopsy, a unilateral pedicular channel is created, giving access to at least 50% of the vertebral body.⁽¹⁹⁾ The narrow biopsy track conserves the supporting tissue, thereby avoiding localised haemorrhage and contamination or injury to surrounding tissue. The relatively narrow wound heals timeously and does not complicate with radiotherapy.^(10,20)

In a review article by Nourbakhsh in 2015 it is stated that spine biopsy complications vary at a rate from 0 to 10%. Complications associated with percutaneous transpedicular biopsy can be divided into early and late. Intra-operative (early) complications include bleeding (haematoma), pneumothorax and neural injury. Late complications include radiculopathy, paraplegia, local and systemic infections including meningitis.^(11,21)

Rationale

In a study by Liang *et al.* (2019), it was determined that percutaneous image guided biopsy of a vertebral lesion is a safe, effective and accurate diagnostic tool and is preferred over open techniques when possible.⁽²²⁾ Chang *et al.* (2001) further states that the fluoroscopy guided percutaneous transpedicular vertebral biopsy obviates the need for major surgery and can expedite appropriate management of patients. Many of the potential complications of more invasive investigative procedures can also be avoided with the transpedicular approach.^(23,24)

The advancement of imaging modalities has enhanced the diagnosing and differentiating of spinal lesions. However, an accurate diagnosis based on histopathological confirmation is still required for directed management, hence the need for biopsy.^(10,25) The common indications for a vertebral biopsy are histological diagnosis of a focal vertebral lesion; identification of suspected or known spinal metastasis; diagnosis of spondylodiscitis for histopathology and microbiological studies.^(20,26,27)

In a 2020 study Kelly *et al.* performed a 7-year retrospective review of spinal biopsy results at a single South African academic hospital. Through this study they were able to determine that 84% of the biopsies performed were open and 16% were percutaneous image guided biopsies. They acknowledged that percutaneous biopsies were safer, more cost effective and incurred less blood loss; however they still had a significantly higher percentage of open compared to closed biopsies. The above finding was attributed to spinal unit protocol and facilities available, a substantial percentage of the biopsies performed was for spinal Tuberculosis (TB) and usually this forms part of a mini-costotransversectomy procedure to drain a paravertebral abscess and obtain a specimen, as part of their study this was recorded as an open biopsy.⁽³⁾

Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) is a quaternary level state hospital based in Johannesburg and serves as a referral centre covering a large feeder area. The protocol within the CMJAH spine unit is that any patient presenting with a suspected spinal infection, neoplasm or lesion of interest requires a biopsy sample for a definitive diagnosis. The biopsy modality of choice is a fluoroscopy guided percutaneous transpedicular biopsy. There are however exceptional situations in which an open biopsy is necessary such as a patient presenting with deteriorating neurology and urgent decompression and stabilisation is required, a biopsy sample is then taken at this point.

Fluoroscopy guided percutaneous transpedicular spinal biopsies are performed regularly within the spine unit at CMJAH. Based on the above literature analysis; there is justification for a study that would audit and quantify the indications and outcomes of percutaneous spinal biopsies and allow us to ascertain the types of pathology present within our patient demographics as well as evaluate any complications that may have arisen from this procedure. Therefore the aim of the study would be to review percutaneous fluoroscopy guided transpedicular spinal biopsies at CMJAH over a 6-year period.

OBJECTIVES

The objectives of the study are:

- To determine the effectiveness of the transpedicular spinal biopsy
- To compare the spinal pathology amongst age and gender
- To identify any complications following the transpedicular spinal biopsy

METHODOLOGY

The research design was a retrospective study of patients who underwent a percutaneous transpedicular spinal biopsy under fluoroscopy guidance. The focus of the study (data collection) was a single centre, namely the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). The time period for the study covered a span of six years i.e. from 1st of January 2016 to the 31st of December 2021.

The **inclusion criterion**: any patient who underwent a percutaneous transpedicular spinal biopsy under fluoroscopy guidance at CMJAH within the stipulated time-frame (1st of January 2016 to the 31st of December 2021).

The **exclusion criterion**: patient files that have incomplete information or poor record keeping were not included in the study.

DATA COLLECTION

In order to perform a retrospective analysis and populate the data collection sheet, the CMJAH spine theatre registry as well as the hospital records system were used as the primary source for data collection, furthermore the spine out-patient department (OPD) files and Picture Archiving and Communication System (PACS) were used to obtain any missing data. The histological findings were accessed from the National Health Laboratory Service (NHLS) *via* the online TrakCare portal.

The following data were captured and placed in a spread sheet format: study number, age, gender, biopsy level, biopsy result, complications and comments.

ETHICS

Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (Clearance certificate number: **M210806**), as well as the Hospital Research Committee and Management. Permission to access NHLS TrakCare portal and PACS was granted by the relevant authorities.

STATISTICAL ANALYSIS

Statistical analysis was performed using IBM SPSS Statistics version 27.0. Descriptive statistics were reported using medians, frequencies and percentages to represent the data.

Categorical variables (qualitative data) were analysed using the following tests: Independent sample t-test was used to test if age was equal for male and female patients, one-way Analysis of Variance (ANOVA) was used to test if age was equal for biopsy result, and Chi-squared test for independence to test for association between gender and biopsy result.

For this study the confidence interval was set at 95% and a *p*-value of less than 0.05 was considered statistically significant. All results have been depicted graphically in tables and graphs such as histograms, bar graphs, box and whisker plots and pie charts.

DEFINING THE STUDY VARIABLES BASED ON OBJECTIVES

- To determine the effectiveness of the transpedicular spinal biopsy:
 - Calculate a percentage of positive yield from the biopsies. A positive yield is regarded as a biopsy that led to a specific result/diagnosis.
 - Spinal pathology was divided into four main categories: spinal TB, neoplastic, pyogenic and other.
- To compare the spinal pathology amongst age and gender:
 - To ascertain any statistical significance between the groups in terms of gender distribution, age, spinal pathology and biopsy level.
- To determine any complications that may have arisen due to the biopsy:
 - A complication rate will be calculated and displayed in the form of a percentage.

RESULTS

Over the six-year period of the study (1st of January 2016 to the 31st of December 2021) 193 patients underwent a percutaneous transpedicular spinal biopsy under fluoroscopy guidance at CMJAH. Of the 193 patients, only 180 were eligible for inclusion in the study. The remaining 13 patients were excluded due to incomplete/missing data (see Figure 1).

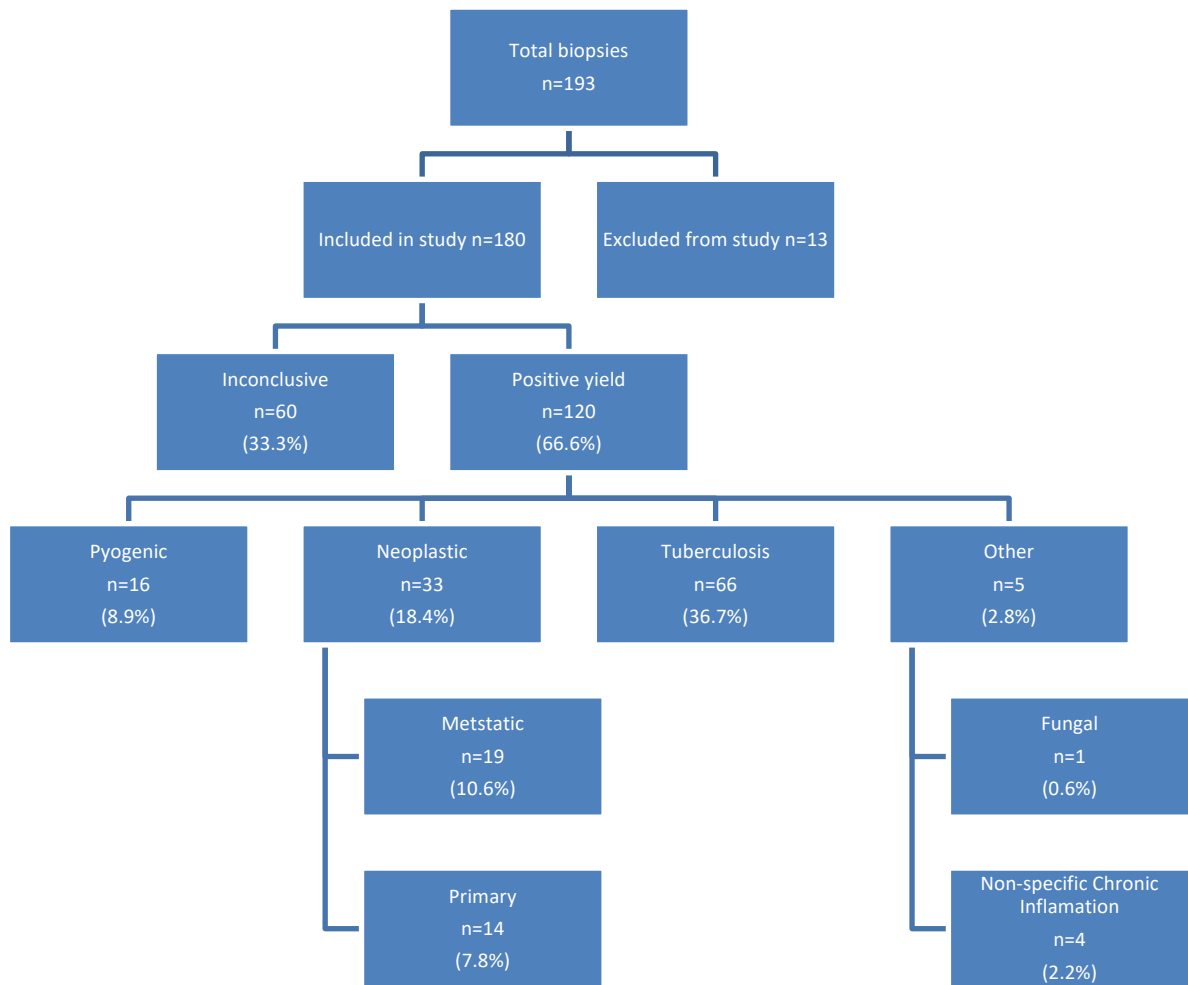


Figure 1. Flow chart demonstrating outcome of percutaneous biopsies

Effectiveness Yield

Regarding the effectiveness of the transpedicular spinal biopsy: 180 biopsies were included in the study, of the 180 biopsies 120 biopsies yielded a positive result with the remaining 60 leading to an inconclusive result whereby no definitive diagnosis could be obtained.

A positive yield is regarded as a biopsy that led to a specific diagnosis. This subtends to a positivity rate of 66.67%. For the purposes of this study, the positive yield results were subdivided into four broad categories, namely: Pyogenic, Neoplastic, TB and Other (see Figure 2).

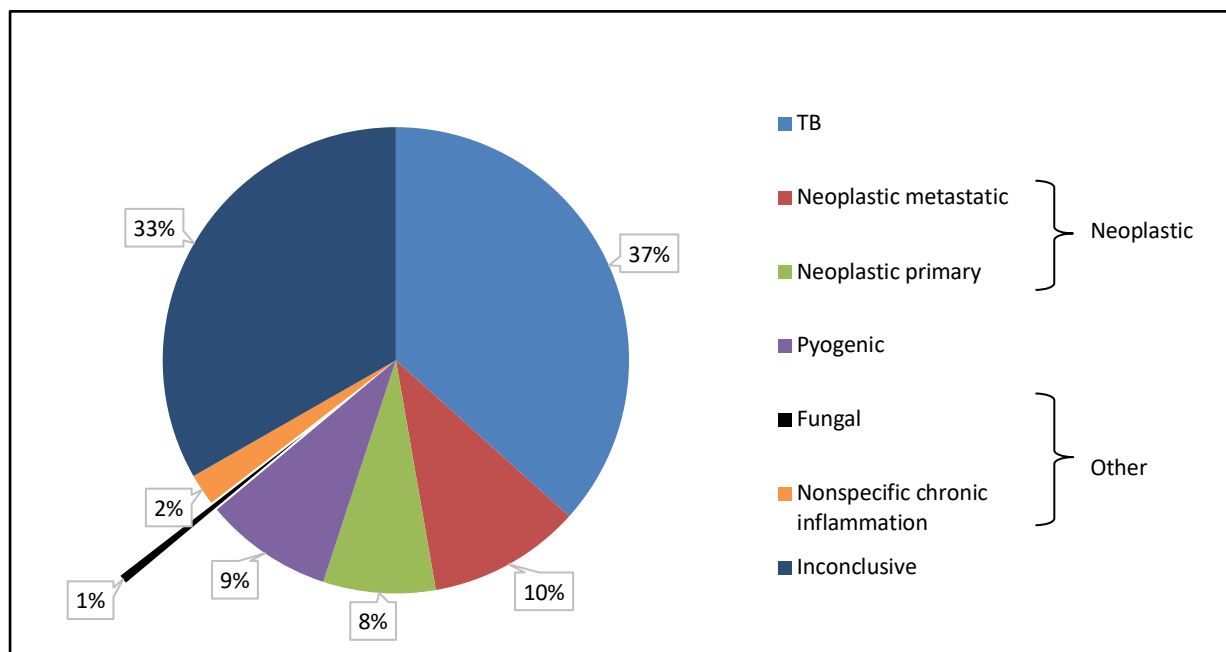


Figure 2. Percentage patients (n = 180) by biopsy result

Analysis of biopsy results

Pyogenic

Of the positive yield of biopsy results, 8.9% were confirmed to be pyogenic infection. Further analysis revealed the causative bacteria in six of the 16 cases to be *Staphylococcus aureus*. Other causative organisms found included two cases of *Acinetobacter baumannii* as well as one case of each of the following organisms: *Enterococcus faecium*, *Escherichia coli*, *Enterococcus faecalis*, *Proteus mirabilis*, *Bacillus species*, *Morganella morganii*, *Streptococcus salivarius* and *Streptococcus agalactiae*.

Neoplasm

A diagnosis of neoplasm made up 18.4% of the positive yield, this subdivided showed 19 cases of metastatic malignancy and 14 cases of primary spinal neoplasm. Further analysis revealed that the primary origin of the metastasis were either from breast (four cases); colorectal (four cases); lung (three cases); liver (one case); gynaecological tract (one case); prostate (one case); melanoma (one case) or indeterminate origin but had histological features of metastatic carcinoma (five cases). Primary spinal neoplasm included histological features of multiple myeloma (eight cases), lymphoma (three cases) or haemangioma (three cases).

Tuberculosis (TB)

Of the 180 biopsies included in the study, 66 tested positive for TB. Thus equating to a positive yield of 36.7% – thereby making up the greatest proportion of positive yield results. To confirm TB positivity, biopsy specimens were subjected to a Ziehl-Neelsen stain to analyse for the presence acid-fast bacilli as well as histological examination to identify foci of necrotising/caseating granulomatous inflammation which is consistent with an active mycobacterial infection. Moreover, TB testing included PCR method molecular/genotypic screening (Xpert MTB/Rif Ultra) to detect Mycobacterium TB complex and to isolate if susceptible to Isoniazid and Rifampicin.

Other

Of the positive yield of biopsy results, five cases were categorised as 'other'. These included four biopsies yielding non-specific chronic inflammation. On histological examination, a focus of calcification was noted, as well as scattered foci of chronic inflammatory cells. In these specimens the differential included causes of inflammation possibly due to auto-immune conditions, fracture or osteoporosis. In these cases neoplasm and infection were ruled out. Under the category of 'other' biopsy results there was only one specimen that flagged positive on mycology culture, with the fungus isolated being *Rhodotorula mucilaginosa*.

Inconclusive

One third of total biopsies were categorised as 'inconclusive' (60 of 180). These biopsy results could not lead to a final or definitive diagnosis and in many cases it was recommended to repeat the biopsy. Pertaining to reasons given by the laboratory for the inability to reach a conclusive diagnosis, was that in majority of these cases the specimen supplied was inadequate for histological investigation. These biopsy samples only contained cortical bone with no representation of bone marrow or cancellous bone deeming the specimen suboptimal for further analysis. There was also a report that stated that the specimen only comprised of blood and a small fragment of bone deeming it poorly preserved and suboptimal for histological assessment. The report further commented that specimen should have been preserved in a 10% formalin solution.

Demographics

Gender Distribution

Of the 180 patients that underwent a transpedicular spinal biopsy, 75 participants were male and 105 participants were female. This accounted for a ratio of 3:2 females to males. Figure 3 below demonstrates the gender distribution based on percentage.

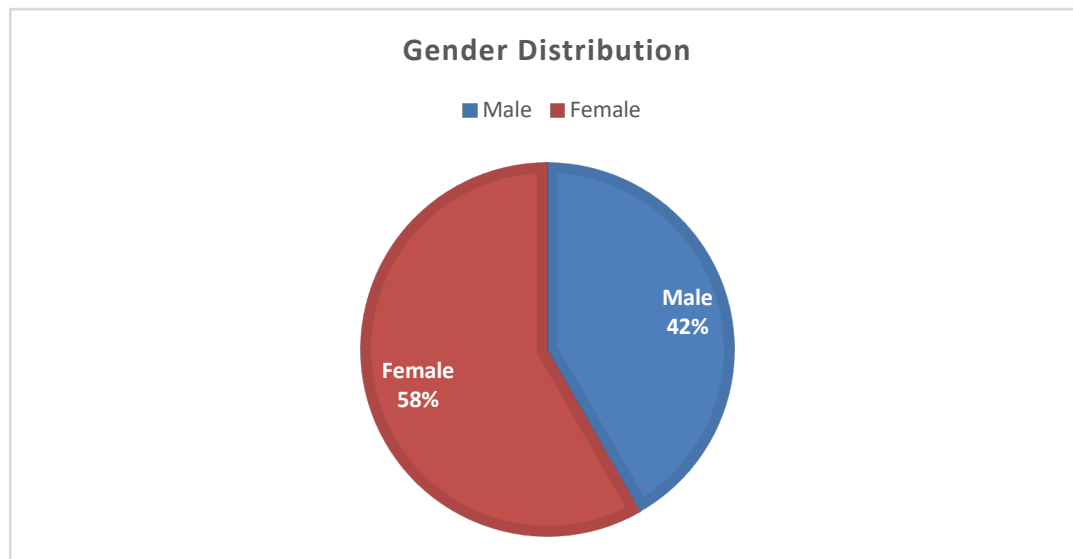


Figure 3. Percentage of patients by gender (n = 180)

Age Distribution

With regards to statistical analysis of age distribution of the patients that underwent a transpedicular spinal biopsy, the range was between 9 and 86 years with the median being 43 years and the mean being 43.44 years. There was a standard deviation of 13.94. A wide range of age is represented with more patients in the middle age ranges. Figure 4 below demonstrates the age range distribution in the study population.

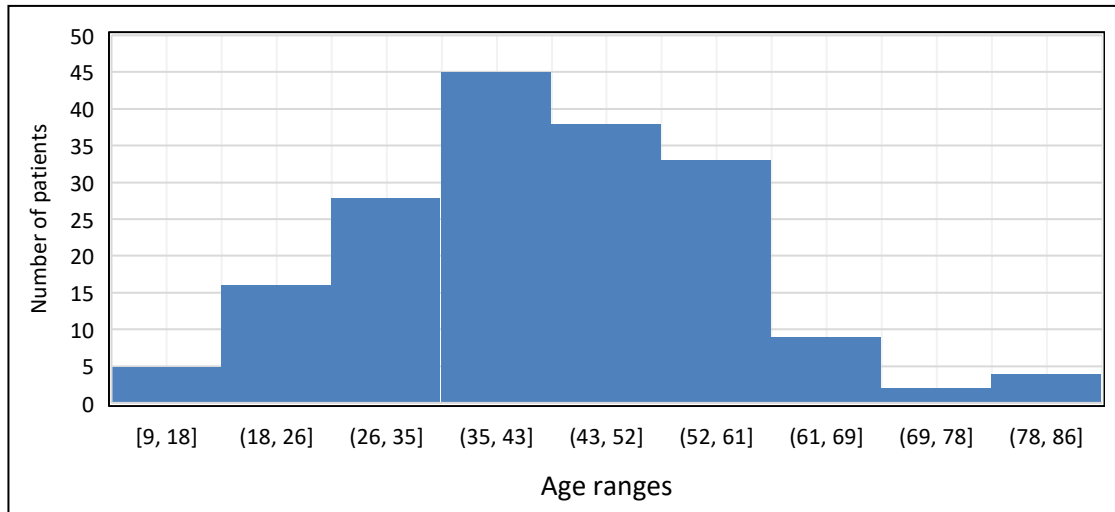


Figure 4. Histogram of age range distribution (n = 180)

Comparison Age and Gender Distribution

With regards to statistical analysis, the independent t-test was used to verify if age distribution was equal for male and female patients. The results yielded that there is no significant difference in age distribution for male and female patients that underwent spinal biopsies in our study population ($t = 0.282$, $df = 178$, $p = 0.778$).

The youngest male patient was 12 years in comparison to the youngest female patient being 9 years. The oldest male patient was 80 years whilst the oldest female patient was 86 years. The median male age was 43 years with the median female age being 42 years. Figure 5 below highlights the comparison of age representation between male and female groups.

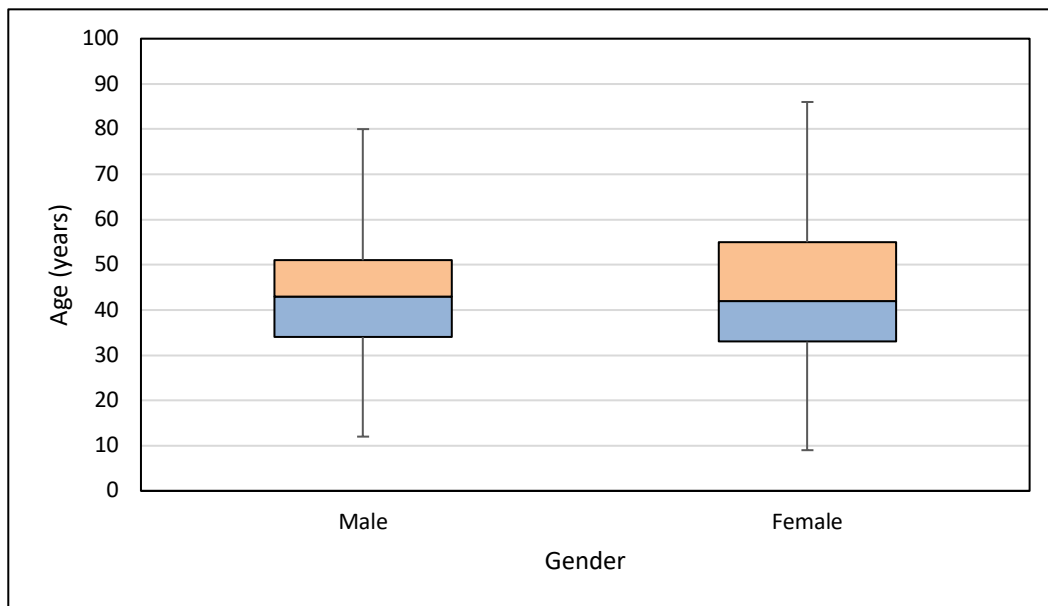


Figure 5. Box and whisker plots of age for male (n = 75) and female (n = 105) patients

Comparison of Biopsy Result and Gender Distribution

In search for an association between biopsy result and gender of patients that underwent a percutaneous spinal biopsy, it was found that there was no statistical significant relationship between gender and biopsy result (Pearson Chi squared = 0.905, df = 5, $p = 0.970$).

Within our study population the comparison of biopsy results between genders found that TB positive cases were identified in 34.7% of males as compared to 38.1% of females. Neoplastic metastatic lesions were found in 10.7% males and 10.5% females. Neoplastic primary lesions were identified in 8% males compared to 7.65% females. Pyogenic infections were identified in 9.3% males as opposed to 8.6% in females. Non-specific chronic inflammation had positive yield in 1.3% of males and 2.9% of females. The solitary fungal case was identified in a female. Results were inconclusive in 36% of males and 31.4% females. Figure 6 below graphically demonstrates the comparison of male versus female percentages per biopsy result.

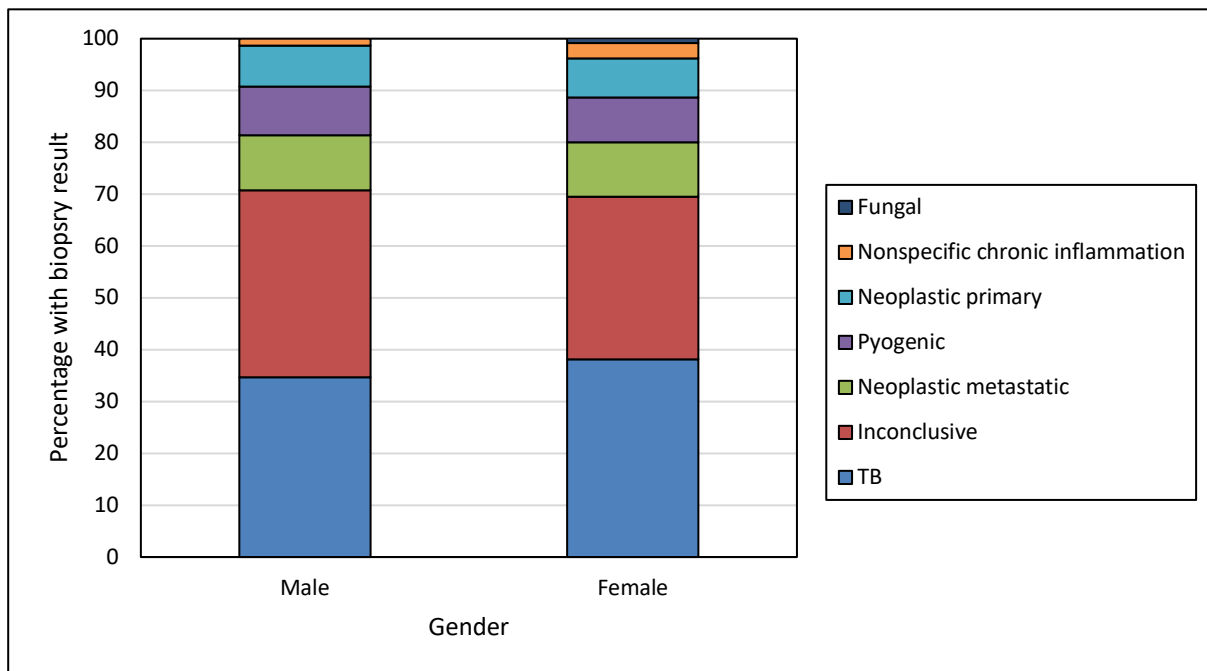


Figure 6. Percentage of male and female patients with different biopsy results

Comparison of Biopsy Result with Age Distribution

When investigating for an association between biopsy result and age distribution the one-way ANOVA was used, this revealed no statistical significant difference in age distribution by biopsy result (Brown-Forsythe = 0,825, $df_1 = 5$, $df_2 = 14,998$, $p = 0,545$). For this purpose robust estimate was used because homogeneity of variance was not equal for groups (Levene statistic = 5.431, $df = 5$, $p = 0.000$). Figure 7 below represents data for age by biopsy result.

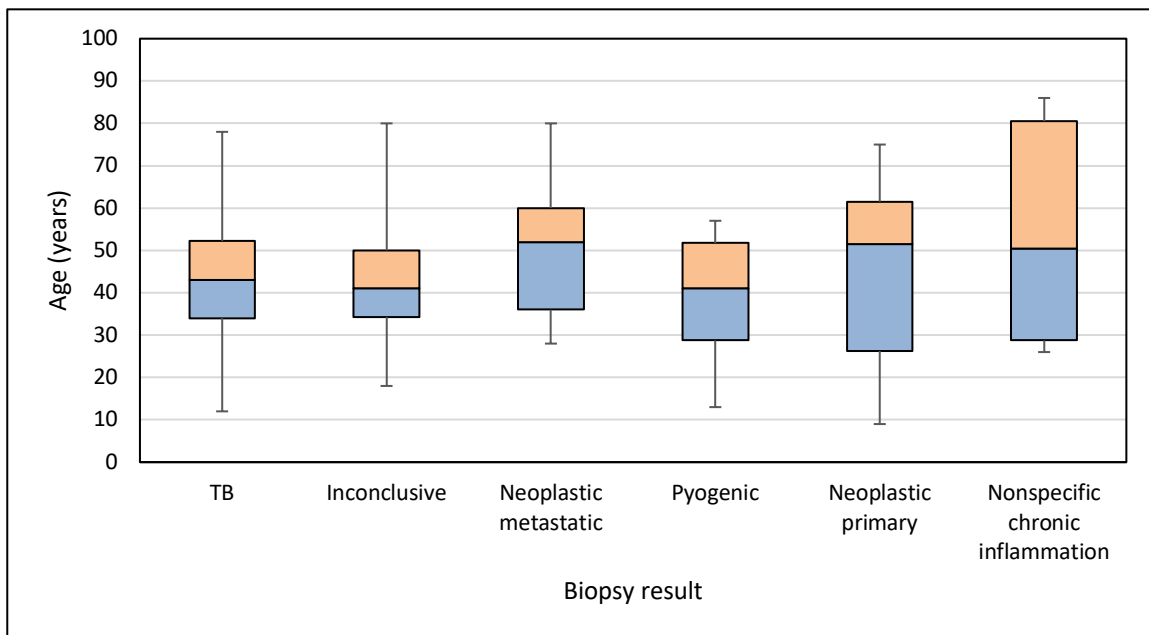


Figure 7. Box and whisker plots of age for biopsy results

Biopsy Level

Biopsy level indicates the specific spinal vertebral level at which the biopsy was performed. The vertebral column is divided into different regions with individual vertebrae being named according to their region and position. Anatomically from top to bottom these regions are: cervical (C1 – C7), thoracic (T1 – T12), lumbar (L1 – L5), sacral (fused S1 – S5) and coccyx.

Analysis of data pertaining to specific level of vertebral biopsy within this study population indicates that percutaneous biopsies were only performed on thoracic and lumbar vertebrae. Table I below is the distribution of percutaneous biopsies per level. The prefix 'T' denotes thoracic region and prefix 'L' denotes lumbar region.

Table I: Biopsy level distribution in the sample (n = 180)

Level	n	%
T1	1	0,6
T2	2	1,1
T3	2	1,1
T4	7	3,9
T5	4	2,2
T6	1	0,6
T7	2	1,1
T8	11	6,1
T9	7	3,9
T10	13	7,2
T11	8	4,4
T12	19	10,6
L1	16	8,9
L2	13	7,2
L3	21	11,7
L4	39	21,7
L5	14	7,8

Biopsy levels do not occur in equal numbers; lumbar biopsies occur in higher frequencies than thoracic biopsies. Levels with higher frequencies are L4, L3, T12, L1 and L5. Levels with lower frequencies are T1, T6, T2, T3 and T7.

When further analysing which biopsy results occur at the different vertebral levels, it is found that the frequency of biopsy results varies within levels. Where there are more patients (more than 10 patients for a level) most results occur (except for L5 and T8), but in different proportions.

When looking at specific biopsy results, TB had the highest positive yield in L4 with 14 cases followed by T12 with eight cases and L5 with seven cases. Neoplastic metastatic had the highest yield in L3 and L4 with four cases each followed by L5 with three cases. Neoplastic primary had the highest yield in T8 with three cases followed by T10, L2 and L3 with two cases each. Pyogenic infection had the highest yield in L4 with five cases followed by T12 with three cases. Non-specific chronic inflammation had two cases in T12 with one case each in T3 and L4. The single case of fungal infection was biopsied in T12. The vertebral level with the highest

number if inconclusive results was L4 with 15 cases. Figure 8 below graphically represents biopsy level with number of patients and biopsy results.

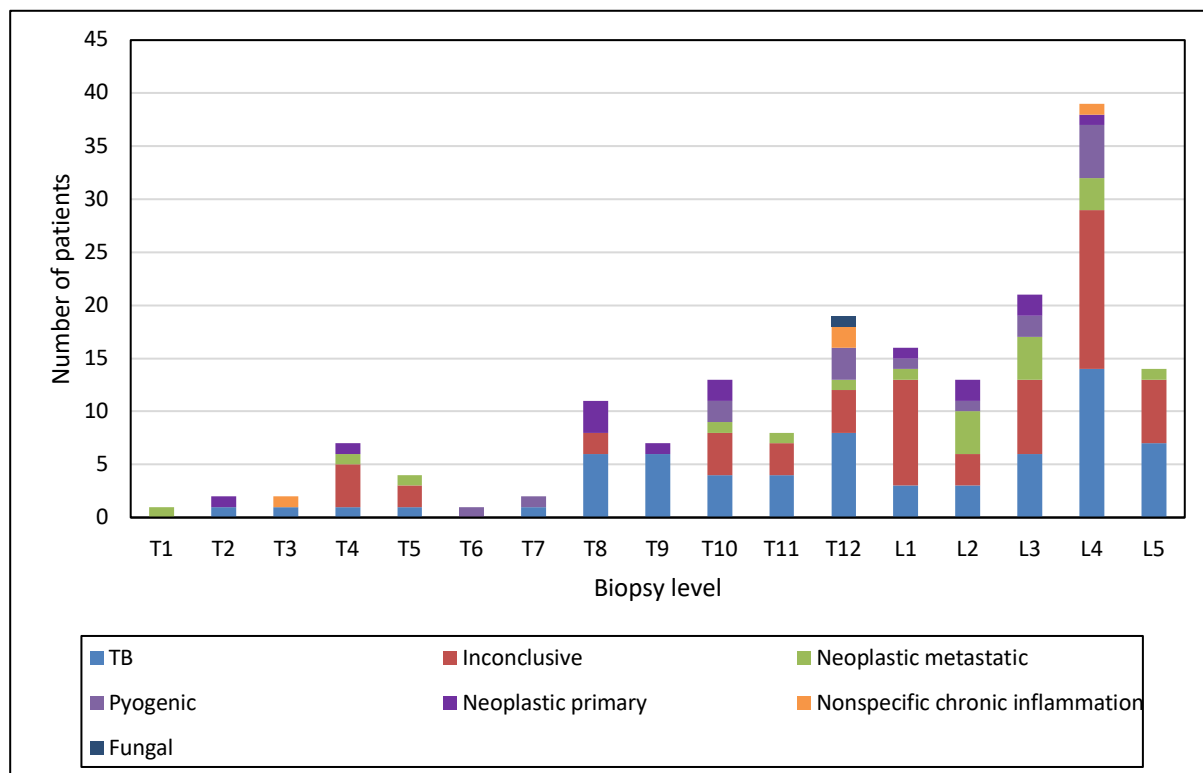


Figure 8. Number of patients with biopsy results per biopsy level

Complications

Of the 180 biopsies performed, a total four complications were identified, indicating a complication rate of 2.22%. These are further broken down into three early and one late complication.

Of the three early complications identified, two patients were reported to have haematoma formation, these resolved spontaneously and no further surgical intervention was needed. One patient was documented to have neurological deterioration in the form of lower limb weakness post biopsy but subsequently resolved without any further intervention. The late complication identified was that of a patient found to have abscess formation of the soft tissues around lumbar biopsy site at the two week clinic follow-up visit. The patient was admitted and underwent incision and drainage of the abscess (see Table II).

Table II: Breakdown of complications post percutaneous spinal biopsy

Early/Late	Complication	Age Gender	Biopsy Level	Biopsy Result	Further Intervention
Early	Haematoma	45 Female	L5	Inconclusive	None
Early	Haematoma	54 Male	T8	Pyogenic	None
Early	Neurological deterioration	38 Male	T12	Inconclusive	None
Late	Abscess	42 Female	L4	TB	Incision + Drainage

DISCUSSION

When a patient with suspected spinal pathology is referred to the CMJAH spine unit, the management protocol includes appropriate radiological investigations (X-ray, CT, MRI) and when a spinal lesion is identified, a tissue diagnosis is needed in order to implement the correct treatment algorithm. At this health institution the biopsy modality of choice is a fluoroscopy guided percutaneous transpedicular biopsy unless certain circumstances warrant an open biopsy.

Effectiveness Yield

A retrospective 6-year review of fluoroscopy guided percutaneous transpedicular biopsies at CMJAH was conducted. One of the objectives of the study was to determine the effectiveness of this biopsy modality. Of the 180 biopsies conducted, 120 led to a positive or specific diagnosis, leaving 60 biopsy results as 'inconclusive' where the final diagnosis could not be established. This equates to a positivity or efficacy rate of 66.67%.

According to Chaudry *et al.* as well as Lee *et al.* the reported efficacy of percutaneous fluoroscopy guided spinal biopsies ranges from 16.1% to 92.3%.^(1,6) When compared to other international studies of a similar nature, our efficacy rate fared sub-par to majority of the studies. However in comparison the current study was the largest in terms of study population, the discrepancy in findings may be due to the smaller sample of patients in majority of compared studies. Table III below depicts a comparison of similar studies and results.

Table III: A comparison of similar studies and outcome of efficacy

Author and Reference	Study Period	Study Design	Study Population	Number of Positive Biopsies	Positive Yield %
Current study	2016-2021	Retrospective	180	120	66.67
Dave (11)	2005-2007	Prospective	71	63	88.7
Mireles (28)	2008-2012	Prospective	100	83	83.0
Kamei (29)	2003-2011	Retrospective	128	120	93.8
Ravikanth (8)	2017-2019	Retrospective	42	38	90.4
Chamkeri (2)	2014-2017	Prospective	23	19	82.6
Bukhari (30)	2009-2014	Prospective	55	38	69.1
Shresta (19)	2013-2015	Retrospective	23	21	91.3
Rosales (31)	2005-2006	Prospective	20	11	55.0
Kim (25)	2003-2010	Retrospective	170	134	78.8

When investigating possible reasons for one third of biopsy results being inconclusive, the common finding was that the biopsy specimens supplied to the lab were sub-optimal or inadequate, thereby leading to an inability to perform histopathological or microbiological analysis. Krishnan *et al.* (2022) states that sample adequacy remains the most important factor for diagnostic accuracy.⁽³²⁾

In a 2016 study by Pagdal *et al.* it was found that 22% of spinal biopsy specimens were suboptimal for diagnostic interpretation, these samples contained scant bone tissue and were contaminated with disc material, the authors attributed this to incorrect routing of the biopsy needle.⁽²⁶⁾ Obtaining an adequate sample is dictated by various factors, including biopsy level, location of the lesion, size of lesion, type of lesion, instrumentation used, experience of the surgeon and technical errors.⁽⁶⁾

When considering characteristics of the lesion, diagnostic yield is higher in metastatic lesions as compared to primary bone neoplasm. The diagnostic yield is lowest in bone lesions caused by haematological malignancies.⁽¹⁾ In 2009, Talac and Mclain stated that the diagnostic yield is higher in spinal lytic lesions versus sclerotic lesions and that inflammatory bone lesions and compression fractures have the highest accuracy rate.⁽³³⁾

In a 2018 study by Yang *et al.* looking at factors affecting biopsy diagnostic yield, using a multivariate analysis it was shown that lesions less than 2 cm in size had significantly lower yields than larger lesions. These findings were attributed to the higher probability of missing

smaller target lesions, leading to sampling errors and insufficient specimens being obtained.⁽⁷⁾ In the current study no record was kept of lesion size and thereby no comment can be made on its role in sample inadequacy.

Studies have led to a better understanding of pedicular anatomy and vertebral morphometry, leading to the use of the pedicle as a biopsy tract. When considering location of the lesion within the vertebral body Dave *et al.* reported that the transpedicular route offers access to over 50% of the total volume of the vertebral body, however lesions located directly anterior to the spinal canal as well as lateral and posterior edges of the vertebral body may be inaccessible to the biopsy needle thereby leading to an inadequate sample being taken.⁽¹¹⁾ This factor may be a consideration for the high yield of inconclusive results within the current study.

Pertaining to instrumentation used, needle type and size have been shown to affect biopsy sample adequacy. Mohan *et al.* (2018) demonstrated that when performing a percutaneous spinal biopsy a needle with a larger inner diameter provides better tissue specimens with minimal crushing effect and that needles with serrated edges are better than those with bevelled edges.^(29,34) Similarly Nourbakhsh also states that a biopsy trephine diameter of greater than 2 mm is more suitable for histology analysis thereby improving the diagnostic yield of the specimen from 59% to 90%.⁽⁵⁾ Although not always documented, the standard practice at this institution is to use an 8 or 10 gauge needle that is part of a commercially available introducer and trocar system. The needle system used in the current study would have been an adequate size to obtain a sufficient specimen without any crush artifacts.

In a 2019 study by Liang *et al.* it was shown that the biopsy diagnostic accuracy improved with an increased number of specimens obtained and with increased specimen length. The study found that the cumulative diagnostic yield plateaued at three specimens.⁽²²⁾ Due to the retrospective nature of the current study, data such as number of specimens and specimen size is not obtainable as this information is not always recorded, hence comment cannot be made on its role in the inconclusive results obtained.

In a 2015 literature review by Nourbakhsh on percutaneous spine biopsy it is stated that in cases of spondylodiscitis, a microbiological analysis of a spinal biopsy sample is only able to identify the causative organism in 35 – 60% of cases and that the positivity yield is adversely influenced by the use of pre-biopsy broad spectrum antibiotics. It is also further mentioned that an improved micro-organism isolation ratio is anticipated when pus is found during the biopsy and in cases of chronic spondylodiscitis the micro-organisms occur in isolated colonies

thereby decreasing specimen adequacy.⁽⁵⁾ Based on the above premise the CMJAH spine unit protocol is that of goal directed or targeted antibiotic therapy in cases of pyogenic spinal infections. Broad spectrum antibiotic cover is only initiated once a biopsy specimen has been obtained therefore this factor should have minimal influence in the lower than expected positivity yield in the current study.

A 2013 local study by Watt and Davis reviewed the yield of spinal TB performed with percutaneous biopsies, it is stated that the classical histological finding of necrotising granulomas with epithelioid macrophages, giant cells and lymphocytes may be altered due to Human Immunodeficiency Virus (HIV) infection and more specifically Acquired Immune Deficiency Syndrome (AIDS). The altered histological findings range from caseating granulomas, to nonspecific chronic inflammation without necrosis. In their study biopsy specimens showing classic TB histology were only correlated in 23% of positive TB culture cases, this was attributed to a high HIV burden within the population subset. Definitive diagnosis of TB ultimately relies on the identification of TB bacilli in biopsy specimens. However, spine TB presents with typically low bacterial loads rendering identification in less than 50% of cases using minimally invasive biopsy techniques. In advanced stages of spine TB nonspecific results are attributed to the start on the bone healing process as the patient may already have been initiated on anti-TB medical treatment.⁽³⁵⁾ Based on the above findings, a correlation between the biopsy results and HIV status of patients in the current study population cannot be drawn as this was not a study parameter, this does however open an avenue for a future research question.

In a 2015 literature review by Nourbakhsh on percutaneous spine biopsy and factors determining outcome it is stated that osseous blood should be treated as a tissue specimen and sent for histological analysis as this increases the accuracy of diagnosis. It is further proposed that any fluid or tissue obtained should be sent for culture as this aids the diagnosis of infection. The combination of aspiration and biopsy is suggested, especially in cases of TB where culture is difficult and delayed.⁽⁵⁾ With the retrospective design of the current study, theatre records reviewed do not highlight if an aspiration was conducted with the biopsy. This finding warrants a possible change in biopsy protocol and points to the need for implementing better record keeping strategies.

Percutaneous spine biopsies have become standard and common procedures within the spine unit at CMJAH. The hospital where the study was based is an academic training facility, this results in the frequent rotation of registrars and fellows within the unit. The subsequent effect

of this is that there is no long term standardisation when performing these biopsies as compared to other similar international studies where the same senior member of staff has performed all the biopsies. In the current study, some of the biopsy procedures may have been conducted by a member of staff undergoing training albeit under consultant supervision there remains an associated learning curve.

Specific biopsy results

Pyogenic

The current study found 8.9% of total biopsies to be pyogenic spinal infections, this finding was regarded to be similar when compared to a 2020 prospective study by Lee *et al.* that diagnosed 10% of biopsy results as being pyogenic.⁽⁶⁾ In the current study the predominant causative organism isolated was *Staphylococcus aureus* accounting for six of the 16 pyogenic cases. Similar findings were reported by Lee *et al.* in the above mentioned study as well as by Kim *et al.* in a 2013 study.⁽²⁵⁾ In the current study other causative organisms found included two cases of *Acinetobacter baumannii* as well as one case of each of the following organisms: *Enterococcus faecium*, *Escherichia coli*, *Enterococcus faecalis*, *Proteus mirabilis*, *Bacillus species*, *Morganella morganii*, *Streptococcus salivarius* and *Streptococcus agalactiae*. Both studies mentioned above reported similar findings with Lee *et al.* identifying one case of each of the following pathogens: *Klebsiella pneumoniae*, *Escherichia coli*, and *Stenotrophomonas maltophilia*. Kim *et al.* reported four cases of *Streptococcus agalactiae*, two cases of *Streptococcus viridans*, and one case of each of the following: *Enterococcus faecalis*, *Escherichia coli*, *Enterobacter cloacae*, *Staphylococcus epididymis*, and *Klebsiella pneumoniae*.

Neoplasm

The current study findings reflected a diagnosis of neoplasm in 33 (18.4%) cases, when subdivided, 19 cases of metastatic malignancy and 14 cases of primary spinal neoplasm were found. Further breakdown revealed that the primary origin of the metastasis were either from breast (four cases); colorectal (four cases); lung (three cases); liver (one case); gynaecological tract (one case); prostate (one case); melanoma (one case) or indeterminate origin but had histological features of metastatic carcinoma (five cases). Primary spinal neoplasm included histological features of multiple myeloma (eight cases), lymphoma (three cases) or haemangioma (three cases). A 2018 study by Yang *et al.* had similar findings to the current

study, they had isolated 31 neoplastic lesions of which 14 were primary malignancies and 17 were metastases. Their findings stated that the two most common origins of metastases were lung (33%) and breast (13%). Primary malignancies were predominantly plasma cell tumours.⁽⁷⁾ Similar results were also found in a 2015 study by Kamei *et al.* that reviewed 128 percutaneous transpedicular vertebral biopsies. A diagnoses of metastatic carcinoma was made in 62 patients, with primary carcinoma sites being identified as prostate in 13 patients, lung in 9, breast in 7, thyroid in 4, kidney, colon, liver, and ureter in 2 patients each and stomach, bladder, uterus, ovary, pharynx, thymus, salivary gland, and sweat gland in 1 case each. In 13 of the patients the primary lesion was not detected. In terms of primary bone malignancy, multiple myeloma was detected in 10 cases and malignant lymphoma in five cases.⁽²⁹⁾

Tuberculosis (TB)

Of the 180 biopsies included in the study, 66 (36.7%) tested positive for TB. Positivity was confirmed either by microscopy for the presence of acid-fast bacilli, histological findings, TB culture or PCR method testing. Findings from a 2013 study by Kim *et al.* diagnosed TB infection in 26 cases out of 170 percutaneous biopsies performed equating to a positivity rate of 15.29%.⁽²⁵⁾ In comparison the current study had a more than double positivity yield for TB, this is possibly owed to the high TB burden amongst the local population. When looking at a 2009 study from India, a similarly high TB endemic country, Dave *et al.* reports a TB positive diagnosis in 21 (29.57%) cases out of 71 percutaneous spinal biopsies performed. Similarly another Indian study performed by Sahoo *et al.* in 2018 had a positive TB diagnosis in 28 (68.29%) out of 41 cases.⁽³⁴⁾ A local study performed by Kelly *et al.* reported a TB positive diagnosis in 71 out of 126 spinal biopsies, however it is pertinent to mention that only 20 of these biopsies were performed percutaneously and the rest were open biopsies.⁽³⁾ According to a World Health Organisation report, South Africa has one of the highest TB incidence rates globally, this is likely the rationalisation for TB making up the greatest proportion of positive yield results in the current study.

Other

Four biopsies results revealed non-specific chronic inflammation. On histological examination, a focus of calcification was noted with scattered foci of chronic inflammatory cells. In these specimens the differential included causes of inflammation possibly due to auto-immune conditions, fracture or osteoporosis. In these cases neoplasm and infection were ruled out. Shrestha *et al.* (2015) reported a similar finding of two cases that had histological features of chronic non-specific inflammation.⁽¹⁹⁾ In a 2016 study Pagdal *et al.* reported a diagnosis of osteoporosis based on histology findings in five cases of vertebral compression fractures that underwent percutaneous spinal biopsy⁽²⁶⁾, similarly Chamkeri *et al.* reported osteoporotic fractures in three cases (13%) of their biopsy findings.⁽²⁾

With regards to other positive yield biopsy results there was only one specimen that flagged positive on mycology culture, the isolated fungus was *Rhodotorula mucilaginosa*. A detailed literature search was conducted, nonetheless no cases of the above fungus causing spinal infection has been reported in literature however there are cases in which it has been isolated as the causative organism in meningitis.

Demographics

Gender and Age Distribution

Of the 180 patients that underwent a transpedicular spinal biopsy, 75 participants were male and 105 participants were female. This accounted for a ratio of 3:2 females to males. Table IV below offers a comparison of similar studies in terms of gender and age distribution. Findings in the current study are not in keeping when compared to international studies, whereby in most studies males made up the greater proportion of patients that underwent percutaneous spinal biopsies. The findings in the current study could reflect the current societal norms where anecdotally females present sooner seeking healthcare treatment than males.

With regards to statistical analysis of age distribution of the patients that underwent a transpedicular spinal biopsy, the range was between 9 and 86 years with the mean being 43.44 years. A wide range of age is represented with more patients in the middle age ranges. The findings in the current study are comparable to international studies with only one study by Mireles *et al.* having a wider age range due to the youngest patient being two years old and the oldest being 83.

When comparing age and gender distribution with each other, statistical analysis verified that there was no significant difference in age distribution for male and female patients that underwent spinal biopsies in our study population (p -value of 0.778).

Table IV: A comparison of similar studies in terms of gender and age distribution

Author and Reference	Study Population	Males n (%)	Females n (%)	Mean Age	Age Range
Current study	180	75 (41.6%)	105 (58.3%)	43.44	9-86
Dave (11)	71	51 (71.8%)	20 (28.2%)	42.8	21-81
Mireles (28)	100	57 (57%)	43 (43%)	53.8	2-83
Chooi (12)	30	22 (73.3%)	8 (26.7%)	52.0	16-75
Ravikanth (8)	42	28(66.7%)	14(33.3%)	46.0	12-76
Chamkeri (2)	23	9 (39.1%)	14 (60.9%)	41.1	30-70
Bukhari (30)	55	37 (67.3%)	18 (32.7%)	53.54	18-80
Shrestha (19)	23	17 (73.9%)	6 (26.01%)	47.0	22-73
Kim (25)	140	70(50%)	70 (50%)	65.1	16-89
Ashizawa (4)	26	14 (53.8%)	12(46.1%)	61.0	29-85
Chaudhary (1)	52	36 (69.2%)	16(30.7%)	54.17	2-87

Comparison of Biopsy Result and Gender Distribution

In search for an association between biopsy result and gender of patients that underwent a percutaneous spinal biopsy, no statistical significant relationship was found between the two groups ($p = 0.970$).

Within our study population the comparison of biopsy results between genders found that TB positive cases were identified in 34.7% of males as compared to 38.1% of females. Neoplastic metastatic lesions were found in 10.7% males and 10.5% females. Neoplastic primary lesions were identified in 8% males compared to 7.65% females. In contrast to the current study, results of a study by Kelly *et al.* found a gender comparison in the neoplastic group to be 49% males and 51% females. In the TB group there was a finding of 62% males and 38% females. They further added that despite a clinical trend in the TB group towards increased males being afflicted, statistical analysis was not significant ($p = 0.15$).

Comparison of Biopsy Result with Age Distribution

In the current study the mean ages for the following groups are as follows: pyogenic group was 41 years, neoplastic metastatic was 52 years, neoplastic primary was 51.5 years, TB was 43 years and other was 50.5 years. When investigating for an association between biopsy result and age distribution the one-way ANOVA test was used, this revealed no statistical significant difference in age distribution by biopsy result ($p = 0,545$). In a study by Kelly *et al.* results revealed the mean age distribution in the neoplastic group was 54.1 years and the TB group was 40.5 years. Based on the age difference between the two groups a high statistical significance was demonstrated ($p < 0.001$).

Biopsy Level

Analysis of data pertaining to specific level of vertebral biopsy within the current study indicates that percutaneous biopsies were only performed on thoracic and lumbar vertebrae. More specifically 77 (42.8%) thoracic compared to 103 (57.2%) lumbar vertebral biopsies, this reveals that biopsy levels do not occur in equal numbers. Lumbar biopsies occur in higher frequencies than thoracic biopsies. Levels with higher frequencies are L4, L3, T12, L1 and L5. Levels with lower frequencies are T1, T6, T2, T3 and T7.

A 2020 study by Ravikanth showed similar results having performed percutaneous biopsies on 14 thoracic and 26 lumbar vertebrae. Further analysis revealed higher frequency biopsies were conducted in L1 (23.6%), T12 (16.4%), L3 (14.6%), L5 (13.3%) (8). Padgal *et al.* in 2016 demonstrated similar results having conducted a total of 84 percutaneous spinal biopsies of which 28 (33.33%) were thoracic spine, 37 (44.05%) were lumbar spine and 19 (22.62%) were taken from both regions on the same patient.⁽²⁶⁾

At our health institution fluoroscopy guided percutaneous spinal biopsies are limited to thoracic and lumbar vertebrae only due to reasons of access and safety. Cervical vertebra have altered pedicle morphometry and therefore an open biopsy is preferred or percutaneous *via* an anterior/posterior lateral approach. The same applies for sacral lesions.

When further analysing which biopsy results occur at the different vertebral levels, it is found that the frequency of biopsy results varies within levels. When looking at specific biopsy results, TB had the highest positive yield in L4 with 14 cases followed by T12 with eight cases and L5 with seven cases. Neoplastic metastatic had the highest yield in L3 and L4 with four

cases each followed by L5 with three cases. Neoplastic primary had the highest yield in T8 with three cases followed by T10, L2 and L3 with two cases each. Pyogenic infection had the highest yield in L4 with five cases followed by T12 with three cases. Non-specific chronic inflammation had two cases in T12 with one case each in T3 and L4. The single case of fungal infection was biopsied in T12. The vertebral level with the highest number of inconclusive results was L4 with 15 cases.

Gehlot *et al.* (2012) performed a retrospective analysis of MRIs in 70 patients with TB spine, findings revealed that thoracic and lumbar vertebrae were the commonest involved and multiple vertebrae were often affected. L3 was the commonest affected vertebrae in their study (36). In a literature review looking at diagnosis and management of spine TB, Moon (2014) stated that 5% of patients with TB present with extrapulmonary TB, with the thoracic spine being the most common site affected.⁽³⁷⁾ The results in the current study are in keeping with the findings of the above two mentioned studies.

In a 2007 prospective study by Chooi *et al.* 30 patients underwent percutaneous transpedicular biopsy of thoracic and lumbar vertebrae. Neoplastic conditions were found in 11 patients with the commonest presentation in levels were L3 (30%), and L1 (20%). Pyogenic conditions were diagnosed in five cases with the commonest levels be T11 and L1 (20% each).⁽¹²⁾ The findings in the current study are in keeping with the studies above.

Complications

The literature reported complication rate of percutaneous transpedicular spinal biopsies varies from 0 to 10%. Reported complications include pneumothorax, transient paresis, hematoma, neural injury, radiculopathy, tuberculous sinus tract, meningitis and even death. The complications are thought to be associated with the anatomic location of the lesion, path used and size of needle used.^(5,29)

In the current study a total four complications were identified, indicating a complication rate of 2.22%. These are further broken down into three early and one late complication. Of the three early complications identified, two patients were reported to have haematoma formation, these resolved spontaneously and no further surgical intervention was needed. One patient was documented to have neurological deterioration in the form of lower limb weakness post biopsy but subsequently resolved without any further intervention. The late complication identified was that of a patient found to have abscess formation of the soft tissues around lumbar biopsy

site at the two week clinic follow up visit. The patient was admitted and underwent incision and drainage of the abscess.

In 2022, Roschan reported a complication rate of 3.57%, with two out of 56 patients presenting with biopsy site haematoma formation, no perioperative intervention was needed.⁽³⁸⁾ A 2012 study by Gasbarrini reported three complications out of 69 patients undergoing percutaneous spine biopsy, this equates to a complication rate of 4.3%. The reported complications included one case of a subcutaneous caseous collection that required incision and drainage of the biopsy tract. The second reported complication was a patient that had progressive neurological deterioration post biopsy, upon surgical decompression it was found that the abscess had extended into the spinal canal and caused compression. The transpedicular tract of the biopsy needle had been too medial, creating a communication between the spinal canal and abscess. The third reported complication was that of a patient that presented with fever and fatigue post biopsy, was treated empirically for meningitis.⁽³⁹⁾

Kamei *et al.* states that to avoid complications, extensive knowledge of vertebral morphometry is required. Appropriate sized biopsy needles can be passed through the pedicles into the vertebral body without injuring the adjacent anatomic structures as long as integrity of the medial and inferior walls of the pedicle is maintained.⁽²⁹⁾ Suggestion is made to utilise a high resolution image intensifier to enhance the detail of visualised vertebral anatomy and select the correct transpedicular path.⁽⁴⁰⁾

Strengths of the study

The study is based on a significant sample size conducted over an extensive period of 6 years. The study encompassed a large variety of spinal pathologies drawing correlations to patient demographics. There was less variability as the procedures were conducted in a dedicated spine theatre by spine unit team members. A large study database was populated creating the opportunity for further research studies to be conducted.

Limitations and Recommendations

The retrospective design of the study has inherent limitations where some data may have been overlooked, hence reasons could not be fully justified for the lower than anticipated efficacy rate, as this information was not recorded. Future studies may take into account correlation of radiographic findings (lesion location and size) to biopsy findings, technical aspects should also be recorded for example, type and size of needles used, size and quality

of specimen obtained. Furthermore, patient clinical condition should be correlated and documented. Looking at operating times with comparison to level of surgeon may also be of value. Based on other local and international studies there may be value in performing a comparative study of open versus closed biopsy findings within our spinal unit. Other comparisons may be drawn from the type of imaging modality used, CT versus fluoroscopy guided. The above suggestions may be beneficial when conducted as a prospective study with randomisation of any of the elements mentioned.

The current study was set within a single centre affording the opportunity to monitor trends amongst the patient demographics attending that specific unit. However, opportunity lies in performing a larger multi-centre study with collaboration of the three larger academic hospitals within the Johannesburg region.

CONCLUSION

Patients presenting with suspected spinal pathology are referred for the appropriate radiological investigations and when a spinal lesion is identified, a tissue diagnosis is needed in order to implement the correct treatment protocol. Through this study it was shown that fluoroscopy guided percutaneous transpedicular biopsy is an effective modality in obtaining a spine biopsy. Even though the efficacy rate was 66% this may be improved by factors mentioned in the discussion. This modality is recommended over open techniques when possible, thereby obviating the need for major surgery and expediting appropriate management of patients. The biopsy modality is useful in obtaining specimens in thoracic and lumbar vertebrae, in all ages groups and is used in the full spectrum of spinal pathological lesions encompassing pyogenic, neoplastic, tuberculous and chronic inflammatory. The study also proves that it is a safe procedure with no long term complications identified.

DECLARATIONS

Author contributions

- Shivam Bhikha. This author helped with study design, data collection, literature review and analysis, article drafting, final approval and submission.
- Shazad Khan. This author helped with report design, literature review and analysis, article drafting and final approval
- Maxwell Jingo. This author helped with report design, literature review and analysis, article drafting, final approval and submission.

Ethics approval and consent to participate

Ethics approval was obtained from Human Research Ethics Committee (Medical), University of the Witwatersrand.

Consent for publication

Consent waived for retrospective research.

Availability of data and materials

Data sharing applicable to this article as datasets were generated or analysed from CMJAH during the current study.

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Competing interests

The authors declare that they have no competing interests.

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APPENDICES

Appendix A: Ethics Clearance Certificate

Appendix B: Hospital CEO Letter

Appendix C: Orthopaedics HOD Letter

Appendix D: CMJAH HOD Letter

Appendix E: Permission request Letter to Radiology HOD

Appendix F: Student's contribution to the "submissible" paper

Appendix G: SAOJ Guidelines

Appendix A: Ethics Clearance Certificate



R49 Drs S Bhikha and M Jingo

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL) CLEARANCE CERTIFICATE NO. M210806

NAME:
(Principal Investigator)

Drs S Bhikha and M Jingo

DEPARTMENT:

School of Clinical Medicine
Department of Surgery
Division of Orthopaedic Surgery
Medical School
University

PROJECT TITLE:

*A review of fluoroscopy-guided percutaneous
transpedicular spinal biopsies at Charlotte Maxeke
Johannesburg Academic Hospital*

DATE CONSIDERED:

2021/08/27

DECISION:

Approved unconditionally

CONDITIONS:

NOTE:

If contact information regarding student study participants is required,
please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>

SUPERVISOR:

Dr S Khan

APPROVED BY:


Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL:

2021/10/27

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

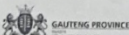
To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

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 submit details to the Committee. **I agree to submit a yearly progress report.** When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in August and therefore reports and re-certification will be due in the month of **August** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).


Signature of Principal Investigator

2021-10-27
Date

Appendix B: Hospital CEO Permission Letter

	GAUTENG PROVINCE HEALTH REPUBLIC OF SOUTH AFRICA
CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL (CMJAH) OFFICE OF THE SENIOR CLINICAL MANAGER	
<i>Enquiries: Ms. TT Mahlangu</i> <i>Email: Thandi.Mahlangu4@gauteng.gov.za</i> <i>Tel: 011 488 3365</i> <i>Ref: 1/7/2</i> <i>Date: 11 October 2021</i>	
GP_202109_014	
Dear Dr Shivam Bhikha	
RE: PROVISSIONAL APPROVAL OF STUDY	
TITLE: A REVIEW OF FLUOROSCOPY GUIDED PERCUTANEOUS TRANSPEDICULAR SPINAL BIOPSIES AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL	
Permission to conduct the above-mentioned study is provisionally granted subject to:	
1. Submitting an Ethics Postgrad Assessor Group Approval.	
Please submit the above document at your earliest convenient within 3 months from the date of this letter. This will prompt the Chief Executive Officer (CEO) of Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) to grant you a final approval. It is important to note that your research can only commence once a final approval is granted. Failure to comply with the above-stated requirements may result in the withdrawal of your application.	
Supported / ~~Not Supported~~ Signed by: Jayshina Punwasi Signed at: 2021-10-11 05:41:25 +02:00 Reason: Witnessing Jayshina Punwasi	
 Dr J. Punwasi Clinical Director	
Approved / ~~Not Approved~~ Signed by: Gladys Magugudi Bogoshi Signed at: 2021-10-13 22:32:35 +02:00 Reason: Witnessing Gladys Magugudi Bo	
  Ms. G Bogoshi Chief Executive Officer	

Appendix C: Orthopaedics HOD Letter

Shivam Bhikha
4 Panorama Complex
24 Julius Wernher Road
Bruma, Johannesburg
2198
14 May 2021

The HOD
Orthopaedic Surgery Department

Dear Prof Ramokgopa

Re: Request for permission to conduct study

My name is Shivam Bhikha and I am a registrar in the department of Orthopaedic Surgery at the University of Witwatersrand. I am currently in the process of completing my research protocol towards my MMed. I would like to inform you of the research study that I would like to conduct. The aim of this research study is to review percutaneous fluoroscopy guided transpedicular spinal biopsies at CMJAH over a 5-year period.

The following are the objectives of the study:

1. To compare the primary spinal pathology amongst age and gender
2. To determine the effectiveness of the transpedicular spinal biopsy
3. To identify any complications following the transpedicular spinal biopsy

The research will be a retrospective study of data from the spine registry and records of patient's files from the spine unit in the department of orthopaedic surgery at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

With regard to confidentiality, no patient identities will be published. Confidential patient details will be known only by the researcher. Ethics clearance will be applied for *via* the Human Research Ethics Committee (HREC) (Medical) at the University of the Witwatersrand.

I would appreciate your permission/consent to conduct this study at the CMJAH.

Yours sincerely,

Shivam Bhikha
Cell: 082 39 39 990
shivam.bhikha@gmail.com

Kindly indicate if permission to conduct this study is granted:

YES: ☒ NO: ☐

Signature / Stamp.....

AJ Hlobetson
Acting HOD

Appendix D: CMJAH HOD Letter



**health and
social development**

Department: Health and Social Development
GAUTENG PROVINCE

**CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC
HOSPITAL**

DEPARTMENT OF ORTHOPEADICS
CMJAH
Tel (011)488-4990

Ms G Bogoshi
The CEO
CMJAH

01\09\2021

Dear Ms Bogoshi

Re: Request to conduct research titled: A review of fluoroscopy guided percutaneous transpedicular spinal biopsies at Charlotte Maxeke Johannesburg Academic Hospital

The above matter refers. I support this research and recommend that he be granted permission to conduct the study as proposed.

Yours sincerely

Professor AJF Robertson
HOD-Orthopedics
CMJAH

Appendix E: Permission request Letter to Radiology HOD

4 Panorama Complex
24 Julius Wernher Road
Bruma, Johannesburg
2198
30 August 2021

Clinical Head Radiology Department
Charlotte Maxeke Johannesburg Academic Hospital

Dear Prof Ramaema

Re: Request for permission to conduct study

My name is Shivam Bhikha and I am a registrar in the department of Orthopaedic Surgery at the University of Witwatersrand. I am currently in the process of completing my research protocol towards my MMed. I would like to inform you of the research study that I would like to conduct. The aim of this research study is to review percutaneous fluoroscopy guided transpedicular spinal biopsies at CMJAH over a 5-year period.

The following are the objectives of the study:

1. To compare the primary spinal pathology amongst age and gender
2. To determine the effectiveness of the transpedicular spinal biopsy
3. To identify any complications following the transpedicular spinal biopsy

The research will be a retrospective study of data from the spine registry and records of patient's files from the spine unit in the department of orthopaedic surgery at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). I will also be accessing the PACS system in order to complete data capturing in relevant cases.

With regard to confidentiality, no patient identities will be published. Confidential patient details will be known only by the researcher. Ethics clearance will be applied for *via* the Human Research Ethics Committee (HREC) (Medical) at the University of the Witwatersrand.

I would appreciate your permission/consent to conduct this study at the CMJAH.

Yours sincerely,

Shivam Bhikha
Cell: 082 39 39 990
shivam.bhikha@gmail.com

Kindly indicate if permission to conduct this study is granted:

YES: ☐ NO: ☐

Signature / Stamp..... 18 Sept 2021

Appendix F: Student's contribution to the research and writing of the "submissible" paper

Division of Orthopaedic Surgery

Faculty of Health Sciences, 4M Room 12, Wits Medical School, 7 York Road, Parktown 2193
• Tel: +27 11 717-2538 • Fax: +27 11 717-2551

06/04/2023

Faculty of Health Sciences, University of the Witwatersrand

RE: SHIVAM BHIKHA'S CONTRIBUTION TO THE RESEARCH AND WRITING OF THE "SUBMISSIBLE" PAPER

To whom it may concern,

This letter serves to confirm that the co-authors of the "submissible" research paper have agreed to its use by Shivam Bhikha, student number 0601497P as part of his MMed research report. Shivam Bhikha made a substantial contribution to conducting the research study and writing the manuscript.

Yours sincerely,



.....
Dr SA Khan
Primary Supervisor
08/03/2023



..... 06-04-2023
Shivam Bhikha
MMed Candidate

Appendix G: South African Orthopaedic Journal Guidelines

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 interpercentile 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.gov/should>
- The following format should be used for references:

Abstract

A structured abstract (maximum of 350 words), summarising the most important points in the article is required.

The abstract consisting 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 6 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 in 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 randomization (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.
- Description of procedure or intervention, including post-operative protocol.
- The outcome measures or scores were used.
- The minimum follow-up period.
- A statistical analysis section 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 procedure for common operations. Only include new procedures or adaptations to standard procedure.
- If you name any specific product, then it requires the name, city, and state/country of the manufacturer.
- Present in narrative format and use past tense.
- Where relevant, tables or figures may be included to provide information more clearly.
- Generally, no data should normally 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 the 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 supported or rejected.
- The results must be interpreted clearly, and any deficiencies expressed. All possible confounding factors, sources of bias, 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 should be clearly stated
- Should 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 but put emphasis on previous findings that agree (or disagree) with those of the present study.
- Do not repeat the introduction.
- The limitations of the study must be presented and suggest how the study could have been improved for a future study.
- Authors should avoid making inferences from non-significant trends unless they believe their study is adequately powered to answer the question; in that case, provide a power analysis.

Conclusion

Summary statement which conveys the conclusions of the findings. Do not draw conclusions not supported by the data obtained from the specific study presented.