Performance of Computed Tomography-Guided Spine Biopsy for the Diagnosis of Malignancy and Infection

Lauren Harris, MChem, MBBS, MRCS (Eng)
Devika Rajashekar, MBBS, MRCS (Eng)
Puneet Sharma, PhD, FRCS (Neurosurg)
Karoly M. David, MD, FRCS (Neurosurg)

Neurosurgery Department, Queen's Hospital, Barking, Havering and Redbridge University Hospitals NHS Trust, London, UK

Correspondence:
Devika Rajashekar, MBBS, MRCS (Eng),
Neurosurgery Department,
King's College Hospital,
68 Chancellor House,
395 Rotherhithe New Rd,
London SE16 3FP, UK.
Email: devika.rajashekar@nhs.net

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BACKGROUND: Computed tomography (CT)-guided percutaneous biopsies are used to guide treatment in vertebral osteomyelitis and spinal malignancy, but the efficacy of this study remains unclear.

OBJECTIVE: To investigate the performance of CT-guided spinal biopsy, and factors that may influence its success.

METHODS: Retrospective study of all consecutive patients who underwent a CT-guided spine biopsy at a UK teaching hospital between April 2012 and February 2019. Biopsies were performed by 3 consultant neuroradiologists for a lesion suggestive of either malignancy or infection. Data collection included patient factors, biopsy factors, further investigations required, and diagnosis. Data were analyzed using contingency tables, analysis of variance, unpaired t-test, chi-squared test, and Fisher's exact test.

RESULTS: A total of 124 percutaneous biopsies were performed on 109 patients with a mean follow-up of 34.5 mo (range 4-86 mo) and a mean age of 66 yr (range 27-93). Approximately 32.3% (n = 40) of the biopsies investigated possible infection, and 67.7% investigated malignancy. The sensitivity for infected cases was 37.0%, and for malignancy 72.7%. The diagnostic accuracy was 57.5% and 78.6%, respectively. Complication rate was 1.6%. In our study, neither needle gauge, anatomic level of the biopsy, or bone quality significantly affected the rate of positive biopsy.

CONCLUSION: Both in our study and in the wider literature, CT-guided biopsy has a vastly superior sensitivity for malignancy compared with suspected infection. These procedures may be painful, poorly tolerated, and are not entirely risk free. As such we advocate judicious use of this modality particularly in cases of suspected infection.

KEY WORDS: CT-guided biopsy, Spinal biopsy, Percutaneous, Spondylodiscitis, Malignancy

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The first percutaneous vertebral bone biopsy was described in 1934, used in conjunction with computed tomography (CT) in 1981.[1,2] Today, CT-guided percutaneous biopsies of spinal lesions are commonly used to diagnose cases of suspected malignancy and infection. Percutaneous needle biopsy has several perceived advantages over open biopsy: it is less invasive, minimizing infection risk and wound-related complications; it does not require a general anesthetic, operating theater, or scrub team; and can be performed in an outpatient setting. These features translate to a safer profile compared with open surgery, reduced cost, shorter procedural length, shorter hospital stay, and fewer complications. Critical constraints on their use, however, include limitations of sensitivity, patient tolerance, and technical challenges in select cases.

ABBREVIATIONS: ANOVA, analysis of variance; **TB,** tuberculosis; **VO,** vertebral osteomyelitis

Vertebral osteomyelitis (VO), with an incidence of 2.4/100 000, can form a serious, life-threatening condition.[3] It can follow an initially indolent clinical course with equivocal imaging features on magnetic resonance imaging (MRI) and CT. These infections commonly arise, however, from hematogenous dissemination from a remote site of infection, usually the urinary tract.[4] If left undiagnosed/untreated,

VO can lead to deformity, instability, sepsis, neurological sequalae including paralysis, and has a mortality rate of 6%.[5]

A clear microbiological diagnosis is required for pathogen-guided antibiotic therapy. This reduces treatment cost, adverse events, eg, *Clostridium difficile* infection, relapse, and the development of resistant organisms. In the absence of sepsis or impending cord compression, best practice is to isolate the organism prior to starting empirical antibiotics.[6] Blood cultures, however, have a positive yield of only 58% (range 30%-78%), and often identify only one organism when a polymicrobial infection is suspected.[4]

Vertebral malignancy can be classified into primary tumors or metastatic disease. Bone metastasis from a solid tumor has an incidence of 2.9% at 30 d and 4.8% at 1 yr.[7] More than 98% of spinal metastases are extradural, and can occur via direct local extension, retrograde spread though the valve-less Batson's plexus and from arterial emboli though the cortical veins.[8,9] Indications for biopsy include confirming metastasis, determining the nature of a solitary bone lesion and excluding malignancy in vertebral body compression.

The role of CT-guided biopsies in suspected infection or malignancy remains a topic of debate. A key factor is its efficacy in reaching a diagnosis. This study aims to determine the performance of CT-guided spine biopsies for malignancy and infection and to investigate possible factors that may affect its success.

METHODS

This study was registered locally with the Clinical Effectiveness Unit as a Service Evaluation prior to data collection. Data were fully anonymized so formal consent was not required.

All consecutive patients who underwent a CT-guided percutaneous spine biopsy at a large teaching hospital in the United Kingdom between April 2012 and February 2019 were included. The decision to biopsy was taken by the referring team after multidisciplinary team discussion with input from neuroradiology, neurosurgery, oncology, and microbiology teams. Patients were not biopsied if they (1) were not fit for intervention or further treatment; (2) had other sites of malignancy that were more easily accessible surgically; (3) patients' wishes; (4) had clinical improvement with treatment negating need for a biopsy. Children (age <18 yr) and sacral biopsies were excluded.

Biopsies were performed by 3 consultant neuroradiologists for a lesion in the spine suggestive of either malignancy or infection. Core biopsies were obtained using a combination of Jamshidi needles (Somatex, Berlin, Germany) for intact cortical bone or Tru-cut needles (Geotek, Ankara, Turkey) for lesions with a large soft tissue component, supplemented by fine-needle aspiration as required. Samples underwent histopathological and microbiological analysis (including Gram stain, fungal culture, mycobacterial culture, and polymerase chain reaction).

Patients were identified from the hospital's Information Department based on coding. This was cross-checked with the Radiology Department's records. Patients' notes, imaging using picture archiving and communication system, microbiology and histopathology results were retrospectively reviewed. Data collected included patient demographics, past medical history, suspected clinical-radiological diagnosis, anatomical level of the lesion, lesion bone matrix, needle gauge, volume of sample collected, complications, biopsy results (malignancy, infection, nondiagnostic, negative), and overall diagnosis. Bone matrix was categorized as lytic, sclerotic, or mixed based on the prebiopsy CT (either from a neuroradiology consultant report or an independent assessment by 2 authors, with a third acting as a mediator). The sample was considered nondiagnostic if the histopathologist ascertained that inadequate or nonrepresentative tissue had been obtained. The final diagnosis for nondiagnostic biopsies were determined by repeat biopsy, open biopsy, and clinical and radiological follow-up.

Data were analyzed on excel and GraphPad prism using 4 by 4 contingency tables, analysis of variance (ANOVA), unpaired t-test, chi-squared test, and Fisher's exact test as appropriate. P values $< .05$ were considered statistically significant.

The primary aim of this study was;

(1) To measure the performance of CT-guided spine biopsies for the diagnosis of infection and malignancy.

Secondary aims included;

(1) To determine whether needle gauge alters the volume of sample obtained;
(2) To determine whether volume of sample, anatomical level of lesion, and quality of bone impacts results.

RESULTS

A total of 124 percutaneous biopsies were performed on 109 patients with a mean follow-up of 34.5 mo (range 4-86 mo) (Figure 1). The mean patient age was 66.0 ± 14.9 with a range of 27 to 93 yr. A total of 60 patients were females (55%) and 49 were males.

Approximately 32.3% (n = 40) of the biopsies were performed due to a clinical and radiological suspicion of infection, and 67.7% (n = 84) for a suspicion of malignancy.

The sensitivity of CT-guided biopsy for infected cases was 37.0%, and for malignancy 72.7% (Table 1). One suspected infection was found to be a tumor (lymphoma) and 2 suspected tumor cases were found to be infection. No cases with a positive biopsy result had the diagnosis overturned by a subsequent test. Thus, both the specificity and positive predictive value were 100%. The negative predictive value was 43.3% for infection and 50% for malignancy. The diagnostic accuracy was 57.5% and 78.6%, respectively, with a yield of 25.0% and 57.1%.

Breast and lymphoma were the most commonly diagnosed malignancies (Table 2). *Mycobacterium tuberculosis* (TB) was the most common infection (Table 3).

There were 2 biopsy-related complications (1.6%) with no permanent sequalae: 1 patient could not tolerate the procedure and 1 patient had a pneumothorax.

In the cases where the CT-guided biopsy was nondiagnostic, a diagnosis was achieved by open biopsy (in 37.5% of cases), repeat CT-guided biopsy (31.3%), further blood cultures (25.0%), and repeat imaging (6.3%). Eleven patients had repeat biopsies which yielded results in 100% of these cases.

A total of 39 (31.5%) patients had a past medical history of malignancy, and 1 (0.8%) had a previous infection. Of the

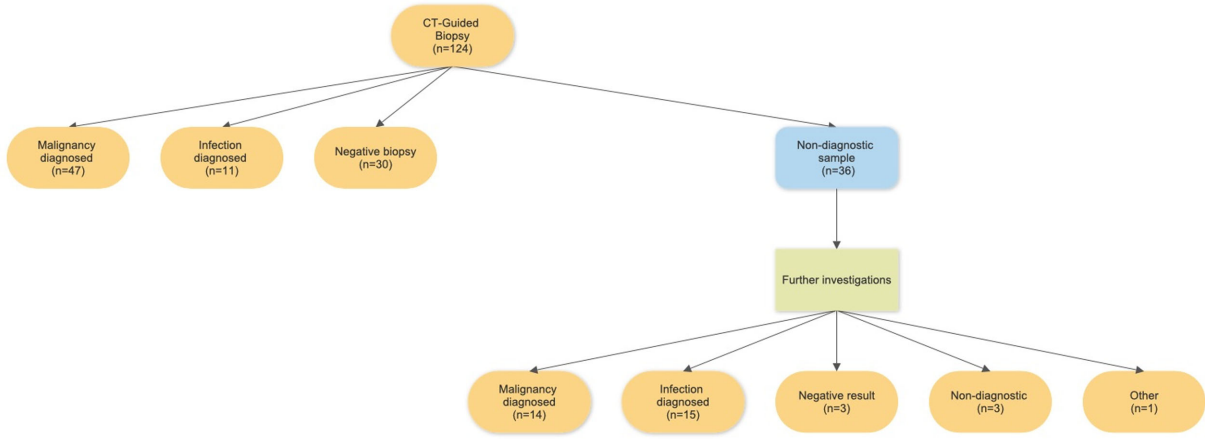

FIGURE 1. *Patient flowchart detailing the results obtained from our cohort of patients who underwent a CT-guided biopsy.*

TABLE 1. Comparison of Diagnostic Statistics for CT-Guided Biopsy for Infection and Malignancy

Variable (%)	All cases (n = 124)	Infection (n = 40)	Malignancy (n = 84)
Sensitivity	62.4	37.0	72.7
Specificity	100	100	100
PPV	100	100	100
NPV	47.0	43.3	50.0
Diagnostic accuracy	71.8	57.5	78.6
Diagnostic yield	46.8	25.0	57.1

PPV = positive predictive value. NPV = negative predictive value.
The performance of CT-guided spine biopsies, for all cases and broken down into infection and malignancy. Performance was quantified using sensitivity, specificity, PPV, NPV, diagnostic accuracy and yield..

TABLE 2. Malignancies Diagnosed From Diagnostic and Nondiagnostic CT-Guided Biopsy

Malignancy	Diagnosis from CT biopsy, n (%)	Nondiagnostic CT biopsy, n (%)
Breast	9 (19.1)	2 (14.3)
Lymphoma	9 (19.1)	5 (35.7)
Unable to classify	9 (19.1)	–
Plasmacytoma	7 (14.9)	4 (28.6)
Prostate	3 (6.4)	–
Sarcoma	2 (4.3)	–
Lung	2 (4.3)	–
Melanoma	2 (4.3)	–
Chordoma	2 (4.3)	–
Myeloma	1 (2.1)	1 (7.1)
Bladder	1 (2.1)	–
Endometrial	–	1 (7.1)
Meningioma	–	1 (7.1)

Breakdown of malignancy diagnosis including those diagnosed from CT-guided biopsy, and those with nondiagnostic CT-guided biopsy which required further investigations. Data given as raw number with percentage in parenthesis.

patients with a known malignancy, CT-guided biopsy diagnosed the same malignancy in 48.7%, showed no malignancy in 23.0%, and a different malignancy in 12.3% (results were inconclusive in 17.9%). Two patients with known breast cancer had a diagnosis of lung cancer and myeloma, respectively. One patient with a history of lymphoma had a biopsy positive for prostate cancer and one patient with a history of prostate cancer had a biopsy positive for sarcoma.

The needle gauge used for the biopsy did not significantly alter the volume of sample obtained (ANOVA test, P value = .5618, Figure 2). Additionally, the volume of sample obtained did not affect the outcome (unpaired t-test, P = .2826). There was no significant outcome difference at any anatomic level (Pearson's chi-squared test, P = .9159).

The diagnostic accuracy was higher in the sclerotic group (n = 19) at 89% versus the lytic group (n = 89) at 66%. The false negative rate was 11% and 34%, respectively. Whilst there was a trend toward sclerotic bone producing a higher proportion of true results, this was not significant (Fisher's exact test, P = .0539).

DISCUSSION

The sensitivity for CT-guided spinal biopsies was 37.0% for infection and 72.7% for malignancy. The diagnostic accuracy was 57.5% and 78.6%, respectively, with a yield of 25.0% and 57.1%. These results are reflected in the literature. A 2019 systematic review identified that the diagnostic culture yield of CT-guided biopsies for suspected spinal infections was 33%.[10] For malignancy, CT-guided biopsy yield has been reported to be approximately 77% to 80%, with some reports up to 97%.[8,11-13]

TABLE 3. Infection Diagnosed From Diagnostic and Nondiagnosis CT-Guided Biopsy

Infection	Diagnosis from CT biopsy, n (%)	Nondiagnostic CT biopsy, n (%)
Mycobacterium tuberculosis	4 (36.4)	7 (46.7)
Staphylococcus aureus	1 (9.1)	–
Pseudomonas	1 (9.1)	1 (6.7)
Streptococcus	1 (9.1)	–
Salmonella	1 (9.1)	–
Micrococcus luteus	1 (9.1)	–
Coagulase-negative *Staphylococcus*	–	2 (13.3)
Unknown	2 (18.2)	5 (33.3)

Breakdown of infective diagnosis including those diagnosed from CT-guided biopsy, and those with nondiagnostic CT-guided biopsy which required further investigations. Data given as raw number with percentage in parenthesis.

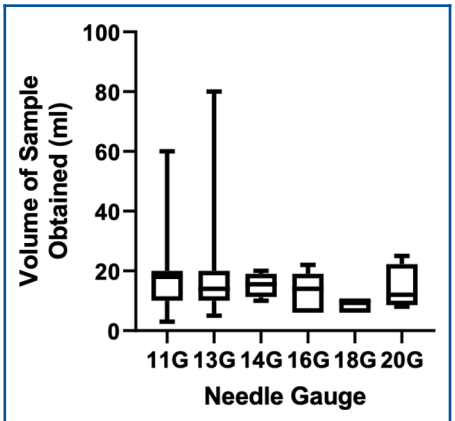

FIGURE 2. *Volume of biopsy sample obtained with variation in needle gauge. These results are statistically not significant.*

In all cases where the biopsy result was positive, the case was treated as "disease positive"; hence, the positive predictive value was 100% throughout. However, a negative biopsy result did not imply an absence of the disease, with a negative predictive value of 43% for infection and 50% for malignancy. Thus, biopsies appear not to be useful in excluding the presence of disease. Echoing others, we propose that a negative result must be confirmed with either close follow-up and/or repeat image-guided biopsy.[14]

A patient's previously known malignancy was diagnosed on CT-guided biopsy in under half the cases. One quarter of patients had no malignancy, with one-eighth having a diagnosis of a different malignancy. This has obvious implications for treatment.

Staphylococcus and then *Streptococcus* are the most common organisms present in vertebral osteomyelitis in the developed world, with TB being one of the most infectious pathogens worldwide.[4,15] The high number of cases of TB in our study reflects the local population, with a high percentage of Bangladeshi nationals. Empirical antibiotics would not target this pathogen, necessitating the need for a culture diagnosis.

Our results suggest that biopsies in cases where infection is the principal differential might not be the optimal diagnostic modality as sensitivity is 37%. This needs to be interpreted in the broader context, balancing the risk of an operation and need for a tissue diagnosis. The positive infectious yield from CT-guided biopsies is lower than that from blood cultures.[6] Hematogenous seeding typically starts in the subchondral bone of the vertebral body and then spreads to the intravertebral discs. Paravertebral abscesses and intravertebral fluid are usually sterile, resulting in nondiagnostic biopsies.[10] Other reasons may include pre administration of antibiotics, biopsy technique, specimen transfer methods, and culture techniques.[10] To what extent patients with no clinical or imaging findings suspicious for atypical pathogens may be better managed with empirical antibiotics is yet to be determined.[16]

Our study showed that (i) needle size did not affect volume of sample obtained, and (ii) volume of sample obtained did not affect diagnostic yield. Studies are inconsistent with regard to whether needle size and sample volume affect rates of accuracy.[12,17] Some hypothesize that the aim of the needle gauge is to avoid crush artifact within the sample, which can be achieved by a needle core above 3 mm.[18] A 2019 systematic review showed no relationship between needle gauge and yield, which is consistent with our results.[10]

It is conceivable that the anatomic level of the lesion could impact outcome, owing to technical challenges with the biopsy, or the bone quality. Our results did not suggest this and the literature is inconclusive.[14,17-20]

It is unclear whether bone architecture affects diagnostic accuracy and the literature is conflicting. Lytic bone may be conceivably devoid of tissue compared with sclerotic bone, and so poorer at providing tissue. On the other hand, lytic bone is likely to be replaced by abnormal soft tissue, rather than empty space, so may be better at providing samples compared with hard, sclerotic bone. Some suggest that diagnostic yield is significantly higher for lytic lesions than for sclerotic lesions, due to the partial liquid content of lytic bone.[11,12,14,20] Explanations include lower cellularity and reactive bone changes (eburnation) in sclerotic lesions and crushing artifacts from biopsy technique.[11,21] Chronic inflammation leads to increased sclerosis and decreased blood supply, which some argue leads to lower yields.[22,23] No consensus has been reached.

Our complication rates were low (1.6%) and consistent with published studies (1.1% as described by Rimondi).[24-26] In contrast, complication rates of open biopsy have been reported as high as 16%.[27]

Limitations

There were several limitations to this study. It was a retrospective, single-center study. Whilst 124 patients reflect a good

sample size, subgroup analysis for both the cervical and sclerotic cohort was small. We were unable to quantify the number of patients who had been commenced on empirical antibiotics or anti-tuberculous treatment prior to biopsy. The presence of a histopathologist during the procedure to evaluate the sample immediately may help to reduce the number of nondiagnostic biopsies, but this was not available at our institution. No attempt was made to correlate lesion size with diagnostic accuracy. In addition, we did not analyze the approach taken (eg, posterolateral, transpedicular) or where the biopsy was taken from (eg, pedicle, body) as this was individualized, making useful analysis difficult. The treatment algorithm for each patient, and a comparison with MRI to assess the accuracy of radiological diagnosis for malignant and infectious cases, was beyond the scope of this study. Despite this, we believe our study accurately reflects the performance of CT-guided spine biopsies for the investigation of malignancy and infection.

CONCLUSION

CT-guided biopsy is more useful for the diagnosis of malignancy than for infection. Performance is independent of sample volume, lesion location, or bone quality. Biopsy appears unhelpful in excluding the presence of disease, and a negative result must be confirmed with clinical follow-up and further investigation.

We advocate caution with the routine use of CT-guided spine biopsies in cases of suspected infection. Further prospective studies and randomized controlled trials are needed to guide best practice.

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