• Clinical Research •

Accuracy between clinical and radiological diagnoses compared to surgical orbital biopsies

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Abstract

● **AIM:** To assess the concordance between diagnosing orbital lesions by clinical examination, orbital imaging, and histological evaluation, in order to help guide future research and clinical practice.

● **METHODS:** A retrospective analysis was undertaken at a large regional tertiary referral centre of all surgical orbital biopsies performed over a 5-year period, from 1st January 2015 until 31st December 2019. Accuracy and concordance between clinical, radiological and histological diagnoses are reported as percentage sensitivity and positive predictive value.

● **RESULTS:** A total of 128 operations involving 111 patients were identified. Overall, sensitivities of 47.7% for clinical and 37.3% for radiological diagnoses were found when compared to the histological gold standard. Vascular lesions that have characteristic clinical and radiological features had the highest sensitivity at 71.4% and 57.1%, respectively. Inflammatory conditions showed the lowest sensitivity in both clinical (30.3%) and radiological (18.2%) diagnoses. The PPV for inflammatory conditions were 47.6% for clinical and 30.0% for radiological diagnoses.

● **CONCLUSION:** Accurate diagnoses are difficult to reach by relying on clinical examination and imaging alone. Surgical orbital biopsy with histological diagnosis should remain the gold standard approach for definitively identifying orbital lesions. Although larger scale prospective studies would help further refine concordance and guide future research avenues.

● **KEYWORDS:** orbital biopsy; orbital lesion; histological diagnosis; radiological diagnosis; clinical diagnosis

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INTRODUCTION

The orbit is a bony compartment containing a complex interplay of structures including the globe, fibrous septae, neurovasculature, lacrimal gland, orbital fat and extra-ocular muscles. Orbital lesions may impact one or more of these structures resulting in the common presenting symptoms of proptosis, visual decline and deficits in ocular movement[1]. It is possible to categorise orbital masses in many ways and usually include histopathological groups of inflammatory, vascular, infective, primary neoplastic and metastatic lesions[2-3].

Surgical biopsy is regarded as the gold standard approach for a definitive diagnosis of orbital lesions[3-4]. However, in certain circumstances there may be pathognomonic clinical presentations and characteristic radiological appearances of certain lesions. This may allow justification for clinicians to judiciously monitor these lesions in the first instance, especially if obtaining a biopsy can be associated with a high risk of resultant comorbidity such as in apical lesions. Although in such circumstance if any doubt arises, due to for example clinical progression, then an orbital biopsy is strongly recommended[5-6]. It has been long established that surgical orbital biopsy is a relatively safe and accurate diagnostic tool[3,5], although it is vital for surgeons to fully consent patients for uncommon but serious complications such as loss of vision. A 10-year review of orbital biopsies at a UK tertiary centre reported 7 complications from 166 orbital biopsies, of which diplopia was the most common[5]. Although there can be a concern of spreading malignant cells to surrounding tissues when performing surgical orbital biopsy, the study by Ting *et al*[5] did not report any complication on malignant seeding despite 34.6% of the orbital lesions obtained from surgical orbital biopsy were malignant in nature.

Fine needle aspiration biopsy (FNAB) is another technique for diagnosing orbital lesions. With the use of a fine hollow needle tumour cells can be obtained under direct visualisation for

anterior palpable lesions or with radiological guidance for more deeper masses. It has been used in cases where orbital lesions have high risk of seeding such as pleomorphic adenoma as well as minimising blood loss for patients with coagulopathies and hypervascular lesions[2]. However, in comparison to open biopsy the diagnostic potential is limited by the small volume of specimen and the disaggregation of cells from their natural histopathological architecture[7-8]. Additionally this approach has been shown to have less diagnostic value for lymphoproliferative and inflammatory lesions[2,8-9].

Advances in imaging technology is making radiological prediction of orbital masses a more viable alternative in certain circumstances to the historical histopathological gold standard. Over the years, new imaging modalities and protocols such as diffusion-weighted magnetic resonance imaging (DWI), fluoro-2-deoxy-d-glucose positron emission tomography computerised tomography (FDG-PET CT)[10] and MRI positron emission tomography (PET-MRI) scans[11] have assisted in improving diagnostic accuracy of orbital lesions. Although neuroimaging is a valuable addition to the armamentarium of orbital mass diagnostic tools, it is still challenging to accurately distinguish between the broad spectrum of benign, inflammatory and malignant lesions[10]. For example DWI has been used to characterize orbital lesions using ADC values, however, there is still considerable variation in the reported specificities and sensitivities of detecting benign and malignant lesions[12]. Although promising in certain circumstances, on the whole, the current literature to date is limited by low case numbers to achieve statistically significant outcomes and draw accurate clinical conclusions. Further research into the efficacy and accuracy of imaging modalities for orbital lesion diagnoses is warranted and requires large scale prospective trials.

There are two main indications for surgical orbital biopsy: 1) Suspicion of a malignant tumor from clinical and radiological findings. An excisional biopsy can be both diagnostic and therapeutic. 2) Inability to establish an accurate diagnosis from clinical or radiological information alone. A biopsy will serve as a diagnostic tool to aid the clinician in formulating a management plan[3].

Currently, there is limited research comparing the consistency between clinical, radiological and histological diagnoses by surgical orbital biopsy[3]. The aim of this study was to further evaluate the accuracy of clinical and radiological diagnosis of orbital lesions when compared to histological diagnosis by building on the 12-year study by Koukkoulli *et al*[3] in order to assess for changes in outcomes over time, inform future research and potentially clinical practice. The concordance results from this study can help clinicians identify the categories of orbital lesions that have higher clinical and radiological rates of diagnosis, in order to minimize risks of surgical biopsy in challenging cases such as in apical lesions. The results can also be applied when counselling patients about the accuracy of clinical or radiological diagnosis before opting for orbital biopsy.

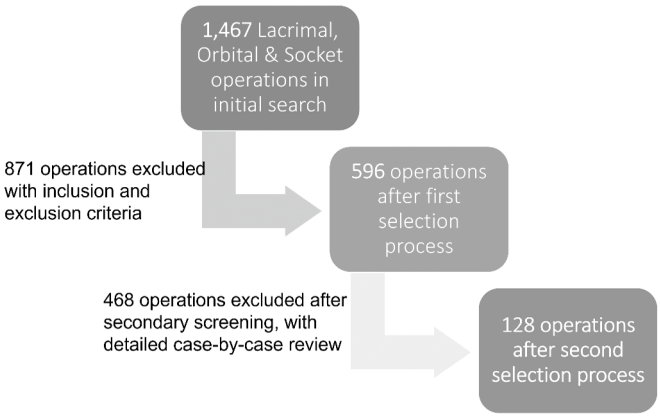

Figure 1 Case identification and selection process.

SUBJECTS AND METHODS

Ethical Approval Although formal ethical approval was not required as this study was an audit, local governance procedures were followed as well as adherence to the tenets of the Declaration of Helsinki[13].

This was a retrospective study of orbital biopsies performed at Leeds Teaching Hospitals NHS Trust over a 5-year period from 1st January 2015 until 31st December 2019.

Clinical Governance Local research and clinical governance procedures were followed with the study being categorised and registered as a clinical audit (registration number 8780).

Case Identification Case search and identification was undertaken by Tang A and Ng HHL by using electronic and paper medical record systems: Medisoft, Histology Databank, and theatre logbooks. The initial search identified 1467 periorbital operations.

Case Selection After applying the inclusion and exclusion criteria 596 cases remained. Further secondary case-by-case review using electronic and paper records (PPM+, Medisoft, EPRO, ICE) resulted in 128 operations judged eligible for the final data analysis (Figure 1). This was undertaken by Tang A and Ng HHL, although case discussion and arbitration if required was undertaken by Gout T, Kalantzis G, and Chang B.

Inclusion criteria: 1) Biopsy due to suspicion of orbital malignancy. 2) Biopsy to aid diagnosis of non-malignant systemic conditions (*e.g.* granulomatosis with polyangiitis and sarcoidosis). 3) Biopsy to assist surgical management (cavernous haemangioma debulking).

Exclusion criteria: 1) Orbital procedures excluded: trauma related (*e.g.* orbital fracture repair with bone fragment removal), therapeutic (orbital floor injections with scar excision); socket reconstruction (*e.g.* socket implants). 2) Lacrimal procedures excluded: trauma (with no requirement

for traumatic implanted material biopsy), lacrimal apparatus evaluation and stenting (with no lesions for biopsy). 3) Oculoplastics procedures excluded: complex reconstructions including the orbit (with no suspicious lesions for additional biopsy).

Data Collection The retrospective data retrieved from the patient's records included demographic material, presumptive clinical diagnosis prior to neuroimaging, radiological reports (CT and/or MRI) and histology results. Morbidity and mortality rates were recorded.

The results were categorised into six major pathological groups based on histological diagnosis as outlined by Koukkoulli *et al*[3]: inflammatory, haematological, neoplastic (primary or metastatic; sub-categorised into benign and malignant), vascular, infective and miscellaneous.

Arbitration Classification of pathologies was in accordance to the categories reported by Koukkoulli *et al*[3]. If there were uncertainties to diagnosis or classification highlighted by Tang A and Ng HHL, then individual case discussion and arbitration was undertaken by Gout T, Kalantzis G, and Chang B. This was made with respect to World Health Organization International Classification of Diseases 11th revision for cases with complex pathophysiology that could span more than one category[14].

Statistical Analysis Presumptive radiological and clinical diagnosis, if provided before the surgical orbital biopsy, was compared to the histological diagnosis. If the clinical or radiological diagnosis assessed independently were in line with the histological diagnosis, this was categorised as correct diagnosis (CD). However, if the presumptive diagnosis was different from the tissue diagnosis, this was classified as a new (incorrect) diagnosis (ND). If no presumptive clinical or radiological diagnosis was provided, it was automatically classified as ND. If more than one presumptive diagnosis was made by the clinician or radiologist, this was deemed as no definite diagnosis and would be categorised as ND. Inconclusive diagnosis (ICD) by histology was classified under miscellaneous.

Sensitivity is the proportion of test positive results given disease positive; and was measured by the proportion of correct diagnoses divided by the total of new incorrect diagnoses and correct diagnoses. Positive predictive value (PPV) is the proportion of disease positive cases given test positive; and was assessed to determine the rate of accuracy. The PPV of clinical diagnoses was the proportion of correct clinical diagnoses divided by the total of false negatives and correct diagnoses. The PPV of radiological diagnosis was assessed in a similar fashion.

RESULTS

Data Collection and Patient Demographics Totally 128 orbital biopsies involving 111 patients were identified between 1st January 2015 to 31st December 2019. Totally 74 cases were performed in the left eye and 54 in the right eye. Three histological samples from biopsies were inconclusive and fifteen cases had no clinical diagnosis offered. Radiological imaging was done in 110 cases, and no diagnoses were offered in 14 cases. The mean age of patients was 44.7y, ranging from 7mo to 87y. The male-to-female ratio was 49:62.

Histological Diagnosis Four patients in this cohort had repeat biopsies. The indications for repeat biopsies were poor quality sample; further debulking; and worsening symptoms, with one patient who had a previous chronic inflammation histology continued to complain of pain despite being on treatment, a re-biopsy was done which showed the same result.

The following shows the respective number and percentage in brackets of histological lesions in each category: inflammatory 33 (25.0%); haematological 18 (13.6%); vascular 7 (5.3%); infective 0; primary neoplastic malignant 11 (8.3%); primary neoplastic benign 14 (10.6%); secondary neoplastic 2 (1.5%); miscellaneous 40 (30.3%) cases (Table 1). Of the inflammatory category, majority of the lesions were chronic in nature.

The overall concordance rates between histological and clinical diagnoses is 47.7%; histological and radiological diagnoses is 37.3%; and clinical and radiological diagnoses is 47.3%. Lowest concordance was seen between histological and radiological diagnoses (Table 2).

Clinical Diagnosis CD were offered in 61 (47.7%) cases, while ND not in concordance with histology were given in 52 (40.6%) cases (Table 3). The overall concordance rates between clinical and radiological diagnoses are 47.3%.

The sensitivity and PPV of clinical diagnosis were 30.3% and 47.6% respectively for inflammatory lesions; 66.7% and 66.7% for haematological lesions; 45.5% and 33.3% for primary neoplastic malignant lesions; 35.7% and 25.0% for primary neoplastic benign lesions; 50.0% and 100% for secondary neoplastic lesions; 71.4% and 62.5% for vascular lesions; and 60.0% and 68.6% for miscellaneous lesions (Table 4).

Radiological Diagnosis Imaging reports were in concordance with the histological results in 41 (37.3%) cases (Table 5). The sensitivity and PPV of radiological diagnoses were 18.2% and 30.0% for inflammatory lesions; 55.6% and 50.0% for haematological lesions; 36.4% and 36.4% for primary neoplastic malignant lesions; 28.6% and 44.4% for primary neoplastic benign lesions; 50% and 50% for secondary neoplastic lesions; 57.1% and 36.4% for vascular lesions; and 30.0% and 52.2% for miscellaneous lesions (Table 6).

DISCUSSION

This is a five-year retrospective single centre case series reviewing the diagnostic accuracy of clinicians and radiologist with respect to orbital lesions. Building on the work done by

Table 1 Histological categories of orbital biopsies

Category	Diagnosis based on histology
Inflammatory	33 (25.0%)
Chronic inflammation	11
Chronic dacryoadenitis	3
Chronic dacryocystitis	2
Chronic sialadenitis	1
Idiopathic inflammation	2
Non-specific inflammation	2
IgG4 associated inflammation	1
IgG4-related chronic sclerosing dacryoadenitis	1
Sarcoidosis	3
Inflammatory pseudotumour	2
Reactive changes	5
Haematological	18 (13.6%)
Lymphoma	18
Vascular	7 (5.3%)
Lymphovenous malformation	1
Cavernous haemangioma	6
Infective	0
Primary neoplastic malignant	11 (8.3%)
Adenocarcinoma	2
Rhabdomyosarcoma	3
Malignant melanoma	1
Nodular BCC	1
Transitional cell carcinoma	1
Squamous cell carcinoma	1
Adenoid cystic carcinoma	1
Multiple myeloma	1
Primary neoplastic benign	14 (10.6%)
Neurofibroma	1
Solitary fibrous tumour	2
Choriostoma	1
Schwannoma	1
Benign eccrine hydrocystoma	2
Pilocytic astrocytoma	1
Pleomorphic adenoma	4
Traumatic neuroma	1
Lacrimal mucocele	1
Secondary neoplastic	2 (1.5%)
Breast	2
Miscellaneous	40 (30.3%)
Amyloidosis	2
Dermoid	12
Lipodermoid	3
Lipoma	3
Epidermoid cyst	2
Extensive calcification	1
Fibrofatty tissue	1
Florid lymphoid hyperplasia	4
Lacrimal gland hyperplasia	1
Lacrimal gland cyst	1
Normal tissue	10
Inconclusive histology	3

BCC: Basal cell carcinoma.

Table 2 Concordance between histological diagnoses and clinical or radiological diagnoses

Parameters	Histological *vs* clinical	Histological *vs* radiological	Clinical *vs* radiological
Concordance (%)	47.7	37.3	47.3

Table 3 Accuracy of clinical diagnosis

Clinical diagnosis	*n*
Correct diagnosis	61
New diagnosis (clinical diagnosis not in concordance with histology)	52
New diagnosis (no clinical diagnosis offered)	15

Koukkoulli *et al*[3] we hope to help guide future research and potentially clinical practice.

In comparing our results to the previous study by Koukkoulli *et al*[3], there was overall similarity of outcomes with less than 50% of CD was reached by both ophthalmologists and radiologist alike. Interestingly, there was an increase in the concordance between clinical and histological diagnosis from 35.7% to 47.7%. This most likely may be attributed to the previous study reporting clinician diagnoses provided by generalists as opposed to our study that reported opinions from orbital specialists. As may be expected this suggests a clinician's sub-specialty experience and knowledge correlates to their accuracy of clinical diagnosis.

On the other hand, there was an increase in the concordance between radiological and histological diagnosis from 30.4% to 37.3% when comparing to the study by Koukkoulli *et al*[3]. This is likely multifactorial and may result from improvements in imaging technology and protocols; improved radiologists experience with managing orbital lesions over time; and added insight from referral reasoning made by an orbital specialist.

The improved diagnostic accuracy of both clinicians and radiologists in our study therefore emphasises how the diagnosis can be dependent on the years of experience of the physician. However, it is worth noting that orbital specialists with over 20y of experience involved in our study may also find it challenging to reach a precise clinical diagnosis as suggested by our concordance values. Therefore, having a regular Multi-Disciplinary Team (MDT) involving orbital specialists, radiologists and pathologists to jointly discuss cases can potentially improve diagnostic accuracies and patient outcomes. By combining the knowledge of orbital specialists and the expertise of radiologists in interpreting scans in a MDT, a more accurate primary diagnosis may be reached as this will be based on history, examination and imaging findings altogether. Depending on the diagnosis this may guide any immediate management, need for a biopsy, and timing of the biopsy.

There have been multiple studies investigating the effects of clinical information on the accuracy of radiological diagnosis. Castillo *et al*[15] systemic review concluded that the

Table 4 Sensitivity and PPV for clinical diagnoses by category

Categories	No. of lesions excised	No. of clinical diagnosis	No. of correct clinical diagnosis	Sensitivity (%)	PPV (%)
Inflammatory	33	21	10	30.3	47.6
Haematological	18	18	12	66.7	66.7
Primary neoplastic malignant	11	15	5	45.5	33.3
Primary neoplastic benign	14	15	4	35.7	25.0
Secondary neoplastic	2	1	1	50.0	100
Vascular	7	8	5	71.4	62.5
Infective	0	3	0	0	0
Miscellaneous	40	32	24	60.0	68.6
No clinical diagnosis offered			15		

PPV: Positive predictive value.

Table 5 Accuracy of radiological diagnosis

Radiological diagnosis	*n*
Correct diagnosis	41
New diagnosis (radiological diagnosis not in concordance with histology)	55
New diagnosis (no radiological diagnosis offered)	32

Table 6 Sensitivity and PPV for radiological diagnoses by category

Categories	No. of lesions excised	No. of radiological diagnosis	No. of correct radiological diagnosis	Sensitivity (%)	PPV (%)
Inflammatory	33	20	6	18.2	30.0
Haematological	18	20	10	55.6	50.0
Primary neoplastic malignant	11	11	4	36.4	36.4
Primary neoplastic benign	14	9	4	28.6	44.4
Secondary neoplastic	2	2	1	50.0	50.0
Vascular	7	11	4	57.1	36.4
Infective	0	0	0	0	0
Miscellaneous	40	23	12	30.0	52.2
No radiological diagnosis offered			14		

PPV: Positive predictive value.

clinical information provided can have a positive effect on radiological reporting and improve accuracy of interpretation. Similarly, Lacson *et al*[16] also demonstrated how incomplete or discordant clinical requests can impact on the radiological interpretation. This can potentially highlight the importance of clinical information in the formulation of radiological diagnosis and reinforces the main principle behind diagnostic radiology which is to interpret imaging to guide management and predict patient outcomes[17]. Therefore, recommending a regular MDT to jointly discuss scans can possibly increase concordance and improve patient outcomes.

Bacorn *et al*[18] retrospectively reviewed 242 orbitotomy procedures over a nine-year period. They found that the clinical and radiological diagnosis agreed with the histological diagnosis in 75.7% and 52.4% of the cases respectively. In contrast, our study showed less concordance clinically and radiologically, with 47.7% and 37.3% respectively. Although both studies involved orbital subspecialists, the clinical diagnosis in their study was reached after both clinical assessment and interpretation of orbital imaging[18], meaning that the clinical diagnosis is not purely based on clinical findings but a combination of clinical and radiological aspects. This is likely to account for the difference in concordance between clinical and histological diagnoses. The difference in medical systems can also contribute to the discrepancy in concordance values. While neuroimaging may not always be available or performed prior to the initial clinic visit and therefore not factor into the clinical diagnosis, this is common practice in some centres and may contribute to their higher diagnostic accuracy[3,16-17]. In real-life practice clinicians would reach a preliminary diagnosis based on the combination of both clinical and radiological findings before taking a biopsy. In the future it may be valuable to compare the clinical diagnosis before imaging studies to the clinical diagnosis made by orbital surgeons with access to neuroimaging scans.

In our study, clinical and radiological diagnosis were not offered in 15 and 14 cases respectively. The is because some lesions had a high potential for metastases and urgent biopsies were therefore performed without the need to formulate a precise clinical or radiological diagnosis. Another reason for no clinical diagnosis is because a group of patients who came through accident and emergency department normally had imaging done before seeing the ophthalmologist, therefore providing the orbital specialist imaging reports to help

guide their clinical diagnosis. There were also cases where radiologists only described radiological features without offering a definite diagnosis and this was deemed as no radiological diagnosis offered (a type of ND). Interestingly, advancements in diagnostic imaging modalities have allowed for conservative management or medical treatment as opposed to immediate surgical biopsy[10,19].

As a referral centre the case load reviewed provided a reasonable sample to represent the likely population distribution of orbital lesion pathologies, which resembles the study findings by Ting *et al*[5] that found inflammatory and lymphoproliferative lesions as the two most common orbital pathologies in his retrospective study of orbital biopsy at the Newcastle Eye Center.

There was a total of 3 inconclusive histology cases in our study. One patient was clinically suspected to have thyroid eye disease and the other with Erdheim-Chester disease, but for both cases histology was inconclusive with non-specific inflammatory changes that were not re-biopsies as there was no clinical progression. The accuracy of histological diagnosis has been reported as dependent on the skills of the individual obtaining the sample and the experience of the pathologist[2], which is similar to how clinical and radiological diagnosis can be dependent on the experience of physician as mentioned previously. For example, there was a case where the patient had two repeat biopsies, with the first biopsy suggesting lacrimal hyperplasia, second suggesting adenocarcinoma and final biopsy showing malignant melanoma. This suggests that an accurate histological diagnosis is not only dependent on the quality of the biopsy sample, but also on the histopathology investigations and systemic work up as well.

Both ophthalmologists and radiologists demonstrated their highest sensitivity in vascular lesions, with 71.4% clinically and 57.1% radiologically, which is a finding consistent with the previous study by Koukkoulli *et al*[3]. Since vascular lesions present with characteristic features, this allows for more accurate diagnosis both clinically and radiologically[3]. On imaging, vascular orbital tumours characteristically have vessels within or connected to the mass and tend to also have more contrast enhancement than non-vascular lesions[20]. Various imaging features have been reported to help differentiate vascular lesions that include enhancement patterns, superior ophthalmic vein enlargement, and phleboliths[20].

On the other hand, inflammatory lesions presented with the lowest sensitivity for both clinical (30.3%) and radiological (18.2%) diagnosis which is similar to the previous study[3]. Inflammatory lesions comprise a broad overlapping category of conditions. This makes it challenging for both clinicians and radiologists to provide a specific diagnosis, which results in either a list of differentials or no diagnosis being provided. This therefore contributes to the low sensitivity of this subset. For example, sarcoid and idiopathic orbital inflammatory lesions have been reported to be difficult to differentiate without performing a biopsy[3].

The PPV is highest for secondary neoplastic lesions clinically but not radiologically. This could possibly be the result of a small sample size (only two lesions) and the fact that imaging only echoed the clinical suggestion by describing the lesion seen with no diagnosis given. Furthermore, the higher PPV for miscellaneous lesions could be attributed to the fact that the centre has seen more lesions categorised as “miscellaneous”, which can include normal tissue, cysts and hyperplasia; and there were 42.9% increased number of lesions compared to Koukkoulli *et al*[3].

In our study, the CT technique used was 64 slice with contrast; while the MRI protocol used were T1/2 weighted with FLAIR, fat saturation and DWI with and without contrast. It is widely known that MRI is the preferred choice for imaging the orbit due to its better visualisation of soft tissues[10,21]. Our study reflects this finding as 44.2% of CD is reached with MRI imaging, compared with 29.8% when imaged with CT. Interestingly, our results show that using both CT and MRI does not increase the accuracy of diagnoses, with 36.4% of these combined imaging cases reaching a CD. Over half of these cases (6 out of 11 cases) were suggested by imaging as lymphoma or other malignancies. The nature of the lesion could be the reason for both imaging modalities being requested as well as the diagnostic challenge in their diagnosis. This study reinforces the findings of previously reported literature. There may be an element of increased clinician and radiologist experience since the previous study by Koukkoulli *et al*[3] that relates to the improved clinical and radiological concordance with histological diagnosis, respectively. However, reaching a precise clinical diagnosis is still challenging even by an experienced orbital specialist and this reinforces the value of a multidisciplinary approach for challenging cases as a way to improve the diagnostic accuracy from clinical and radiological findings combined. This approach may help clinicians better diagnose orbital lesions prior to surgical biopsy, which is especially valuable for challenging high-risk apical cases. As well as allow patients to be better informed for their decisions on proceeding with surgical biopsies.

Our study has limitations associated with retrospective studies such as being prone to mis-classification bias and being subjected to confounding bias. Retrospective data collection is also prone to having incomplete, inconsistent or inaccurate records. However, this approach was most practical given the availability of the data set. Precautions were taken to address these issues with arbitration of diagnostic or classification

uncertainty as outlined in the methodology section. The study also only assessed the excised lesions as the assumption was that the non-excised lesions were benign, which potentially increased the 'true' sensitivity rate and PPV. Therefore, a prospective study to see how many orbital lesions that are not biopsied will allow for capturing the complete dataset.

In conclusion, based on this study surgical orbital biopsy should remain the gold standard for diagnosing orbital lesions of unknown aetiology.

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REFERENCES

1 Héran F, Bergès O, Blustajn J, Boucenna M, Charbonneau F, Koskas P, Lafitte F, Nau E, Roux P, Sadik JC, Savatovsky J, Williams M. Tumor pathology of the orbit. *Diagn Interv Imaging* 2014;95(10):933-944.

2 Mombaerts I, Ramberg I, Coupland SE, Heegaard S. Diagnosis of orbital mass lesions: clinical, radiological, and pathological recommendations. *Surv Ophthalmol* 2019;64(6):741-756.

3 Koukkoulli A, Pilling JD, Patatas K, El-Hindy N, Chang B, Kalantzis G. How accurate is the clinical and radiological evaluation of orbital lesions in comparison to surgical orbital biopsy? *Eye* (*Lond*) 2018; 32(8):1329-1333.

4 Jamison A, Gregory ME, Lyall DAM, Kemp *E.G.* Visual outcomes following orbital biopsy. *Orbit* 2013;32(5):304-308.

5 Ting DSJ, Perez-Lopez M, Chew NJ, Clarke L, Dickinson AJ, Neoh C. A 10-year review of orbital biopsy: the Newcastle Eye Centre Study. *Eye* (*Lond*) 2015;29(9):1162-1166.

6 Medel R, Balaguer Ó. Approach to diagnosis of orbital tumours. *Orbital Surgery* 2014:46-72.

7 Jose P, Barão R, Matos D, Pinto F, Fonseca A, Teixeira F. Orbital biopsy: is it worth it? a 10-year review. *Pan Am J Ophthalmol* 2020;2(1):38.

8 Alkatan HM, Alyousef NA, Alshabib NS, Aljasser IHJ. A comprehensive review of biopsy techniques for oculoplastic and orbital surgeons from ophthalmic pathologists' perspective. *Saudi J Ophthalmol* 2021; 35(3):174-178.

9 Alkatan HM, Helmi KA, Maktabi AMY. Pitfalls in diagnosing orbital malignancy through orbital incisional biopsy: A report of two cases with different scenarios. *Saudi J Ophthalmol* 2021;34(3):205-208.

10 Purohit BS, Vargas MI, Ailianou A, Merlini L, Poletti PA, Platon A, Delattre BM, Rager O, Burkhardt K, Becker M. Orbital tumours and tumour-like lesions: exploring the armamentarium of multiparametric imaging. *Insights Imaging* 2016;7(1):43-68.

11 Kalemaki MS, Karantanas AH, Exarchos D, Detorakis ET, Zoras O, Marias K, Millo C, Bagci U, Pallikaris I, Stratis A, Karatzanis I, Perisinakis K, Koutentakis P, Kontadakis GA, Spandidos DA, Tsatsakis A, Papadakis GZ. PET/CT and PET/MRI in ophthalmic oncology (review). *Int J Oncol* 2020;56(2):417-429.

12 Sepahdari AR, Politi LS, Aakalu VK, Kim HJ, Abdel Razek AAK. Diffusion-weighted imaging of orbital masses: multi-institutional data support a 2-ADC threshold model to categorize lesions as benign, malignant, or indeterminate. *AJNR Am J Neuroradiol* 2014;35(1):170-175.

13 World Medical Association. WMA declaration of helsinki – ethical principles for medical research involving human subjects. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/. Updated 2022. Accessed on 18th November, 2022.

14 World Health Organization. International classification of diseases 11th revision. https://www.who.int/standards/classifications/classification-of-diseases. Accessed 18th November, 2022.

15 Castillo C, Steffens T, Sim L, Caffery L. The effect of clinical information on radiology reporting: a systematic review. *J Med Radiat Sci* 2021;68(1):60-74.

16 Lacson R, Laroya R, Wang AJ, Kapoor N, Glazer DI, Shinagare A, Ip IK, Malhotra S, Hentel K, Khorasani R. Integrity of clinical information in computerized order requisitions for diagnostic imaging. *J Am Med Inform Assoc* 2018;25(12):1651-1656.

17 Sim R, Young SM, Agrawal R, Sundar G. Clinical, radiological and histological correlation in diagnosis of orbital tumours. *Cogent Med* 2019;6(1):1607128.

18 Bacorn C, Gokoffski KK, Lin LK. Clinical correlation recommended: accuracy of clinician versus radiologic interpretation of the imaging of orbital lesions. *Orbit* 2021;40(2):133-137.

19 Tailor TD, Gupta D, Dalley RW, Keene CD, Anzai Y. Orbital neoplasms in adults: clinical, radiologic, and pathologic review. *Radiographics* 2013;33(6):1739-1758.

20 Poon CS, Sze G, Johnson MH. Orbital lesions: differentiating vascular and nonvascular etiologic factors. *AJR Am J Roentgenol* 2008;190(4):956-965.

21 Karcioglu ZA. Overview and imaging of orbital tumors. *Surgical Ophthalmic Oncology*. Cham: Springer International Publishing, 2019:107-116.