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**Original Article**

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# A Retrospective Study to Assess the Impact and Importance of Pursuing a Second Opinion Surgical Pathology on Continuum of Treatment

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## Abstract

***Objective:*** The aim of this study is to identify the rate of major and minor disagreements with diagnoses from external institutions for patients with head and neck lesions or clinical contexts. ***Design:*** Considering the high significance of referral in pathology, it seems that no planned retrospective or prospective study has been conducted in Saudi Arabia. ***Subjects/Patients:*** We decided to review the diagnoses of patients that were referred to our hospital over 24 months from 2015 to 2016. ***Methods:*** Both paper and electronic health records were used for data collection at King Fahad Medical City. A retrospective review of all consecutive referral cases starting from January 1, 2015, to September 30, 2016, was performed for diagnostic errors, adverse events and near misses' diagnosis. ***Results:*** The major diagnostic discrepancy, defined as diagnostic or staging differences resulting in major alterations in treatment, were seen in 26 (10.6%) of the cases. The observed discrepancy rate of 10.6%. ***Conclusion:*** Our mandatory second review policy in pathology referral cases leads to 10.57% major diagnostic changes across all sites of head and neck. In conclusion, the second opinion in pathology should be obtained before any major therapeutic endeavour as it reveals diagnoses discrepancy, particularly in challenging sites and cases.

**Keywords:** ***Surgical pathology, Pursuing a second opinion surgical pathology, Surgical pathology on continuum of treatment, Head and neck lesions, Diagnostic errors.***

## Introduction

The primary goal of pathology is to provide a correct and accurate diagnosis as the errors in pathology may lead to many adverse consequences such as mortality, morbidity, and disability (Ahmed *et al*., 2004; Kronz *et al*., 2005). As per American Medical Association, diagnostic error was associated with annual mortality rate of 44,000 to 98,000 (Maria *et al*., 2013). Despite advances in diagnosis, head and neck cancer remains the area of diagnostic discrepancies because of complex, diverse, and difficult pathology. Thus, obtaining Secondary opinion is the best method to prevent diagnostic errors (Seo *et al*., 2017). In general, 74.8% of pathologists recommended, whereas 19.8% contended the second opinion of a pathologist depending on the type of lesion and primary diagnosis. Additionally, 2.7% (n = 3) accepted both of these components were advantageous. Furthermore, one pathologist didn't consider referral as a valuable option instead suggested it for controversial cases. Furthermore, two pathologists found referral to be time consuming and confusing but might be necessary in certain situations (Razavi *et al*., 2018).

The aim of this study is to identify the rate of major and minor disagreements with diagnoses from external institutions for patients with head and neck lesions or clinical contexts

The development of head and neck squamous cell carcinoma (HNSCC) is influenced by pre-existing medical conditions, infectious agents, family history, oral hygiene, diet and Exposure of carcinogen, individually or in combination. Smoking of tobacco is considered as a predominant risk factor for HNSCC, and this risk is related with the duration and intensity of smoking. Smoking cessation reduces but doesn't completely stop the danger of cancer advancement (Schlecht *et al*., 1999).


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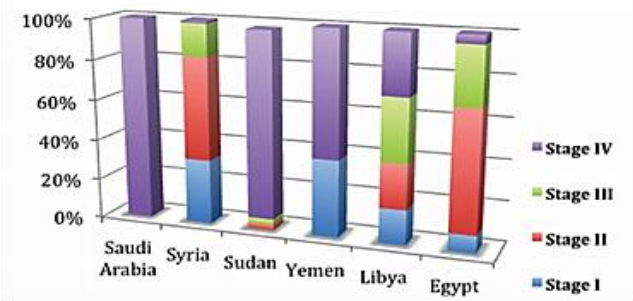


**Figure 1: Distribution of oral cancer histological stage at the time of diagnosis by Arab country**

The criterion for identification of cases to be sent for second opinion is not mentioned in any guidelines. However discrepancy in diagnosis have been identified in almost all major organs with certain sites of the body and lesions being more prone towards yielding errors (Tsung., 2004). Head and neck area have been highlighted as high risk area in site specific studies (Woolgar *et al*., 2011).The most disturbing finding of this was that 66.7% biopsy for squamous cell carcinomas were misdiagnosed as non-malignant or dysplasia. Obscuring inflammation (3.3%), insufficient tissue (13.3%), and discrepancy (23.3%) were among other reasons for misdiagnosis of incisional biopsy. The factor contributes to errors in surgical pathology are shown in table 1.

**Table 1: Factor contribution to errors in surgical pathology**

| Factor | Contribution |
|---|---|
| Variable input | Variable input in patient identification and in clinical history leads to errors in surgical pathology. |
| Complexity | The chance of error increases as a system is more complex. |
| Inconsistency | Errors may occur with inconsistency in training, individual performance, procedures, communication, and language or diagnostic taxonomy. |
| Human intervention | Humans do poorly at routine repetitive tasks. Machines are best for routine repetitive tasks but tend to have problems with unanticipated situations. |
| Time constraints | Batch work and deadlines may force individuals to cut corners or at least work in a hurried mode that may result in errors. |
| Hand-offs | In surgical pathology, hand-offs of the specimen include specimen collection, labeling, delivery, accessioning, dissection, transfer to cassette, transfer to block, transfer to slide, transcription of findings, and report delivery. |
| Inflexible hierarchical culture | This type of culture leads to failure because of the inability to adapt and change and the inability to acknowledge the source of errors. |

The challenges with the funding for second opinion diagnosis depend upon the country. The healthcare system is differently financed in each country. In an ideal scenario the second opinion shall be mandatory and free of charge for improving the patient's management. If the pathology report of the referred patient is incomplete and he physician at the referral centre asks for a full diagnostic biopsy than charging a fee can become counterproductive. Telepathology may also help to reduce the time of a second review (Etit *et al*., 2013).

## Methods

### Data abstraction instrument

Both paper and electronic health records were used for data collection at King Fahad Medical City (KFMC). The validity, reliability, and reproducibility of data gathering instruments were tested through a pilot study.

### Sample size

A retrospective analysis of 397 pathology referrals cases with demographic data and clinical information (slide or block and outside report) was performed for original diagnosis in the KFMC, Saudi Arabia, starting from January 1, 2015, to September 30, 2016 (20 months). Cases were categorized by anatomic site/organ systems as per WHO Head and Neck Classification 2016_ updates 2017. The primary diagnosis was compared with the second review to assess the disparity rates and the impact on management.

### Ethics approval

The requisite approval from KFMC Department of Pathology and Institutional Ethics Committee was taken to collect data and use it for research.

### Eligibility of referral cases

### Inclusion and exclusion criteria

A retrospective review of all consecutive referral cases starting from January 1, 2015, to September 30, 2016, was performed for diagnostic errors, adverse events and near misses diagnosis. Cases with diagnostic discrepancies based on histologic tissues recut and/or additional material were included. Exclusion criteria included those cases that demand secondary opinions from physicians other than pathologists and lack of accompanying slides or blocks. Also, challenging cases, that were sent to KFMC pathology department, without a previous or tentative diagnosis were excluded from the study (Westra *et al*., 2002, Mullin *et al*., 2015).

### Methodology to be Adopted for Answering the Research Questions

The clinical diagnostic process in pathology is shown in figure 2.

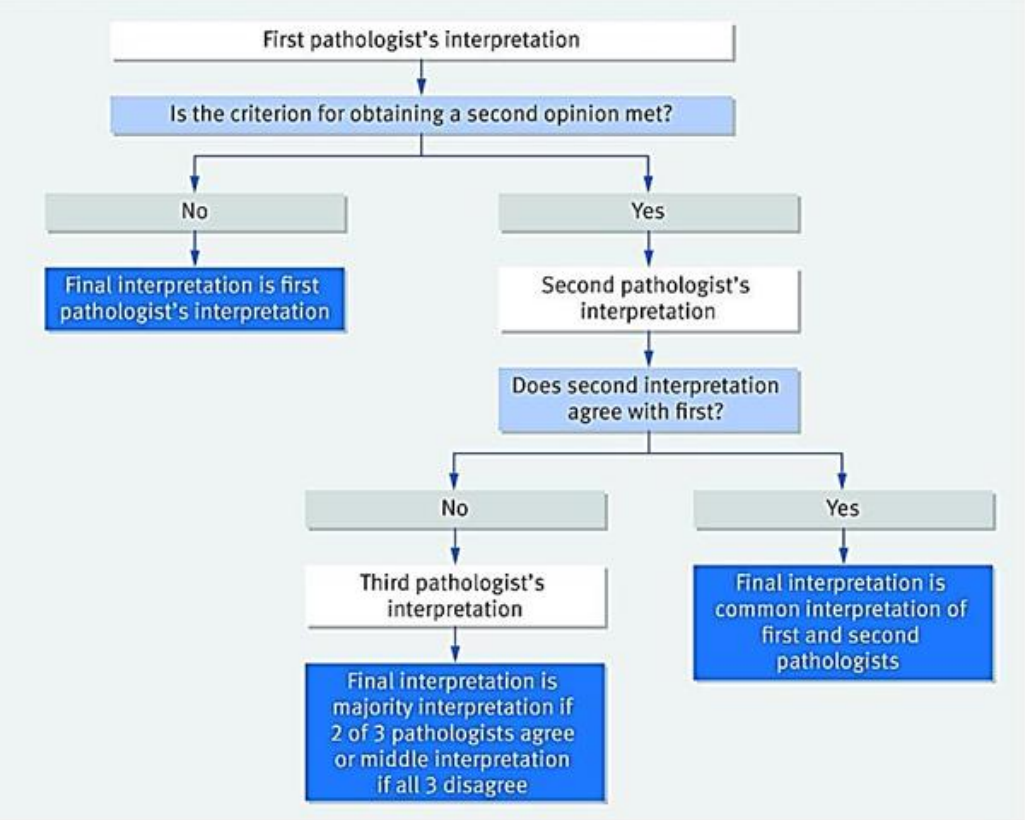


**Figure 2: Process of pathologic interpretation**

**Demographic, clinical, and pathologic data**

Demographic data, clinical diagnosis, patient history and examination were assessed retrospectively from registered records or clinical database. Patient data were screened for sex, age, primary cancer site, site region, referral base (community hospitals, commercial laboratories and academic centres) and stage of the disease (metastatic vs. Non-metastatic) whether malignancy was histopathologically confirmed, outside diagnosis, second opinion and post review diagnosis. Gross description of tissue included size, site and consistency. Process at KFMC to compare in house and outside diagnosis

At the KFMC, there is no process of mandatory second opinion. However, the department of Pathology KFMC recommends a formal examination of the tissue section, removed at other institutions, before developing, advocating, or continuing a treatment plan.

**Defining the qualification**

A general pathologist must have completed a primary degree in medicine and have had 5-year training in histopathology.

**Distribution of cases**

In our department of pathology, OSS cases are allocated to the general surgical pathologists, while bone marrows, neuropathology, and renal cases are examined directly by specialists. Also, referral cases with head and neck cancers had been re-examined and notified by the oral and maxillofacial pathologists in our institute.

**Categorizing discrepancy**

The original diagnosis of the referred cases was compared with the second review for discrepancies as it may cause modification in therapy or prognosis.

**Process of histopathological examination**

Tissues of the primary carcinomas, the surgical margins, and the lymph nodes were processed and sectioned for accurate and consistent histopathological evaluation. For this, OCT-embedded frozen specimens (Optimum Cold Temperature medium, Tissue-Tek, Miles, Elkhart, Ind.) were cut with a cryostat to get the smooth even section. First, the tissues were sectioned (2 in number) at 5 µmm thickness for haematoxylin-and-eosin staining and microscopic examination. The slides were then evaluated by a pathologist blinded to the primary interpretation as negative, positive, or non-diagnostic for the presence of squamous cell carcinoma. Secondly, twenty tissue sections of 12 µmm thickness were cut and put in sodium dodecyl sulphate and proteinase K solution. The DNA was extracted from the tissue sections using phenol and chloroform method and then precipitated it using the ethanol. Similarly, the second set of 2 and 20 sections were cut for microscopic and DNA analysis, respectively. After the second one, we obtained the third set of two tissue sections for microscopic examination. Thus, 240 µmm of tissue for DNA analysis from each margin was immediately sandwiched between sections examined by light microscopy.

## Statistical analysis

Statistical analysis was performed using the SPSS software Version 11.5 (SPSS Inc., Chicago, IL, USA). Patient variables such as sociodemographic and clinical parameters, second-opinion referrals, information needs were related to patient motives for second-opinion seeking. The relative contributions of the different patient variables were estimated by logistic regression analysis.

## Results

**Demographic results/ Patients characteristics**

The pathologic material from 246 patients referred to pathology department for evaluation of head and neck cancer from January 1, 2015 to September 30, 2016 was reviewed. This material was received from King Fahad Medical City (KFMC), Saudi Arabia. The minimum patient age was 13 and the maximum age was 93 with a

mean age of 49.63 years with standard deviation of 16.13. 131 (53.03%) patients were male and the remaining 115 (46.07%) patients were female. The male to female ratio was 1.14. Of the total 246 patients, 36.6% (90 patients) came from private hospitals, 35.4% (87 patients) from government hospitals, 26.0% (64 patients) directly from university hospitals and the remaining 2% (5 patients) came from the outside kingdom (Figure 5). Site distribution was oral cavity (n=37, 15%), oropharynx/hypopharynx (n=6, 2.4%), nasopharynx (n=40, 16.3%), larynx (n=36, 14.6%), thyroid (n=98, 39.8%), neck (n=4, 1.6%), ear (n=2, 0.8), sinonasal (n=9, 3.7%), skull base (n=1, 0.4), and ear + nasopharynx(n=1, 0.4).

**Age distribution**

Figure 3 shows the age-specific incidences of head and neck cancer from January 1, 2015, to September 30, 2016, in Saudi Arabia. The incidence was 9.8% in populations <30 years compared to 45.5%, 32.5, and 12.2% for patients aged 31-50 years, 51-70 years, and >70 years, respectively.

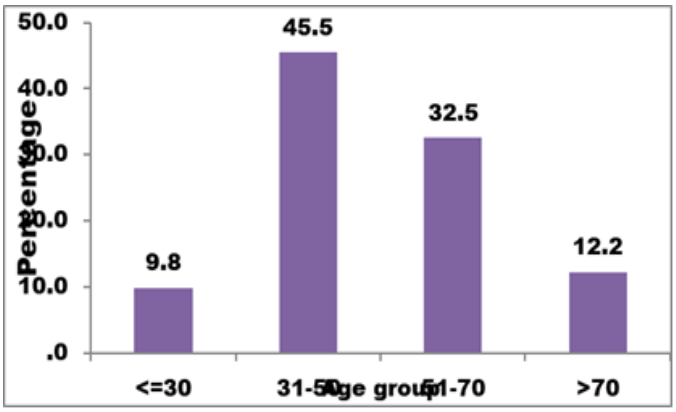


**Figure 3: Age distribution among head and neck cancer patients**

**Percent of patients referred from other hospitals**

Of 246 patients referred to pathology department for evaluation of head and neck cancer, 90 (36.59%) came from private hospitals, 87 (35.37%) from public hospitals, 64 (26.02%) from university hospitals and the remaining 5 (2.03%) came from outer kingdom hospitals respectively as shown in figure 4.

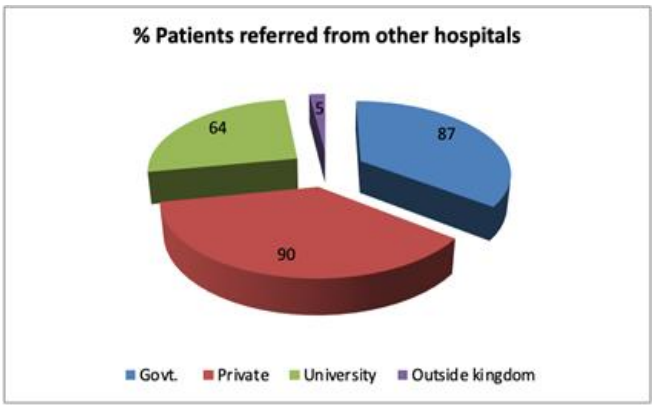


**Figure 4: Patient referrals and transfers**

**Second opinion**

Of 246 reviewed referral surgical pathology cases, 202 (82.1%) concurred with the findings from referral hospitals while the remaining 44 (17.9%) did not (Table 2). No specific site was more prone to change in diagnosis.

In 44 cases (17.9%), the discrepancy rate varied by anatomic site, ranging from 2% for the skull base, oropharynx & nasopharynx to 61% for the thyroid. By anatomic sites, these included 27 cases (61.4%) from the thyroid, 6 cases (13.6%) from the sinonasal, 3 cases (6.8%) from oral cavity, 3 cases (6.8%) from the larynx, 2 cases (4.6%) from the odontogenic cases, 1 cases (2.3%) from the nasopharynx, 1 cases (2.3%) from the oropharynx cases, and 1 cases (2.3%) from the skull base. The detail of the referrals number and anatomical sites is shown in figure 5.

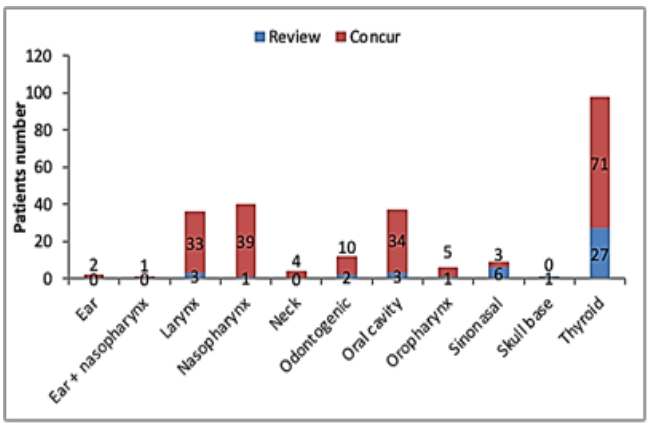


**Figure 5: Number of anatomical sites according to diagnostic agreement and disagreement**

Of 44 (17.9%) outside surgical pathology cases (whose reports did not concur with reports from outside laboratories), 17 came from private hospitals, 16 came from university hospitals and 11 came from government hospitals. The detail of the hospitals is shown in figure 6.

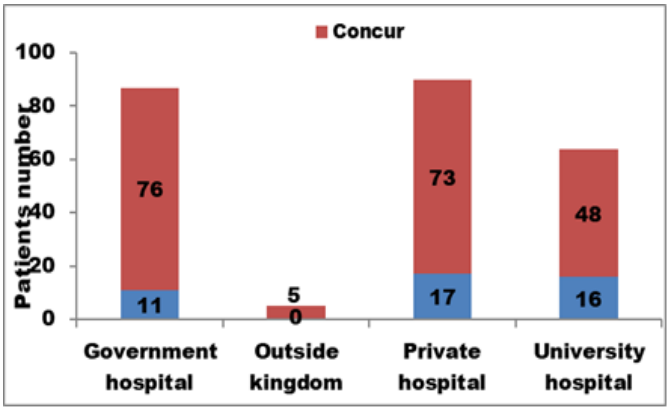


**Figure 6: Number of referrals cases according to diagnostic agreement and disagreement**

**Discrepancy (Major and Minor)**

Major discrepancies (defined as diagnostic or staging differences resulting in altered treatment) were seen in 26 (10.6%) of the cases while minor in 18 (7.3%) cases (Figure 7).

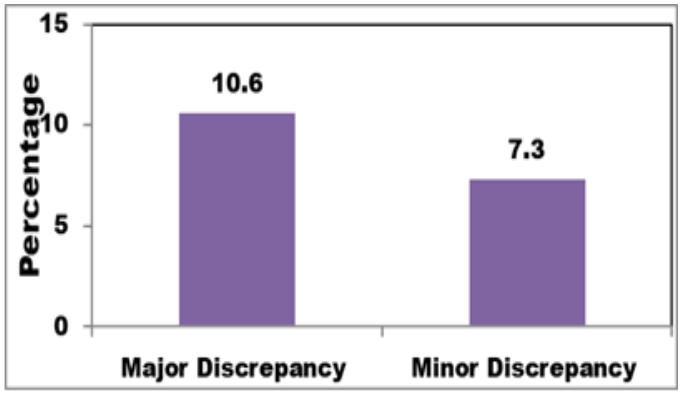


**Figure 7: Percentage of major and minor diagnostic agreement in review cases**

Among 26 major discrepancies, the discrepancy rate varied by anatomic site ranging from 4% (skull base) to 62% (thyroid). The detail of the referrals number and anatomical sites is shown in figure 8.

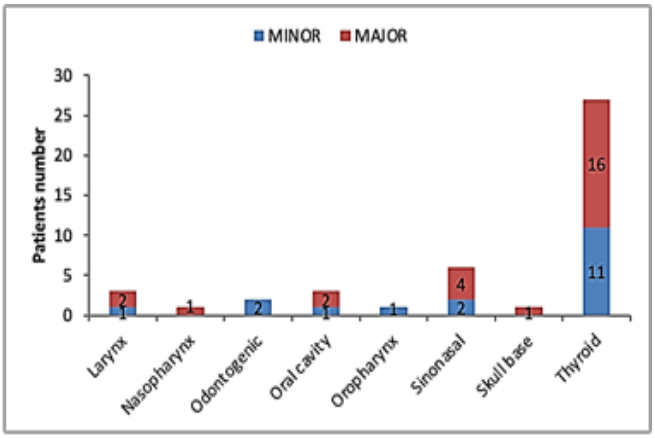


**Figure 8: Distribution of major and minor discrepancies as per anatomic site**

Of the 26 major discrepancy cases, 11 came from public hospitals, 8 from private hospitals and the remaining 7 came from university hospital respectively. (Figure 9).

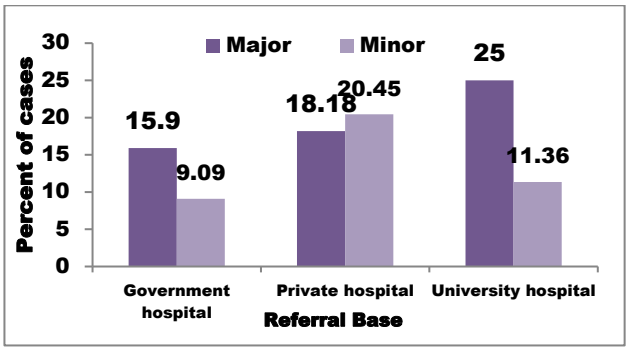


**Figure 9: Distribution and percentage of patients came from other public, private or university hospitals for second opinion**

**Diagnostic discrepancies according to anatomic sites**

**Larynx cases**

Of 3 (6.8%) larynx discrepancy cases (whose reports did not concur with reports from outside laboratories), 2 cases were major and 1 was minor as shown in table 2. For the major disagreements, 1 case initially diagnosed with "Plasma cell myeloma" by the physician pathologist was changed to "Lymphohistocytic infiltration" in the second-opinion report. One case submitted with an "adenocarcinoma" diagnosis was changed to "neuroendocrine carcinoma".

**Table 2: Major and Minor diagnostic disagreements between original and second-opinion diagnoses in larynx cases**

| | Submitted diagnosis | Second opinion diagnosis | Pts. (N) |
|---|---|---|---|
| **MAJOR** | Plasma cell myeloma | Lymphohistocytic infiltration | 1 |
| | Poorly differentiated adenocarcinoma with signet ring cells | Poorly differentiated neuroendocrine carcinoma with signet ring cells | 1 |
| **MINOR** | Invasive moderately differentiated squamous cell carcinoma | Superficial fragments of squamous epithelium showed mild to moderate dysplasia | 1 |

**Oral cavity cases**

Of 3 (6.8%) oral cavity discrepancy cases, 2 cases were major and 1 was minor as shown in table 3. For the major disagreements, 1 case initially diagnosed with "Atypical epithelial proliferation consistent with carcinoma ex pleomorphic adenoma" by the physician pathologist was changed to "Pleomorphic adenoma with squamous metaplasia" in the second-opinion report. One case submitted with a "Well differentiated squamous cell carcinoma" diagnosis was changed to "Invasive well differentiated squamous cell carcinoma".

**Table 3: Major and Minor diagnostic disagreements between original and second-opinion diagnoses in oral cavity cases**

| Discrepancy | Submitted diagnosis | Second opinion diagnosis | Pts. (N) |
|---|---|---|---|
| **MAJOR** | Atypical epithelial proliferation consistent with carcinoma ex pleomorphic adenoma | Pleomorphic adenoma with squamous metaplasia | 1 |
| | Well differentiated squamous cell carcinoma | Invasive well differentiated squamous cell carcinoma | 1 |
| **MINOR** | High grade mucoepidermoid carcinoma | High grade salivary gland tumour consist with salivary ductal carcinoma | 1 |

**Sinonasal cases**

Of 6 (13.6%) sinonasal discrepancy cases, 4 cases were major and 2 were minor as shown in table 8. For the major disagreements, 1 case initially diagnosed with "Intraosseous ameloblastoma, basaloid pattern tumor" by the physician pathologist was changed to "Adenoid cystic carcinoma, cribriform pattern" in the second-opinion report. One case submitted with a "Malignant neoplasm consistent with sinonasal undifferentiated carcinoma" diagnosis was changed to "Malignant neoplasm suggestive of primitive neuroectodermal tumor/ ewing sarcoma" and the remaining major discrepancies are shown in table 4.

**Table 4: Major and Minor diagnostic disagreements between original and second-opinion diagnoses in sinonasal cases**

| Discrepancy | Submitted diagnosis | Second opinion diagnosis | Pts. (N) |
|---|---|---|---|
| **MAJOR** | Intraosseous ameloblastoma, basaloid pattern tumor | Adenoid cystic carcinoma, cribriform pattern | 1 |
| | Malignant neoplasm consistent with sinonasalundiffrentiated carcinoma | Malignant neoplasm suggestive of primitive neuroectodermal tumor/ ewing sarcoma | 1 |
| | Retiform hemangioendothelioma | Granulation tissue with underlying vascular proliferation/ hemangioma | 1 |

| | | | |
|---|---|---|---|
| | Sinonasal undifferentiated carcinoma | Poorly differentiated neoplasm consistent with ewing sarcoma /pnet | 1 |
| **MINOR** | T-cell lymphoma with t cell anaplastic cell lymphoma | Poorly differentiated malignant neoplasm | 1 |
| | Ulcerated basal cell carcinoma | Baso-squamous carcinoma | 1 |

**Nasopharynx cases**

Only one major discrepancy was observed among nasopharynx cases. In this, diagnosis changed from "Minimal chronic inflammatory changes" to "Non-keratinizing undifferentiated nasopharyngeal carcinoma" as shown in table 5.

**Table 5: Major diagnostic disagreements between original and second-opinion diagnoses in nasopharynx cases**

| Discrepancy | Submitted diagnosis | Second opinion diagnosis | Pts. (N) |
|---|---|---|---|
| **MAJOR** | Minimal chronic inflammatory changes | Non-keratinizing undifferentiated nasopharyngeal carcinoma | 1 |

**Skull base cases**

**Table 6: Major diagnostic disagreements between original and second-opinion diagnoses in skull base cases**

| Discrepancy | Submitted diagnosis | Second opinion diagnosis | Pts. (N) |
|---|---|---|---|
| **MAJOR** | Basal cell carcinoma | Eccrine hidradenoma | 1 |

**Thyroid cases**

Of 27 (61.4%) thyroid discrepancy cases (whose reports did not concur with reports from outside laboratories), 16 cases were major and 11 was minor as shown in table 7.

**Table 7: Major and Minor diagnostic disagreements between original and second-opinion diagnoses in thyroid cases**

| Dis | Submitted diagnosis | Second opinion diagnosis | N |
|---|---|---|---|
| **MAJOR** | Ectopic thymic tissue associated with diffuse micro abscesses formation | Classical hodgkins lymphoma mainly in extrathyroid tissue | 1 |
| | Encapsulated follicular variant of papillary thyroid carcinoma | Thyroid tissue with focal lesion showing micro follicular pattern; no definite nuclear features of ptc seen | 1 |
| | Encapsulated well differentiated tumor of undetermined malignant potential | Cellular nodule arising in nodular hyper plasia | 1 |
| | Follicular carcinoma | Follicular adenoma with hurthle cell changes | 1 |
| | Follicular carcinoma with capsular invasion | Cellular nodule arising in nodulorgoiter | 1 |
| | Follicular neoplasm mostly on top of hemorrhagic cystic colloid lesion | Cellular nodule with hurthle cell changes | 1 |
| | Follicular variant of papillary thyroid carcinoma | No evidence of malignancy | 1 |
| | Hashimoto's thyroiditis with encapsulated nodule with focal capsular invasion | Hashimotos thyroiditis | 1 |
| | Hurthle cell adenoma | Minimally invasive hurthle cell carcinoma | 1 |
| | Multifocal papillary thyroid carcinoma, follicular variant | Follicular neoplasm with no features of papillary thyroid carcinoma changes | 1 |
| | Papillary thyroid carcinoma | Follicular carcinoma | 1 |
| | | Hashimotos thyroiditis | 1 |
| | | No evidence of malignancy | 1 |
| | | Nodular hyperplasia with hurthle cell changes | 1 |
| | | Suspicious for papillary thyroid carcinoma with hurthle cell | 1 |
| | Papillary thyroid microcarcinoma | No evidence of malignancy | 1 |
| **MINOR** | Encapsulated and solid follicular carcinoma of clear cell variant | Metastatic renal cell carcinoma | 1 |
| | Encapsulated follicular carcinoma | Encapsulated follicular variant of papillary thyroid carcinoma | 1 |
| | Encapsulated follicular lesion with capsular and multifocal vascular invasion consistent with minimally invasive follicular carcinoma | Papillary thyroid carcinoma | 1 |
| | Encapsulated follicular variant of papillary thyroid carcinoma | Follicular variant of papillary thyroid carcinoma | 1 |
| | Follicular variant of papillary thyroid carcinoma | Encapsulated follicular variant of papillary thyroid carcinoma | 2 |
| | Hashimotos thyroiditis with micro papillary thyroid carcinoma (mean < 1cm) | Papillary thyroid carcinoma | 1 |
| | Microscopic extrathyroidal extension is seen/ ptc with anaplastic transformation | Papillary thyroid carcinoma with poorly differentiation | 1 |

| | | | |
|---|---|---|---|
| | Microscopic foci of papillary thyroid microcarcinoma | Follicular lesion of uncertain malignant potential with hurthle cell changes | 1 |
| | Single focus of papillary microcarcinoma | Multinodular hyperplasia | 1 |
| | Well differentiated tumor of uncertain malignant potential | Encapsulated follicular variant of papillary thyroid carcinoma | 1 |

**Odonogenic cases**

There were two minor discrepancies was observed among odonogenic cases as shown in table 8.

**Table 8: Minor diagnostic disagreements between original and second-opinion diagnoses in odontogenic cases**

| Discrepancy | Submitted diagnosis | Second opinion diagnosis | Pts. (N) |
|---|---|---|---|
| **MINOR** | Desmoplastic fibroma | Fibroblast / myofibroblast neoplasm | 1 |
| | Low grade polymorphous adenocarcinoma | Adenoid cystic carcinoma with poorly differentiated carcinoma element | 1 |

**Oropharynx cases**

There was only one minor discrepancy among oropharynx cases as shown in table 9.

**Table 9: Minor diagnostic disagreements between original and second-opinion diagnoses in oropharynx cases**

| Discrepancy | Submitted diagnosis | Second opinion diagnosis | Pts. (N) |
|---|---|---|---|
| **MINOR** | Suggestive of malignant neoplasm | Atypical lymphoproliferative proliferation | 1 |

**Reconfirmation of second opinion diagnosis**

Although most cancers were easily diagnosed after second opinion, additional opinion was asked for diagnostic purposes in 3 patients with head and neck cancer as shown in table 10.

**Table 10: Cases of additional review by subspecialized pathologist**

| Submitted diagnosis | Second opinion diagnosis | Second pathologist review |
|---|---|---|
| Poorly differentiated adenocarcinoma with signet ring cells | Poorly differentiated neuroendocrine carcinoma with signet ring cells | Revised by sub-specialized in house head and neck |
| Follicular carcinoma | Follicular adenoma with hurthle cell changes | Dr. Adelalnajjar agrees with our diagnosis |
| Papillary thyroid carcinoma | Follicular carcinoma | Rendered by subspecialized pathologist |

## Discussion

To identify the rate of major and minor disagreements with diagnoses from external institutions for patients with head and neck lesions or clinical contexts

The second opinion is the double reading of pathology specimens, by a specialist pathologist, at the request of the treating physician or institute or as standard practice before the implementation of a treatment plan to minimize diagnostic errors and to improve quality. Our retrospective analysis of 246 head and neck oncology referral specimens over 21 months revealed an overall discordance rate of 17.9%. The anatomical sites like the thyroid gland (11.0%), sinonasal space (2.4%), larynx (1.2%), and oral cavity (1.2%) were more prone to diagnostic errors or change in diagnosis. While the odontogenic (0.8%), nasopharynx (0.4%), oropharynx (0.4%), and skull base (0.4%) were less likely to have discordance. These sites all averaged a 0.4–11% change in the diagnosis rate.

Observing the rates of major and minor diagnostic discordances among referral patients with head and neck lesions are considered the primary goal. The present study classified the diagnostic discrepancy, following the previous studies, as the minor when the second review doesn't significantly modify the treatment and/or prognosis and the major one when the second review modifies the treatment plan. Of 44 (17.9%) diagnostic discordance in the present study, 26 (10.6%) were major while 18 (7.3%) were minor. Other studies have reported the discrepancy rate ranging from 0.1% to 7%, which is lower than the present study (Westra *et al*., 2002; Kronz *et al*., 1999; Manion *et al*., 2008; Tsung JS, 2004; Cooper *et al*., 2006). Interpretation differences due to challenging clinical situations could be one of the explanations of higher diagnostic discordance compared to previous published studies. The cases in which the secondary diagnoses did not agree with the primary or outside diagnosis, the department of pathology KFMC tried to recognize the accurate diagnoses by using the third review and extra follow-up information.

**To determine the impact of second opinion surgical pathology on cancer staging and diagnosis**

Some studies have reported a profound impact of the second surgical pathology review on the results of clinical studies. Westra *et al*. observed a 61% change in tumor classification on specialist review and the significant impact of this change on patient's survival (Westra *et al*., 2002). In an attempt to decrease the diagnostic errors, some studies have suggested a review of all surgical pathology material by the second pathologist before making the final diagnosis. Thus, our department reviewed 246 cases over 21 months that were determined to have a significant change in diagnosis. A total of 44 cases (17.89%) with head and neck cancer had changes in diagnosis in the present study, which is higher than those reported by other studies (7% by Westra and colleagues, 1–6% by large general surgical pathology series, and 0.1–7% by survey studies of pathology laboratories) (Westra *et al*., 2002; Kronz *et al*., 1999; Manion *et al*., 2008; Tsung JS, 2004; Cooper *et al*., 2006). In 2016, a systematic review analyzing the benefits and risks of second opinion found changes in the diagnosis, treatment or prognosis among 12–69% cases (Ruetters *et al*., 2016). Similarly, several other meta-analyses have also reported the changes in these factors ranged from 10-62% and 2-51%, respectively (Payne *et al*., 2014; Hillen *et al*., 2017). The reasons for higher diagnostic change in the present study may be related to sample size differences, difficulty to

interpret the report by other pathologists due to complex clinical situations and intensive expertise of our oncologic pathologists.

**To determine specific anatomic sites or specimen types which are particularly susceptible to discrepant diagnoses?**

Expert opinions and follow up until a definitive diagnosis have been suggested by several studies to identify the diagnostic discordance according to the anatomic site. Given the high rate of diagnostic discordance for all the major sites in head and neck cancer observed in the present study by specialists pathologists, these sites must be considered among the high-risk areas and also be considered for routine second opinion review. By anatomic site and specimen types, the discrepancy rates ranged from 0% (ear, neck, and ear + nose) to 61% (sinonasal). In this study, most diagnostics errors identified in four head and neck tumor categories such as Thyroid (61.4%), Sinonasal (13.6%), Oral cavity (6.8%), and Larynx (6.8%). Three sites, though limited in number, appeared to have no change in diagnoses such as neck (4), ear (2), and ear + nose (1) cases, respectively. So, anatomic sites like the thyroid gland, Sinonasal space, Oral cavity, and Larynx were more prone to major diagnostics changes, though organ sites also had diagnostic changes. A policy of mandatory second opinion for all surgical pathology material will equally address errors of commission and omission.

The high discordance rate observed in the clinical pathology of our study suggest a routine institutional review of all pathology specimens before initiating definitive treatment and is also supporting the recommendations of the Association of Directors of Anatomic and Surgical Pathology (Westra *et al*., 2002). The present study also identified the adenocarcinomas, poorly differentiated carcinomas, and specimens of uncommon histology (<10 reports) that warrants the closest attention for the second review.

**To characterize the nature and impact of discordant diagnoses on treatment continuum**

In the present study, the major diagnostic discrepancy, defined as diagnostic or staging differences resulting in major alterations in treatment, were seen in 26 (10.6%) of the cases. The observed discrepancy rate of 10.6%, in this study, was high compared to previous studies showing diagnostic discrepancies ranged from 2.3% to 6.8%, respectively (Manion *et al*., 2008; Tsung JS, 2004; Weir *et al*., 2003).

**To evaluate the limitations or factors behind discordant diagnoses**

Compulsory second opinion pathology does not only change the diagnosis but also improves accuracy. In the present study, the precision of the second opinion analysis was 95% for which adequate centre or pathologic follow-up data was accessible.

In 15 cases, for example, the primary diagnosis was modified after obtaining the diagnostic errors in tumor classification during section analysis (IHC). Aldape *et al*. observed a high discrepancy rate in those cases, which were from the community hospital with limited access to subspecialty expertise (Aldape *et al*., 2000).

**To characterize the nature and impact of discordant diagnoses on patient care and prognosis**

Our study has several important weaknesses. Missing clinical and radiological information, size of tissue received for interpretation, sub optimal quality of slides and block and difficulty in sample recruitment were the major problems in this study. Also, we did not analyse the treatment course of the studied cases. Finally, we also did not analyze the cost variables in this study. Although the second opinion in pathology is a function of cost, previous work has shown the second review as a cost-savings approach (Epstein *et al*., 1996). A more comprehensive analysis for for head and neck oncology examples is entangled by methodological contemplations in deciding the expense of individual pathology reports, however is painfully required.

Despite a policy of mandatory second opinion in pathology for referred patients and the Association of Directors of Anatomic and Surgical Pathology recommendations, current trends in health economics have put the second review practice at risk (Simpson *et al*., 1993 and Monaco, 1997).

## Recommendations

Although secondary pathology review occurs in a variety of different clinical settings, some areas of head and neck cancer pathology are highly prone to diagnostic errors, and thus require frequent second opinion consultations. Also, the differences in diagnosis need to be addressed professionally, so the patient receives prompt and optimal care.

## Limitations of the study

**Limitations in data collection**

- Missing clinical and radiological information
- Variance in quality of information record by pathologist
- Difficulty in sample recruitment –more material

**Ways to overcome limitation**

- Multidisciplinary meeting with head and neck surgeon
- Oncologist and radiologist to review slides by sub-specialized head and neck pathologies to reach clear diagnosis
- Request to more large size (excision biopsy) for better interpretation

**Scope of future research**

Numerous studies have found the second review in pathology as one of the perfect ways to reduce morbidity and mortality among head and neck cancer patients. We also aim to present the programme to the patients in a different way, to improve compliance. These changes will have to be evaluated. Instead, changes in the programme for specific subgroups will have to be compared to the result for the same subgroup earlier. Another possibility is to compare results from cases managed at other organizations.

In conclusion, all surgical pathology material should be reviewed by the second pathologists to minimize the diagnostic errors regardless of the organ system or nature of the institution initially diagnosed the patients with cancer. Our mandatory second review policy in pathology referral cases leads to a 10.57% major diagnostic changes across all sites of head and neck. In conclusion, the second opinion in pathology should be obtained before any major therapeutic endeavour as it reveals diagnoses discrepancy, particularly in challenging sites and cases.

## Declarations

## Conflict of interest

None

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None

## Ethical Clearance

Not Applicable

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