



# OPEN Utility of Sydney system for reporting the neck lymphadenopathy underwent real-time ultrasound guided fine-needle aspiration

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The Sydney lymphadenopathy cytology system was proposed in 2020, but its validation for neck ultrasound-guided fine-needle aspiration cytology remains to be explored. Patients with lymphadenopathy who underwent ultrasound and cytology were included. The final diagnosis relies on histology and consensus of the multidisciplinary team. Cytology results follow the Sydney system (L1-L5); L3-L5 categories indicate malignancy, and we further calculate sensitivity, specificity, and overall accuracy. From July 2020 to April 2023, a total of 208 patients were included, of which 68 had malignant tumors and 140 were benign cases. According to the Sydney system, the malignancy rates for L2 to L5 are 2%, 89%, 100%, and 98%, respectively. The Sydney system demonstrated 97% sensitivity, 99% specificity, and 99% accuracy in the diagnosis of neck lymphadenopathy. The study shows that the Sydney system is highly effective in reporting neck lymphadenopathy.

**Keywords** Ultrasound, Fine needle aspiration cytology, Sydney system, Elastography, Neck lymphadenopathy

Head and neck cancers (HNC) are one of the most common cancers in the world<sup>1</sup>. A retrospective study of over 70,000 patients with HNC revealed that 52% have neck lymph node metastases at presentation<sup>2</sup>. Therefore, it is important to differentiate benignity and malignancy for neck lymphadenopathy. Ultrasound (US) examination is a useful tool to examine neck masses<sup>3</sup>. Abnormal lymphadenopathy is usually larger in size, irregular/burred in border, more heterogeneous in echotexture, rounder in size, harder in elastography, and absent of hilum in Doppler and contrast ultrasound<sup>4</sup>.

Since no single US characteristic is specific for malignancy, we combined age and three ultrasound characteristics to develop a comprehensive an ultrasound scoring system for assessing neck lymph nodes<sup>5</sup>. The validity of this scoring method has been previously confirmed<sup>6</sup>. Additionally, recent US elastography and contrast-enhanced US have also been applied to check in the evaluation of lymph nodes(LNs)<sup>7</sup>.

Excision biopsy is a method for harvesting tissue to determine its etiology. However, it's important to note that most neck lymphadenopathies are benign and do not typically require excisional biopsy, which can result in skin wounds<sup>8</sup>. Fine needle aspiration serves as a viable alternative method for obtaining tissue samples without the need for excision. When performed under the guidance of real-time ultrasound (US-FNA), this procedure can yield more precise cytology specimens, especially in the case of non-palpable small lymph nodes<sup>9</sup>. This approach helps minimize invasiveness and provides valuable diagnostic information in a less invasive manner.

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Cytology reporting relies on established systems, the Bethesda system and Milan system, are used for thyroid and salivary glandular tumor/nodule cytology<sup>10,11</sup>. Recently, the Sydney system was proposed for reporting lymphadenopathy<sup>4</sup>. Similar to the Bethesda system, the Sydney system categorizes lymphadenopathy five groups: inadequate/insufficient, benign, atypical undetermined significance/atypical lymphoid of uncertain significance (AUS/ALUS), suspicious, and malignant. This classification system was reported to be effective in lymphadenopathy<sup>12–15</sup>. Kanhe et al. reported that the accuracy of Sydney system for reporting lymphadenopathy was higher than 99%<sup>15</sup>. The study combined US guided and non-US-guided; rapid on-site evaluation and non-rapid on-site evaluation; neck lymphadenopathy and other sides.

Based on previous reports and meta-analyses<sup>12,16,17</sup>, use of the Sydney reporting system exhibits significant heterogeneity and is subject to inherent partial validation bias. This heterogeneity results from different operators, nodal sites, and clinical settings.

Therefore, the performance of Sydney system is still not well understood in cervical lymphadenopathies. In our setting, all procedures were performed in the cervical region by experienced head and neck surgeons under ultrasound guidance. This result can verify the effectiveness of the Sydney system in diagnosing cervical lymphadenopathy after US-FNA. We intend to check the performance of the ultrasound scoring system, elastography and Sydney system in reporting neck lymphadenopathy.

## Methods

This is a cross-sectional study and the institutional ethics committee review board approved this study plan. (FEMH-IRB-109074-E). All patients signed written informed consent forms. Research was performed in accordance with the Declaration of Helsinki.

## Patients

The inclusion criteria included patients more than 20 years old who had enlarged neck lymphadenopathy and at least one US characteristic abnormality<sup>5,18–21</sup> (i.e., size, shape, hilar echogenicity, margin, or vascular pattern) that permitted US-FNA. Patients with lymph node enlargement identified by the Otolaryngology or Oncology departments at Far-Eastern Memorial Hospital were referred for ultrasound examination. The ultrasound scans were primarily conducted by Dr. Liao (the first author), with a smaller portion performed by Dr. Lo (the fourth author). Informed consent was obtained either by Dr. Liao or a research nurse who explained the study and invited patients to participate. Pathological examinations were mainly conducted by Dr. Wu (the second author) in the Pathology department. In the determination of the final diagnosis, pathology results are employed whenever accessible. In cases where pathology findings are unavailable, a collaborative approach is undertaken through a multidisciplinary team meeting, involving experts from the Pathology, Radiology, and Oncology departments. Patients who had negative cytopathology results were followed for a minimum of 6 months to verify that no malignancy had developed in these LNs afterward.

## US examination

Sonograms were performed with one high-resolution 7- to 18-MHz real-time linear-array transducer (Aplio MX, Toshiba, Tokyo, Japan). The detailed method was described in our previous study<sup>5</sup>. In brief, all patients in our study underwent thorough neck US examination using grayscale, power Doppler US and US elastography. We measured the lengths of the short and long axes and the diameter ratio of the short to long axis (S/L ratio) of enlarged LNs. The nodal margin was classified as regular or irregular. Echogenicity compared to the adjacent muscles was speculated and classified as hypoechoic, isoechoic, or hyperechoic. The echogenic hilum was differentiated and classified as its presence or absence. The internal echotexture was examined and classified as a homogenous or heterogeneous pattern. The vascular pattern was evaluated with power Doppler US and grouped into avascular or hilar type versus mixed, spotted, or peripheral type. All the morphological US data were entered into our Marosis PACS system (Marotech Inc., Seoul, South Korea). A predictive scoring scale was proposed as:  $0.06 \times (\text{age}) + 4.76 \times (\text{S/L ratio}) + 2.15 \times (\text{internal echo}) + 1.80 \times (\text{vascular pattern})$ . Cervical lymphadenopathy was regarded as malignant with a score  $> \text{or} = 7^5$ .

## Elastography

For our elastographic technique, real-time elastographic images were demonstrated together with grayscale sonograms in a two-panel format. We further compressed with light pressure followed by decompression, which repeated the cycle until the size and color distribution of the region of interest (ROI) in numerous sequential images appeared nearly identical. Compression was directed along the radiation axis, with a focus on preventing any motions that deviate from the plane. Real-time elastographic visual employed a color-coded graphic format, with emphasis on the selected target area. Stiffness was denoted by blue, intermediate firmness by green and yellow, and softness by red within this representation. We used the 4-point scoring system<sup>22</sup> to evaluate lymphadenopathy as follows: Elastographic score (ES) 1 represents soft (less than 10% of red areas), ES 2 represents moderately soft (10–50% of red areas), ES 3 represents moderately stiff (10–50% of blue, green, and yellow areas), and ES 4 represents stiff (less than 10% of blue, green, and yellow areas). An LN with RTE of ES 3 or 4 was classified as malignant.

Another elastographic technique employed in this study was shear wave elastography (SWE). Shear wave elastographic images were also displayed along with the grayscale sonograms in two-panel images for comprehensive evaluation. A high-intensity pulse is generated by the ultrasound probe toward the target, where perpendicular shear wave propagation is detected. The shear wave propagation is then converted and recorded as shear velocity (m/s) and Young's modulus (kPa). The mean SWE value of the included lymphadenopathy was used as a cutoff value for evaluation. An LN with SWE higher than the cutoff value of SWE is classified as malignant.

## US-FNA procedure

In US-guided FNA procedure, each patient underwent the process by placing the array probe parallel to the needle for guidance and with a 22-G needle within the node that was the most suspicious to be malignant. All procedures were performed after injection of local anesthesia and visualization of the needle as it advanced toward the desired target. During the US-FNA procedure, only one specimen was obtained through a single needle aspiration. The syringe needle unit was quickly withdrawn when the appropriate amount of material filled the plastic portion of the needle. Following the aspiration, two slides were prepared for cytological analysis: One of the two slides was air-dried for Liu's stain, and the other was rapidly fixed in alcohol for the Papanicolaou stain. This meticulous approach ensured the acquisition of high-quality cytological specimens for accurate diagnostic evaluation. On-site examination was not available in this study.

## Sydney system

The cases were classified according to the Sydney system<sup>4</sup> into five groups, denoted as L1 to L5: L1: Inadequate/Insufficient; L2: Benign; L3: Atypical (cells) Undetermined Significance/Atypical Lymphoid (Cells) of Uncertain Significance (AUS/ALUS); L4: Suspicious and L5: Malignant. The categories L3 to L5 were classified as malignant, and calculate the sensitivity, specificity, and overall accuracy for the malignancy classification. This comprehensive approach allowed for a thorough assessment of diagnostic performance.

## Statistical analysis

Mann-Whitney U tests and chi-squared tests were used to determine the differences in clinical parameters (i.e., age, sex, side and site of occurrence, diameter of short and long axes, S/L ratio, echogenicity, internal echo, margin, echogenic hilus, vascular pattern, real-time elasticity score and our combined US L/N score<sup>5</sup>) between benign and malignant LNs as appropriate. The optimal cutoff point of ES in shear wave elastography was determined at the point of highest accuracy for malignancy. The diagnostic accuracy was expressed as the sensitivity, specificity and area under the ROC curve (AUC). A *p* value < 0.05 was interpreted as statistically significant. All statistical analyses were accomplished using Stata software, version 12.0 (StataCorp. LP, College Station, TX).

## Results

From July 2020 to April 2023, this study enrolled 208 patients presenting with neck lymphadenopathy, comprising 68 cases with malignancy and 140 with benign condition. Of these patients with malignant LNs, 61 underwent pathological examination (21 underwent lymphadenectomy and 5 underwent core needle biopsy of cervical LNS; 36 of these underwent biopsy at the primary site). After collaborative discussion by a multidisciplinary team, 7 patients were also diagnosed as malignant. Another 140 patients with negative cytopathology results were followed for at least 6 months to verify the subsequent presence of malignancy in these LNs. Nine of the patients underwent resection surgery.

The prevalence of malignant LNs was 33% (68/208). Of the enrolled patients, 117 were males, accounting for 56% of the patients, while 91 were females, constituting the remaining 44%. The mean age of the participants was 46 years old, with ages spanning a range from 20 to 82 years. Among the malignant LNs, 14 had nasopharyngeal carcinoma, 10 had hypopharyngeal cancer, 8 had oral cancer, 8 had papillary thyroid carcinoma, and 6 had esophageal carcinoma. Among individuals diagnosed with benign nodal disease, the majority (*N* = 122) were found to have reactive lymphoid hyperplasia. The patients' final diagnoses are summarized in Table 1.

Table 2 presents the rate of malignancy based on the Sydney system classification. We found that the specimen inadequate rate of US-FNA was 2% (4/208). The malignancy rates varied across different Sydney system categories with rates of 2%, 89%, 100% and 98% for the L2 to L5 groups, respectively. Moving from L1 to L5, the probability of malignancy increases.

Table 3 demonstrates the patient and US characteristics for benign and malignant lymphadenopathies. In patients with malignant lymphadenopathies, there is a higher proportion of males, and the average age is comparatively older (55.9 years vs. 41.4 years) when compared to the benign group. However, there is no significant difference observed between the left and right sides of the lymph nodes. Malignant lymph nodes frequently tend to be larger in size, rounder in size (S/L ratio), and greater stiffness in both RTE and SWE. We also found that the LN score was notably higher in malignant lesions as compared to benign lesions, with respective mean scores ( $\pm$  SD) of  $9.2 \pm 2.6$  versus  $5.9 \pm 1.8$  (*p* value < 0.01).

A comparison of the diagnostic performance of elastography, shear wave elastography, the US scoring system and the Sydney system in reporting neck lymphadenopathy is demonstrated in Table 4. The real-time elastography (ES 3&4) demonstrated a sensitivity of 62.7%, specificity of 58.2% and an overall accuracy of 59.8%. For shear wave elastography (> 44 kPa), the sensitivity was 63.9%, specificity was 62.0%, and the accuracy reached 62.6%. When utilizing the US scoring system, we observed a sensitivity of 81%, specificity of 77%, and an accuracy of 78%. Conversely, the Sydney system exhibited remarkable performance, with a sensitivity of 97%, specificity of 99% and a high accuracy of 99%.

## Discussion

The aim of this study was to investigate the performance of the US scoring system, elastography, and the Sydney system in their ability to distinguish between benign and malignant LNs. Most patients with enlarged LNs first visited an otolaryngologist and arranged an ultrasound. Therefore, most LNs was metastatic cancer from the head and neck region. Under the guidance of US, FNA had a low rate of inadequate specimens, with only 2% (4/208) falling into this category. The variation in nondiagnostic rate, which ranged from 3.58 to 10.57% in other studies<sup>13,14,23–25</sup>, contrasts with the low nondiagnostic rate observed in our study. The low nondiagnostic

Item		Numbers (%)
Malignant nodal disease	NPC	14 (7)
	Hypopharyngeal cancer	10 (5)
	Oral cancer	8 (4)
	Thyroid cancer	8 (4)
	Esophageal cancer	6 (3)
	Oropharyngeal cancer	5 (2)
	Lung cancer	5 (2)
	Unknown primary carcinoma	5 (2)
	Laryngeal cancer	2 (1)
	Other cancer	6 (3)
	B cell lymphoma	2 (32)
	Prostate cancer	1 (17)
	Pancreas cancer	1 (17)
	Endometrial cancer	1 (17)
	Breast cancer	1 (17)
Benign nodal disease	Reactive lymphoid hyperplasia	122 (58)
	Tuberculosis	1 (1)
	Kikuchi disease	1 (1)
	Negative follow-up	15 (7)

**Table 1.** Final diagnosis of patients.

Sydney system/Final diagnosis	N (%)	Benign (%)	Malignant (%)
Inadequate/Insufficient	4 (2%)	4 (100%)	0/4 (0%)
Benign	137 (65%)	135 (98%)	2/137 (2%)
AUS/ALUS	9 (4%)	1 (11%)	8/9 (89%)
Suspicious	2 (1%)	0 (0%)	2/2 (100%)
Malignant	56 (27%)	0 (0%)	56/57 (98%)

**Table 2.** Risk of malignancy according to the Sydney system classification. AUS/ALUS, Atypical (cells) Undetermined Significance/Atypical Lymphoid (cells) of Uncertain Significance.

rate in our study might be due to real-time US guidance with experience and superficial location of the neck LNs. In our opinion, the Sydney System is a very effective classification system for reporting the cytology of neck lymphadenopathy. It demonstrates a remarkable level of sensitivity (97%), specificity (99%), and overall accuracy (99%). These findings underscore the system's reliability and utility in clinical practice.

FNA cytology remained one of the most accurate method for evaluating lymphadenopathy. The accuracy of FNA cytology in diagnosing malignant neck lymphadenopathy was approximately 82–97%<sup>26</sup>. However, there is no standard criterion for reporting the results of FNA cytology. The Sydney system plays a good role in reporting lymphadenopathy and showed good results in our study. A recent international, multi-institutional study reported the Sydney system had adequate interobserver concordance with digitally whole-slide images<sup>27</sup>. Another previous study in southern India applied the Sydney system to evaluate neck lymphadenopathy, used L3–L5 as malignancy and reported a sensitivity and specificity of 93% and 95%, respectively<sup>25</sup>. The study had a nondiagnostic rate of 11%, while in our series, the nondiagnostic rate (L1) was only 2%. This highlighted the importance of real-time US guidance. The sensitivity, specificity and overall accuracy of FNAB when considering category L3 ~ L5 to represent malignant cytopathology in this study were 92.6%, 95.1% and 92.8%, respectively. The results were comparable to our study and support the useful of the Sydney system. It has been documented that cancer cells may be arranged as scattered infiltrative nests, often intermixed with fibrous stroma, which might hamper the chance of correct sampling and increase the possibility of false negative results<sup>28</sup>. In our series, we had two cases with false-negative cytology results. One patient with NPC underwent concurrent chemoradiotherapy, and another patient had thyroid papillary cancer. The cytology for thyroid cancer revealed no malignancy; however, there was a high thyroglobulin level in the washing examination. The final surgical pathology shown metastatic papillary cancer. Therefore, a washing thyroglobulin exam for residual material in the FNA needle is useful in diagnosing metastatic lymphadenopathy from thyroid cancer.

US characteristics play a pivotal role in distinguishing between benign and malignant neck lymphadenopathy. Because the malignant lymphadenopathy keep growth, therefore the size is bigger for malignancy. Additionally, the malignant lymph nodes invade in multiple directions, leading to rounder in shape and irregular in border, which are indicative features. Furthermore, due to the angiogenesis process, the malignant nodes often display atypical vascular features. The elastography can reveal increased tissue hardness in malignant nodes,

Item		N (%) / mean ± SD			P-value
		Total N = 208	Benign N = 140	Malignant N = 68	
Gender	Male	117 (56)	68 (58)	49 (42)	0.001*
	Female	91 (44)	72 (79)	19 (21)	
Age		46.2 ± 14.3	41.4 ± 13.5	55.9 ± 10.7	< 0.001**
Side	L	109 (52)	73 (67)	36 (33)	0.914
	R	99 (48)	67 (68)	32 (32)	
Level	I	34 (16)	29 (85)	5 (15)	0.024*
	II	74 (36)	43 (58)	31 (42)	
	III	15 (7)	12 (80)	3 (20)	
	IV	15 (7)	7 (47)	8 (53)	
	V	55(27)	40 (73)	15 (27)	
	VI	15 (7)	9 (60)	6 (40)	
Boundary	Clear	179 (86)	138 (77)	41 (23)	< 0.001**
	Vague	29 (14)	2 (7)	27 (93)	
Internal echo	Homogenous	142 (68)	125 (88)	17 (12)	< 0.001**
	Heterogenous	66 (32)	15 (23)	51 (77)	
Echogenicity	Hypochoic	206 (99)	139 (67)	67 (33)	0.600
	Isoechoic	2 (1)	1 (50)	1 (50)	
Calcification	Absent	200 (96)	139 (70)	61 (30)	0.001*
	Present	8 (4)	1 (12)	7 (88)	
Architecture	Solid	205 (99)	139(68)	66 (32)	0.206
	Cystic < 50%	3 (1)	1 (33)	2 (67)	
Hilar echo	Absent	129 (62)	65 (50)	64 (50)	< 0.001**
	Linear/Oval	79 (38)	75 (95)	4 (5)	
Vascular pattern	Avascular/Hilar	181 (87)	131 (72)	50 (28)	< 0.001**
	Other	27 (13)	9 (33)	18 (67)	
Size(short) cm		0.94 ± 0.55	0.7 ± 0.3	1.4 ± 0.6	< 0.001**
Size(long) cm		1.71 ± 0.89	1.4 ± 0.6	2.3 ± 1.1	< 0.001**
S/L ratio		0.56 ± 0.18	0.50 ± 0.14	0.68 ± 0.20	< 0.001**
SWE (kPa)	SWE(kPa)	44.6 ± 24.3	40.4 ± 22.8	52.8 ± 25.2	0.001*
	SWE SD(kPa)	23.2 ± 13.9	19.8 ± 12.6	29.9 ± 13.9	< 0.001**
SWE (m/s)	SWE(m/s)	3.8 ± 2.5	3.4 ± 1.04	4.5 ± 4.0	0.008*
	SWE SD(m/s)	1.2 ± 0.7	1.0 ± 0.6	1.5 ± 0.7	< 0.001**
RTE	1	23 (13)	14 (61)	9 (39)	0.008*
	2	73 (40)	59 (81)	14 (19)	
	3	80 (43)	45 (56)	35 (44)	
	4	8( 5)	4 (50)	4 (50)	
Score LN <sup>5</sup>		7.0 ± 2.6	5.9 ± 1.8	9.2 ± 2.6	< 0.001**

**Table 3.** Demonstrate the patients and US characteristics for benign and malignant lymphadenopathy. \*p value < 0.05, \*\*p value < 0.001.

Items	Sensitivity (95%CI)	Specificity (95%CI)	Overall accuracy (95%CI)
RTE (3 + 4)	62.71% (50.4–75.1%)	58.18% (49.0–67.4%)	59.76% (52.4–67.2%)
SWE (> 44 kPa)	63.93% (51.9–76.0%)	61.98% (53.3–70.6%)	62.64% (55.6–69.7%)
SWE(> 3.8 m/s)	54.10% (41.6–66.6%)	68.33% (60.0–76.7%)	63.54% (56.5–70.5%)
LN Score <sup>5</sup> (> 7)	80.60% (71.1–90.1%)	77.37% (70.4–84.4%)	78.43% (72.8–84.1%)
Sydney system (L3-5)	97.06% (93.0–100.0%)	99.26% (97.8–100.0%)	98.53% (96.9–100.0%)

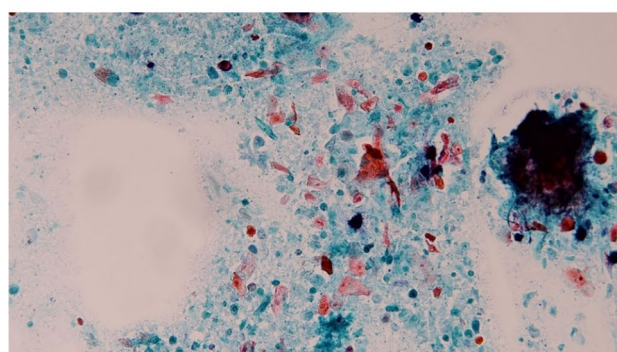
**Table 4.** Comparison of the diagnostic performance by the RTE/SWE/LN scoring system and the Sydney system.



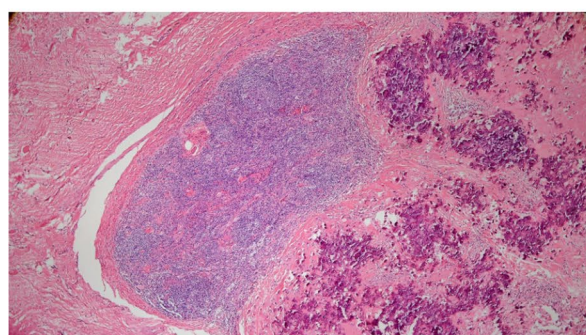
(A)



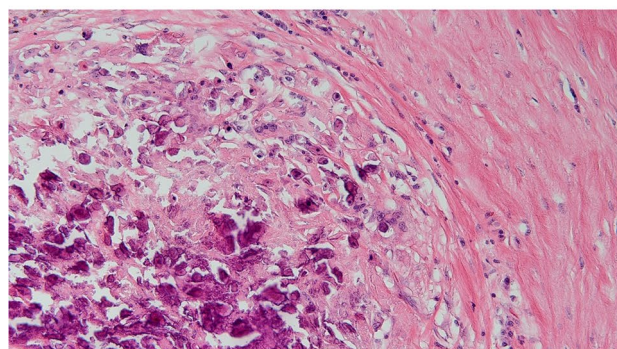
(B)



(C)



(D)



primarily attributable to tissue fibrosis. All these characteristics can provide the information for malignant lymphadenopathy. However, most of these features are subjective and operator dependent and no single one characteristic has high sensitivity, specificity and accuracy.

◀ **Fig. 1.** There was one false-positive case in our study. Preoperative ultrasound found lymph nodes with heterogeneous echo texture overriding the common carotid artery (A). On cytology, the smear showed a tumor necrotic debris background with some keratinocyte-like cells (in orange color) and some cell shadows with enlarged nuclei (in green color). This finding was comparable to malignancy in cytology according to the Sydney system (B). In the final pathology with H&E staining, calcifications, histiocytes, and necrotic debris with necrotic keratinocyte-like cells were observed (C: low power & D: high power). Because there were no viable carcinoma cells, the final diagnosis was no metastatic carcinoma.

Table 3 provides an overview of the US characteristics of benign and malignant lymphadenopathies in our cases series. Malignant lymph nodes were more common in male and older patients, tended to be larger in size and rounder in shape (as indicated by the S/L ratio) and were more likely to have vague boundaries, heterogeneous internal echotexture, calcifications, absent hilar echotexture, and other vascular patterns. We previously reviewed these characteristics and developed an US scoring system that also showed significant differences between benign and malignant lymphadenopathies in our study. Malignant lymph nodes also exhibited increased stiffness on both real-time elastography (RTE) and shear wave elastography (SWE). These findings suggest that clinical data, US features, and elasticity characteristics can serve as indicators for distinguishing between benign and malignant lymphadenopathies. The US scoring system demonstrated acceptable diagnostic performance. These findings highlight the importance of combining multiple diagnostic approaches to improve the accuracy of diagnosing neck lymphadenopathy. The US scoring system can be used as a screening tool, while the Sydney system can serve as the gold standard before the final histopathology.

Table 4 presents a comparison of the diagnostic performance of real-time elastography, shear wave elastography, the US scoring system, and the Sydney system. The US scoring system achieved a sensitivity of 81%, specificity of 77%, and overall accuracy of 78% in distinguishing between benign and malignant lymphadenopathy. On the other hand, the Sydney system exhibited higher sensitivity (97%), specificity (99%), and accuracy (99%). The post-hoc power analysis demonstrated a power of 86% for sensitivity and 99% for both specificity and accuracy. These findings suggest that the US scoring system can be used as a screening tool for diagnosing malignant LNs, while the Sydney system demonstrates superior performance and can serve as the gold standard before the final histopathology.

US elastography, on the other hand, showed poor diagnostic performance in this study. The sensitivity, specificity, and accuracy were 63%, 58%, and 60% for RTE with the 4-point scoring system, 64%, 62%, and 63% for SWE higher than 44 kPa, and 54%, 68%, and 64% for SWE higher than 3.8 m/s, respectively.

It is difficult to diagnose LNs after radiation therapy. Figure 1 demonstrates another case of a false-positive result; this is a hypopharyngeal cancer patient. He received an US exam 3 months after concurrent chemoradiotherapy. On US, multiple heterogeneous LNs above the carotid artery were found. US-FNA with the Sydney system was positive for malignancy. Preoperative US found lymph nodes with heterogeneous echo texture overriding the common carotid artery (Fig. 1A). On cytology, the smear showed a tumor necrotic debris background with some keratinocyte-like cells (in orange color) and some cell shadows with enlarged nuclei (in green color). This finding was comparable to malignancy in cytology according to the Sydney system (Fig. 1B). In the final pathology with H&E staining, calcifications, histiocytes, and necrotic debris with necrotic keratinocyte-like cells were observed (C: low power & D: high power). Because there were no viable carcinoma cells, the final diagnosis was no metastatic carcinoma.

Diagnosing neck lymphadenopathy becomes challenging after radiation therapy due to the alterations in ultrasound and cytology findings. Documentation indicates that radiation therapy can lead to the disappearance of certain lymphoid tissues and the replacement of parts of lymph nodes with fibrous tissue. These changes can complicate the diagnostic process and necessitate careful evaluation to distinguish between benign and malignant conditions in the post-radiation context<sup>28</sup>. In our previous study, radiation therapy had influence on sonographic characteristics, ultimately impacting diagnostic accuracy in this patient population<sup>29</sup>. On computed tomography (CT) scans, the criteria used for detecting pathological lymph nodes, such as nodal necrosis or a short-axis diameter, can at times be deemed unreliable in the evaluation of irradiated neck regions<sup>30</sup>. According to previous systematic review and meta-analysis, the pooled sensitivity and specificity for identifying malignant lymph nodes in patients with a history of prior irradiation were found to be relatively modest, with values of 69.1% and 84.2%, respectively<sup>31</sup>. Therefore, it should be very careful in interpretation of the cytology results of LNs after radiation.

There are some limitations need to be mention. First, our study is constrained by a relatively small cases number and a single institution setting. Second, there is a degree of selection bias as most patients with a US scoring less than 7 did not received US-FNA examination. Third, we encountered a rarity of lymphoma cases in our study, and in such instances, we opted for ultrasound-guided core needle biopsy (US-CNB) when lymphoma was suspected. Therefore, the cases in our series is selected. In our opinion, ancillary techniques usually are still necessary to classified different types of lymphoma<sup>32</sup>. Further study focus on Sydney system in lymphoma diagnosis is still mandatory. Fourth, our dataset lacks contrast-enhanced ultrasound (CEUS) data, which could have provided additional valuable insights. Fifth, this study is still not well external validated, which should include more cases numbers and demographic information such as ethnicity, and make the results more robust.

## Conclusion

In conclusion, this study provides valuable insights into the characteristics of neck lymphadenopathy and the diagnostic capabilities of various US methods. Specifically, the Sydney System demonstrated superior performance with higher sensitivity, specificity, and overall accuracy compared to the conventional US scoring

system and elastography. Our findings observed that the Sydney System is very effective for reporting neck lymphadenopathy.

## Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Conception and design: L.L.J. and H.W.L. Analysis: L.L.J., H.W.L. Interpretation of data: L.L.J., W.C.H., C.P.C., L.W.C., C.C.M., W.M.H., and H.W.L. Drafting of the manuscript: L.L.J. Revising: L.L.J., W.C.H., C.P.C., L.W.C., C.C.M., W.M.H., and H.W.L. Final approval of the version to be published: L.L.J., W.C.H., C.P.C., L.W.C., C.C.M., W.M.H., and H.W.L.

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### Declarations

### Competing interests

The authors declare no competing interests.

### Informed consent

All patients signed written informed consent forms.

### Additional information

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