**Localisation of tongue lesions according to subsite: bad and better neighbourhoods**

**Running title:**

**Keywords:** tongue, subsites, biopsy, clinicopathological, neighbourhood

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**Abstract**

**Objective:** Tongue lesions constitute a considerable proportion of oral mucosal pathologies. These lesions appear in different subsites of the tongue—dorsal, ventral, lateral and tip—and may be reactive, infectious, immunologic or neoplastic. We analysed the potential differences among these subsites regarding lesion type and clinicopathological concordance.

**Methods:** In this retrospective analysis of human tongue lesions diagnosed over a 7-year period (2016-2022) in our institution, we divided the tongue into subsites—lateral, dorsal, ventral and tip—and classified diagnoses into different categories.

**Results:** The lateral aspect of the tongue was the most affected site (43.6%). Most lesions (64.8%) were classified as reactive, infectious or tumour-like. More malignant or premalignant lesions were found on the lateral aspect (31%) compared with the other aspects, and almost all lesions observed on the tip of the tongue (96%) were reactive, infectious or tumour-like. The clinical and histopathological diagnoses concurred in only 62.3% of cases on the lateral aspect compared with 92.6% at the tip.

**Conclusions:** Our findings support the perception of the tongue as a diverse organ comprising better and worse neighbourhoods regarding both lesion type and clinicopathological concordance. These findings should be further supported by preclinical studies focusing on the microenvironmental properties of the different subsites of the tongue.

**Introduction**

The human tongue is a unique and mainly muscular organ that participates in major functions of the oral mucosa, including tasting, phonation, mastication, deglutition, maintenance of oral hygiene, protection of deeper structures and facilitation of orofacial growth (du Toit, 2003). The easy clinical accessibility of the tongue makes it a good health indicator for clinical examinations (Costa et al., 2012). The condition of the tongue has been considered a reflection of local and systemic diseases, such as candidiasis, anaemia, endocrine disorders, metabolic diseases, storage diseases and neurological deficits (Bhattacharya, Sinha & Pal, 2016; Mangold, Torgerson & Rogers, 2016). While some diagnoses can be made on the basis of clinical appearance, the tongue may occasionally be affected by pathological conditions that necessitate a biopsy and a consequent histopathological diagnosis (Logan & Goss, 2010).

Epidemiological studies have shown that tongue lesions constitute a considerable proportion of oral mucosal lesions and that prevalence rates vary around the world (Darwazeh & Pillai, 1993). The variable prevalence rates indicate a lack of consistency in the reference data (Bhattacharya et al., 2016). The lesions might be reactive, arising in response to local trauma (e.g., irritation fibroma, pyogenic granuloma, mucocele), inflammatory or immunologic (e.g., lichen planus, lichenoid reaction), or neoplastic, which can be either benign (e.g., lipoma, schwannoma) or malignant (e.g., squamous cell carcinoma, sarcoma) (Allon, Vered & Kaplan, 2019).

The tongue encompasses the dorsal, lateral and ventral aspects and the tip. Little is known about the distribution of lesions according to these subsites. However, it is well known that oral squamous cell carcinoma is more prevalent on the lateral aspect of the tongue (Mangold et al., 2016) and relatively rare on the dorsal aspect (Okubo et al., 2017).

The present study was conducted with a special focus on the different subsites of the human tongue. The purpose of the study was to view the tongue as a whole, as a comparison to its different subsites. Specifically, we aimed to analyse the potential differences among these subsites regarding the type of lesion and the clinicopathological concordance, a finding that could potentially enhance the clinical accuracy of tongue lesion diagnosis.

**Materials and Methods**

The present study was approved by the local Institutional Review Board (#0011-22) and conducted as a retrospective analysis of human tongue lesions diagnosed over a period of 7 years (2016-2022) in the Institute of Pathology of our institution. We included all diagnostic biopsy records from the tongue, studied patients’ clinical records and collected the following relevant data: demographic information (age and sex), the aspect of the tongue involved (lateral, dorsal, ventral and tip), the histopathological diagnosis and the pre-biopsy clinical differential diagnosis. The collected data were summarised, and the clinical and histopathological diagnoses were classified into one of the following categories: reactive, infectious or tumour-like lesions, benign lesions, immune/autoimmune lesions, lichenoid lesions or those of undetermined significance, premalignant lesions and malignant lesions (Table 1).

Statistical analysis of the results was conducted by expert biostatisticians (A.R.B. and N.L.Z.) using R statistical software (R Core Team, 2023). Lesion types and tongue aspects are described by counts and percentages. Regarding the clinicopathological concordance, when the pre-biopsy clinical diagnosis and histopathological diagnosis were classified in the same lesion type category, it was considered a ‘match’. The categories were further divided into two groups to compare the clinicopathological match rates between the groups: the first group included malignant and premalignant lesions while the second group included the remaining categories (non-malignant or non-premalignant lesions). Fisher’s test was used to compare the distributions of tongue aspects among the lesion types and to compare the clinicopathological match rates among tongue aspects according to diagnosis type. P-values less than 0.05 were considered significant.

**Results**

From 2016 to 2022, 3536 biopsies of the oral cavity were performed in the Institute of Pathology of Barzilai University Medical Center; 383 (10.8%) comprised tongue biopsies, 174 from males (45.4%) and 209 from females (54.6%), giving a male to female ratio of 1:1.2. The age range of the patients was 5 to 99 years and the mean age was 52±21.7 years. Most of the histologically observed lesions (64.8%) were reactive, infectious or tumour-like lesions while 14.8% were malignant or premalignant (Figure 1). Most of the tongue lesions were encountered at the lateral aspect of the tongue (43.6%), followed by the dorsal aspect (26.4%), tip (19.1%) and ventral aspect (8.6%) (Table 2 and Figure 2).

***Tongue lesions according to subsite***

**Lateral aspect:** lesions observed on the lateral aspect of the tongue were reactive, infectious or tumour-like (44%), malignant (21.1%), lichenoid lesions or those of undetermined significance (16.3%), premalignant (10.2%), immune/autoimmune (4.8%) or benign (3.6%) (Table 5 and Figure 3). The clinical diagnosis ‘matched’ the histopathological result in only 62.3% of cases (Table 6).

**Dorsal aspect:** lesions on the dorsal aspect of the tongue were reactive, infectious or tumour-like (72.3%), benign (12.9%), lichenoid lesions or those of undetermined significance (11.9%) or malignant (3%); no premalignant lesions or immune/autoimmune lesions were encountered (Table 5 and Figure 3). The clinical diagnosis ‘matched’ the histopathological result in 73.1% of cases (Table 6).

**Ventral aspect:** lesions on the ventral aspect of the tongue were reactive, infectious or tumour-like (72.7%), lichenoid lesions or those of undetermined significance (18.2%), immune/autoimmune (6.1%) or malignant (3%); no benign lesions and no premalignant lesions were observed (Table 5 and Figure 3). The clinical diagnosis ‘matched’ the histopathological result in 76.7% of cases (Table 6).

**Tip of tongue:** lesions on the tip of the tongue were almost always reactive, infectious or tumour-like (95.9%); a minority were lichenoid lesions or those of undetermined significance (1.4%), malignant (1.4%) or benign (1.4%) (Table 5 and Figure 3). The clinical diagnosis ‘matched’ the histopathological result in 92.6% of cases (Table 6).

Regarding the clinicopathological concordance and the differences in match rates, the pre-biopsy clinical diagnosis generally matched the histopathological diagnosis and was correctly classified in the same category in 252 of all cases (65.8%). In the malignant or premalignant lesion group, only 31 cases matched (52.5%), while for the second group, which included the remaining categories, 221 cases matched (76%). In terms of the differences in match rate according to subsite (neighbourhood), the match rate was highest for the tip of the tongue (92.6%) and lowest for the lateral aspect (62.3%).

***Tongue lesions according to age***

Thirty-two cases (8.3%) occurred in paediatric patients aged 18 years and below. The most affected subsite in such patients was the ventral aspect (37.4%) while the most prevalent category was reactive, infectious or tumour-like lesions (78.12%) (Table 3). In addition, 160 cases (41.7%) were found in elderly patients (aged 60 and above), where the most affected subsite was the lateral aspect (62.5%) and the most prevalent category was reactive, infectious or tumour-like lesions (43.1%) (Table 4). It should be noted that, while the lateral aspect was the most affected subsite in elderly patients, it was the least affected subsite in paediatric patients (3%). In addition, while the ventral aspect was the most affected subsite in the paediatric patient group, it was the least affected subsite in the elderly group of patients (7%). The most prevalent category across all age groups was reactive, infectious or tumour-like lesions. The elderly patient group exhibited the highest proportion of malignant and premalignant lesions (28.75%).

**Discussion**

As far as we are aware, this is the first study to examine the prevalence and clinicopathological correlations of tongue lesions that focuses on the different subsites of the tongue. Tongue lesions constituted an appreciable percentage (10.8%) of all histologically diagnosed cases of oral cavity biopsies in our institution, which is higher than the 4%-9.2% reported by some authors (Alaeddini, Barghammadi, Eshghyar & Etemad-Moghadam, 2014; Byahatti & Ingafou, 2010; Dhanuthai, Kintarak, Subarnbhesaj & Chamusri, 2020; Lasisi & Abimbola, 2017; Shamloo, Motazedian & Lotfi, 2016) but lower than the 18.52%-52.3% reported by others (Avcu & Kanli, 2003; Bánóczy, Rigó & Albrecht, 1993; Darwazeh & Pillai, 1993; Koay, Lim & Siar, 2011; Vörös-Balog, Vincze & Bánóczy, 2003) in most clinical studies. The prevalence of tongue lesions in the clinical studies may be higher than in the present study because lesion diagnoses such as geographic, coated or fissured tongue can be made on the basis of clinical appearance and do not usually require histopathological examination.

In the present study and in accordance with the studies by Costa et al. (2012), Gambino et al. (2015) and Miyake et al. (2018), reactive, infectious or tumour-like lesions were the most diagnosed tongue lesions. This is in contrast to the study by Alaeddini et al. (2014), where tongue lesions were primarily classified into the immune-mediated group and the reactive/inflammatory category, respectively. Moreover, according to our analysis, the reactive, infectious or tumour-like lesion category was the most prevalent category across all subsites. The mean age of the patients in the present study was 52 years, which is comparable to the 45-48-year age range reported by Lasisi and Abimbola (2017), Dhanuthai et al. (2020), Shamloo et al. (2016) and Alaeddini et al. (2014).

Most of the tongue lesions were found on the lateral aspect of the tongue (43.6%), which is in accordance with the results obtained by Aittiwarapoj et al. (2019), Shamloo et al. (2016), Gambino et al. (2015) and Miyake et al. (2018). However, studies by Lasisi and Abimbola (2017) and Alaeddini et al. (2014) found the most affected subsite to be the dorsum of the tongue, followed by the lateral aspect.

In the present study, the distribution of the type of lesion varied among the different subsites. More malignant/premalignant cases were diagnosed on the lateral aspect (31%), and almost all lesions observed at the tip of the tongue (96%) were reactive, infectious or tumour-like lesions. Accordingly, the tip of the tongue could be considered the best neighbourhood of the tongue from the patients’ point of view and the lateral aspect the worst.

The match between the clinical and histopathological diagnosis was also best achieved on the tip of the tongue, making it the best neighbourhood from the clinician's perspective as well, followed by the ventral and dorsal aspects and finally the lateral aspect, which could also be considered the worst neighbourhood from that point of view. The differences in match rates between the clinical and histopathological diagnoses emphasise the importance of the histopathologic analysis in the final diagnosis, particularly in the lateral aspect.

When considering the pre-biopsy evaluation and clinicopathological correlation, the clinical diagnosis was correctly classified in the same category as the histopathological result for 252 of all cases (65.8%). For malignant or premalignant clinical diagnoses, the accuracy was significantly lower, with only 31 cases matched (52.5%), while 221 matched (76%) for other diagnoses. This demonstrates our relatively limited clinical ability to assess neoplastic lesions.

Examination of the incidence and distribution of tongue lesions according to age revealed that reactive and benign tongue lesions mostly affected younger age groups in the ventral aspect, whereas malignant and premalignant tongue lesions affected older age groups, particularly in the lateral aspect. This finding suggests that advancing age is a significant risk factor for cancer.

The differences among the subsites of the tongue may be attributed to extrinsic factors, such as oral habits, or to intrinsic factors, such as cell population. In a recent study discussing the composition and the transcriptional landscape of the tongue immune system, Lyras et al. (2022) successfully identified distinct local immune cell populations and described two specific subsets of tongue-resident macrophages occupying discrete anatomical niches. Further studies are needed to determine whether the differences among the different subsites can be attributed to differences in the microenvironmental niches that contain different subpopulations of fibroblastic or immunological cells.

In conclusion, different subsites of the tongue do not behave in the same manner and thereby constitute different neighbourhoods: worse and better. Both from the patients’ and the clinicians’ perspective, the best neighbourhood is the tip of the tongue while the worst is the lateral aspect. This study provides a novel point of view by demonstrating the differences among the different subsites of the tongue in terms of types of lesions and clinicopathological concordance.

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**Data Availability Statement**

**Author Contributions**

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**Table 1.** Age, sex and tongue lesion location according to type of lesion category

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Serial No. | Age | Sex | Pre- biopsy clinical diagnosis | Type of lesion (according to clinical diagnosis) | Histopathological diagnosis | Type of lesion (according to histopathological diagnosis) | Involved aspect of tongue | Clinicohistopathological correlation |

\*Type of lesion: **A**. Reactive, infectious or tumour-like lesions; **B**. Lichenoid lesions or those of undetermined significance; **C**. Benign lesions; **D**. Malignant lesions; **E**. Premalignant lesions; and **F**. Immune/autoimmune lesions.

**Table 2.** Tongue lesion distribution according to subsite

|  |  |  |
| --- | --- | --- |
| **Category** | **n** | **%** |
| Dorsal aspect | 101 | 26.4% |
| Lateral aspect | 167 | 43.6% |
| Tip of tongue | 73 | 19.1% |
| Ventral aspect | 33 | 8.6% |
| Not available | 9 | 2.3% |
| Total | 383 | 100% |

**Table 3.** Tongue lesion distribution according to category and subsite in paediatric patients (age < 18 years)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of lesion (histopathology)** | **Dorsal aspect** | **Lateral aspect** | **Tip of tongue** | **Ventral aspect** |
| Benign lesions | 4 (44.4%) | 1 (100%) | 0 | 0 |
| Lichenoid lesions or those of undetermined significance | 1 (11.1%) | 0 | 0 | 0 |
| Malignant lesions | 1 (11.1%) | 0 | 0 | 0 |
| Reactive, infectious or tumour-like lesions | 3 (33.3%) | 0 | 10 (100%) | 12 (100%) |
| Total | 9 (100%) | 1 (100%) | 10 (100%) | 12 (100%) |

**Table 4.** Tongue lesion distribution according to category and subsite in elderly patients (age > 60 years)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of lesion (histopathology)** | **Dorsal aspect** | **Lateral aspect** | **Tip of tongue** | **Ventral aspect** |
| Benign lesions | 4 (12.5%) | 1 (1%) | 1 (5.6%) | 0 |
| Immune/autoimmune lesions | 0 | 8 (8.2%) | 0 | 1 (8.3%) |
| Lichenoid lesions or those of undetermined significance | 6 (18.8%) | 18 (18.4%) | 1 (5.6%) | 5 (41.7%) |
| Malignant lesions | 2 (6.2%) | 28 (28.6%) | 0 | 1 (8.3%) |
| Premalignant lesions | 0 | 15 (15.3%) | 0 | 0 |
| Reactive, infectious or tumour-like lesions | 20 (62.5%) | 28 (28.6%) | 16 (88.9%) | 5 (41.7%) |
| Total | 32 (100%) | 98 (100%) | 18 (100%) | 12 (100%) |

**Table 5.** Tongue lesion distribution according to category and subsite (all ages) p-value = 0.00049

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of lesion (histopathology)** | **Dorsal aspect** | **Lateral aspect** | **Tip of tongue** | **Ventral aspect** |
| Benign lesions | 13 (12.9%) | 6 (3.6%) | 1 (1.4%) | 0 |
| Immune/autoimmune lesions | 0 | 8 (4.8%) | 0 | 2 (6.1%) |
| Lichenoid lesions or those of undetermined significance | 12 (11.9%) | 27 (16.3%) | 1 (1.4%) | 6 (18.2%) |
| Malignant lesions | 3 (3%) | 35 (21.1%) | 1 (1.4%) | 1 (3%) |
| Premalignant lesions | 0 | 17 (10.2%) | 0 | 0 |
| Reactive, infectious or tumour-like lesions | 73 (72.3%) | 73 (44%) | 70 (95.9%) | 24 (72.7%) |
| Total | 101 (100%) | 166 (100%) | 73 (100%) | 33 (100%) |

**Table 6.** Clinicopathological correlation according to subsite (all ages)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Match** | **Dorsal aspect** | **Lateral aspect** | **Tip of tongue** | **Ventral aspect** |
| **Yes** | **68 (73.1%)** | **96 (62.3%)** | **63 (92.6%)** | **23 (76.7%)** |
| **No** | **25 (26.9%)** | **58 (37.7%)** | **5 (7.4%)** | **7 (23.3%)** |
| **Total** | **93 (100%)** | **154 (100%)** | **68 (100%)** | **30 (100%)** |

**Figure Legends**

**Figure 1.** Incidence of tongue lesions according to type of lesion

**Figure 2.** Distribution of tongue lesions according to subsite

**Figure 3.** Distribution of tongue lesions according to category and subsite