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Original Research

Pre-operative staging of carcinoma of tongue using ultrasonography and magnetic resonance imaging

Nilu Malpani Dhoot[1], Suman Hazarika[2], Binoy Choudhury[3], Amal Chandra Kataki[4], Hridayananda Goswami[2], Ranjan Baruah[2], Rajib Sharma[2]

[1]Department of Radiology, Dr. B. Borooah Cancer Institute, International Hospital, Guwahati, Assam, India, [2]Department of Radiology, International Hospital, Guwahati, Assam, India, [3]Department of Radiology, Dr. B. Borooah Cancer Institute, Guwahati, Assam, India, [4]Department of Radiology, Dr. B. Borooah Cancer Hospital, Guwahati, Assam, India

Address for correspondence:
Dr. Nilu Malpani Dhoot, Dr. B. Borooah Cancer Institute, International Hospital, Guwahati, Assam, India. E-mail: drniludhoot@gmail.com

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ABSTRACT

Purpose: To assess the accuracy of staging tongue cancer using ultrasound (US) and magnetic resonance imaging (MRI) when compared to histopathology (HPE). **Method:** Biopsy confirmed, 28 cases of carcinoma of tongue were prospectively studied. A tumor, node, metastasis stage was assigned to each patient using MRI and US in this double-blind study. The gold standard stage on HPE was then correlated with MRI/US stage. Statistical analysis was performed. **Results:** Most of the patients 75% (21/28) at presentation were stage II or more. MRI staging had an overall accuracy of 82.1% (23/28) while US had 57.1% (16/28) overall accuracy. The difference in staging was not statistically significant on Fischer's exact test. US was more accurate in evaluating larger tumors. For stage 1, II and III MRI was 83.3% accurate. US achieved an accuracy of 16.6% for stage I and an accuracy of 66.6% for stage II and III. For stage IV, both MRI and US attained 100% accuracy. **Conclusion:** US has an accuracy of 57.1% in staging tongue cancer, while MRI attains 82.1% accuracy. The difference is not significant statistically. US achieves high accuracy in evaluating advanced cancers. It can be used where MRI is unavailable or contraindicated.

KEY WORDS: Cancer, magnetic resonance imaging, staging, tongue, ultrasound

INTRODUCTION

An accurate analysis of the stage of tongue tumor is vital in deciding the therapy offered to the patient [1]. Even though tongue is an organ, which is visible to the eye, clinical examination is difficult as most of the patients with carcinoma of tongue cannot open their mouth wide and many cannot tolerate palpation. Furthermore, these tumors are infiltrative, and if they cross the barrier of lingual aponeurosis, they will grow beneath it extensively involving the musculature while the mucosal surface shows a small or even no abnormality [2]. Hence pre-therapy imaging and staging of the tongue cancer is indispensible.

Computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound (US) are the available imaging modalities for cancer of tongue. MRI allows good visualization of oral cancer and is the imaging technique of choice for studying head and neck tumors [3]. The abnormalities detected on MRI are well correlated pathologically [4]. MRI imparts detailed view of the tongue tumor and its nodal extensions. Although, CT can be used for imaging the tongue but MRI is superior owing to its better soft tissue resolution and hence it is preferred. However, MRI is generally expensive and sometimes unavailable. Apart from that, claustrophobia, incompatibility with metallic implants, and the long duration of the procedure are additional issues restricting MRI use in many situations. Even though the

risk of contrast agent reactions in MRI is less than that of CT, they are known to occur [5]. MRI contrast agents are to be avoided in patients with renal insufficiency [6,7].

US is a substantial investigative tool in head and neck pathologies due to its high resolution, convenience, and adaptability [8]. It can be done bedside and can be performed repeatedly as it is relatively safe, is universally available, and generally less expensive. There is no absolute requirement of contrast agents in US. In addition to all this, it can be performed in claustrophobic, restless, uncooperative patients and also in patients with metallic implants. In our study, we have used US in assessing the stage of tongue cancer in patients who were posted for surgery on the basis of MRI findings and clinical evaluation. We compared the US assigned tongue cancer stage with MRI stage and histopathology.

METHODS

We selected 43 tongue cancer patients for our prospective study who were referred to our institute from April 2013 to March 2014. Following institutional ethical committee approval and written informed consent from each patient, these 43 biopsy-proven cases of squamous cell carcinoma of the anterior tongue were included in our study. Cases with cancer in the base of the tongue or buccal mucosa without anterior tongue involvement were excluded. The patients who were considered clinically inoperable based on age, general condition, associated medical conditions, and advanced disease were excluded. This study was performed over a period of 1 year in our departments of radiology and imaging.

Each patient was evaluated in detail by a dedicated head and neck oncosurgeon having more than 10 years of experience. A clinically assessed tumor, node, metastasis (TNM) [9] stage was assigned to each patient. Further a MRI of oral cavity was performed within a day or two of clinical examination. A MRI based TNM [9] stage of tongue cancer was assigned to each patient by two radiologists working in consensus and having more than 5-year experience in head and neck radiology. If there was a discrepancy between clinical and MRI stage, MRI stage was considered superior and assigned to the patient. Surgical treatment was offered to all these patients depending on MRI stage, general health factors such as age, physical fitness, and other coexisting medical conditions. After explaining the risks and the benefits of the surgery to the patients, 6 patients opted out of surgical therapy.

The contrast enhanced MRI examinations of the oral cavity was performed on a 1.5-T magnet (Achieva Level 5; Philips Healthcare, Best, the Netherlands) with the use of a body coil. The imaging protocol consisted of T1- and T2-weighted fast spin echo images in axial and coronal planes and short-tau inversion recovery (STIR) sequences in axial, sagittal, and coronal planes. T1-weighted post contrast (gadopentatate dimeglumine, dose 0.2 ml/kg) fat-suppressed images were obtained in all three planes. The imaging parameters were as follows - T1-weighted imaging: Repetition time/echo time, 400/8 milliseconds; field of view, 20 cm; matrix size, 512 × 512; T2-weighed imaging: Repetition time/echo time, 2341/50 milliseconds; field of view, 20 cm; matrix size, 512 × 512; and STIR: Repetition time/echo time, shortest/80 milliseconds; field of view, 20 cm; matrix size, 512 × 512. The average scan time was about 35 min. A slice thickness of 5 mm covered the area of interest from the floor of the orbit to the cricoid cartilage. The same protocol was followed in all patients. The MRI examinations were read in consensus by two head and neck radiologists. The radiologists were aware that all patients had confirmed tongue cancer but were blinded to patient identities and clinical examination results. Nine cases were either T4b or N2b/N3 or both on MRI, these were surgically irresectable due to advanced disease.

There were 28 patients out of 43 (6 patients opted out of surgery and 9 patients had extensive local and nodal disease on MRI) cases who consented for surgery and were found surgically resectable on MRI. These patients were evaluated on US by a sonologist with more than 5 years of experience in head and neck US. The sonologist was blinded to clinical/MRI stage, but was aware of the proven diagnosis of tongue cancer. Using a systematic US technique, the sonologist assigned a US based TNM stage for each patient. The patient was placed in supine position with the neck extended. The systematic sonographic technique was done using a high resolution probe (7-12 mHZ) of a high-resolution US machine (Nemio 30 SSA-550A; Toshiba Medical Systems Co, Ltd, Tokyo, Japan). Starting from the submental region, with the probe in a transverse orientation, the neck was scanned to the hyoid bone. The mylohyoid muscle, intrinsic tongue muscles, sublingual space, sublingual neurovascular bundle, base of the tongue, and lingual septum were identified and examined in this plane. The probe was then moved to a longitudinal orientation, with the long axis parallel to the midline in the submental region and tilted on either side to view the genioglossus muscle, mylohyoid muscle, submandibular glands, and submandibular duct. The neck was scanned later for detection of the neck nodes. A US based TNM stage was assigned to each of the 28 tongue cancer patients.

All these patients were operated within 15 days of US and MRI examinations. A TNM stage assigned on histopathology (HPE) for each patient was considered the gold standard. Comparisons were made between the TNM stage on MRI and US with HPE gold standard stage. The accuracy of each modality was calculated. Fischer's exact test was used to evaluate any statistically significant difference between US and MRI stage. $P < 0.05$ was considered statistically significant.

RESULTS

In our cohort of 28 patients, there were 17 males and 11 females. The age range of this study group was between 30 and 55 years. Most of the patients (75%, 21/28) at presentation were stage II or more. MRI staging had an overall accuracy of 82.1% (23/28) while US staging had an overall accuracy of 57.1% (16/28) when compared to gold standard HPE staging. On Fischer's exact test, the *P* value obtained was 0.079. Thus, the difference in staging of tongue cancer on MRI and US was not quite statistically significant. US was more accurate in evaluating larger tumors and less accurate in assessing smaller

Table: 1 Stage wise accuracy on MRI and US when compared to HPE

Stage of the disease	Number of patients staged on HPE (gold standard stage)	Number of patients correctly staged on MRI	Stage wise accuracy in MRI when compared with HPE (%)	Number of patients correctly staged on US	Stage wise accuracy in US when compared with HPE (%)
Stage 0 TIS	1	0	0/1, 0	0	0/1, 0
Stage 1	6	5	5/6, 83.3	1	1/6, 16.6
Stage 2	12	10	10/12, 83.3	8	8/12, 66.6
Stage 3	6	5	5/6, 83.3	4	4/6, 66.6
Stage 4	3	3	3/3, 100	3	3/3,100
Total	28	23	23/28, 82.1	16	16/28, 57.1

HPE: Histopathology, MRI: Magnetic resonance imaging, CIS: Carcinoma *in situ*, US: Ultrasound

tumors. The stage wise accuracy is shown in [Table 1]. Both MRI and US were unable to detect one case of carcinoma *in situ* (CIS) in our cohort. This patient had speckled leukoplakia with ulceration. One patient was downstaged on MRI and 4 patients were upstaged [Table 2]. On US 7 patients were downstaged, while 5 patients were upstaged as depicted in [Table 3]. If stage 0 and stage 1 diseases were to be excluded, US would achieve an accuracy of 71% (15/21) whereas MRI would be 85% (18/21) accurate. This suggests that US is more accurate for advanced disease and most of our patients at presentation were stage II or more.

DISCUSSION

A definite diagnosis of tongue cancer is obtained primarily by biopsy. The principal role of imaging is for staging the disease to provide an accurate staging work-up for the planning of therapy.

MRI is indispensible for staging tongue cancer is well-known fact. Contrast enhanced MRI has become the cornerstone in the pretreatment evaluation of tongue cancers and provides accurate information about the extent and depth of disease that can help decide the appropriate management strategy and indicate prognosis. There are multiple papers proving the worth of MRI in tongue cancer time and again [4,10-13]. The reported accuracy of MRI in evaluation of tongue carcinoma by Zeng *et al*. [14] was 83-100%. We achieved an accuracy of 82.1% in our study.

Sonography is not a modality of choice for defining tongue pathology. It is exacting, as bony mandible outlines the oral cavity allowing only limited field of view. It is fundamentally used in neck for evaluating neck nodes and guiding fine needle aspirations and biopsies [15,16] However, there are accessible sites that can be used for transmission of the US beam to the tongue lesion, for example, the submental region and intraoral access. The intraoral approach provides a limited view and is more useful for tumor thickness assessment. A few studies have indicated the usefulness of intraoral sonography while evaluating tumor thickness in oral cancers [17,18]. Submental access has also been successfully used attaining sensitivity of 61% [19]. Wakasugi-Sato *et al*. [20] evaluated the usefulness of intraoral and intraoperative sonography in tumor thickness assessment and tumor margin clearance during surgery. Even in the larynx and hypopharynx, US has been attempted with encouraging results [21].

Management of the tongue cancer is primarily decided on stage of the disease, [22] likewise at our institutes. Stage I and II cancers (T1-T2, N0) are treated with a single modality therapy at our institutes. Surgery or radiotherapy (RT) is advised for the primary at early stages, the former being favored. Locally advanced cancers (stage III and IV) are treated with combination of surgery, RT and chemotherapy for both the primary and the neck. Distant tumor metastasis is well assessed by CT and Positron emission tomography (PET) CT. If distant tumor spread is detected, the management changes even if there is minor regional spread. USG has limited role in assessing distal tumor spread apart from spread to the neck nodes. PET CT and/or CT are indispensible modalities with regards to confirming or ruling out distant metastasis.

In a study of 50 tongue cancer cases, Fruehwald *et al*. [23] could stage all but 1 case correctly using US. In our study group of 28 patients, we could perfectly stage 16 patients using US. In another study by Bruneton *et al*., [24] sonography did not visualize tumors in 9 of 42 cases of tongue cancer (7 stage T1 and 2 anterior stage T2 tumors). We could not correctly recognize the stage of 12 tongue tumors out of 28 (6 stage 1 and 4 stage 2). One of our patients was CIS, where both MRI and US failed. This patient had speckled leukoplakia with ulceration, having high suspicion of malignancy clinically. This patient was biopsied which was positive for cancer. US and MRI were done to know the extent of the disease as well as the nodal status. US was more accurate in detecting advanced disease, stage II and more. In cases of stage 1 disease, sonography failed to identify all except one [Figures 1a and b, 2a and b] small intrinsic tongue muscle tumor, primarily because of the depth. The high frequency probe we used through submental approach provided coronal and sagittal sections of the tongue. The intrinsic tongue muscle being located farthest from the probe had the least resolution. Similarly, involvement of the mylohyoid muscle by the tumor was difficult to detect due to depth. However, in our study, we could identify all three cases of mylohyoid invasion [Figure 3] correctly. Genioglossus is a fan-shaped muscle [Figure 4a], easy to identify on US, therefore, a tumor involving the fan-shaped genioglossus [Figure 4b and 5a] is simple to locate. The hypoechoic tumors extending to sublingual space could not be overlooked due to striking contrast with the hyperechoic sublingual glands. The use of Doppler could tell us the encasement of the lingual neurovascular bundle by the tumor [Figure 5a and b]. Doppler also allowed differentiation between the lingual artery and submandibular

Table 2: Demonstrates number of patients upstaged or down staged or correctly staged on MRI when compared with HPE

Number of patients in each stage on HPE (gold standard)						
Number of patients in each stage on MRI	CIS	Stage 1	Stage 2	Stage 3	Stage 4	Total
Normal	1					1
CIS						0
Stage 1		5				5
Stage 2		1	10			11
Stage 3			2	5		7
Stage 4				1	3	4
Total	1	6	12	6	3	28

HPE: Histopathology, MRI: Magnetic resonance imaging, CIS: Carcinoma *in situ*

Table 3: Demonstrates number of patients upstaged or downstaged or correctly staged on US when compared with HPE

Number of patients in each stage on HPE (gold standard)						
Number of patients in each stage on US	CIS	Stage 1	Stage 2	Stage 3	Stage 4	Total
Normal	1	4				5
CIS						0
Stage 1		1	1			2
Stage 2		1	8	1		10
Stage 3			3	4		7
Stage 4				1	3	4
Total	1	6	12	6	3	28

HPE: Histopathology, MRI: Magnetic resonance imaging, CIS: Carcinoma *in situ*, US: Ultrasound

gland duct encasement by the tongue mass [Figure 6a and b]. In all, large growths [Figure 7a and b] can be assessed reasonably well on US, whereas it is not very sensitive for small tumors. One of the fundamental advantages of using sonography is the high resolution it affords [8]. In addition, sonography is inexpensive, does not involve ionizing radiation, can be performed in patients with metallic implants, at the bedside, in patients with renal failure, and is suitable for restless, claustrophobic, or uncooperative patients.

The many frailties of sonography would restrict it from becoming the sole imaging modality for evaluation of tongue malignancies. We used sonography despite the fact that MRI is the modality of choice in this study to evaluate this option in case MRI is unavailable or contraindicated. There are several situations were MRI may not be feasible. Apart from claustrophobia, the contrast agents used in MRI are also contraindicated in certain situations. In restless patients, MRI is extremely limited for evaluation of tumor invasion. Therefore, in the patient population in which MRI is contraindicated, unaffordable, and unavailable, sonography can be used as an alternative modality and for posttreatment follow-up.

There are multiple limitations of this study. The first and main limitation of this study is its small sample size that describes our first routine use of US in tongue. For a wider acceptance of US, a further study with a larger study group would be needed. Second, we included operable cases of cancer involving the anterior

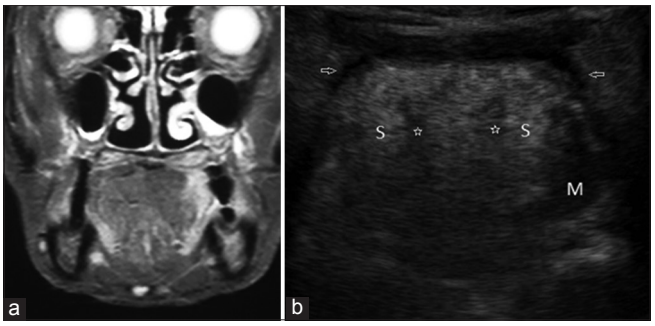

Figure 1: (a) A 42-year-old male patient having tongue ulcer, a coronal T2 fat saturated section of magnetic resonance imaging of the tongue shows a small intrinsic muscle T2 hyperintense lesion on the left side. (b) Coronal section ultrasound of tongue of the same patient shows small hypoechoic growth on the left side intrinsic muscles marked as M. The stars shows the genioglossus muscles. The hyperechoic sublingual glands are marked as S. The arrows show mylohyoid muscles on both sides

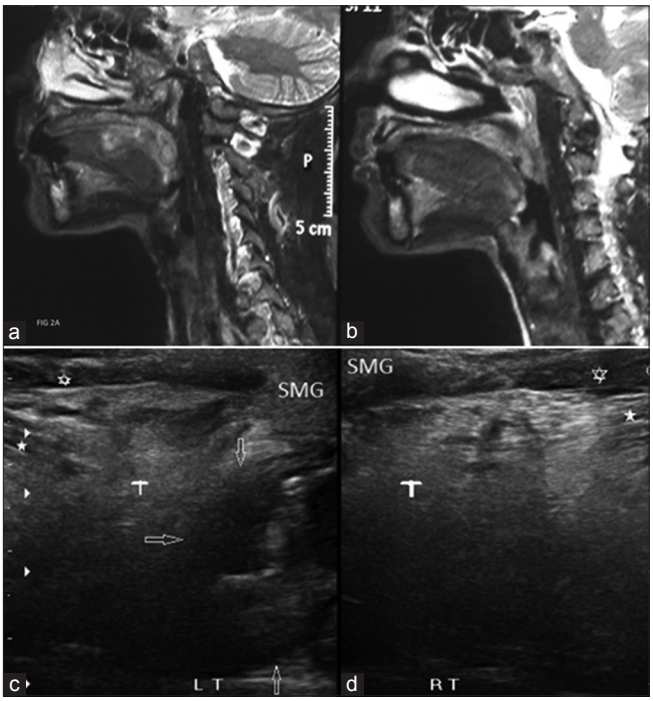

Figure 2: (a) A 54-year-old male patient having pain and tongue lesion, sagittal short-tau inversion recovery magnetic resonance imaging (MRI) images show small hyperintense growth involving only the intrinsic muscles of the tongue on the left. The right side is normal on MRI. (b) Same patient as in Figure 2a, sagittal section on ultrasound shows hypoechoic growth in intrinsic muscles on the left marked by arrows. The intrinsic muscles are marked as T on both sides. SMG is submandibular gland. Star sign is on the hypoechoic normal mylohyoid muscle

tongue, inoperable tumors and those infiltrating the base of tongue were excluded amounting to selection bias. Third, we did not use contrast-enhanced sonography to assess the tumors. The use of contrast in US of tongue cancer could be an avenue for further research. Fourth, we have used high frequency probe for our study, which has limited depth resolution and intrinsic tongue muscles were the farthest from submental

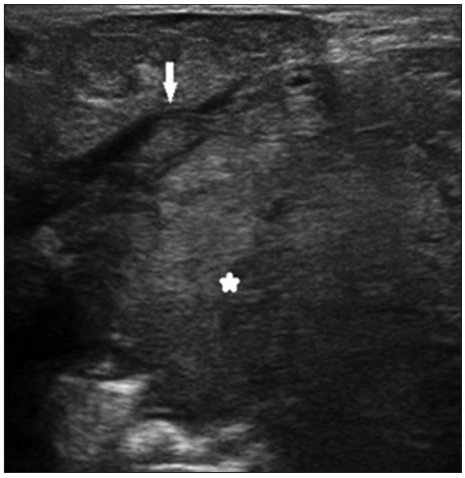

Figure 3: Patient having large tongue mass since 4 months, transverse section through the submental window on ultrasound shows a large heterogeneously hypoechoic growth marked by solid star, it infiltrates the mylohyoid muscle shown by the solid arrow

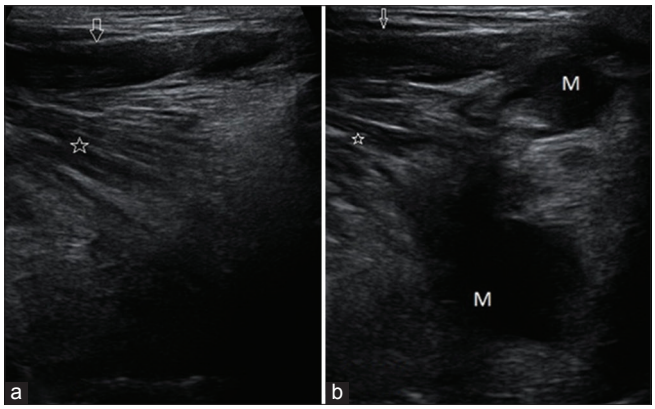

Figure 4: (a) A 34-year-old lady having tongue tumor, the sagittal section of tongue on ultrasound shows the normal fan-shaped genioglossus muscle marked by star. The arrow marks the normal mylohyoid muscle on the right side. (b) Same patient on the left side has a hypoechoic mass (M) on ultrasound sagittal section infiltrating the genioglossus marked by star. The arrow shows the mylohyoid muscle

approach. Thus, reducing the ability of US to interpret only intrinsic muscle growth. Lower frequency probe usage through the submental window can also be an area of further research. Fifth, all of our cases were biopsy-proven tongue cancers, and we evaluated role of sonography for detection of extension of the disease but not for detection of the disease itself. Finally, the use of US in tongue itself has several inherent limitations. These include poor visualization of the posterior regions, such as intrinsic tongue muscle growths (missed in all, but one cases in our study), the unproven role of sonography, and the difficulty in showing small tumors on sonography.

CONCLUSION

To conclude, we reached an accuracy of 57.1% in the evaluation of tongue cancer using US, which was statistically not significantly different when compared with MRI, which attained 82.1% accuracy. Although small tumors were inaccessible on

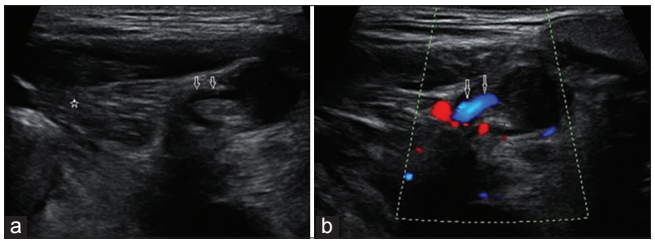

Figure 5: (a) Same patient of Figure 4a/b, has a linear hypoechoic structure marked by arrows on ultrasound could be lingual artery, which is encased by the hypoechoic mass infiltrating the genioglossus muscle, marked by a star. (b) Use of Doppler signal in Figure 5a, confirms that the lingual artery is encased by the tongue mass

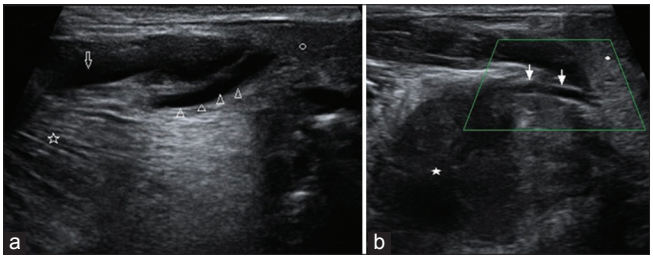

Figure 6: (a) A 38-year-old male patient, sagittal ultrasound (US) shows the submandibular gland duct shown by arrowheads. The star marks the genioglossus muscle and arrow marks the mylohyoid muscle. The circle is in the submandibular gland. (b) Same patient on the other side sagittal US image shows, hypoechoic mass (marked by star), arrows point the submandibular gland duct (there is no flow on Doppler) encased by the mass. Solid circle is the echogenic submandibular gland

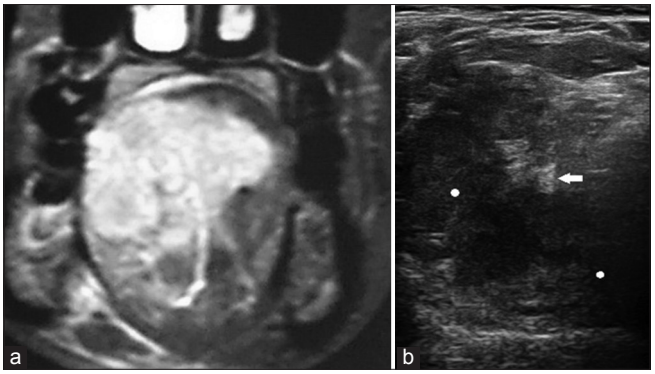

Figure 7: (a) A 30-year-old female patient has a large tongue ulcer, a coronal short-tau inversion recovery magnetic resonance imaging shows a large hyperintense tongue growth going across the lingual septum. (b) Same patient ultrasound image, coronal section shows a large hypoechoic mass marked by solid circles going across the midline. The arrow point to the lingual septum

sonography, we think that it can play a significant role in the staging of tongue tumor for advanced disease.

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