Abstract
Sonographic elastography is a new technique for measurement of the tissue stiffness, and is currently under investigation for tissue characterization in several anatomic sites. This article introduces methodologies of sonographic elastography, and mentions the possibility of its application to oral and maxillofacial regions. Sonographic elastography seems to be suboptimal for salivary gland malignancies, because there are many pathological types, and overlap between pleomorphic adenoma and malignant tumors. As to cervical lymph nodes, most studies have documented promising results of high accuracy for malignancy, although further larger studies are required to validate these findings. Therefore, sonographic elastography may become a useful ancillary technique in the routine diagnostic work-up for lymph nodes in the near future. For the masseter muscle, sonographic elastography has a possibility for exploring the causes of muscle pain, understanding the state of the muscle, selecting therapeutic methods, and evaluating therapeutic effect.

ABBREVIATIONS
EI: Elasticity Index; ARFI: Acoustic Radiation Force Impulse; SWE: Shear Wave Elastography; TMD: Temporomandibular Disorder

INTRODUCTION
High-resolution sonography is a sensitive imaging test for the detection of superficial masses. In experienced hands, many lesions can be diagnosed using a combination of grayscale and power Doppler sonographic features. Sonographic elastography is one of the latest technologies that can be applied to conventional sonography for reconstructing tissue elasticity. Many kinds of applications for sonographic elastography have been developed.

As classification by technical methods, vibration energy is classified into manual compression, and acoustic compression, and imaging information is classified as strain imaging and shear wave imaging [1].
In this article, we outline the types of sonographic elastography. We discuss the possibility of application of sonographic elastography to the oral and maxillofacial fields, such as salivary glands, cervical lymph nodes, and masseter muscles.

**Principals of sonographic elastography**

Sonographic elastography is that the information of tissue strain or shear wave are imaged, when the vibration energy is given to the target tissue. The vibration energy is classified into manual compression and acoustic compression (Table 1). The former is achieved by vibration caused by manual compression or involuntary movement of arm muscles, or vibration caused by patient muscular contraction or breathing. The latter is achieved by the ultrasound irradiation force from a probe. The imaging information is classified as strain imaging, which is calculated based on strain, and shear wave imaging, which is calculated based on the propagation speed of shear waves [1]. This article will be described separately in the following three groups: i.e., Strain Elastography, Acoustic Radiation Force Impulse (ARFI) Imaging, and Shear Wave Elastography.

**Strain elastography:** Strain elastography depicts the stiffness of soft tissue by measurement of the tissue strain induced by manual compression [2]. The various methods and names have been applied to measure tissue strain for each company or equipment [1-3]. The strain data are converted into color-scale images and superimposed on B-mode images to easily recognize the relationship between the strain and lesion [4]. The hard tissue shows low strain, and is displayed as blue-color in general; the soft tissue shows high strain, and is displayed as red-color [4].

The qualitative evaluation is performed using elasticity score in differentiating benign and malignant masses on strain elastography [1,5]. It is a 5 or 4-point visual scoring system based on the degree and uniformity of the color in the target mass. A higher score indicates a higher diagnostic confidence of malignancy (Figure 1).

As a semi-quantitative method, the diagnostic approach of evaluating stiffness is proposed [1]. Strain ratio is defined as a ratio of the strain in a target mass to that in a reference tissue on mainly Hitachi’s machine [2,6]. Elasticity ratio, which is defined as the ratio of the elasticity indices of two target tissues on GE Healthcare’s machine, is also expressed numerically like the strain ratio [7,8] (Figure 2). The elasticity index is a value expressed from 0 to 1.0 for softer than the average, and from 1.0 to 6.0 for stiffer than the average, assuming that the average strain in the displayed ROI is 1.0.

The applied compression loads on strain elastography are not standardized in free-hand operation, and this may affect the reliability of the elasticity [9]. Accuracy differs between shallow and deep sites due to problems associated with the propagation of vibration energy [1]. The cut-off values of strain ratio were variously reported, and therefore, the unified cut-off value should be recommended through the multicenter prospective study [1].

**Acoustic radiation force impulse imaging:** Acoustic

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*The table is quoted from Reference 1 and simplified.*

**Figure 1** Elasticity scoring system based on Itoh's report. (Reference 5). (A) –Score 1; mass is similar in elasticity to surrounding tissue. (B) –Score 2; mass is predominantly soft similar with the surrounding tissue, with some stiffer area present. (C) –Score 3; mass indicates soft at the periphery, with stiff of the center. (D) –Score 4; mass is entirely stiff. (E) –Score 5; entire mass and the surrounding area are stiff.
Radiation Force Impulse (ARFI) technology requires no external compression and exploits short-duration acoustic radiation forces to small volumes of tissue. When the focused ultrasound beam is transmitted with the probe, the tissue is displaced posteriorly. The tissue displacements are detected and imaged [10]. A stiffer region of tissue exhibits smaller displacements than a softer region, and it is expressed as black [1]. Shear waves are generated when the restorative force of the tissue propagates horizontally [10]. ARFI technology allows not only qualitative visual evaluation, but also quantitative measurement of shear wave velocity in ROI [11]. The stiffer the tissue is, the greater the shear wave velocity will be.

This technique does not need manual compression, and therefore, the reproducibility is good and there is little measurement error between examiners [12,13]. Because the shear wave velocity of malignant lesions is higher than that of benign lesions, ARFI images is useful for differential diagnosis between benign and malignant lesions [11,12,14]. Another advantage is that the internal structure can be visualized well [1,15]. ARFI technique is especially useful in diagnosing the complicated cyst accompanied by bleeding, protein-rich fluid, septum or calcification, because compression is given to each tissue [15]. However, there is still little equipment with this technology, and the choice of probe is limited.

Shear wave elastography: Shear Wave Elastography (SWE) is based on the combination of a radiation force and an ultrafast imaging sequence, which capable of catching the propagation of the resulting shear waves in real time [1,16-18]. The velocity information is converted to a color code, and displayed as a color map by superimposing it on the B-mode image [16,19,20]. The propagation speed of shear waves is fast in hard tissue, and slow in soft tissue [1,18]. The soft lesions are displayed as blue, and the hard lesions are displayed as yellow-red [1,17]. The speed of propagation of the shear wave is proportional to the square root of the tissue’s elastic modulus [1,17]. Therefore, SWE allows expression of the shear wave velocity in m/s and estimation of Young’s modulus in kPa [1,16,20,21].

SWE is a highly reproducible technique without relying on the skill of the operator [1,16,19,20]. SWE is excellent in the quantitative diagnosis of tissue elasticity. The optimal cut-off value for distinguishing benign and malignant lesions is advocated, and high diagnostic accuracy has been reported [22,23]. Intraductal cystic change or calcification did not influence SWE indices [17,21,24]. Only size is significantly correlated with SWE indices. For nodule with a larger diameter, adequate compression of the whole nodule may not be obtained [17,24]. As this new technology is commercialized only fairly recently, there is a global paucity of evidence in the form of journal articles, and diagnostic criteria have not been established [1].

Clinical applications of sonographic elastography to the oral and maxillofacial region

Salivary glands: Sonography is the first-choice imaging in evaluation of salivary neoplasms. Several studies have reported features of the salivary tumors using sonographic elastography [25-31] (Figure 3). Klintworth et al. qualitatively evaluated strain pattern distribution on strain elastography for parotid tumors, and documented that a pattern of heterogeneous reticular distribution was more frequent in malignant tumors than in benign tumors [29]. The stiffness of the malignant tumors was higher than that of the benign neoplasms [27,31], and that of pleomorphic adenoma was higher than that of Warthin tumors [26]. However, the discriminatory performances for detection of malignancy are poor, because there is appreciable overlap between stiffness of pleomorphic adenomas and malignant neoplasms [27,31].

Mansour et al. evaluated performances of ARFI in comparison with strain elastography [30]. ARFI presented different mean
values between pleomorphic adenomas and Warthin tumors, whereas strain elastography did not visualize any significant difference between the two entities. Bhatia et al. evaluated focal salivary lesions using SWE. They documented overlap in elastic moduli between benign and malignant neoplasms, so that there was no clinically useful cut-off [25].

In general, the preliminary data suggest that sonographic elastography is suboptimal for detection of malignancy in the salivary glands. In the future, we should consider whether sonographic elastography can be useful for evaluation the pathological status of the salivary lesions, such as sialolithiasis, sialoadenitis, and Sjögren’s syndrome.

Cervical lymph nodes

The status of the cervical lymph nodes should be clarified for selecting the therapeutic methods, and determining the prognosis. A combination of grayscale and power Doppler sonography is sensitive imaging for the detection of lymph nodes, and most extensively used for classification of lymph nodes. However it has limitation in accuracy. Several studies have evaluated the stiffness of the lymph nodes using sonographic elastography for the diagnosis of malignancy [9,32-35].

The stiffness of the lymph nodes were qualitatively assessed by 4 or 5-point score on strain elastography, and the cut-off value were advocated between 2 and 3 [33] (Figure 1). The node with the higher score was diagnosed as malignancy, because the malignant nodes generally show higher stiffness than benign nodes (Figure 4). Alam et al. have modified the scoring system, and adopted the specific pattern classification, including the pattern of central softer area with peripheral stiffer area to account for the possibility of central necrosis in metastatic nodes [32]. The modified classification showed high accuracy of 84% for diagnosing metastatic lymph nodes.

The strain ratio of the lymph nodes have been examined, using either the sternodeidomastoid muscle or the surrounding loose connective tissue, as reference tissue [9,34,36]. Lyshchik et al. calculated the strain ratios of lymph nodes against muscles, and documented that a high accuracy of 92% in diagnosing malignancy was achieved at a cut-off value of strain ratio over 1.5 [9]. Ying et al. analyzed the performance of strain elastography on diagnosis of the malignant lymph nodes, based on meta-analysis of a total of 9 studies including 835 lymph nodes [37]. The qualitative evaluation using elasticity score showed sensitivity of 0.74 and specificity of 0.90. The semi-quantitative evaluation using strain ratio showed 0.88 and 0.81, respectively.

The lymph nodes partially infiltrated by tumors can be hardly diagnosed using scoring systems and strain ratios. Quantitative sonographic elastography may overcome this limitation by permitting analysis of specific regions within lymph nodes [36]. Bhatia et al. performed the pilot study of evaluation of lymph nodes using SWE [38]. However, accuracy for malignancy was not sufficient at the cut-off of 30.2 kPa [38]. Further improvement is required.

Overall, the preliminary evidence suggests that sonographic elastography may be useful to differentiate benign and malignant cervical lymph nodes. The status of the malignant lymph nodes would be different according to the histopathological types. Therefore, further sufficiently large and detailed research should be required to enable stratification.

Masseter muscles: Hardness or stiffness of skeletal muscles is widely used as an index for diagnosing patients with myalgia in the fields of orthopedics or sports medicine. The pathogenesis of myofascial pain is not well understood. Of them, muscle edema may be involved in provoking muscles pain or fatigue [39-43]. Sustained contraction may produce a high intramuscular pressure and significantly impede local muscle blood flow [44]. Blood vessel compression may cause local hypoperfusion hypoxia, which is related to the release of well-known pain mediators, such as serotonin, norepinephrine, and bradykinin [44-46]. Concerning the masseter muscle which is covered with a thick fascia, an increase in intramuscular pressure accompanied by an increase in the water content may increase muscle hardness [47].

Sonographic elastography appears to be feasible as an additional imaging tool for evaluating the muscles hardness in the maxillofacial region [7]. We performed experiment of static contraction of the masseter muscle in order to observe the status of muscle edema on strain elastography [48]. We examined the elasticity ratio of the masseter muscle against the subcutaneous tissue and the distribution of soft and hard area to the whole area of the muscle, and clarified that the elasticity ratio and
Figure 4 Strain elastography of the cervical lymph nodes. (A) –Metastatic lymph node indicates uniformly stiff mass. (B) –Reactive lymph node indicates largely softer with the inconstant appearance of stiffer areas.

Figure 5 Strain sonography before and immediately after exercise in 28-year-old man. (A)–Before exercise. (B)–Immediately after exercise. (C)–The range of the red color was specified, and the number of pixels of the red-colored area was calculated automatically. The soft area ratio was obtained as the ratio of the red-colored area against the whole area of the masseter muscle. (D) –Hard area ratio was calculated similarly. After exercise, Elasticity ratio, soft area ratio, and hard area ratio increased.
the ratios of soft and hard areas increased immediately after exercise (Figure 5). An increase in the soft area would raise the intramuscular pressure and, consequently, increase hardness around the edematous area, leading to enhancement of the total muscle stiffness [48]. We also examined the masseter muscle in Temporomandibular Disorder (TMD) patients using strain sonography, and clarified that the elasticity ratio of masseter muscle of the symptomatic side in TMD patients was larger than that of the healthy volunteers, and that a significant difference was seen between the elasticity ratios of the symptomatic and asymptomatic sides in patients [7] (Figure 6, 7).

Information as to the muscle stiffness can be one of the key features for determining the regimen for treatment or presuming the state of progress of treatment [49]. We have performed a clinical trial of massage treatment of the masseter and temporal muscles for TMD patients using an oral rehabilitation robot, and observed the state of the masseter muscle on sonographic elastography before and after massage treatment [50]. The masseter muscle stiffness was related to the most comfortable massage pressure, and therefore, it can be one index for determining the massage pressure [49]. The stiffness of affected muscles is reduced after massage treatment together with improvement of sonographic indices of edematous change [7,51] (Figure 8).

Myofascial trigger points are discrete hypersensitive hard palpable nodules located within taut bands of skeletal muscle [52]. In recent reports, myofascial trigger points can be visualized as the hard masses on sonographic elastography of the upper trapezius muscles in patients with acute spontaneous cervical pain [45,53].

Overall, sonographic elastography has a possibility for exploring the causes of muscle pain, understanding the state of the muscle, selecting therapeutic methods, and evaluating therapeutic effect.

DISCUSSION AND CONCLUSION

Sonographic elastography is a recent technique, which can present the information of stiffness. The vibration energy is classified into manual compression and acoustic compression, and the imaging information is classified as strain imaging and shear wave imaging. Strain elastography depicts the stiffness of soft tissue by measurement of the tissue strain induced by manual compression. The qualitative evaluation is performed using visual scoring system, and the semi-quantitative evaluation is done using strain ratio or elasticity ratio.

Acoustic Radiation Force Impulse (ARFI) technology exploits short-duration acoustic radiation forces. The resulting tissue displacements are detected and imaged. ARFI technology allows not only qualitative visual evaluation, but also quantitative measurement of shear wave velocity in ROI. Shear Wave Elastography (SWE) is based on the combination of a radiation force and an ultrafast imaging sequence. The velocity information is converted to a color code. SWE allows expression of the shear wave velocity in m/s and estimation of Young’s modulus in kPa.

The possibilities of application of sonographic elastography to oral and maxillofacial regions were discussed. The discriminatory performances of strain elastography for detection of malignancy of the salivary glands were insufficient, because...

Figure 6 Strain elastography of the masseter muscle in patient and healthy volunteer. (A)– Strain elastography of the symptomatic masseter muscle in 51-year-old man with myofascial pain. Elasticity ratio was 1.44. (B)– Strain elastography of the right masseter muscle in 53-year-old man without symptom. Elasticity ratio was 0.85.
there is appreciable overlap between stiffness of pleomorphic adenomas and malignant neoplasms. Pilot studies of ARFI and SWE indicated similar results. Therefore, sonographic elastography is still suboptimal for detection of malignancy in the salivary glands.

The performance of strain elastography on diagnosis of the malignant lymph nodes based on meta-analysis showed high sensitivity and specificity using the qualitative scoring system and the semi-quantitative strain ratio. As to SWE, further improvement is required. The preliminary evidence suggests
that sonographic elastography may be useful to differentiate benign and malignant cervical lymph nodes.

Application of ultrasound elastography to the masseter is a challenging work. Through experiment of contraction of the masseter muscle, an increase in the soft area would raise the intramuscular pressure and, consequently, increase hardness around the edematous area, leading to enhancement of the total muscle stiffness. The elasticity ratio of masseter muscle of the symptomatic side in TMD patients was larger, and it is reduced after massage treatment. The masseter muscle stiffness can be one index for determining the massage pressure. Overall, Sonographic elastography has a possibility for exploring the causes of muscle pain, understanding the state of the muscle, selecting therapeutic methods, and evaluating therapeutic effect.

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