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SHORT COMMUNICATION

Development of a standardized evaluation of endobuccal adverse events induced by repeated tongue protrusion with both a dedicated questionnaire and an endobuccal examination

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Abstract

Introduction A new approach to treat obstructive sleep apnea (OSA) is upper airway stimulation therapy (UAS). Electrical pulses applied to the hypoglossal nerve induce tongue protrusion, increase airway patency and decrease the frequency of apneic and hypopneic events. Thus, the main objective of this study was to design a standardized evaluation of endobuccal adverse events induced by repeated tongue protrusion with both a dedicated questionnaire and an endobuccal examination.

Method This study has designed the Tongue Adverse Event and Satisfaction Questionnaire (TAESQ) and an endobuccal examinations divided into an endobuccal lesion examination (ELE) and an endobuccal risk factor examination (ERFE). Evaluations were conducted at month 6 post-implantation.

Results The study population after implantation of UAS device consisted of ten Caucasian males with a mean age of 51.9 ± 11.8 years, and a mean BMI of 28.6 ± 3.3. The AHI of the ten participants ranged from 46.7 ± 12.2/h at baseline to 14.5 ± 8.9/h with the Inspire therapy at the 6-month follow-up. The TAESQ revealed pain (30%), followed by less tongue sensitivity (20%) and tongue weakness (10%). The ELE did not reveal any lesions. The ERFE revealed that some participants had tissue and dental risk factors but not associated to more adverse events.

Conclusion The TAESQ, ELE and ERFE have been designed and studied on a small number of participants. These evaluations could systematically be included in the care pathway of patients treated by UAS to better investigate tongue discomfort and tongue lesion for patients treated with this technology.

Keywords Sleep medicine · Obstructive sleep apnea · Upper airway stimulation (UAS) · Oral cavity · Quality of life · Tongue adverse event · Satisfaction Questionnaire

Abbreviations

UAS	Upper airway stimulation
BMI	Body Mass Index
AHI	Apnea Hypopnea Index

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OSA	Obstructive sleep apnea
CPAP	Continuous positive airway pressure
IPG	Implantable pulse generator
HGN	Hypoglossal nerve
STAR	Stimulation treatment for apnea reduction
TAESQ	Tongue Adverse Event and Satisfaction Questionnaire
CSQ8	Client Satisfaction Questionnaire 8
DISE	Drug-induced sleep endoscopy

Introduction

Obstructive sleep apnea (OSA) is characterized by repeated episodes of airway collapse (apnea) or narrowing (hypopnea) during sleep. Current OSA treatments include both non-surgical methods such as weight loss, continuous positive airway pressure (CPAP) and mandibular advancement devices, and surgical methods such as upper airway soft tissue and skeletal surgery. CPAP is the first-line treatment for mild–severe OSA [1]. However, a substantial proportion of patients are unable or unwilling to adhere to it [2]. Alternative non-surgical and surgical treatments are less effective than CPAP and have several adverse events [3, 4]. A new approach is to stimulate the hypoglossal nerve electrically. Among the various techniques [5], selective upper-airway stimulation (UAS) therapy is the most promising. Selective electrical stimulation of the hypoglossal nerve fibers governs the genioglossus muscle, the largest tongue protrusor [6]. Electrical pulses applied to the hypoglossal nerve induce tongue protrusion, increase airway patency and decrease the frequency of apneic and hypopneic events [7, 8]. Recently, a 5-year follow-up confirmed the effectiveness of UAS therapy [9].

Follow-up has found that serious adverse events are rare and include device explantation [6], device repositioning and fixation [8, 10], pain at the neck incision and post-implantation infection [10]. Minor adverse events are more frequent, especially tongue discomfort associated with stimulation and tongue lesion after activation of the UAS [6, 8, 10–16]. These minor endobuccal adverse events could reduce UAS adherence and effectiveness by inducing difficulties to fall asleep with therapy or disrupting sleep [23]. Despite UAS therapy expands and is used for the routine clinical management of OSA in the USA and in several European countries, there is a lack of studies evaluating systematically minor endobuccal adverse events and their impacts on the UAS therapy follow-up. To conduct such studies, we first need recommendations and tools for the standardized evaluation of patients implanted with UAS therapy for the treatment of OSA [17, 18]. Thus, the main objective of this study was to design a standardized evaluation of both patient-reported and examination-based measures of minor endobuccal adverse events induced by repeated tongue protrusion (tongue discomfort and lesion). The secondary objective was to investigate some preliminary elements of psychometric validation of the proposed self-reported questionnaire by exploring the relationship between patient-reported tongue adverse events and: (1) self-reported overall satisfaction, (2) the endobuccal examinations, in the Bordeaux cohort of patients implanted with UAS therapy [23].

Methods

Patient selection

Selection was based on the STAR trial criteria [8]. Adults with moderate-to-severe OSA (AHI > 25/h and < 65/h, central apnea index < 25%), who had failed on or did not tolerate CPAP therapy as defined by a monthly usage < 3 h/night and an Epworth Sleepiness Score (ESS) > 10 were eligible for enrollment in the UAS program. Screening included clinical evaluation, a polysomnography (PSG) and a drug-induced sleep endoscopy (DISE). Patients had to have a BMI < 35 kg/m^2, and demonstrate a lack of complete concentric or lateral collapse at the level of the velopharynx during DISE and clinical examination. The study was conducted in accordance with the Declaration of Helsinki and French Good Clinical Practices. Standard informed consent process was given to all patients and written informed consent was obtained.

Participants included underwent surgical implantation of the Inspire system (Minneapolis, MN) UAS device. The entire operative technique was the same as previously described [6, 7], and no complications (e.g. infection or device displacement) were reported. The device was activated approximately 1 month after implantation to detect sensation and functional thresholds during an out-patient visit. After 1 month of nocturnal acclimatization, the UAS therapy was further titrated during inpatient polysomnography at month 2 post-implantation. During the titration night, the amplitude was adjusted to minimize the occurrence of obstructive events and had to not exceed the arousal threshold. The titration procedure was the same as previously described [6, 7]. At month 6 post-implantation, a polysomnography was conducted to ensure that stimulation remained efficient. Questionnaires were administered and endobuccal examinations were performed on the same day as the polysomnography.

Tongue Adverse Event and Satisfaction Questionnaire (TAESQ)

Patient reported of minor endobuccal adverse events were measured through a dedicated self-rated questionnaire. The TAESQ was specifically designed for this study. It is a short

7-item auto-questionnaire scored on a four-point Likert scale ranging from "strongly disagree" (score = 0), "somewhat agree" (score = 1), "agree" (score = 2) to "strongly agree" (score = 3) and takes less than 3 min to complete. The rating was determined according to the patients' experience in the preceding weeks. The total score was the sum of the scores for each item. The total score ranges from 0 to 21. The questionnaire contains three dimensions (Table 1).

1. Overall self-reported satisfaction with UAS therapy (question n°1);
2. Information perceived regarding any related endobuccal adverse events during the standard informed consent process (questions 2–3);
3. Functional and painful endobuccal adverse events related to the UAS therapy (questions 4–7).

Client satisfaction questionnaire (CSQ-8)

The CSQ-8 is an self-reported questionnaire to assess overall patient satisfaction [19, 20]. It was found that the CSQ-8 is correlated with treatment dropout, number of therapy sessions attended, and with changes in client-reported symptoms. The CSQ-8 consists of 8 items rated on a balanced four-point Likert scale ranging from 1 to 4 and takes less than three minutes to complete. The total score ranges from 8 to 32.

Endobuccal examinations

Endobuccal clinical examination was a concise and standardized soft, periodontal and dental tissue examination conducted by a dental surgeon. It was divided into: (1) an endobuccal soft tissue examination based on the search for oral lesions, hereafter called the endobuccal lesion examination (ELE), (2) an examination to detect endobuccal risk factors of erosion, hereafter called the endobuccal risk factor examination (ERFE).

Table 1 Tongue adverse event and satisfaction questionnaire (TAESQ)

Please tick the appropriate box:

0: strongly disagree

1: somewhat agree

2: agree

3: strongly agree

Satisfaction regarding the stimulation therapy	0	1	2	3
1- You are satisfied with the stimulation therapy	□	□	□	□
Information regarding the stimulation therapy	0	1	2	3
2- You received information about the operation and the purpose of the therapy	□	□	□	□
3- You have been informed about the potential tongue side effects that can be induced by the therapy (discomfort, lesion)	□	□	□	□
Tongue discomforts related to stimulation therapy	0	1	2	3
4- You have the feeling of having less strength in the tongue	□	□	□	□
5- You have the feeling of having less tongue sensitivity	□	□	□	□
6- You have pain on the undersurface of your tongue	□	□	□	□
7- You have pain on the boarder of your tongue	□	□	□	□

Endobuccal lesion examination

Therapy-related endobuccal lesion mainly concerned the soft tissues. The soft tissue inspection was performed according to the three-circle examination, from the outside to the inside oral cavity (Fig. 1) [21]. At the end of this examination, the dental surgeon reported the different degrees of endobuccal lesion using the dedicated schemas in Table 2.

Endobuccal risk factor examination

This examination concerned the endobuccal soft tissues, periodontal and dental tissues, as well as restorative (dental fillings) and prosthetic repair. Soft tissues inspection evaluated the presence of macroglossia (protrusion beyond the teeth during resting posture and impression of a tooth on the lingual border) and/or short lingual frenulum (limitation of tongue protrusion beyond the lower incisor teeth). Periodontal and dental tissues inspection evaluated the presence of edentulous, examination evaluated the mandibular teeth to establish if they were fractured and/or mobile [22] (Fig. 2a, b). Finally, the same method was used to assess prosthetic repairs (filling, crowns and removable denture). The dental surgeon reported his findings on the dedicated schemas in Table 3.

Statistical analysis

Descriptive statistics included frequencies and percentages of categorical variables together with means and standard deviations of continuous variables. The Spearman correlation was used to evaluate the relationship between the TAESQ and the CSQ-8 scores. The Mann–Whitney test was used to compare TAESQ scores according to the presence or absence of endobuccal lesions or endobuccal risk factors. For all the tests, the accepted significance level was 5%. Data analysis was performed using SPSS software (Version 18 for Mac, PASW Statistics).

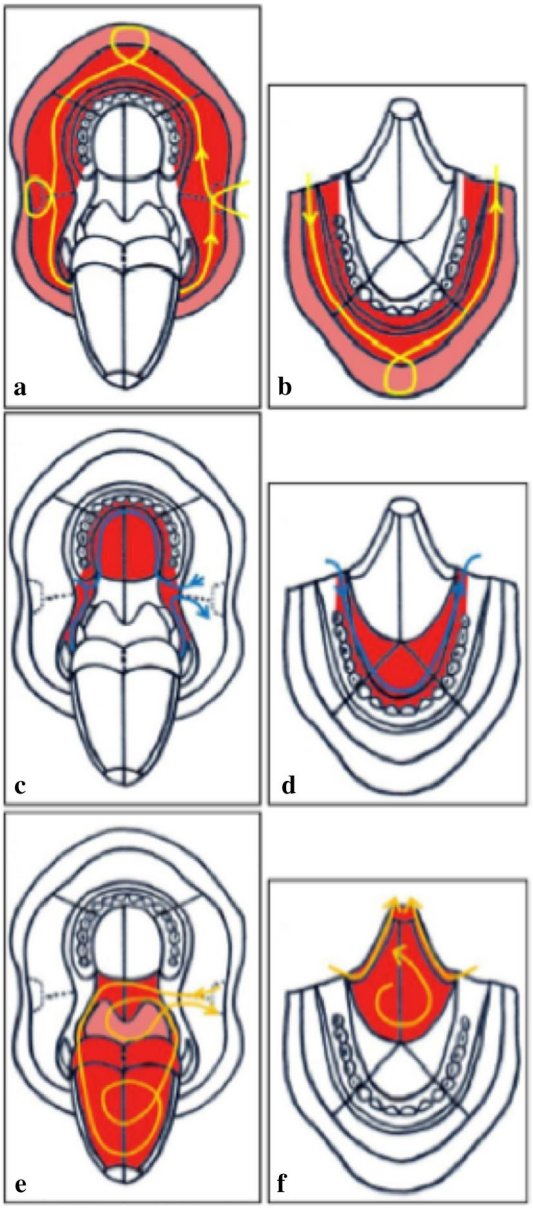


Fig. 1 The three-circles examination for soft tissue inspection, from the outer to the inner oral cavity. **a, b** First circle outside of teeth: examination of one of the two labial corners up to the opposite corner, including examination of gingivojugal folds, mucous aspects and vermilion edges of the lower and upper lips, and vestibular faces of the jaw and mandible. **c, d** Second circle inside of teeth, and examination of the hard palate, the retromolar trigone, the floor of the mouth, the lingual face of the gum up to the contralateral tuberosity. **e, f** Third circle to examine tongue and aero-digestive junction

Results

Characteristics of implanted participants

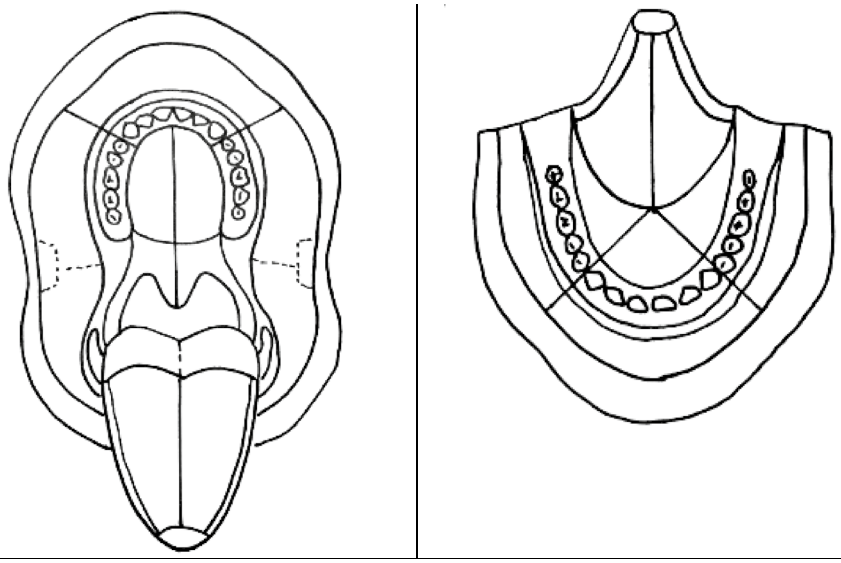
The study population after implantation consisted of ten Caucasian males with a mean age of 51.9 ± 11.8 years, and a mean BMI of 28.6 ± 3.3. The AHI of the ten participants ranged from 46.7 ± 12.2/h at baseline to 14.5 ± 8.9/h with the Inspire therapy at the 6-month follow-up. The ESS ranged from 15.9 ± 3.5 to 10.9 ± 6.1. The population was the same as that previously published [23].

TAESQ

Results are shown Table 4.

Table 2 Schemas for intraoral lesion examination (ILE)

Type of lesions observed during examination are reported on schemas with appropriate symbol:
□ *Ulceration*
○ *Erosion*
× *Keratosis*
△ *Erythema*



Endobuccal clinical examination

The endobuccal examination did not detect any endobuccal lesions. Regarding endobuccal risk factors: (1) two patients presented macroglossia and two had a short lingual frenulum (Fig. 3a, b), (2) one patient was posteriorly edentulous, one had tooth mobility and four had fractured teeth (Fig. 3c), and (3) none of the participants presented restorative and/or prosthetic risks factor.

Client Satisfaction Questionnaire CSQ-8

Scores on this questionnaire varied between 21 and 32 (mean 27.5 ± 3.4).

Relationship between the TAESQ and CSQ-8

TAESQ total scores and CSQ-8 scores was not correlated (rho = 0.58, $p = 0.078$).

Relationship between endobuccal clinical examination and TAESQ

The TAESQ total score ($Z = -1.4$, $p = 0.22$) was not different between patients with endobuccal risk factors and those without.

Discussion

The main objective of this study was to design a standardized evaluation of minor endobuccal adverse events induced by repeated tongue protrusion (tongue discomfort and lesion) with a dedicated self-reported questionnaire and an endobuccal examination. The secondary objective was to propose a preliminary psychometric validation of the proposed self-reported questionnaire by investigating the relationship between patient-reported endobuccal adverse events and: (1) overall satisfaction, (2) the result of standardized

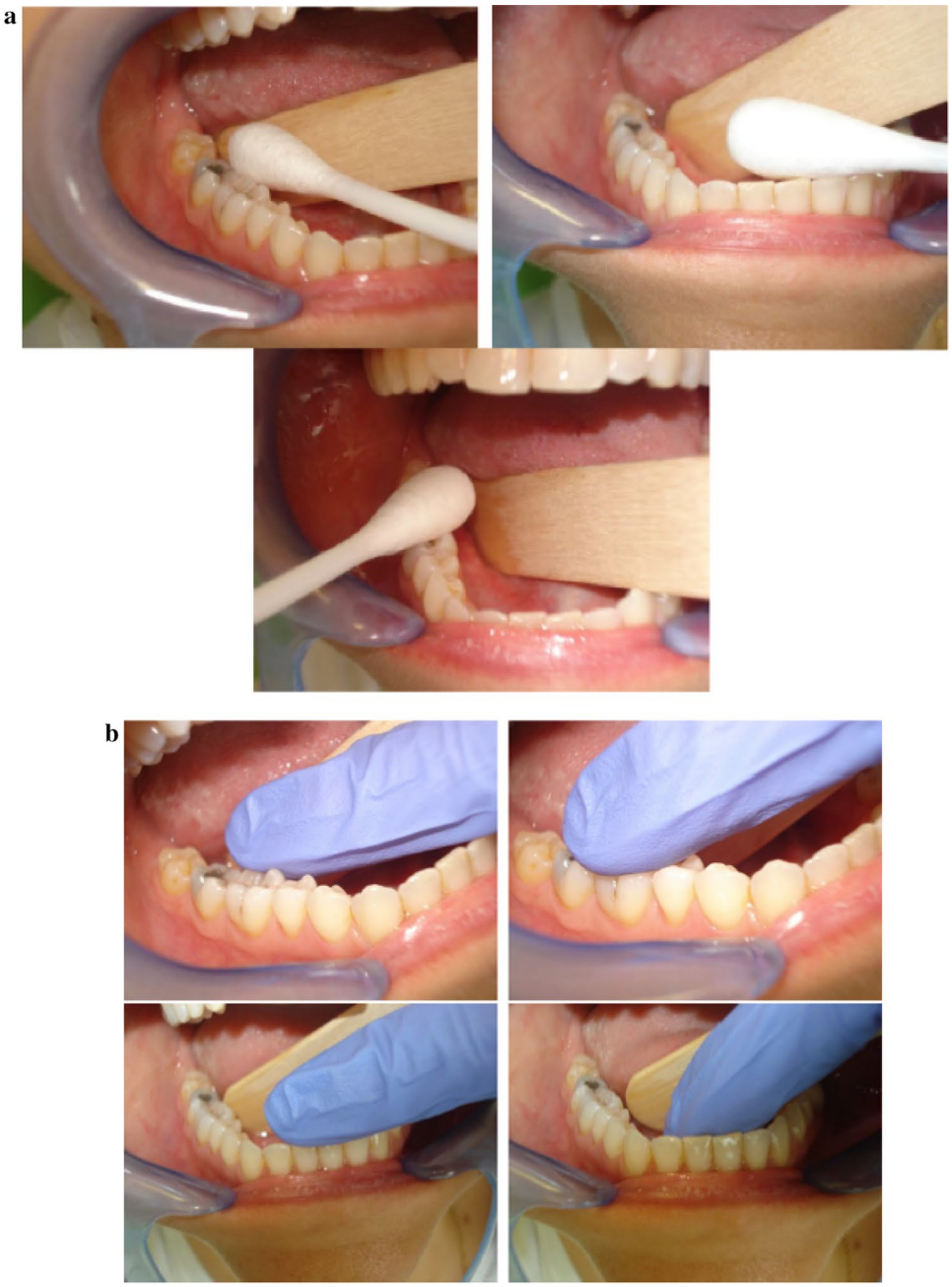


Fig. 2 Evaluation of dental surfaces using distemper (**a**) and finger (**b**) for hard tissue inspection in search of dental/prosthetic risk factors

endobuccal examinations in ten patients implanted with UAS evaluated 6 months post-implantation.

The self-reported questionnaire designed in this study to investigate tongue discomfort and lesion induced by UAS has been called the Tongue Adverse Event and Satisfaction Questionnaire (TAESQ). Most complaints revealed by the TAESQ concerned pain (30%), followed by less tongue sensitivity (20%) and tongue weakness (10%). This is in agreement with previous studies. In the studies by Strollo et al. [8] and Kerizian et al. [15], 21% and 55% of patients reported pain, respectively. Woodson et al. [9] and Strollo et al.[8] reported that around 18% of their patients experienced tongue weakness. Importantly, the scores on the satisfaction item in the TAESQ (Item 1) show that participants were globally satisfied. Nevertheless, patients receiving UAS therapy should be made more aware of the potential endobuccal adverse events that it can cause. Concerning the psychometric validation of the TAESQ, this preliminary study did not find any relationship between self-reported tongue adverse events (TAESQ scores) and overall satisfaction (CSQ-8 scores).

The endobuccal examination designed in this study to investigate tongue discomfort and lesion induced by UAS, was divided into: (1) the endobuccal lesion examination

Table 3 Schemas for intraoral risks factors examination (IRFE)

Check to indicate ABSENCE or PRESENCE for each item and add details if necessary			
		ABSENCE	PRESENCE
Soft tissues risks factors	Macroglossia	☐	☐
	Short lingual frenulum	☐	☐
Periodontal and dental risk factors	Edentulous	☐	☐ No. of tooth/teeth concerned
	Fractured tooth/teeth	☐	☐ No. of tooth/teeth concerned
	Tooth/teeth mobility	☐	☐ No. of tooth/teeth concerned
Restorative and prosthetic risk factors	Fractured filling(s)	☐	☐ No. of tooth/teeth concerned
	Fractured crown(s)	☐	☐ No. of tooth/teeth concerned
	Fractured removable denture	☐	☐ No. of tooth/teeth concerned

Table 4 Response to Tongue Side Effect and Satisfaction Questionnaire (TSESQ) in ten patients implanted with Inspire therapy, evaluated 6 months post-implantation

TSESQ items	Mean ± SD	% Response/item			
		Score = 3 (%)	Score = 2 (%)	Score = 1 (%)	Score = 0 (%)
Item 1	1.8 ± 1.2	40	20	20	20
Item 2	2.8 ± 0.4	80	20	0	0
Item 3	1.9 ± 1.1	40	20	30	10
Item 4	0.2 ± 0.6	0	10	0	90
Item 5	0.2 ± 0.4	0	0	20	80
Item 6	0.5 ± 0.8	0	20	10	70
Item 7	0.7 ± 1.0	10	10	20	60

SD standard deviation

(ELE), (2) the endobuccal risk factor examination (ERFE). The ELE did not reveal any lesions. The ERFE revealed endobuccal risk factor in most of the patients. However, we did not find any relationship with the TAESQ score.

The principal limitation of this study is the small number of patients ($n = 10$), that (1) reduce the possibility of complete investigation of psychometric evaluations of the reliability and validity properties of the TAESQ, and (2) reduce the possibility to investigate the relationship between specific endobuccal risk factor and endobuccal adverse events. Further studies are needed to evaluate construct, internal structural and external validity of the questionnaire in a larger population. The second limitation is the absence of a control group and a short follow-up period of only 6 months of active treatment. Further evaluation in a well-controlled trial with long-term assessment using the same procedures is essential. Third, impact of electrode configuration or stimulation amplitude on self-reported endobuccal adverse event or examination findings has not been studied and should be investigated in further studies.

Nevertheless, given the high prevalence of minor endobuccal adverse events induced by repeated tongue protrusion described in the literature, our preliminary study highlights the need of further studies that carefully and systematically investigate these adverse events to better understand the impact on adherence and effectiveness of UAS therapy. Such studies should use standardized and validated tools. The development of a standardized evaluation of endobuccal adverse events induced by repeated tongue protrusion with both a dedicated questionnaire and an endobuccal examination proposed in this article can be considered as a first step in this way. Given the worldwide implantation of UAS, the multi-language availability of these tools should also be encouraged to conduct multicentral study using the same parameters.

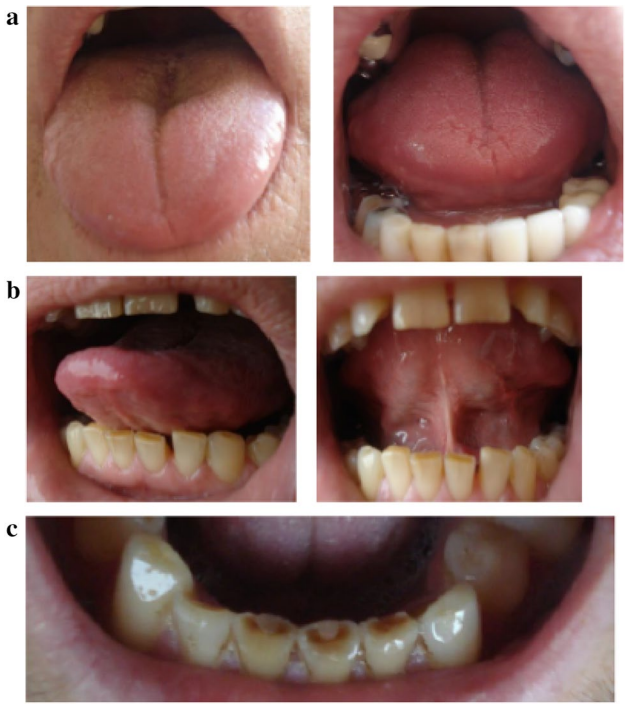


Fig. 3 Patients with macroglossia (**a**), short lingual frenulum (**b**) and fractured free edge mandibular incisors (**c**)

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants and/or animals All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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