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Measuring tongue volumes and visualizing the chewing and swallowing process using real-time TrueFISP imaging—initial clinical experience in healthy volunteers and patients with acromegaly

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Abstract This study assessed both two-dimensional (2D) TrueFISP imaging for quantifying tongue volume and real-time TrueFISP imaging for evaluating chewing and swallowing in healthy volunteers and patients with acromegaly. In 50 healthy volunteers, tongue volumes were measured using a 2D TrueFISP sequence. Chewing and swallowing were visualized using a real-time TrueFISP sequence. Ten patients with acromegaly were examined twice with the same magnetic resonance imaging protocol: once prior to therapy and a second time 6 months after therapy. Prior to therapy, healthy volunteers had an average tongue volume of 140 ml for men and 90 ml for women, and patients with acromegaly had an average tongue volume of 180 ml for men and 145 ml for women. However, 6 months after therapy the mean tongue volumes in patients with acromegaly had decreased to 154 ml in the men and to 125 ml in the women. The chewing and swallowing process was normal in all volunteers. Prior to therapy, just two patients showed a chewing and swallowing pathology, which disappeared after therapy. Patients with acromegaly had larger tongue volumes than healthy volunteers, and TrueFISP imaging proved feasible for visualizing chewing and swallowing in real time and is capable of detecting possible pathologies. Furthermore, TrueFISP imaging can be used to monitor therapeutic approaches in patients with acromegaly.

Keywords Tongue volume · Chewing · Swallowing · Acromegaly · TrueFISP

Introduction

Micro- and macroadenoma of the pituitary gland with hypersecretion of growth hormone (GH) and insulin-like growth factors 1 (IGF-1) lead to acromegaly because of swelling of soft tissues and stimulation of cartilage growth [1, 2]. Compared with healthy volunteers, patients with untreated acromegaly have a significantly higher incidence of cardiovascular disease [3, 4]; malignancies, including colorectal carcinoma; and sleep apnea syndrome, with increased mortality rates [5, 6]. In addition, patients with acromegaly are usually characterized by facial changes (longer nose, thicker lips) and oral cavity abnormalities such as macroglossy, causing chewing and swallowing disorders.

Several diseases are associated with chewing and swallowing problems. They can occur primarily by structural aberrations—for instance, due to oropharyngeal tumors—or secondarily due to functional disorders that can be caused by different neurologic, metabolic, or myopathic diseases, including acromegaly [7–11]. Many studies have documented oropharyngeal airway complications in patients with acromegaly, such as sleep apnea syndrome [10–12]. However, the diagnosis of chewing and swallowing problems is generally based on functional and real-time rendering of the chewing and swallowing process. The examination of chewing and swallowing calls for an imaging modality with high temporal resolution and adequate soft-tissue visualization. Magnetic resonance (MR)-based approaches have been promising in this regard [13], indicating that real-time MR techniques are able to monitor the chewing and swallowing process [14, 15].

The aim of this study was to assess both a 2D TrueFISP sequence for quantifying tongue volumes and high-resolution real-time TrueFISP imaging for evaluating the chewing and swallowing act in patients with acromegaly compared with healthy volunteers, and to determine whether the outlined protocol is suitable for follow-up studies in patients with acromegaly.

Materials and methods

Subjects

Within a 4-month period, 50 healthy volunteers (25 men, 25 women, mean age 43.6 years) with no history of acromegaly, as well as 10 patients (four men, six women, mean age 58 years) with proven acromegaly (IGF-1 583±48 μg/l; GH 13.5±7.0 μg/l) were enrolled in the study. The mean body mass index (BMI) in all male and female volunteers was normal (male 22, female 19.3, range 19–23.5). The 10 patients with acromegaly were obese (BMI male 26.3, BMI female 25.9, range 25.7–26.8).

The study was performed according to good clinical practice rules and was approved by the local ethical committee. Written informed consent was obtained from all volunteers and patients, who were not charged for the examination. Vital signs and adverse reactions were monitored for up to 24 h following the MR examination.

MR imaging

All imaging was performed on a 1.5 T MR system (Magnetom Sonata, Siemens Medical Systems, Erlangen, Germany) equipped with a high-performance gradient system characterized by an amplitude of 40 mT/m and a slew rate of 200 mT/m/ms. A head/neck phased-array surface coil was used for signal reception.

In the 50 healthy volunteers, tongue volumes were measured by employing a 2D TrueFISP sequence in a sagittal slice orientation without a distance factor (TR/TE/flip 190/4.8/70°, matrix 205×256, slice thickness 4 mm, slice number 20, acquisition time of all slices 76 s). To avoid motion artifacts, the volunteers were asked to not move their tongues during the exams.

The healthy volunteers also underwent a chewing and swallowing MR examination using a high-resolution real-time TrueFISP sequence (TR/TE/flip 3.79/1.9/87°, matrix 208×256, acquisition time 20 s, acquisition time per image 0.5 s) with an oral contrast bolus. For oral contrast administration, 0.5 ml gadopentetate dimeglumine (Magnevist, Schering, Berlin, Germany) was mixed with 100 ml of commercially available vanilla pudding (Ravensberger, Humana Milchunion, Everswinkel, Germany, concentration 1:200). After that, a small piece of banana was mixed into this solution to increase the volume and viscosity of the contrast solution.

Before the examination, all volunteers and patients with acromegaly were asked to test-chew and swallow a small bolus in supine position outside of the magnet. None of the volunteers or patients with acromegaly showed signs of aspiration. For the examinations, a plastic spoon was used to administer the contrast agent bolus while the subjects were in supine position with their heads placed in the head coil.

The 10 patients with proven acromegaly were examined with both MR protocols twice: once prior to therapy and a second time 6 months after therapy with sandostatin analogues (Sandostatin LAR 10–30 mg intramuscularly every 4 weeks) and/or transsphenoidal resection of the hypophysis.

Image evaluation

All images were transferred to a workstation (Virtuosos, Siemens Medical Systems, Erlangen, Germany) and reviewed by a board-certified radiologist. The chewing and swallowing act was assessed with regard to possible anatomical variants and pathologies. Furthermore, tongue volumes of all volunteers and all patients were measured by manually marking the anatomical borders of the tongue on each of the sagittal 2D TrueFISP slices (up to 20 slices) and calculating the respective areas (in milliliters) (Fig. 1a, b). The total volume was then determined by adding all single areas and multiplying the sum by 0.4, as the employed slice thickness was 4 mm.

Signal-to-noise ratio

For quantitative analysis, regions of interest (ROI) were placed in the middle of the tongue. Image noise, defined as the standard deviation of signal intensities measured in an ROI placed outside the body, was determined. Based on these measurements, signal-to-noise

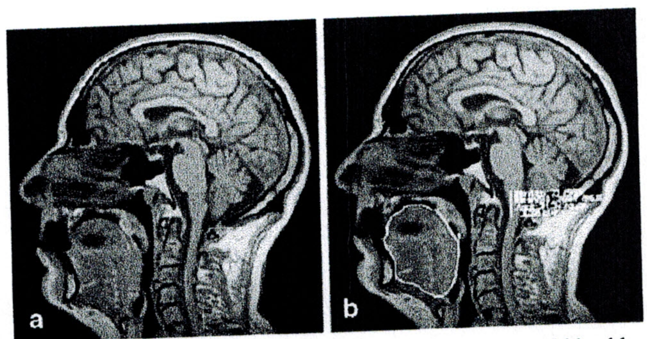

Fig. 1 a–b TrueFISP image, sagittal plane, in a 43-year-old healthy male volunteer (**a**). The sagittal plane is manually marked for tongue volume measurement (**b**). The tongue volume on this slice amounts to 21 ml; however, the tongue volume on all sagittal planes amounted to 101 ml.

Table 1 Demographic and tongue volume data of the 50 volunteers

	Sample	Age (years)	Min (ml)	Max (ml)	Mean (ml)	Weight (kg)	Size (cm)	Body mass index
Men	25	29–64 (mean 45)	94	140	117	72–120 (mean 88)	169–195 (mean 180)	22
Women	25	33–56 (mean 43)	67	90	77	50–70 (mean 59)	165–178 (mean 168)	19.3

Table 2 Demographic and tongue volume data of the 10 patients with acromegaly

	Sample	Age (years)	Min (ml)	Max (ml)	Mean (ml)	Weight (kg)	Size (cm)	Body mass index
Men	4	59–63 (mean 60)	164	204	180	75–110 (mean 83)	162–176 (mean 171)	26.3
Women	6	37–66 (mean 56)	101	175	145	55–75 (mean 64)	mean (165)	25.9

ratios (SNR) for representative parts were calculated as follows: $\mathrm{SNR} = ((\mathrm{SI}\,(\mathrm{tongue})/\mathrm{IS}\,(\mathrm{SD})\ \mathrm{noise}))$.

Statistical analysis

Differences between the two groups were tested using the Mann–Whitney *U*-test as a nonparametric procedure. Absolute differences between time points (for example, tongue volume at baseline and after therapy) were analyzed per group using the paired Wilcoxon signed rank test. For all statistical analyses, a *p*-value <0.05 was considered statistically significant.

Results

All MR examinations in the volunteers as well as in the patients with known acromegaly were performed without any complications. All subjects were able to chew and swallow in supine position without aspiration.

The mean MR examination time for assessing the tongue volumes was 10 min (range 7–13) and 22 min (range 19–25), respectively, including the chewing and swallowing study. The average tongue volume in the volunteers measured by MRI was 117 ml in men and 77 ml in women (Table 1). The mean SNR in the volunteers was 70±10. The patients with acromegaly showed an average tongue volume of 180 ml in men and 145 ml in women (Table 2).

Chemical shift and susceptibility artifacts were low and did not render the image quality. Thus, all data sets were diagnostically sufficient. The chewing and swallowing process was normal in all volunteers (Fig. 2a–c). The pharyngeal and laryngeal space was normal in all patients. No stenoses, wall irregularities, or other pathologies were observed. Two of the 10 patients with acromegaly showed a conspicuous chewing and swallowing process prior to therapy that disappeared after therapy: A 53-year-old female patient showed involuntary swallowing while chewing (Fig. 3), with no aspiration observed. In a 63-year-old male patient, the tongue involuntarily dropped back into the pharyngeal space while swallowing, but this did not hamper the act of swallowing itself (Fig. 4). In the eight remaining patients with acromegaly, no chewing or swallowing abnormalities were observed.

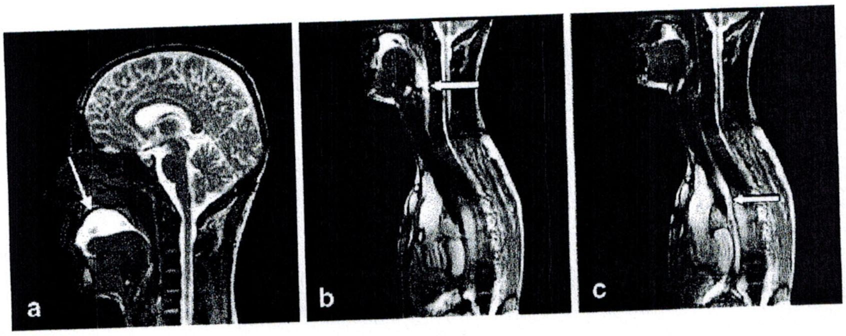

Fig. 2 a–c A 38-year-old healthy male volunteer with a normal chewing (**a**, *arrow*) and swallowing process (**b–c**) shown by using a real-time TrueFISP sequence. The bolus is in the hypoharyngeal space (**b**, *arrow*) and after that in distal part of the esophagus (**c**, *arrow*).

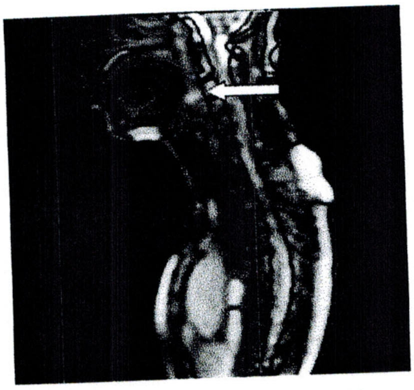

Fig. 3 Real-time 2D TrueFISP sequence in a 50-year-old patient with acromegaly (sagittal view). During the chewing process, an involuntary swallowing act can be observed (leaking). There were no signs of aspiration or other complications.

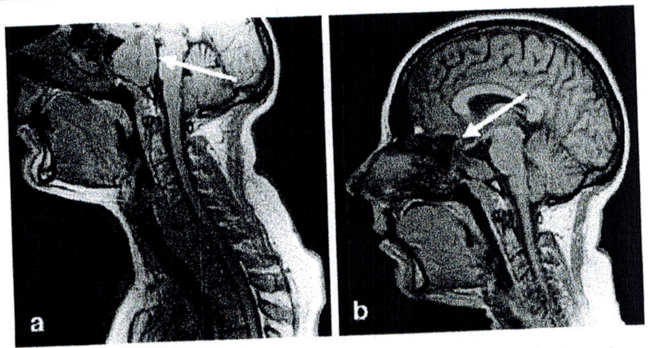

Fig. 5 a–b Two-dimensional TrueFISP image, sagittal plane, in a 37-year-old female acromegaly patient with hypophyseal macroadenoma (*arrow*) and a tongue volume of 117 ml prior to therapy. Six months after therapy with sandostatin analogue and surgical therapy (transsphenoidal resection of the hypophyseal adenoma), the tongue volume decreased to 88 ml.

Six months after therapy there was no statistically significant difference of BMI in the patients with acromegaly, and the mean tongue volumes were 154 ml for male patients (180 ml prior to therapy) and 125 ml in the female patients (145 ml prior to therapy) (Fig. 5a, b). Furthermore, the mean SNR of the tongue in patients with acromegaly decreased from 114 to 93 after therapy.

Discussion

The presented data carry three messages we believe are important: (1) Patients with acromegaly have a greater tongue volume than healthy subjects do, (2) the TrueFISP sequence is feasible for visualizing the chewing and swallowing act in real time and can be used for monitoring therapeutic approaches in patients with acromegaly, and (3) the reduction of SNR of the tongue in patients with acromegaly after therapy is due to the decrease in tongue volume and thus the water content of the tongue.

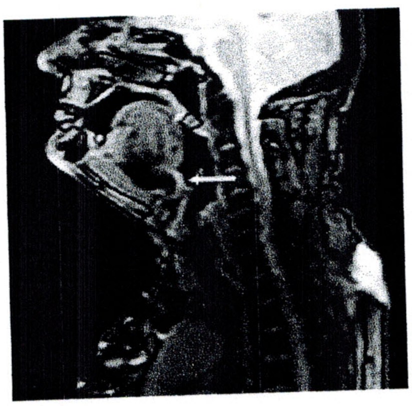

Fig. 4 Real-time 2D TrueFISP sequence in a 63-year old patient with acromegaly. During swallowing the tongue dropped to the pharyngeal space.

Chewing and swallowing problems are frequent and increase with age and in conjunction with different diseases [8, 16]. The chewing and swallowing process is a very fast one: The oropharyngeal and hypopharyngeal transport amounts to 300 ms only and shows a speed between 9 and 25 cm/s, but the esophageal transport needs 4–8 s and has a speed of 2–4 cm/s [17]. Therefore, real-time imaging is mandatory for monitoring these processes [13]. Patients with acromegaly suffer from multiple functional problems within the upper airway, such as sleep apnea syndrome and macroglossy [9–11].

Respiratory motion artifacts in conjunction with susceptibility effects had for a long time prohibited the MR-based analysis of the heart and gastrointestinal tract. Reflecting recent hardware and software developments, functional MRI has become possible by allowing the acquisition of fast imaging with steady-state precession sequences (TrueFISP). The initial technical reports suggest that real-time TrueFISP MRI can provide a noninvasive alternative characterized both by good diagnostic accuracy and patient acceptance. Thus, real-time TrueFISP MR imaging is capable of depicting functional processes with sufficient temporal and spatial resolution for a qualitative as well as quantitative assessment [18–20]. Motivated by inherent noninvasiveness, operator independence, and lack of ionizing radiation, TrueFISP MRI has in the past been proposed for evaluating the stomach [19, 20]. Despite initial enthusiasm, the clinical utility of MRI for detecting and staging gastric malignancies [21–23] has remained rather limited. This reflects the lack of sufficient spatial resolution to depict the gastric mucosal surfaces. The MR-based analysis of functional heart and gastric disorders, on the other hand, seems to have considerably more potential [20, 24–26].

Primarily designed for cardiac imaging, FISP is based on a steady state built up in both the longitudinal and transverse directions. Whereas in FISP only one or two of the gradients are balanced, TrueFISP is characterized by balanced gradients in all three directions, ensuring maximum recovery of the transverse magnetization. In direct comparisons with 2D FLASH cine MR imaging, TrueFISP was characterized by shorter acquisition times and superior image quality in a volunteer study aiming to quantify ventricular motion [27]. Although a relatively high frame rate with one image per second was achieved, the SNR for anatomic display was not a limiting factor. Even higher frame rates are conceivable without running into SNR limitations, given the unique signal characteristics of TrueFISP. Although not evaluated, echo-sharing techniques or radial projection TrueFISP imaging might be an alternative to maintain the TrueFISP contrast mechanisms while enhancing the temporal resolution even further [27].

In a volunteer study, real-time imaging of gastric peristalsis was achieved with a TrueFISP sequence offering both high temporal and spatial resolution [28]. This study also demonstrated the ability of time-resolved 3D MRI to identify patients with gastric dyspepsia and reduced gastric emptying rates in comparison with the mean determined in healthy volunteers [29]. The real-time imaging technique proposed in this study complements the aforementioned efforts by providing a real-time analysis of gastric motion. The peristaltic wave itself can be resolved with both sufficient temporal and spatial resolution to permit both a qualitative and quantitative assessment.

Reflecting its noninvasive character that spares the patient any exposure to ionizing radiation, real-time MRI offers several potential advantages compared with videofluoroscopy, advantages that became evident when assessing the patients [13, 30]. Real-time TrueFISP sequences provide excellent soft tissue contrast and allow direct visualization of the chewing and swallowing act [13, 30]. In an initial study that included eight volunteers and six patients with dysphagia, Barkhausen et al. proposed assessing the swallowing act based on a TrueFISP MR fluoroscopy technique using different oral contrast agents [13]. However, the best image quality was rendered using semolina pudding [13], due to the high signal intensity in the TrueFISP sequence, the high inherent viscosity, and the long pharyngeal transit time compared with water–gadolinium solution or yogurt [13]. This study confirmed the feasibility of TrueFISP MR fluoroscopy to visualize the swallowing process in real time. Abolmaali et al. used real-time TrueFISP sequence for visualizing the articular disk during opening and closing of the mouth [31]. In this study, 12 healthy volunteers and 17 patients with temporomandibular joint dysfunction were included. Using a sliding window technique of 7 mm, one image could be acquired each 0.5 s. High image quality and real-time visualization of the articular disk motions allowed the assessment and quantification of articular disk pathologies.

The soft-tissue swelling of the tongue might be responsible for upper airway obstruction [32–34]. Previous studies tried to characterize anatomical differences of acromegalic patients in comparison with healthy nonacromegalics by using lateral x-ray films with cephalometric landmarks and reference lines. From those studies [33, 34–37], patients were shown to be predisposed to obstructive sleep apnea because of anatomical skeletal abnormalities: maxillary and mandibular retrognathism, dorsocaudal rotation of the mandible, enlargement of the anterior and posterior facial height, and narrowing of the depth of the bony framework of the nasopharynx. Moreover, compared with the healthy population, patients with acromegaly have a larger uvula and a narrowed pharyngeal airway space caused by changes in pharyngeal soft-tissue swelling [33, 35–37].

Macroglossia also narrows pharyngeal airway space. Magnetic resonance imaging, compared with radiographs, has the advantage of more precise delineation of soft tissue and determination of tongue volume. The present study has shown that MRI of the pharynx revealed a significant higher tongue volume in patients with active acromegaly compared with a healthy control group.

The volunteers in our study had a mean tongue volume of 140 ml in men and 90 ml in women. Pharyngeal and laryngeal anatomy was normal in all 50 volunteers. The chewing and swallowing act was regular. There was no aspiration or regurgitation observed in any of the examined volunteers. In the patients with acromegaly, the oral cavity was tight due to the large tongue. The pharyngeal and hypopharyngeal space was not narrowed. The somatostatin analogues have been shown to reduce GH secretion by pituitary adenomas and lead to amelioration of clinical features of acromegaly such as reduction of soft-tissue swelling [38, 39]. Magnetic resonance images are able to calculate the tongue volume and determine the effect of treatment with somatostatin analogues in patients with acromegaly. Prior to therapy, the patients with acromegaly had a mean tongue volume of 180 ml in men and 145 ml in women. After therapy the mean tongue volume was reduced by 14% in the female patients (mean 125 ml) and 15% in the male patients (mean 154 ml). This change was predicted after drug therapy with sandostatin analogues and surgical resection of the hypophysis through reduction of the water content in soft tissues and in the tongue [37, 38]. This could be confirmed by a decrease in the mean SNR after therapy.

This study has shown that real-time TrueFISP imaging can be used to visualize the chewing and swallowing process in volunteers as well as in patients with acromegaly and that the applied protocol is capable of detecting several pathologies associated with acromegaly. Furthermore, the outlined MR protocol is suited for measuring tongue volumes and can therefore be used as a noninvasive imaging modality for follow-up studies in patients with acromegaly after drug or surgical therapy.

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