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Published in:
Radiotherapy and Oncology

DOI:
10.1016/j.radonc.2018.09.022

Radiotherapy and Oncology 130 (2019) 68–74

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

Functional Swallowing Units (FSUs) as organs-at-risk for radiotherapy. PART 2: Advanced delineation guidelines for FSUs

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ARTICLE INFO

Article history:
Received 23 January 2018
Received in revised form 13 August 2018
Accepted 10 September 2018
Available online 11 December 2018

Keywords:
Head and neck cancer
(chemo)Radiation
Delineation
Swallowing organs at risk
Hyolaryngeal elevation
Tongue base retraction

ABSTRACT

Background and purpose: In a separate article (PART 1), a rationale and explanation of the physiology-and-anatomy-based concept of Functional Swallowing Units (FSUs) was presented. FSUs are swallowing muscles not included in the set of commonly defined swallowing organs at risk (SWOARs). They are involved in three crucial swallowing components: hyolaryngeal elevation (HLE), tongue base retraction (TBR) and tongue motion. This paper is a continuation of PART 1 and it provides detailed computed tomography (CT)-based delineation guidelines for FSUs, which presumably are also at risk of radiation-induced dysphagia.

Material and methods: Following analysis of swallowing physiology and human anatomy, presented in PART 1, CT-based delineation guidelines for defined FSUs were created. Delineation was performed by the first author and revised by a panel of experts.

Results and conclusions: Detailed delineation guidelines are presented for seven FSUs involved in HLE, TBR and tongue motion. The guidelines are supplemented by CT and MRI-based exemplary illustrations and complete CT/MRI-based delineation atlases (available online). This paper provides information essential to the implementation of the FSU concept in radiation practice, and supports uniform contouring, data collection and further improvement of swallowing sparing radiation-based strategies.

Since radiation-based, organ-preserving treatment protocols for head and neck cancer, with or without chemotherapy, yield comparable oncological results to surgery, many patients can be cured from the disease with definitive (chemo)radiotherapy [1,2]. However, a substantial percentage of survivors suffer from, often severe, treatment-related (late) toxicity [3]. One of commonly observed side effects are broadly definable, swallowing problems, significantly deteriorating the quality of life of the patients [4,5]. In the last 15 years, effort has been made to develop radiation-based swallowing sparing strategies [6–10]. As a first step, dysphagia/aspiration-related structures have been identified, including pharyngeal constrictor muscles and larynx [11]. However, other swallowing muscles, in particular those involved in hyolaryngeal elevation (HLE) and tongue base retraction (TBR) (swallowing components crucial for safe and efficient swallowing) have been considered irrelevant. As a consequence, they are still not taken into account by many radiation oncologists [12,13].

The rationale behind the physiology-and-anatomy-based concept of Functional Swallowing Units (FSUs) was presented in a separate publication (PART 1), covering all, previously not defined, swallowing muscles involved in HLE, TBR and tongue motion. This paper (PART 2) is a continuation of the FSU concept, providing detailed CT-based delineation guidelines for all FSUs, which are required for implementation of the proposed functional approach in radiotherapy practice.

Abbreviations: SWOARs, swallowing organs at risk; HLE, hyolaryngeal elevation; TBR, tongue base retraction; FSUs, Functional Swallowing Units; FOM, floor of mouth; THM, thyrohyoid muscles; PDS, posterior digastric/stylohyoid muscles complex; SCM, sternocleidomastoid muscle; LPM, longitudinal pharyngeal muscles; HSG, hyoglossus/styloglossus muscles complex; GGS, genioglossus muscles complex; BOT, base of tongue; ITM, intrinsic tongue muscles; NTCP, normal tissue complication probability; DVH, dose–volume histogram; PCM, pharyngeal constrictor muscle; VF, videofluoroscopy.

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https://doi.org/10.1016/j.radonc.2018.09.022
0167-8140/

General method

The final structures definition represents the outcome of a structured learning process, based on the delineation of multiple CT/MRI scans. Every contour made by the first author has been revised by two other head and neck radiation oncologist (JL and HB) and, subsequently, by two independent head and neck radiologist (AV and BD). Required corrections and adjustments have been discussed and introduced. Definitive consensus has been reached after revision of all contours in multidisciplinary setting, serving as an independent panel and consisting of, additionally, two otolaryngologists (GH and JW), one oral and maxillofacial surgeon (MW) and one Speech-Language pathologist (MH).

The FSUs were delineated using RayStation Treatment Planning System (version 6.1, RaySearch Laboratories AB, Stockholm, Sweden) on the axial view of contrast enhanced CT-scan. A complete CT-based delineation atlas is available online as Supplementary Material (Supplement 1). Since complementary MRI for delineation is common practice, the additional value of the MRI (T-2 sequence) has been noted and a separate MRI-based atlas is provided online (Supplement 2). Anatomical delineation borders are summarised in Table 1.

Delineation guidelines for FSUs

FSUs involved in hyolaryngeal elevation

Floor of mouth (FOM, pink contour), also known as suprahyoid muscles; the caudal border is formed by the caudal edge of the anterior digastric muscles, their hyoid- or mandible-ends, whichever appears first on the CT. The border appears as a soft tissue mass with muscular density situated anteriorly to the body of the hyoid. From that point, this soft tissue will be defined as FOM, with the anterior digastrics situated most anteriorly and laterally to the lymph nodes in level 1a. Moving further cranially, the mylohyoid muscles appear medially and posteriorly to the anterior digastric muscle. The posterior parts of mylohyoids are especially easy to define and appear as thin oblong structures reaching at their very end to the submandibular glands. Medially, they are separated from the posterior part of the tongue (hyoglossus muscle) by the thin fat layer. The geniohyoid muscles appear between the anterior digastrics and posteriorly to the level 1a, forming the middle part of the FOM. Their lateral borders are difficult to define because there is no fatty space visible between the geniohyoids and the remaining FOM muscles. The posterior edge of geniohyoids forms a transition line between FOM and tongue muscles. Since structures of the tongue have a slightly lower density, it can be identified easily. (Fig. 1b) Further above, the tongue, consisting of the intrinsic tongue musculature, fills the whole middle part of the oral space and the geniohyoids are no longer visible. From that point the FOM is formed only by the mylohyoids, anteriorly attached to the mandible and posteriorly reaching the submandibular glands and slightly above them – as a free muscle edge [14]. (Table 1; Fig. 1a–d).

Thyrohyoid muscles (THM, purple contour) both left and right are easily defined on the CT as one structure. They are attached to the anterior surface of the frontal part of the thyroid cartilage at the first visible point. Part of the THM, which runs above the thyroid cartilage, is attached to the anterior surface of the thyroid membrane (not visible on CT). Here the contouring of THM should be continued until the hyoid bone becomes visible. (Fig. 1a, e) This way of THM delineation may partly include cranial parts of three other infrahyoid (strap) muscles, but reliable distinguishing of those on CT is barely possible.

Two aforementioned FSUs (FOM and THM) can be combined simply by adding of these two contours. In this way an additional composite structure can be created, if needed, forming an *anterior segment* of swallowing apparatus (Fig. 1a, pink and purple contour).

Posterior digastric/stylohyoid muscles complex (PDS, orange contour) Posterior digastric appears as an oblong, muscle-like soft tissue mass attached to the mastoid notch, which, as a bony landmark, is easy to localise on CT. PDS runs in the space between the transverse process of the first cervical vertebrae and the jugular vein (located medially) and the posterior part of the sternocleidomastoid muscle (SCM) and the parotid gland (located laterally). Running further downwards, it 'outruns' the SCM and the jugular vein; laterally it is still limited by parotid deep lobe (Fig. 1g, h). At that point, the stylohyoid may also become visible as a very thin muscle located slightly anteriorly to the posterior digastric. However, it often looks like a part of the posterior digastric and as such it is rather difficult to define as a separate structure. Both muscles run further down together, reaching the medial edge of the submandibular gland. Here, at the level where the greater cornu of hyoid bone becomes visible, the whole PDS complex ends as tendon intermediate of digastric muscle. It appears as an oval structure a few millimetres long, with a slightly higher density than the muscle tissue (Fig. 1i).

As mentioned, identifying these two muscles separately may be difficult. The most important part while contouring is the posterior digastric, since it constitutes approximately 90% of the PDS complex volume. Furthermore, one is more likely to include the tiny stylohyoid while contouring the PDS than exclude it. The origin of the stylohyoid is usually invisible or difficult to separate from two other tiny muscles originating on the styloid process: the *stylopharyngeal muscle* and *styloglossus muscle.* The ipsi- and contralateral PDS complexes should be delineated separately.

Longitudinal pharyngeal muscles (LPM, dark blue contour) The LPM contour begins from its *cranial border,* (torus tubarius) on both sides, at the level where the hard palate appears. (Fig. 1j) From the point where the soft palate (and thus *palatopharyngeal muscle)* becomes visible the soft palate should also be included. At that point, the whole structure has an inverted U-shape with its ends bent outwards. (Fig. 1k) From the level where the pharyngeal constrictor should be defined (caudal tip of the pterygoid plates, where both humuli are still visible) [15], the LPM is limited to the soft palate and the inner layer of the lateral part of the pharyngeal wall. (Fig. 1l) Since the fibres of both *palatopharyngeal muscles* blend with each other through the midline, the uvula should be included in LPM as long as it is connected (laterally) with the rest of the palate. From the point where the uvula appears as a free part, it should be excluded, as at that level the *palatopharyngeal muscles* do not intermesh with each other anymore. The LPM contour should continue downwards, including both palatopharyngeal folds along the lateral inner part of the pharyngeal wall, variably visible on the CT as small reliefs of the mucous membrane into the lumen of the pharynx. (Fig. 1m) The caudal border of the LPM is simply the last slice where the palatopharyngeal folds are visible. While contouring LPM as described above, the part of the third longitudinal muscle- *stylopharyngeal muscle-* will be automatically included, as it inserts the inner layer of the pharyngeal wall and blends with two other muscles. Its origin and proximal part though, can be challenging to define especially on CT. As one of three muscles attached to the styloid process, it appears at the medial side of the base of the styloid and as such it may be difficult to separate from the two other styloid muscles. Therefore inclusion of the proximal part of *stylopharyngeal muscle* in LPM is optional.

FSUs involved in tongue base retraction

Hyoglossus/styloglossus muscles complex (HSG, yellow contour) The HSG contour begins from the caudal border of the

Table 1
Overview of all FSUs and their corresponding anatomic borders.

FSU involved in HLE	Anatomical border					
	Cranial	Caudal	Anterior	Posterior	Lateral	Medial
Floor of mouth FOM	Free edges of mylohyoids	Caudal edge of anterior digastric	Caudally: platysma Cranially: posterior border of level 1a/mandible	Hyoid/tongue muscles/posterior edges of mylohyoids (anterior border of submandibular glands)	Lateral edge of anterior digastric/ lateral edge of mylohyoids (medial border of level 1b)	Not defined
Thyrohyoid muscles THM	Caudal edge of hyoid	Slice where lamina of thyroid cartilage appears	Anterior end of the muscle reaching laryngeal prominence	Posterior end of the muscle (oblique line of the thyroid)	Platysma	Thyroid cartilage
Posterior digastric/ stylohyoid muscles complex PDS	Mastoid notch of temporal bone	*Tendon intermediate* medially to submandibular gland (cranial tip of grater cornu of hyoid appears)	Anterior end of stylohyoid or posterior digastric	Posterior end of posterior digastric	Posterior part of sternocleidomastoideus, deep lobe of parotid gland	Cranially: transversal process of C1, jugular vein lateral border of level 2 Caudally: hyoglossus muscle (HSG)
Longitudinal pharyngeal muscles LPM	Torus tubarius (left and right)/ first slice where hard palate appears	The last slice where posterior pharyngeal folds are visible	Cranially: anterior edge of torus tubarius and soft palate Caudally: anterior edge of posterior pharyngeal folds	Posterior edge of soft palate and posterior pharyngeal folds/superior PCM	Lateral edge of torus tubarius/ superior PCM	Pharyngeal lumen or not defined
FSU involved in TBR/ Tongue motion	Cranial	Caudal	Anterior	Posterior	Lateral	Medial
Hyoglossus/ styloglossus muscles complex HSG	One slice under the point where styloglossus appears as separate muscle not connected with the body of the tongue	Lateral part (greater cornu) of hyoid	Caudally: anterior end of hyoglossus Cranially: anterior edge of styloglossus	Caudally: posterior edge of hyoglossus Cranially: posterior edge of styloglossus (lingual part)	Caudally: PDS (*tendon intermediate* of digastric muscle)/submandibular gland/ mylohyoid Cranially: mylohyoid/mandible	Caudally: pharyngeal lumen/ BOT Cranially: ITM (inferior longitudinal muscle)/BOT
Genioglossus muscles GGS	Cranial end of septum linguae/ ITM	Caudal end of septum linguae just above hyoid	Caudally: posterior border of FOM Cranially: apex of the tongue	Anterior border of BOT	Caudally: anterior ends of hyoglossus muscles (HSG) Cranially: ITM (inferior longitudinal muscles)	Not defined
Intrinsic tongue muscles ITM	The last slice where the body of the tongue is visible	The first slice where the inferior longitudinal muscles become visible (between GGS and HSG)	Anterior edge of the body of the tongue	BOT/posterior edge of the body of the tongue	Caudally: medial border of HSG Cranially: lateral edge of the body of the tongue	Lateral edge of GGS or not defined

HLE-hyolaryngeal elevation, TBR-tongue base retraction; BOT-base of tongue.

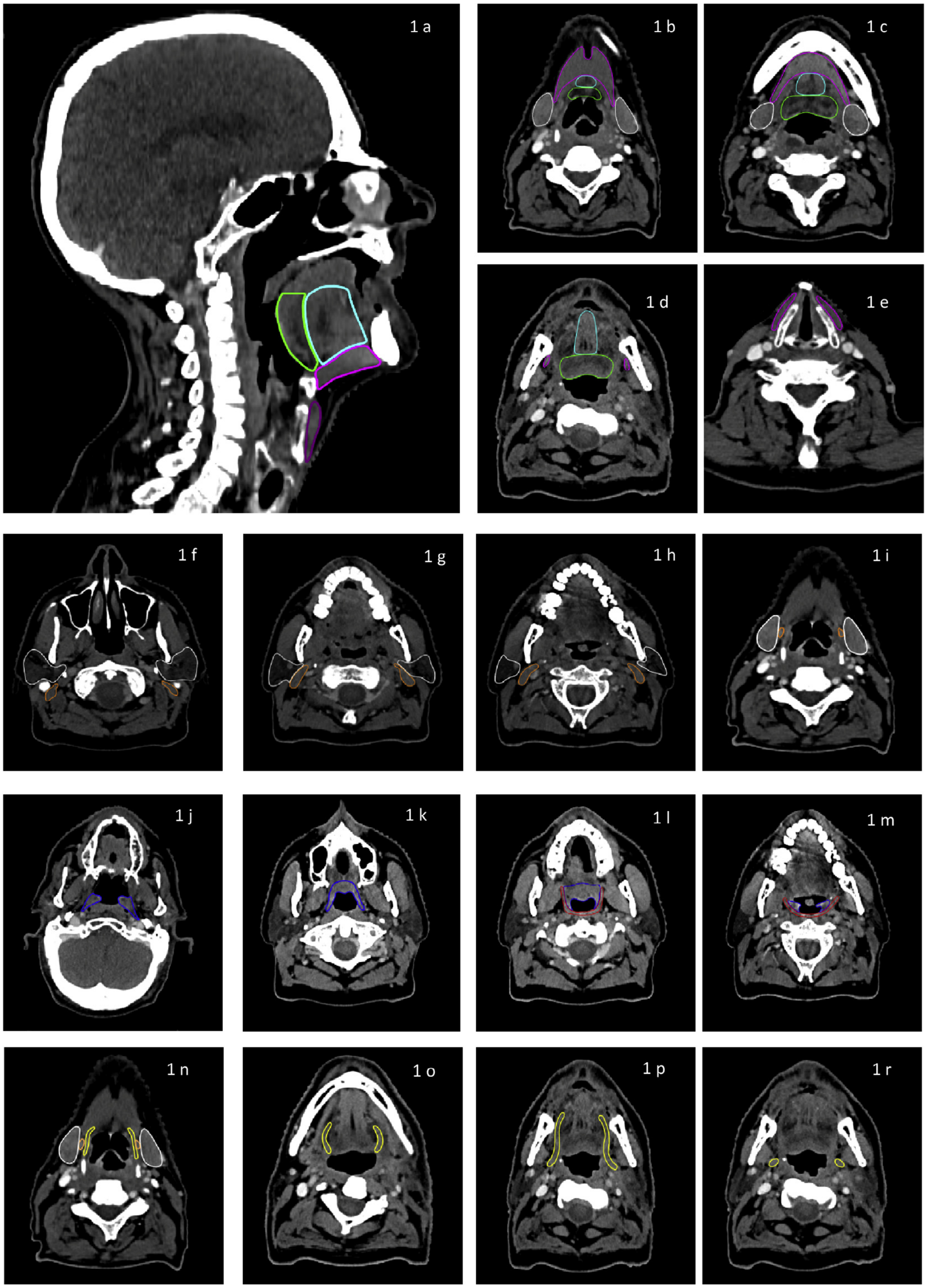

Fig. 1. (a) Anterior segment (pink and purple); (a-e) FOM (pink), THM (purple), GGS (light blue), BOT (light green), submandibular glands (white); (f–i) PDS complex (orange) from cranial to caudal (i: tendon intermediate), parotid/submandibular glands (white); (j–m) LPM (dark blue) from cranial to caudal, superior PCM (red); (n–p) HSG complex (yellow) from caudal to cranial, PDS caudal end (orange), submandibular gland (white); (r) one slice above cranial border of HSG (styloglossus visible as separate muscle not attached to the body of the tongue, delineation optional).

hyoglossus muscle, formed by lateral parts of the hyoid (Fig. 1n). Further upwards the definition of hyoglossus muscle becomes easier due to the density difference between muscle and fatty/connective tissue. Its lateral border is formed by medial edge of mylohyoid muscle and its medial border is formed by base of tongue and, more anteriorly, by fibres of intrinsic tongue muscles, running between hyoglossus and genioglossus muscle. The delineation should be continued upwards following the typical, arched-shape of the muscle. (Fig. 1o) At the upper end of hyoglossus muscle, slightly in front and laterally to it, the *styloglossus muscle* appears. Distinguishing these two muscles is difficult. To include the whole lingual part of styloglossus muscle, the contour should continue until the point where it appears as a separate tiny muscle, unconnected to the rest of the tongue and located posteriorly to it. (Fig. 1p, r) The definition of this relatively short part of the styloglossus muscle (running further cranially up to the apex of styloid process) may be difficult on CT. Therefore, its inclusion in HSG is optional. Ipsi- and contralateral HSG complexes should be delineated separately.

FSUs involved in tongue motion

Genioglossus muscles (GGS, light blue contour). The GGS contour starts caudally and includes both (left and right) muscles as one structure. As such it appears between the middle part of FOM and base of tongue (BOT). It can be recognised by a typical chink between both genioglossus muscles (*septum linguae*), and a slightly different density than darker BOT posteriorly and brighter FOM anteriorly. Lateral borders of GGS are easily defined by lateral edges of both muscles, visible medially from the sublingual glands, hyoglossus muscles and intrinsic tong muscles. Cranially GGS abuts with intrinsic tongue muscles and the last slice, where the midline fibrous septum is visible, defines its upper border. For the details of the delineation of BOT we refer to the atlas by Christianen et al. [15] (Fig. 1a–d).

Intrinsic tongue muscles (ITM, coral contour)

As the fibres of all intrinsic muscles intermesh with each other, precise definition is difficult. According to the principle of functional unit approach, we consider all eight muscles (four each side) as one structure, which makes the definition somewhat easier and more robust. Based on the delineation of other tongue structures, described above, creation of the ITM is recommended as follows:

1. Create a composite structure, the sum of structures BOT, GGS and both HSG.
2. Copy the new structure and name it TONGUE. Adjust the copied structure by including the anterior and superior part of the tongue. Start adjusting upwardly, from the point where the inferior longitudinal muscle becomes visible between hyoglossus and genioglossus (Fig. 2d; Fig. 4g in PART 1) until the body of the tongue is no longer visible.
3. Create the ITM structure by subtracting the composite structure (Step 1) from the TONGUE (Step 2). (Fig. 2b-e).

This way of creating ITM covers most of the intrinsic muscle volume, including longitudinal inferior, which is challenging to contour manually. Furthermore, it provides an additional structure (TONGUE), encompassing the complete lingual part of the tongue musculature.

MRI: additional value for delineation of FSUs

Using MRI for contouring organs at risk may substantially improve the precision and robustness of structure definition. T-2 MRI sequence is particularly useful due to its high discrimination value between the muscle and (fibro-) fatty tissue. Using MRI for the delineation of FSUs provides several advantages:

- Location of free edges of mylohyoids and therefore cranial (and posterior) border of the FOM (Fig. 3a).
- Exact location of hyoglossus between mylohyoid and genioglossus/intrinsic tongue muscles and the caudal border of the HSG, defined as the point where the extra-lingual part of the styloglossus appears (Fig. 3b).
- Exact location of posterior digastric muscle (and thus PDS complex), especially at the point where it runs between the parotid gland and the lymph nodes level 2 (Fig. 3c).
- Location of the LPM, including its cranial border (Fig. 3d) and, in particular, its relation to pharyngeal constrictor superior (Fig. 3e).
- Identification of the origins and proximal parts of three styloid muscles: *stylohyoid muscle* (a part of PDS), *styloglossus muscle* (a part of HSG) and *stylopharyngeal muscle* (a part of LPM) (Fig. 3f).

Discussion

This article is the second of a two-part series and it constitutes a practical tool for the implementation of the Functional Swallowing Units concept, comprehensively discussed in PART 1. To our knowledge, this is the first paper providing detailed systematic delineation guidelines, accompanied by complete CT and MRI-based atlases, for muscles involved in hyolaryngeal elevation, tongue base retraction and tongue motion.

In their retrospective study, Kumar et al. [16] assessed and confirmed the relevance of post-radiation injury of suprahyoid

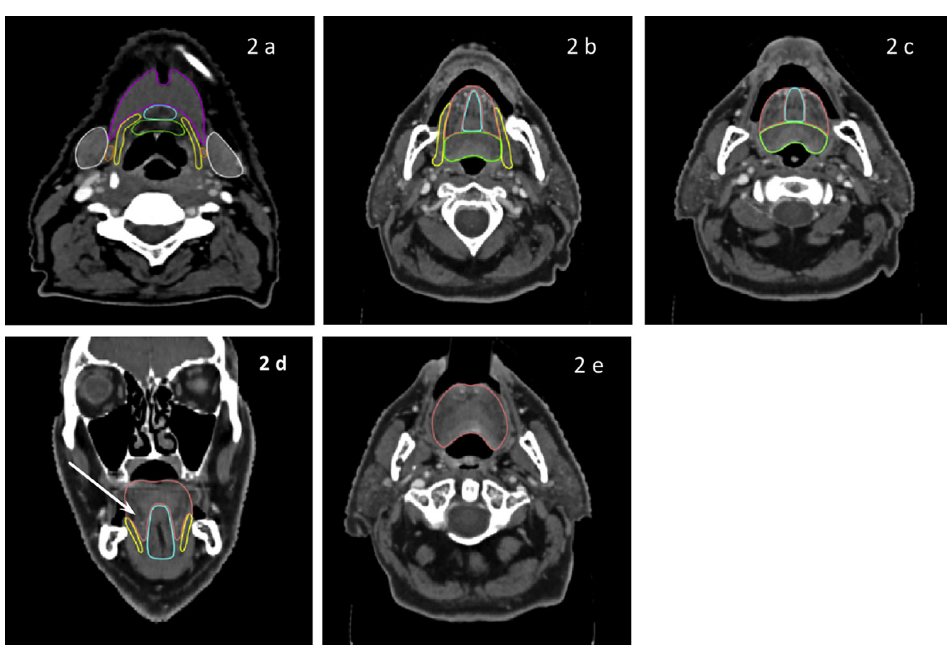

Fig. 2. (a) Relationship of FOM (pink), GGS (light blue), BOT (light green), HSG (yellow), PDS (orange) and submandibular glands (white); (b–d) relationship of ITM (coral), GGS, BOT and HSG; intrinsic inferior longitudinal muscle (white arrow); (e) ITM cranial part.

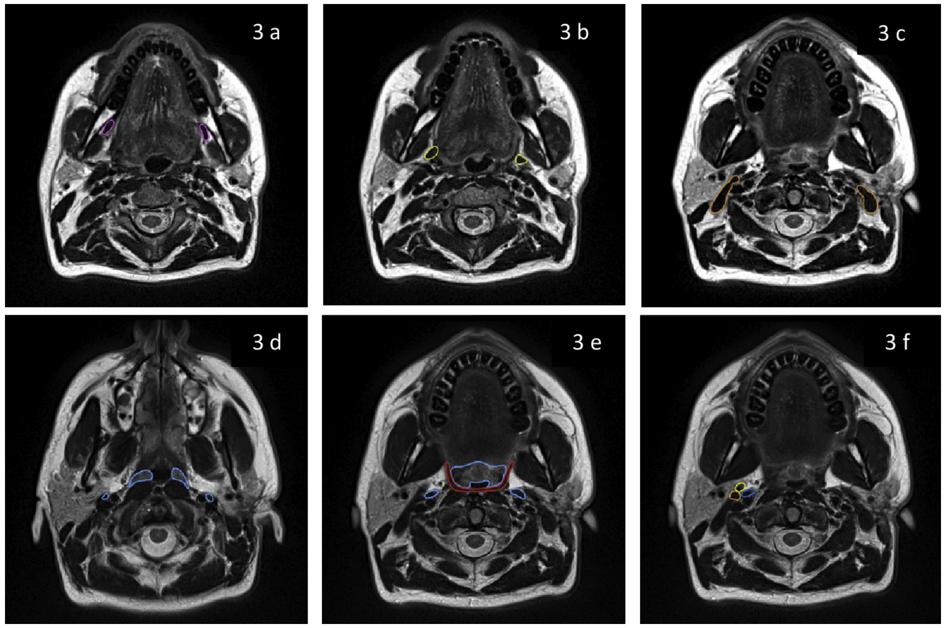

Fig. 3. Some aspects of FSUs on MRI T2 sequence: (a) cranial border of FOM (free edge of mylohyoid muscles); (b) insertion of styloglossus muscle into the body of the tongue (one slice above the cranial border of HSG); (c) PDS complex (between parotid gland and level 2 lymph nodes); (d) torus tubarius (origin of salpingopharyngeal muscle and cranial border of LPM); (e) relationship of LPM and PCM superior; (f) 3 muscles originating from styloid process: styloglossus muscle (yellow, optional part of HSG), stylopharyngeal muscle (dark blue, optional part of LPM), stylohyoid muscle (orange, part of PDS).

muscles in the development of penetration/aspiration. They also provided a short, practical delineation description (as an Appendix material). The authors delineated the suprahyoid muscles separately (geniohyoid, anterior belly of digastric muscle and mylohyoid), two extrinsic tongue muscles separately (genioglossus, hyoglossus) and a composite structure FOM, including all suprahyoid muscles and hyoglossus muscle. This delineation method resembles our proposed guidelines, with the exception of the FOM definition. We do not recommend including the hyoglossus muscle as it has a different function (tongue base retraction) shared with another tongue muscle, styloglossus (defined in this paper as ***hyoglossus/styloglossus complex, HSG).*** For the delineation of separate muscles, we would refer to Kumar et al. [16] Furthermore, the MD Anderson Group [17] delineated all muscles separately in their recently published retrospective report on chronic radiation-associated dysphagia. This report again confirms the high impact of radiation damage to suprahyoid and tongue muscles on swallowing condition. All structures were auto-segmented using an internal atlas dataset, and subsequently reviewed by two radiation oncologists [17]. Auto-segmentation is a promising method of contouring, if it genuinely saves time. This is particularly useful during adaptive radiotherapy [18–20]. However, experience in our institute suggests that the potential benefit is usually compromised by the propagation of barely distinguishable (swallowing) structures requiring (time consuming) manual adjustments. The use of composite structures, such as FSUs, may make auto-segmentation techniques more efficient.

From a research perspective, contouring muscles as proposed provides another advantage: the physiology-based concept reduces the number of candidate variables and, thus, the risk of overfitting, in regression-type Normal Tissue Complication Probability (NTCP) models [21]. This matters especially for VF-based endpoints, where the number of events is the limiting sample size and the number of potential predictors usually high (low observation-per-predictor ratio). Proper selection of predictors, substantiated by swallowing physiology, seems to be the first step on the way to minimise overfitting. Going further, clustering algorithms (e.g. principal components analysis) may as well be supported by a smart definition of organs at risk and, therefore, DVH parameters (i.e. predictors). Other advantage is the avoidance of further acceleration of co-linearity between various DVH parameters of adjacent small muscles – a common statistical pitfall while creating NTCP models [22]. Nevertheless, the problem of co-linearity will remain. For instance, the proximity of superior pharyngeal constrictor (responsible for propulsion forces of posterior pharyngeal wall) and longitudinal pharyngeal muscles (responsible for larynx elevation) makes it difficult to distinguish the contribution of their damage to dysphagia. Pearson et al. explored their two-sling theory of hyolaryngeal elevation on a population of irradiated patients [12]. Besides the significantly higher rate of aspiration and residue after irradiation, they found that observed reduction of laryngeal kinematics was attributable mainly to functional deficits in the posterior muscle sling (i.e. longitudinal muscles) [12]. Those findings could partially explain the prominent role of the PCM superior as the strongest predictor of radiation-induced dysphagia (especially its persistent pattern) in most of the studies on this topic [6,7,23–29]. Furthermore, the authors noted that longitudinal pharyngeal muscles, because of their function, should be defined as a separate structure (instead of, as previously recommended, being partially included in PCM superior) and analysed in correlation to this function [11,13]. For such a complex problem as dysphagia, this hypothesis-driven analysis may be a better approach than random selection or exclusion of (often correlated) DVH parameters. Finally, we presume that this approach is especially useful for the interpretation of functional radiation-induced swallowing disorders captured on videofluoroscopy (VF), the golden standard for objective swallowing evaluation.

In 2010, we published the first version of systematic delineation guidelines for SWOARs, which has since been included in the international guidelines for organs at risk for head and neck by Brouwer et al., with some minor modifications [15,30]. This paper, in combination with the aforementioned atlas for SWOARs, covers almost all structures involved in most of the pharyngeal swallowing components: hyolaryngeal elevation, tongue base retraction, laryngeal closure, upper oesophageal sphincter opening and pharyngeal contraction [31]. Moreover, we provide delineation guidelines for other tongue muscles (involved in tongue motion), as these muscles may be relevant if correlated with subjective swallowing complaints [17,32]. Presented concept not only complements the guidelines previously published by Christianen et al., but also makes the delineation feasible, due to a smart definition of Organs At Risk. We did not define the palatoglossal muscle, the fourth extrinsic tongue muscle. Even on MRI, it is very difficult to distinguish it from the body (intrinsic muscles) of the tongue and it supports another swallowing component, velopharyngeal closure, preventing nasal regurgitation. Functional swallowing is possible without velopharyngeal closure if all other aspects are normal [33]. It is also not the most typical disorder after irradiation (with possible exception of nasopharyngeal cancer patients) [33–36]. Furthermore, nerves and blood vessels supplying all mentioned structures are not defined separately. These are impossible to reliably distinguish using the current routine imaging techniques.

It is important to realise that sparing regions without detailed contouring may be sufficient to reduce toxicity. Nevertheless, the relevance of precise structures definition in radiotherapy grows, not only due to the need for better understanding of radiation-induced toxicity mechanisms, but also the rapid development of radiation techniques, opening new possibilities for sophisticated, individualised cancer treatment.

Conflict of interest statement

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2018.09.022.

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