Original article

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

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A R T I C L E   I N F O

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 four 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.

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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.
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 Supplementary Material (Supplement 1). Since complementary MRI for delineation is common practice, the additional value of supplementary 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 ‘ourtruns’ 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 digastic 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 stylovahygeal 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. 1i) 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>
<thead>
<tr>
<th>FSU involved in HLE</th>
<th>Anatomical border</th>
<th>Cranial</th>
<th>Caudal</th>
<th>Anterior</th>
<th>Posterior</th>
<th>Lateral</th>
<th>Medial</th>
</tr>
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<tbody>
<tr>
<td><strong>Floor of mouth</strong></td>
<td><strong>FOM</strong></td>
<td>Caudal</td>
<td>Hyoid/tongue muscles/posterior edges of mylohyoids (medial border of level 1b)</td>
<td>Caudally: platysma Crani ally: posterior border of level 1a/mandible</td>
<td>Caudally: platysma</td>
<td>Lateral edge of anterior digastric</td>
<td>Not defined</td>
</tr>
</tbody>
</table>
| **Thyrohyoid**      | **THM**          | Caudal  | Thyroid cartilage | Caudally: anterior edge of torus tubarius and soft palate | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius/ | Thr  
| Posterior digastric/  | stylohyoid        | Slice   | Anterior end of the muscle reaching laryngeal prominence | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius | Anterior end of posterior digastric | Caudally: transversal process of C1, jugular vein lateral border of level 2 
| **muscles complex** | **PDS**          | where lamina of thyroid cartilage appears | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius | Posterior end of posterior digastric | Caudally: transversal process of C1, jugular vein lateral border of level 2 
| **Longitudinal pharyngeal** | **LPM**          | Caudal  | Caudally: anterior edge of torus tubarius and soft palate | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius | Lateral edge of torus tubarius/ | Caudally: transversal process of C1, jugular vein lateral border of level 2 
| **FSU involved in TBR/ Tongue motion** | **HSG**          | Caudal  | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius | Superior PCM | Caudally: transversal process of C1, jugular vein lateral border of level 2 
| **Hyoglossus/ styloglossus muscles complex** | **HSG**          | Caudal  | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius | Caudally: anterior edge of torus tubarius | Superior PCM | Caudally: transversal process of C1, jugular vein lateral border of level 2 
| **Genioglossus muscles** | **ITM**          | Caudal  | Caudally: posterior border of FOM | Caudally: posterior border of BOT | Caudally: posterior border of BOT | BOT/posterior edge of the | Caudally: transversal process of C1, jugular vein lateral border of level 2 
| **Intrinsic tongue muscles** | **ITM**          | Caudal  | Caudally: posterior border of the tongue | Caudally: posterior border of the tongue | Caudally: posterior border of the tongue | BOT/posterior edge of the | Caudally: transversal process of C1, jugular vein lateral border of level 2 

**Table 1**

Overview of all FSUs and their corresponding anatomic borders.

**HLE**-hyolaryngeal elevation, **TBR**-tongue base retraction; **BOT**-base of tongue.
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 mylo- hyoid 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. Ipsilateral 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 tongue 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 Christiansen 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 suprahoid...
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.

References