Assessment of cough in head and neck cancer patients at risk for dysphagia—An overview

Sofiana Mootassim-Billah | Gwen Van Nuffelen | Jean Schoentgen | Marc De Bodt | Tatiana Dragan | Antoine Digonnet | Nicolas Roper | Dirk Van Gestel

1Department of Radiation Oncology, Speech Therapy, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium
2Department of Otolaryngology and Head and Neck Surgery, University Rehabilitation Center for Communication Disorders, Antwerp University Hospital, Antwerp, Belgium
3Department of Translational Neurosciences, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium
4Department of Logopaedics and Audiological Sciences, Faculty of Medicine and Health Sciences, University of Ghent, Ghent, Belgium
5BEAMS (Bio-, Electro- And Mechanical Systems), Université Libre de Bruxelles, Brussels, Belgium
6Department of Radiation Oncology, Head and Neck Unit, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium
7Department of Surgical Oncology, Head and Neck Surgery Unit, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium
8Department of Oto-Rhino-Laryngology and Head & Neck Surgery, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium

Correspondence
Sofiana Mootassim-Billah, Department of Radiation Oncology, Speech Therapy, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium.
Email: sofiana.mootassim-billah@bordet.be

[Correction added on 17 May 2021, after first online publication: The second sentence of the Introduction has been revised.]

Abstract

Background: This literature review explores the terminology, the neurophysiology, and the assessment of cough in general, in the framework of dysphagia and regarding head and neck cancer patients at risk for dysphagia. In the dysphagic population, cough is currently assessed perceptually during a clinical swallowing evaluation or aerodynamically.

Recent findings: Recent findings have shown intra and inter-rater disagreements regarding perceptual scoring of cough. Also, aerodynamic measurements are impractical in a routine bedside assessment. Coughing, however, is considered to be a clinically relevant sign of aspiration and dysphagia in head and neck cancer patients treated with concurrent chemoradiotherapy.

Conclusion: This article surveys the literature regarding the established cough assessment and stresses the need to implement innovative methods for assessing cough in head and neck cancer patients treated with concurrent chemoradiotherapy at risk for dysphagia.

KEYWORDS
aspiration, assessment, cough, dysphagia, head and neck cancer, radiation

Received: 9 December 2020 Revised: 22 February 2021 Accepted: 26 March 2021
DOI: 10.1002/cnr2.1395

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2021 The Authors. Cancer Reports published by Wiley Periodicals LLC.

1 | INTRODUCTION

Late radiation-associated dysphagia (RAD) can be defined as impaired swallowing safety and/or efficiency following intensive non-surgical
treatment regimens in head and neck cancer (HNC) patients. It has been reported by 50 to 79% of HNC-patients treated with concurrent chemoradiotherapy and has a high impact on patients’ reported quality of life.

The two hallmarks of RAD are residue (ie, food sticking in the oral cavity, pharynx, or larynx), and penetration/aspiration. Penetration is defined as an entry of material into the larynx, but which does not pass below the vocal folds. Aspiration is defined as an entry of material below the vocal folds. In case the patient’s sensory system is unimpaired, penetration and aspiration result in a cough reflex that protects the lower airways and lungs by evacuating the material. In HNC-patients, however, the efficacy of the elicited cough is often diminished or absent due to sensory deterioration.

Radiation-induced deterioration is characterized by inflammatory changes, which may result in enhanced cough response (higher sensitivity/reactivity due to inflammation) in the early phase. Because of cell depletion, inflammation (ie, heat, pain, swelling), xerostomia, dysgeusia, mucositis and desquamation may occur. Those acute troubles generally appear within 3 months and resolve within a few months. In the late phase, prolonged radiation injuries may depend on the radiation dose or be the consequence of acute troubles with an exponential decay 12 to 18 months after treatment.

Late radiation injuries involve fibrotic lesions and muscle atrophy. This may alter nerve electrophysiology and lead to hyposensitivity. Sensory deterioration in this head and neck region is a serious threat as it may result in an inefficient cough reflex. Therefore, HNC-patients with RAD are severely at risk of food aspiration.

Literature has reported high incidence rates of aspiration in this population ranging between 20% and 83%. It has been observed that aspiration rates depend on the adjunct of other treatments such as chemotherapy or surgery. Jagtap et al reported a higher risk of penetration/aspiration after combining a tongue base resection with radiotherapy. Moreover, 50% of the patients treated with radiotherapy (RT) presented silent aspirations. Patients treated with concurrent chemoradiotherapy (CCRT) for oral, oropharyngeal, nasopharyngeal and laryngeal cancers have exhibited rates of aspirations as high as 83%. Following RT alone, aspiration occurs in up to 48% of the patients treated for oral, oropharyngeal, and laryngeal cancer and in up to 65.9% of the patients treated for nasopharyngeal cancer.

Hedström et al have developed the DESdC, a study-specific categorical symptom score to determine patient-reported dysphagia (DESdC = presence of Drinking, Eating, Swallowing difficulties and Coughing when eating/drinking [any combination]; scores between 0 and 4 with 0 = no symptom). Their study has reported that 89% of HNC-patients treated with RT or CCRT reported symptoms of RAD. The most commonly reported DESdC score was 3 (33%). Because of the occurrence of silent aspirations, fewer patients (13%) reported four symptoms (including coughing). According to the Penetration-Aspiration scale, these patients were severely at risk of aspiration-pneumonia but they were not aware of it. Besides, Rogus-Pulia et al demonstrated that 83% of aspirations and 100% of penetrations in patients treated with CCRT are silent.

Mortensen et al reported dysphagia-related aspiration and aspiration pneumonia to remain the most life-threatening complications of radiotherapy in HNC-patients. The mortality rate in patients with RAD developing aspiration pneumonia after CCRT ranges from 9% to 34.6%. The risk of aspiration pneumonia in RAD patients may occur up to 10 years after treatment. Early detection of dysphagia and especially aspiration is therefore key in this population.

2 | ESTABLISHED DYSPHAGIA ASSESSMENT

Videofluoroscopic Swallow Study (VFSS) is considered the gold standard for evaluating dysphagia. The direct and continuous visualization of the oral, pharyngeal, and cervical esophageal phase of swallowing, allowing for symptom detection and simultaneously revealing crucial information regarding swallowing physiology, is a major advantage of this instrumental, radiographic examination. As an adjunct to VFSS, the Fiberoptic Endoscopic Evaluation of Swallowing (FEES) is a useful tool in providing direct imaging of superior pharyngeal anatomy, secretions, and vocal fold movement. As each tool has its own strengths and plays a complementary role with regard to the other, combining the two improves their sensitivity for detecting aspiration and residue.

Due to lack of availability, patient compliance, and expertise, it is not possible to carry out instrumental examination in daily clinical practice on every patient suspected of dysphagia. Therefore, evaluation of swallowing efficacy and safety often starts with a “bedside” or clinical swallow examination (CSE). The CSE comprises multiple liquid and food swallowing trials, patient history, assessment of the oral mechanism, and patient-reported outcome. To diagnose dysphagia and aspiration, clinicians often rely on identifiers of dysphagia and aspiration risk like abnormal coughing, dysphonia, dysarthria, abnormal gag reflex, and post-swallowing voice change.

Previous research has shown that CSE underestimates aspiration risk in patients at risk and overestimates aspiration risk in patients without risk. This is possibly due to the clinical markers being unrelated to swallowing (eg, gag reflex) or unreliable indicators of penetration and aspiration (eg, voice quality). Despite limitations in estimating swallowing safety accurately, the CSE represents the more accessible method for assessing dysphagia in daily clinical practice.

3 | COUGH TERMINOLOGY AND COUGH NEUROPHYSIOLOGY

Prior to exploring established cough assessment, cough definition, and cough type categorization, as well as a description of the neurophysiology of coughing, are warranted.

3.1 | Terminology and types of coughing

Coughing is defined as a deep inspiration followed by closure of the glottis (compression), forced expiratory effort, and then opening of the
glottis with expiration. As mentioned, effective coughing plays a crucial role in expectorating foreign bodies from the airways and avoiding aspiration, particularly during swallowing in patients with RAD.

Differences exist with regard to cough sequencing. A single cough is one cough produced after one inspiration. A cough epoch or cough bout, or cough attack as commonly named by patients, represents successive coughs after one single inspiration. By multiple coughs, one designates successive coughs separated from each other by an inspiration.

Coughing may be either voluntary or reflexive. A voluntary cough originates in the cerebral cortex. Voluntary cough testing involves asking a patient to cough. A reflexive cough is elicited by direct activation of receptors on airway sensory nerves. The reflexive cough is induced by stimuli that motivate the subject to protect and clear the airway by coughing and is always preceded by an urge-to-cough, a biological perceived need to cough.

Whereas a (reflexive or voluntary) cough starts with an inspiratory phase, the expiratory reflex following contact of food, liquids, or chemicals with the true vocal folds or the upper tracheal areas, starts with a closure of the glottis without any prior inspiration. This is possible because swallowing (food or liquids) physiologically starts during the expiratory phase and interrupts quiet breathing. The lung volume during quiet breathing is ranging from 42% to 48% of total vital capacity. This lung volume is sufficient to allow the expiratory reflex to occur during swallowing without prior additional inspiration.

The pulmonary stretch receptors are also activated mechanically. The cough receptors, described by Widdicombe in 1954, are myelinated and respond to mechanical stimulators such as food and liquids. Therefore, cough receptors play a key role regarding the detection of penetration and aspiration. They are found in the extrapulmonary airways (larynx, trachea, mainstem bronchi). Mechanoreceptors are insensitive to direct chemical stimulation.

The cerebral cortex plays an important role in the cognitive processes participating in the modulation of voluntary coughing or voluntary suppression of the cough reflex. The involved cortical areas are the motor cortex, the sensory motor cortex, the supplementary motor area, and the limbic system. The magnitude of the cortical activation depends on the area of the cerebral cortex. Voluntary coughs encode the premotor and motor cortex, cerebellum and corticospinal pathway. Voluntary coughs occur without medullary input. The urge-to-cough involves the primary sensory cortex (intensity of the urge-to-cough), insula (magnitude of the input from the airway), and the prefrontal and post-parietal areas (attention and localization of the site of irritation). Voluntary cough suppression encodes different areas such as anterior insula, supplementary motor area, motor cingulate cortex and right inferior frontal gyrus. The limbic brain contributes to affective factors such as unpleasantness associated with airway irritations and cough.

### 3.2.2 | Cortical control

The cerebral cortex plays an important role in the cognitive processes involving the nucleus tractus solitaries where central and peripheral responses involving the nucleus ambiguous, the retroambigualis, and the phrenic nucleus are processed.

### 3.2.3 | Efferent nerves

Vagus, phrenic, and spinal motor nerves are activated after motor information processing in the cerebral cortex and cerebellum.
These activations cause diaphragm relaxation, thoracic, and abdominal muscle contraction (expiratory and accessory muscles).49,59 The nucleus retroambigualis, via phrenic and other spinal nerves, activates inspiratory and expiratory muscles. The nucleus ambiguus, via the recurrent laryngeal nerve (branch of the vagus), sends impulses to the larynx that cause glottal closure.59,60 Expiratory and accessory muscle activations differ between a voluntary and a reflexive cough.60 A voluntary cough involves a sequential and coordinated activation starting with the expiratory muscles. Accessory muscles respond increasingly afterwards. In contrast, for reflexive coughs, expiratory and accessory muscles are activated simultaneously. That difference suggests that the level of activation in voluntary coughs can be modulated depending on the need perceived.60

4 | ESTABLISHED COUGH ASSESSMENT

Established cough assessment currently comprises subjective ratings and recordings of aerodynamic and acoustic features. With regard to the main topic of this overview, various causes and diagnoses of coughing are not addressed.

4.1 | Subjective ratings

Persistent coughing is a common unpleasant reason for seeking medical care.45 Respiratory diseases like chronic cough or chronic obstructive pulmonary diseases are generally addressed by questionnaire completions, patient history interviews, symptom ratings, clinical observations, and non-instrumental assessment (eg, ordinal scores or visual analogue scales of subjective cough severity).61,62

4.2 | Aerodynamic features

When a more thorough examination is warranted, patients are subjected to an instrumental evaluation involving pulmonary function testing.69 To date, voluntary cough testing is usually carried out by recording the airflow rate using a facemask or pipe coupled to a filter and connected to a digital spirometer.43,50 Participants are asked to take in a maximal breath and then produce a volitional cough in the spirometer. They are typically instructed to “cough as hard as they can” or “like they have something stuck in their throat.”

Cough reflex sensitivity testing in general informs on hypersensitivity of the upper or lower airways and the ventilatory capacity.49 Cough reflex sensitivity testing involves an inhalation challenge by known tussive agents. Chemoreceptors described above are sensitive to chemicals such as capsaicin (chili pepper), bradykinin, or other classical nociceptor stimulants.12,63 In contrast, mechanoreceptors are sensitive to mechanical stimulation and acids such as citric acid, low-chloride solutions, and distilled water.12 Citric acid, aerosolized water (fog), and capsaicin are tussive agents widely used in cough testing and can induce cough in a dose-dependent and reproducible manner.46 Typically, three thresholds are relevant during cough reflex sensitivity testing: (1) cough threshold, meaning the lowest dose (eliciting dose) of tussive agent required to induce a single cough53,64 (2) C2: the dose of tussive agent required to elicit two coughs (3) C5: the dose of tussive agent used to produce five successive coughs.46

During sensitivity testing, participants can be instructed either to cough if they need to – that is, the “urge-to-cough” method—or to suppress/inhibit the (urge to) cough as much as possible—the suppressed reflexive cough method.49 It was reported that these two methods help to differentiate between the thresholds for natural and suppressed reflexive coughs. The latter informs on the dose at which suppressing/inhibiting a cough is not possible anymore. According to Monroe et al, the natural reflexive cough threshold might be influenced by cortical expectation of cough occurrence during sensitivity testing.65 Therefore, the suppressed reflexive cough threshold should be explored because it represents the point where participants can no longer voluntarily control their cough response.65 However, Mills et al have demonstrated that healthy subjects may fail to produce suppressed reflexive cough responses (ie, they do not cough) regardless of the dose of citric acid.66 This suggests that this task also involves cortical control participation and higher inhibitor processes.58 To enable a more precise examination of cough reflex sensitivity testing, some studies have combined both approaches.67

Voluntary cough testing and cough reflex sensitivity testing are assumed to provide complementary information.43,50,64 Inconsistent measures between voluntary coughs and suppressed reflexive coughs have been reported in healthy volunteers.64 Examining peak flows rates and areas under the curve for pressure, voluntary coughs turned out to be stronger than suppressed reflexive coughs because of cortical inhibition of the latter.64 Furthermore, the peak expiratory flow rate and the total expired volume have been reported to be features that discriminate between voluntary coughs and natural reflexive coughs (triggered via the urge-to-cough method).68 The feature values are larger for voluntary compared to suppressed reflexive coughs.68 It has been reported that the amount of air inspired prior to coughing (which is larger for voluntary coughs) may significantly influence cough flow rates.69,70

Moreover, some studies that investigated objective aerodynamic cough-related features in airway diseases showed inconsistencies between aerodynamic measurements and patients’ subjective complaints (cough ratings and cough-related quality of life scores mostly).71–73

4.3 | Acoustic features

Cough sound detection has been described as a new challenge to assess respiratory diseases both in humans and animals.74,75 The literature suggests that each acoustic cough emission is a sequence that begins with a burst/release, followed by a “fricaced” fragment ( turbulence noise) and a “voiced” fragment.76,77 These expected phases enable to decide whether a cough episode has occurred.76 Hence, automated acoustic signal monitoring has been proposed to detect
cough episodes successfully.\textsuperscript{76,78–81} Amplitude, frequency, duration, severity (coughs per epoch), and pattern of the cough, for instance, have been considered to be relevant cough features for automatic early detection of respiratory diseases.\textsuperscript{75,78–83}

The literature has reported few parallels between automatic cough sound analysis and auditory perception.\textsuperscript{84,85} While comparing auditory assessment and automatic categorization, strong correlations were found regarding the distinction between productive (audible mucus noise) and unproductive coughs (inaudible mucus noise).\textsuperscript{84} In accordance with perceptual classification, a doctoral thesis has also reported the successful automatic distinction by means of acoustic features between wet (presence of mucus) and dry (ticklish, irritation) coughs.\textsuperscript{80} The gender might also be identified perceptually via cough sounds.\textsuperscript{84}

However, some cough sound features, which have been reliably reported via automatic cough sound analysis, relate inconsistently to perceptual ratings.\textsuperscript{43,86} Laciuga et al have reported perceptual difficulties in differentiating a cough event from a throat clearing, but also from perceptually differentiating a single cough from a cough epoch.\textsuperscript{43} Cough duration may also be auditorily misjudged.\textsuperscript{43} Low agreement between raters with regard to the cough sound strength and the quality (eg, effortful, breathy, strained) was also reported.\textsuperscript{43,86} Furthermore, both the automatic and perceptual identification of a respiratory disease based on cough signals is very poor.\textsuperscript{84,85} These findings highlight the difficulty of interpreting automatic cough signal detection and categorization in terms of perceived timbre as well as the underlying disease.

## 5 | COUGH-RELATED FEATURES AS BIOMARKERS OF LATE RAD IN HNC-PATIENTS

In this section, methods are discussed for assessing coughing and quantifying cough signals in the framework of the evaluation of swallowing in HNC-patients with RAD.

### 5.1 | Perceptual ratings

Abnormal coughing before, during, or after swallowing is a relevant clinical marker of dysphagia in head and neck cancer.\textsuperscript{8,87} Coughing is generally assessed perceptually during a clinical swallowing evaluation. In a retrospective study with 89 patients who aspirated following radiotherapy for HNC, the cough reflex efficacy was graded by two or three speech therapists. Results showed that the cough reflex was frequently ineffective, intermittently ineffective, or absent several months following treatment (median = 10 months).\textsuperscript{8}

The high incidence of silent aspiration in this population makes the occurrence (or absence) of coughing before, during, or after swallowing a weak predictor of penetration/aspiration.\textsuperscript{8,34} In addition, clinicians such as speech therapists, otolaryngologists, and neurologists do not demonstrate strong inter-rater agreement for cough reflex efficacy scoring.\textsuperscript{43} Laciuga et al explain the low agreement by a lack of expertise in cough physiology prior to the perceptual assessment.\textsuperscript{43} Due to proven weak inter- and intra-rater reliability, the auditory assessment of cough alone must be considered to be an unreliable predictor of aspiration.\textsuperscript{88}

As an adjunct to coughing, voice quality is usually assessed immediately following deglutition.\textsuperscript{48} Changes in voice quality are expected to inform about the possible accumulation of saliva or food at the vocal fold level.\textsuperscript{59} Indeed, it has been reported that a change in voice quality may indicate laryngeal dysfunction or the presence of an intruding object at the laryngeal level.\textsuperscript{90} Waito et al (2010) confirm that a normophonic voice after swallowing reflects a lack of aspiration-penetration.\textsuperscript{48} However, they have not corroborated that a strong correlation exists between aspiration and changes in perceived voice quality (eg, wet voice).\textsuperscript{46} Even though a cough reflex or wet voice are unreliable markers of abnormal swallows individually, McCullough et al found that their combination may represent a reliable method for detecting penetration and aspiration perceptually.\textsuperscript{88}

Because cough-related information is considered to be clinically relevant in patients with RAD, but the reliability of the auditory assessment of cough is considered to be insufficient, researchers and clinicians have investigated the added value of objective examinations.

### 5.2 | Aerodynamic features

In the field of dysphagia, cough airflow-related measures are regarded to be useful physiologic metrics to track airway defense capabilities in at-risk individuals.\textsuperscript{3,91} Airflow-related measurements are generally obtained from reflex as well as voluntary coughs. Voluntary coughs are produced upon verbal command, isolated from swallowing. Reflex cough measurements are obtained by means of an inhalation cough challenge according to the guidelines in Section 4.2. Cough airflow-related features used in the framework of dysphagia include\textsuperscript{42,50,92}:

- (i) the total number of coughs;
- (ii) the inspiration phase duration in seconds (s);
- (iii) the total expired volume (TEV) in the cough epoch in liters (L);
- (iv) the total cough epoch duration in seconds (s);
- (v) the peak expiratory flow rate (PEFR) in liters per second (L/s), that is, the peak airflow rate in the expiratory phase;
- (vi) the peak expiratory flow rise time (PEFRT) in seconds (s);
- (vii) the compression phase duration (CPD) in seconds (s); that is, the time interval from the beginning of the expiratory phase of the first cough to the last cough;
- (viii) the compression phase duration in liters (L/s\textsuperscript{2}), that is, the ratio PEF/PEFRT.

Previous studies have found a relation between aerodynamic measurements during voluntary coughs and the detection via VFSS or FEES of a risk of penetration/aspiration.\textsuperscript{93,94} A study investigating voluntary cough in an amyotrophic lateral sclerosis (ALS) population found impairments in inspiratory and expiratory cough airflow...
measurements underlying inadequate airway clearance and secretion management. Moreover, some research has demonstrated the efficacy of voluntary cough airflow features at identifying stroke patients or Parkinson’s disease patients at risk for aspiration. However, a majority of studies focusing on voluntary cough airflow waveforms or rates could not distinguish between audible aspiration, that is, aspiration followed by an audible cough and silent aspiration (aspiration without any cough response).

Recent research supports cough reflex sensitivity as a biomarker for silent aspiration. In 2016, Troche et al investigated the relation between cough reflex, voluntary cough airflow measurements and the risk of penetration/aspiration in a Parkinson’s disease population (PD). The capsaicin inhalation challenge showed that the cough reflex threshold (C2) discriminates better than voluntary cough between the risk of penetration and the risk of aspiration. Moreover, Hegland et al demonstrated that the peak expiratory flow rate and the total expired volume of the cough reflex are reliable markers of cough effectiveness in PD. In contrast, the same markers collected with voluntary coughs are overestimated. The capsaicin cough challenge highlighted the critical role of the cough reflex in preventing aspiration. Besides the capsaicin cough challenge, Miles et al reported that low concentrations of citric acid also enable obtaining aerodynamic features predicting silent aspiration. However, Morice et al observed large inter-individual variability in aerodynamic cough responses to irritants in the healthy population and highlighted the importance of focusing on intra-individual changes rather than differences between healthy subjects and patients.

Regarding head and neck cancer patients with RAD, objective voluntary and reflexive cough measurements are still lacking, although a relation has been found between silent aspirations and an ineffective cough reflex. Moreover, the use of aerodynamic equipment is not widespread in clinical practice and speech therapists may have an uneven understanding of pulmonary function testing. In addition, aerodynamic equipment interferes with an evaluation in a natural setting (eg, during a meal).

5.3 Possible added value of acoustic cough-related features in HNC-patients with late radiation-associated dysphagia

As reported, cough sound analysis is regarded as a growing line of research, especially with a view to assessing respiratory diseases. However, in the framework of dysphagia, acoustic analysis in general is an underresearched topic. Some studies have investigated the added value of cervical auscultation (CA) in assessing dysphagia. CA consists in listening to swallowing sounds with stethoscopes, microphones, or accelerometers in a patient’s natural environment. Due to its inaccuracy, research has demonstrated the risk of using CA as a stand-alone tool for assessing dysphagia.

Comparing healthy swallows and penetration-aspiration swallows with a tri-axial accelerometer, Sejdic et al showed that each axis (three anatomical directions) reported distinct information. This finding suggests that the position and orientation of a sensor influence the recorded signal. Movahedi et al have demonstrated that recordings with distinct transducers (microphones and accelerometers) are idiosyncratic and non-interchangeable. Another issue in CA is the identification/interpretation of acoustic components of swallowing because the sensor is placed on a site that moves and produces extra-sounds. Moreover, CA demonstrates only fair agreement between raters and over-reports post-swallowing aspiration. These findings highlight the need for further investigation to establish CA as a reliable tool before using it for RAD.

Given the importance of effective coughing in patients with RAD and considering the reliability of acoustic cough-related features found as biomarkers of respiratory diseases, the exploration of cough sound analysis in RAD may be relevant. However, this topic is underresearched and no conclusive results have been reported neither in patients with RAD nor in dysphagia in general. Mills et al have investigated three measurements of the strength of voluntary and suppressed reflexive coughs in healthy individuals. The measurements included airflow rate, acoustic signal, and air pressure. Based on the analysis of the peak and the area under the curve of each type of recording, the study emphasized the importance of assessing the strength of reflexive coughs rather than voluntary coughs in the dysphagic population. Voluntary and suppressed reflexive coughs showed low correlations. Also, the conclusions have been based on measures of air pressure and flow rate rather than on acoustic cough signals whose features were less accurate and relevant.

To our knowledge, acoustic cough-related features in HNC-patients with RAD have not been explored yet. As mentioned previously, inadequate coughing is a clinical cause of aspiration in HNC-patients with RAD that needs close monitoring by dysphagia experts. Developing an easy, inexpensive, and repeatable method for testing cough in the framework of dysphagia in daily life would offer an alternative method for tracking swallowing problems in HNC-patients. Such a method would enable exploiting acoustic features related to voluntary and reflex cough as biomarkers of dysphagia and/or aspiration. Recording acoustic cough-related features is easily implementable in clinical practice and could provide valid measurements. In particular, since cough signals are poor in head and neck cancer patients, such a method could provide novel information regarding this population. Also, given that cough features in isolation are not considered to report reliably on the swallowing function per
reflex features in a natural setting (e.g., bedside) could provide additional information for assessing dysphagia amongst head and neck cancer patients with RAD.

6 | LIMITATIONS AND FUTURE DIRECTIONS

Although there is an increasing interest in cough testing in the field of dysphagia, cough investigation is minimal in head and neck cancer patients with RAD. Cough terminology and typing applicable in a RAD framework are lacking. Perceptual ratings of cough efficiency during a clinical swallowing evaluation show low rater agreement. Regarding objective measures, the literature mainly focuses on the assessment of voluntary coughs to predict the risk of aspiration. However, HNC-patients treated with CCRT are at risk of silent aspiration. Silent aspirations in this population may occur in up to 83% of the patients and may lead to death in up to one-third of them. Aspirations cannot be reliably predicted by voluntary coughs. Furthermore, the gold standard for assessing coughing objectively is the instrumental recording of airflow data via a facemask or pipe connected to a digital spirometer. Airflow rate recordings require a piece of equipment that is impractical for routine bedside clinical assessment. This impracticality interferes with daily life assessment, that is, the obtainment of biomarkers during swallowing or meal consumption. Also, research on cough sounds in the framework of dysphagia is infrequent and has not reported conclusive results yet. Therefore, innovative methods allowing for the detection of cough reflex features in a natural setting (e.g., bedside) could provide additional information regarding RAD.

7 | CONCLUSIONS

Studies focusing on objective cough features are scarce, particularly in HNC-patients with RAD. These patients may suffer from sensory deterioration, including an ineffective cough reflex, up to several years after treatment. This may lead to silent aspiration-related pneumonia that can be fatal for a significant number of patients. Automatic or semi-automatic cough sound analysis is a growing line of research that has provided valid measurements, particularly for assessing respiratory diseases. Despite scarce literature regarding cough features in the framework of dysphagia, exploring cough sounds might represent an alternative assessment method in HNC-patients with RAD. Such a method is easily implementable in daily life and could provide novel information regarding these patients. To our knowledge, voluntary and reflexive acoustic cough features in HNC-patients with RAD have never been explored. Hence, research focusing on acoustic cough-related features should be considered for tracking dysphagia and/or aspiration in HNC-patients with RAD.

ACKNOWLEDGEMENTS

This work has been supported by Les Amis de Bordet.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHORS’ CONTRIBUTIONS

All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization, S.M.B., G.V.N., J.S., M.D.B., D.V.G.; Methodology, F.M.L.; Writing - Original Draft, S.M.B., G.V.N., J.S., D.V.G.; Writing - Review & Editing, S.M.B., G.V.N., J.S., M.D.B., T.D., A.D., N.R., D.V.G.; Supervision, G.V.N., J.S., D.V.G., M.D.B.

ETHICAL STATEMENT

Not applicable.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

ORCID

Sofiana Mootassim-Billah https://orcid.org/0000-0003-4917-7360

REFERENCES

1. Awad MJ, Mohamed AS R, Lewin JS, Baron CA, Gunn GB, Rosenthal DI, Holsinger FC, Schwartz DS, Fuller CD, Hutcheson KA. Late Radiation-Associated Dysphagia (Late-RAD) with Lower Cranial Neuropathy after Oropharyngeal Radiotherapy: A Preliminary Dosimetric Comparison. Oral Oncol. 2014;50(8):746-754.
2. Rosenthal DI, Lewin JS, Eisbruch A. Prevention and Treatment of Dysphagia and Aspiration After Chemoradiation for Head and Neck Cancer. Journal of Clinical Oncology. 2006;24(17):2636-2643.
3. Watts SA, Tabor L, Plowman EK. To cough or not to cough? Examining the potential utility of cough testing in the clinical evaluation of swallowing. Curr Phys Med Rehabil Rep. 2016;4(4):262-276.
4. Rinkel RN, Leeuw IMV, Doornaert P, Rene C. Prevalence of swallowing and speech problems in daily life after chemoradiation for head and neck cancer based on cut-off scores of the patient-reported outcome measures SWAL-QOL and SHI. Eur Arch Otorhinolaryngol. 2016;273:1849-1855.
5. Silveira MH, Dedivitis RA. Quality of life in swallowing disorders after nonsurgical treatment for head and neck cancer. Int Arch Otorhinolaryngol. 2015;19:46-54.
6. Kraaijenga SAC, van der Molen L, Jacobi I, Hamming-Vriese O, Hilgers FJM, van den Brekel MWM. Prospective clinical study on long-term swallowing function and voice quality in advanced head and neck cancer patients treated with concurrent chemoradiotherapy and preventive swallowing exercises. Eur Arch Oto-Rhino-Laryngol. 2015;272(11):3521-3531.
7. Langendijk JA, Doornaert P, Leeuw IMV, Leemans CR, Aaronsen NK, Slotman BJ. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. J Clin Oncol. 2008;26(22):3770-3776.
8. Nguyen NP, Moltz CC, Franck C, et al. Effectiveness of the cough reflex in patients with aspiration following radiation for head and neck cancer. Lung. 2007;185:243-248.
9. Hammond CS. Cough and aspiration of food and liquids due to oral pharyngeal. Dysphagia. 2008;18:35-40.
10. Madhavan A, Carnaby GD, Crary MA. ‘Food sticking in my throat’: video fluoroscopic evaluation of a common symptom.
chemoradiation for head and neck cancer. *Radiother Oncol.* 2006;81:143-150.

29. Kwon M, Kim S-A, Roh J-L, et al. An introduction to a head and neck cancer-specific frailty index and its clinical implications in elderly patients: a prospective observational study focusing on respiratory and swallowing functions. *Oncologist.* 2016;21:1091-1098.

30. Garon BR, Sierantz T, Ormiston C. Reproduced with permission of the copyright owner. Further reproduction prohibited without. *J Neurosci Nurs.* 2009;41(4):178-187. https://doi.org/10.1016/j.jnecn.2012.05.050.

31. Hunter KJ, Lee OE, Lyden TH, et al. Aspiration pneumonia after chemo - intensity-modulated radiation therapy of oropharyngeal carcinoma and its clinical and dysphagia-related predictors. *Head Neck.* 2014;36:120-125.

32. Jagtap M. Swallowing skills and aspiration risk following treatment of head and neck cancers. *Indian J Surg Oncol.* 2019;10(2):402-405.

33. Ng LKY, Lee KYS, Chiu SN, Ku PKM, Van Hasselt CA, Tong MCF. Silent aspiration and swallowing physiology after radiotherapy in patients with nasopharyngeal carcinoma. *Head Neck.* 2011;33(9):1335-1339.

34. Mortensen HR, Jensen K, Grau C, Mortensen HR, Jensen K, Grau CAI. Aspiration pneumonia in patients treated with radiotherapy for head and neck cancer. *Acta Oncol.* 2013;52:270-276.

35. Hedström J, Finizia C, Olsson C. Correlations between patient-reported dysphagia screening and penetration – aspiration scores in head and neck cancer patients post-oncological treatment. *Dysphagia.* 2018;33:206-215.

36. Christianen MEM, Leeuw IMV, Doornaert P, et al. Patterns of long-term swallowing dysfunction after definitive radiotherapy or chemoradiation. *Radiother Oncol.* 2015;117(1):139-144. https://doi.org/10.1016/j.radonc.2015.07.042.

37. Abe H, Tsubahara A. Observation of arytenoid movement during laryngeal elevation using videodeposcopic evaluation of swallowing. *Dysphagia.* 2011;26:150-154.

38. Schultheiss C, Nusser-Müller-Busch R, Seidl RO. The semisolid bolus penetration-aspiration scale. *Head Neck Radiother.* 2015;115(1):56-62. https://doi.org/10.1016/j.radonc.2015.07.042.

39. Yoon JA, Kim SH, Jang MH, Kim S, Shin YB. Correlations between patient-reported dysphagia screening and penetration – aspiration scores for fiberoptic endoscopic evaluation of swallowing. *Dysphagia.* 2014;29:223-233.

40. Carrol TL. Chronic Cough. San Diego: Plural Publishing; 2019.

41. Yoon JA, Kim SH, Jang MH, Kim S, Shin YB. Correlations between aspiratory and pharyngeal residue scale scores for fiberoptic endoscopic evaluation and videofluoroscopy. *Yonsei Med J.* 2019;60(12):1118-1186.

42. O’Hor JC. Rogus-pulia N, Garcia-arguello L, Robbins J, Safdar N. Bedside diagnosis of dysphagia: a systematic review. *J Hosp Med.* 2015;10(4):256-265.

43. Leder SB, Espinosa IF. Aspiration risk after acute stroke: comparison of clinical examination and Fiberoptic endoscopic evaluation of swallowing. *Dysphagia.* 2002;17:214-218.

44. Laciuga H, Brandonme AE. Troche MS, Hegland KW. Analysis of clinicians’ perceptual cough evaluation. *Dysphagia.* 2016;31(4):521-530.

45. Mazzoni SB, Canning BJ. Synergistic interactions between airway afferent nerve subtypes mediating reflex bronchospasm in guinea pigs. *Am J Physiol Integr Compar Physiol.* 2002;283:R86-98.

46. Janssens T, Brepoels S, Dupont L, Van Den BO. The impact of harm-fulness information on citric acid induced cough and urge-to-cough. *Pulm Pharmacol Ther.* 2015;31:9-14. https://doi.org/10.1016/j.pupt.2015.01.002.

47. Morice AH, Fontana GA, Belvisi MG, et al. ERS guidelines on the assessment of cough. *Eur Respir J.* 2007;29:1256-1276.

48. Crooks MG, Den Brinker A, Hayman Y, et al. Continuous cough monitoring using ambient sound recording during convalescence from a COPD exacerbation. *Lung.* 2017;195(3):289-294.
48. Waito A, Bailey GL, Molfenter SM, Steele CM. Voice-quality abnormalities as a sign of dysphagia: validation against acoustic and videofluoroscopic data. *Dysphagia*. 2011;26:125-134.

49. Vertigan AE, Gibson PG. *Speech Pathology Management of Chronic Refractory Cough and Related Disorders*. Oxford: Comptin Publishing; 2016.

50. Troche MS, Schumann B, Brandimore AE, Okun MS, Hegland KW. Reflex cough and disease duration as predictors of swallowing dysfunction in Parkinson’s disease. *Dysphagia*. 2016;31(6):757-764.

51. Widdicombe J, Fontana G. Cough: what’s in a name? *Eur Respir J*. 2006;28(1):10-15.

52. McGarvey L, McKeagney P, Polley L, MacMahon J, Costello RW. Are there clinical features of a sensitized cough reflex? *Pulm Pharmacol Ther*. 2009;22(2):59-64. https://doi.org/10.1016/j.pupt.2008.11.003.

53. Davenport PW. Urge-to-cough: what can it teach us about cough? *Thorax*. 2007:62:329-334.

54. Davenport PW. Cough sound analysis to identify respiratory infection in pigs. *Comput Electron Agric*. 2008:64:318-325.

55. Vertigan AE, Gibson PG. Speech Pathology Management of Chronic Refractory Cough and Related Disorders. Oxford: Comptin Publishing; 2016.

56. McGarvey L, McKeagney P, Polley L, MacMahon J, Costello RW. Are there clinical features of a sensitized cough reflex? *Pulm Pharmacol Ther*. 2009;22(2):59-64. https://doi.org/10.1016/j.pupt.2008.11.003.

57. Polverino M, Polverino F, Fasolino M, Andò F, Alfieri A, De Blasio F. Are there clinical features of a sensitized cough reflex? *Thorax*. 2007.62:329-334.

58. Vertigan AE, Gibson PG. *Speech Pathology Management of Chronic Refractory Cough and Related Disorders*. Oxford: Comptin Publishing; 2016.

59. Polverino M, Polverino F, Fasolino M, Andò F, Alfieri A, De Blasio F. Are there clinical features of a sensitized cough reflex? *Thorax*. 2007:62:329-334.

60. Lasserson D, Mills K, Arunachalam R, Polkey M, Moxham J, Kalra L. Comparison of voluntary and reflex cough effectiveness as a sign of dysphagia: validation against acoustic and videofluoroscopic data. *Dysphagia*. 2011;26:125-134.

61. Leconte S, Liistro G, Lebecque P, Degryse J. The objective assessment of cough following citric acid inhalation. *Thorax*. 2011;66:1226-1230. https://doi.org/10.1136/thoraxjnl-2011-200545.

62. Morice AH, Faruqi S, Wright CE, Zito M, Bennet JR, Huckabee M. Cough sound description in relation to respiratory diseases in dairy calves. *Prev Vet Med*. 2010;96:276-280. https://doi.org/10.1016/j.prevetmed.2010.06.013.

63. Smith J, Woodcock A. New developments in the objective assessment of cough. *Lung*. 2008:186(1):107-111.

64. McFarland DH, Harris B, Fortin AJ. Enhancing swallowing-respiration coordination. *Curr Phys Med Rehabil Rep*. 2018;6:239-244.

65. Widdicombe JG. *BRONCH OF THE CAT* from the Nuffield Institute for Medical Research, University of Oxford (1933) who distinguished deflation fibres and slowly adapting fibres excited by of rapidly adapting stretch fibres which they suggested were responsible for the H. J Physiol. 1954;123:71-104.

66. Canning BJ, Chang AB, Bolser DC, Smith JA, Mazzzone SB, McGarvey L. Anatomy and neurophysiology of cough CHEST guideline and expert panel report. *Chest*. 2014;146(6):1633-1648.

67. Perry SE, Miles A, Fink JN, Huckabee M. The dysphagia in stroke protocol reduces aspiration pneumonia in patients with dysphagia following acute stroke: a clinical audit. *Transf Stroke Res*. 2019;10:36-43.

68. Wheeler Hegland K, Troche MS, Brandimore AE, Davenport PW, Okun MS. Comparison of voluntary and reflex cough effectiveness in Parkinson’s disease. *Parkinsonism Relat Disord*. 2014;20(11):1226-1230. https://doi.org/10.1016/j.parkreldis.2014.09.010.

69. Smith JA, Aliverti A, Quaranta M, et al. Chest wall dynamics during voluntary and induced cough in healthy volunteers. *J Physiol*. 2012; 590(3):563-574.

70. Hegland KW, Troche MS, Davenport PW. Cough expired volume and airflow rates during sequential induced cough. *Front Physiol*. 2013;4:1-5.

71. Marsden PA, Smith JA, Kelsall AA, et al. A comparison of objective and subjective measures of cough in asthma. *J Allergy Clin Immunol*. 2008;122(5):903-907. https://doi.org/10.1016/j.jaci.2008.08.029.

72. Smith J, Owen E, Earis J, Woodcock A. Cough in COPD: correlation of objective monitoring with cough challenge and subjective assessments. *Chest*. 2006;130(2):379-385.

73. Decalmer SC, Webster D, Kelsall AA, Mcguinness K, Arthur A, Smith JA. Chronic cough: how do cough reflex sensitivity and subjective assessments correlate with objective cough counts during ambulatory monitoring? *Thorax*. 2007:62:329-334.

74. Ferrari S, Silva M, Guarino M, Marie J, Berckmans D. Cough sound analysis to identify respiratory infection in pigs. *Comput Electron Agric*. 2008:64:318-325.

75. Ferrari S, Piccinini R, Silva M, Exadaktylos V, Berckmans D, Guarino M. Cough sound description in relation to respiratory diseases in dairy calves. *Prev Vet Med*. 2010;96:276-280. https://doi.org/10.1016/j.prevetmed.2010.06.013.

76. Smith J, Woodcock A. New developments in the objective assessment of cough. *Lung*. 2008:186(Suppl 1):48-55.

77. Fontana GA, Widdicombe J. What is cough and what should be measured? *Pulm Pharmacol Ther*. 2007;20:307-312.

78. Id JZ, Zhao L, Gao X, Xu F. An advanced recording and analysis system for the differentiation of Guinea pig cough responses to citric acid and prostaglandin E 2 in real time. *PLoS One*. 2019;14:1-20. https://doi.org/10.1371/journal.pone.0217366.

79. Shi Y, Liu H, Wang Y, Cai M, Xu W. Review article theory and application of audio-based assessment of cough. *J Sensors*. 2018:1-10.

80. Chatzarrin H. Feature Extraction for the Differentiation of Dry and Wet Cough Sounds. Carleton University; 2011.

81. Xaviero P, Pramono A, Imitiaz SA, Rodriguez-villegas E. Automatic identification of cough events from acoustic signals. Paper presented at: 2019 41st Annu Int Conf IEEE Eng Med Biol Soc. 2019:217-220.

82. Fischer P, Gross V, Kroenig J, et al. Description of nighttime cough events in patients with stable COPD GOLD II–IV. *Int J COPD*. 2018;13:1071-1078.

83. Miranda IDS, Diacon AH, Niesler TR. A comparative study of features for acoustic cough detection using deep architectures. Paper presented at: 2019 41st Annu Int Conf IEEE Eng Med Biol Soc. 2019:2601-2605.

84. Smith JA, Ashford JR. Inter- and Intrajudge reliability of a clinical examination of cough following citric acid inhalation. *Thorax*. 2006;61(8):699-705.

85. Monroe MD, Manco K, Bennett R, Huckabee M. Citric acid cough reflex test: establishing normative data. *Speech, Lang Hear*. 2014;17 (4):216-224.

86. Monroe MD, Manco K, Bennett R, Huckabee M. Citric acid cough reflex test: establishing normative data. *Speech, Lang Hear*. 2014;17(4):216-224.

87. Monroe MD, Manco K, Bennett R, Huckabee M. Citric acid cough reflex test: establishing normative data. *Speech, Lang Hear*. 2014;17(4):216-224.

88. Monroe MD, Manco K, Bennett R, Huckabee M. Citric acid cough reflex test: establishing normative data. *Speech, Lang Hear*. 2014;17(4):216-224.

89. Monroe MD, Manco K, Bennett R, Huckabee M. Citric acid cough reflex test: establishing normative data. *Speech, Lang Hear*. 2014;17(4):216-224.

90. Monroe MD, Manco K, Bennett R, Huckabee M. Citric acid cough reflex test: establishing normative data. *Speech, Lang Hear*. 2014;17(4):216-224.
90. Groves-wright KJ, Boyce S, Kelchner L. Perception of wet vocal quality in identifying penetration/aspiration during swallowing. J Speech Lang Hear Res. 2010;53:620-633.

91. Ebihara S, Ebihara T, Kohzuki M. Effect of aging on cough and swallowing reflexes: implications for preventing aspiration pneumonia. Lung. 2012;190:29-33.

92. Tabor-gray LC, Gallestagui A, Vasilopoulos T, Plowman EK. Characteristics of impaired voluntary cough function in individuals with amyotrophic lateral sclerosis. Amyotroph Lateral Scler Front Degener. 2019;20(1-2):37-42.

93. Pitts T, Troche M, Mann G, Rosenbek J, Okun MS, Sapienza C. Characteristics of impaired voluntary cough function in individuals with amyotrophic lateral sclerosis. Amyotroph Lateral Scler Front Degener. 2019;20(1-2):37-42.

94. Hammond CAS, Goldstein LB, Homer RD, et al. Predicting aspiration in patients with. Chest. 2010;138:1426-1431. https://doi.org/10.1378/chest.10-0342.

95. Ebihara S, Ebihara T, Kohzuki M. Effect of aging on cough and swallowing reflexes: implications for preventing aspiration pneumonia. Lung. 2012;190:29-33.

96. Miles A, Moore S, McFarlane M, Lee F, Huckabee M. Comparative analysis of cervical auscultation signals and modern signal-processing techniques.

97. Sejdic E, Dudik JM, Kurosu A, Jestrovic I, Coyle JL. Understanding cervical auscultation sounds and swallowing function characteristics of impaired voluntary cough function in individuals with amyotrophic lateral sclerosis. Amyotroph Lateral Scler Front Degener. 2019;20(1-2):37-42.

98. Frakking TT, Chang AB, O’Grady KAF, Walker-Smith K, Weir KA. Cervical auscultation in the diagnosis of oropharyngeal aspiration in children: a study protocol for a randomised controlled trial. Trials. 2013;14(377):1-8.

99. Frakking TT, Chang AB, O’Grady KAF, Walker-Smith K, Weir KA. Cervical auscultation in the diagnosis of oropharyngeal aspiration in children: a study protocol for a randomised controlled trial. Trials. 2013;14(377):1-8.

100. Jayatilake D, Ueno T, Teramoto Y, et al. Smartphone-based real-time assessment of swallowing ability from the swallowing sound. IEEE J Trans Eng Heal Med. 2015;3:1-10. http://ieeexplore.ieee.org/servlet/opac?punumber=6221039&isnumber=6221039

101. Dudik JM, Coyle JL, Sejdic E. Dysphagia screening: contributions of cervical auscultation signals and mobile cough strength evaluation device using cough sounds. Sensors. 2018;18(3810):1-13.

102. Yagi N, Nagami S, Lin M-K, et al. A noninvasive swallowing measurement system using a combination of respiratory flow, swallowing sound, and laryngeal motion. Med Biol Eng Comput. 2017;55(6):1001-1017.

103. Borr C, Helscher-Fastabend M, Lücking A. Reliability and validity of cervical auscultation. Dysphagia. 2007;22(3):225-234.

104. Dörr C, Jestrovic I, Luan B, Coyle JL, Sejdic E. A comparative analysis of swallowing accelerometry and sounds during saliva swallows. Biomed Eng Online. 2015;14(3):1-15.

105. Frakking TT, Chang AB, O’Grady KAF, Walker-Smith K, Weir KA. Cervical auscultation in the diagnosis of oropharyngeal aspiration in children: a study protocol for a randomised controlled trial. Trials. 2013;14(377):1-8.

106. Frakking TT, Chang AB, O’Grady KAF, Walker-Smith K, Weir KA. Cervical auscultation in the diagnosis of oropharyngeal aspiration in children: a study protocol for a randomised controlled trial. Trials. 2013;14(377):1-8.

107. Leslie P, Drinnan MJ, Zammit-Maempel I, Coyle JL, Ford GA, Wilson JA. Cervical auscultation synchronized with images from endoscopy swallow evaluations. Dysphagia. 2007;22(4):290-298.

108. Stroud AE, Lawrie BW, Wiles CM. Inter and intra-rater reliability of cervical auscultation to detect aspiration in patients with dysphagia. Clin Rehabil. 2002;16(6):640-645.

109. Nozue S, Itaha Y, Takahashi K, et al. Accuracy of cervical auscultation in detecting the presence of material in the airway. Clin Exp Dent Res. 2017;3(6):209-214.

110. Leslie P, Drinnan MJ, Finn P, Ford GA, Wilson JA. Reliability and validity of cervical auscultation: a controlled comparison using videofluoroscopy. Dysphagia. 2004;19(4):231-240.

111. Umayahara Y, Soh Z, Sekikawa K, Kawae T, Otsuka A, Tsuji T. Clinical significance of cough peak flow and its non-contact measurement via cough sounds. Appl Sci. 2020;10(2782):1-12.

112. Umayahara Y, Soh Z, Sekikawa K, Kawae T, Otsuka A, Tsuji T. A mobile cough strength evaluation device using cough sounds. Sensors. 2018;18(3810):1-13.

113. Umayahara Y, Soh Z, Sekikawa K, Kawae T, Otsuka A, Tsuji T. Estimation of cough peak flow using cough sounds. Sensors. 2018;18(2381):1-13.

How to cite this article: Mootassim-Billah S, Van Nuffelen G, Schoentgen J, et al. Assessment of cough in head and neck cancer patients at risk for dysphagia—An overview. Cancer Reports. 2021;e1395. https://doi.org/10.1002/cnr2.1395