The Changes in Pharyngeal Constrictor Muscles Related to Head and Neck Radiotherapy: A Systematic Review

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Abstract
It is well known that radiation damage of the pharyngeal constrictor muscles, the glottic larynx, and the supraglottic larynx may lead to dysphagia, an unwanted effect of head and neck radiotherapy. The reduction of radiotherapy-induced dysphagia might be achieved by adaptive radiotherapy. Although the number of studies concerning adaptive radiotherapy of head and neck cancer is continuously increasing, there are only a few studies concerning changes in dysphagia-related structures during radiotherapy. The goal of this review is to summarize the current knowledge about volumetric, dosimetric, and other changes of the pharyngeal constrictor muscles associated with head and neck radiotherapy. A literature search was performed in the MEDLINE database according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The conclusions of 8 studies that passed the criteria indicate a significant increase in the volume and the thickness of the pharyngeal constrictor muscles during radiotherapy. Moreover, the changes in magnetic resonance imaging signal intensity of the pharyngeal constrictor muscles correlate with the absorbed dose (typically higher than 50 Gy) and also with the grade of dysphagia. This systematic review presents 2 variables, which are suitable for estimation of radiotherapy-related pharyngeal constrictor muscles changes—magnetic resonance imaging signal intensity and the thickness. In the case of the thickness, there is no consensus in the level of the measurement—C2 vertebra, C3 vertebra, and the middle of the craniocaudal axis are used. It seems that reference to a position associated with a vertebral body could be more reproducible and beneficial for future research. Although late pharyngeal toxicity remains a challenge in head and neck cancer treatment, better knowledge of radiotherapy-related changes in the pharyngeal constrictor muscles contributes to adaptive radiotherapy development and thus improves the treatment results.

Keywords
radiotherapy, head and neck cancer, pharyngeal muscles, pharyngeal constrictors, dysphagia

Abbreviations
ART, adaptive radiotherapy; BF, blood flow; BV, blood volume; CBCT, cone-beam computed tomography; CP, capillary permeability; CT, computed tomography; IGRT, image-guided RT; IMRT, intensity-modulated radiotherapy; MRI, magnetic resonance imaging; PCM, pharyngeal constrictor muscles; RT, radiotherapy; VMAT, volumetric modulated arc therapy; V50, volume of PCM receiving more than 50 Gy

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Introduction
Radiation-induced dysphagia is one of the side effects of head and neck radiotherapy (RT) or chemo-RT, responsible for a change in the type of diet, prolongation of meal times,1,2 or even a need for tube feeding.3 These consequences have a strong negative impact on the patient’s quality of life. Dysphagia is possibly the most severe acute and late toxicity for

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patients with oropharyngeal cancer treated by chemo-RT. Consistently, Hunter et al. concluded that reduced quality of life after treatment correlates closely with the development of dysphagia. Moreover, Machta et al. reported that 43% of patients in remission suffer from dysphagia grade. Although other toxicities such as xerostomia have been reduced significantly by developments in RT techniques in recent decades, dysphagia remains a challenge for radiation oncologists.

Radiotherapy is a primary modality in head and neck cancer treatment. New RT techniques such as intensity-modulated RT (IMRT), volumetric modulated arc therapy (VMAT), and image-guided RT (IGRT) for head and neck cancer have 2 main goals: the delivery of a curative dose to the tumor and the sparing of healthy tissues. Intensity-modulated RT has enabled dose escalation to the tumor by steep dose gradients between the target volume and healthy tissue. The use of VMAT has led to more homogeneous tumor coverage and more efficient normal tissue sparing. The development of IGRT, especially daily cone-beam computed tomography (CBCT), has increased interfraction accuracy and shows geometrical and anatomical variations during the treatment. Adaptive RT (ART) as the next logical step in RT progress may achieve an additional reduction of dose to the organs at risk and may reduce the toxicity of the treatment and thus improve quality of life. The goal of ART is the modification of treatment in response to the tumor and the organs at risk using online or offline corrections of the treatment plans. However, the potential of ART remains much untapped. The tissue changes and biological responses need to be thoroughly investigated for the effective implementation of ART.

It is evident that dysphagia can only be reduced after identifying all the structures which should be spared. Swallowing is a complex process, in which many anatomical structures participate: 30 pairs of muscles, 6 cranial nerves, and others. Patients with RT-induced dysphagia have decreased pharyngeal peristalsis and poor synchronization between pharyngeal constrictor muscles (PCM) and other abnormalities. It seems that RT-induced damage of the PCM, the glottic larynx, and the supraglottic larynx contributes to the development of dysphagia. Various planning studies have confirmed a strong relationship between dose in swallowing structures mentioned above and dysphagia incidence. Nevertheless, according to Duprez et al., the most important structures associated with late swallowing disturbances are PCM because their mean dose is the most demonstrative predictor of dysphagia. Currently, a phase III randomized study of dysphagia optimized IMRT versus standard IMRT in head and neck cancer is launched, and the results will probably show us the importance of swallowing structures sparing.

Both the tumor and all organs at risk undergo volumetric changes during treatment. Volumetric, dosimetric, and other changes in the parotid glands have been documented in numerous studies. Most of them reported anatomic and dosimetric changes in the parotid glands associated with the incidence of xerostomia. Castelli et al. published a systematic review focused on ART for head and neck cancer in October 2018, including 29 studies, 11 of which reported benefits of ART, providing either a dosimetric or clinical result. However, none of these studies was engaged with the reduction of dysphagia. A few studies showing the changes in dysphagia-related structures during RT have been published. Thus, the goal of this review is to summarize them along with the current knowledge of volumetric, dosimetric, and other changes of PCM related to head and neck RT.

Materials and Methods

Search Strategy

The search of the articles included in this review (Figure 1) was performed in the MEDLINE database according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The following keywords were used: ((pharyngeal constrictor muscles) OR (pharyngeal constrictors)) AND (radiotherapy) AND (head and neck). The search was completed in January 2019. As the review focused only on this topic has not yet been published, the search duration was not restricted; 58 results were found in the MEDLINE database, and 28 records were identified in references (of which 23 were duplicates). In total, 63 articles were reviewed.

Selection Criteria and Data Synthesis

The articles had to be in accordance with the following criteria in order to be included in this review: (1) describing anatomical, dosimetric, or other changes of PCM related to RT, (2) to be written in English, and (3) to be available in full-text form. To avoid biasing the outcome of this review, no other criteria such as “only statistically significant findings” were added. Two reviewers reviewed the search results independently and agreed on the following data extraction.

In all, 47 articles were excluded because they were dealing with another topic: contouring (6), imaging (3), treatment planning (7), and toxicity of treatment (31). Furthermore, 2 clinical investigations reported anatomical changes but unfortunately did not mention PCM (also excluded). Another 4 studies were written in a language other than English, and 2 articles not relating to RT were not included. In total, 55 reviewed records did not meet the criteria for inclusion. The following studies were found appropriate for this review: 4 articles report anatomical changes (2 of them report dosimetric changes as well), 3 articles deal with magnetic resonance imaging (MRI) signal changes, and 1 study is focused on computed tomography (CT) perfusion changes (Table 1). The risk of bias was assessed according to the Cochrane Handbook for Systematic reviews (Table 1). Although the majority of the articles did not achieve high scoring, they were all included in our study due to the
critically low number of publications focused on the given topic so far.

**Results**

**Anatomical Changes of PCM During RT**

Ricchetti et al\(^{40}\) reported a statistically significant increase in the volume of PCM in 91.6% of analyzed patients treated by chemo-RT (CBCT weekly). The mean volume growth (± standard deviation) of PCM was 0.7 ± 0.9 cm\(^3\) (4.8% ± 6.3%) during the first week. The highest volume increase was measured in the seventh week as 2.5 ± 2.9 cm\(^3\) (16.9% ± 18.9%).

Kumarasiri et al\(^{41}\) analyzed the volume and thickness of PCM at the center of the C3 vertebral body during treatment (CBCT daily, measured on every fifth CBCT). The authors measured the mean volume increase in PCM as 11.9 ± 7.6 cm\(^3\) (54% ± 33%) over the treatment course. The thickness increased by 2.9 ± 1.9 mm (63 ± 39%) as well (Table 2).

Eisbruch et al\(^{42}\) evaluated PCM changes using several techniques, including endoscopy and CT. All patients were scanned by CT pre-RT and 3 months post-RT. Thickness of PCM was measured on both CT scans. The thickness of the PCM was measured at the center of the C2 vertebral body. The cohort of patients was divided into 2 groups according to gemcitabine dose levels. The group at the higher dose (50-150 mg/m\(^2\)) possessed a median pre-RT constrictor thickness of 2.5 mm and a median post-RT thickness of 7 mm (Table 2). The group at the lower gemcitabine dose (10 mg/m\(^2\)) showed no statistically significant difference in PCM thickness between pre-RT and post-RT CT scans.

Popovtzer et al\(^{43}\) measured the thickness of PCM in the middle of their craniocaudal axis. The PCM thickness significantly increased from 2.9 ± 0.9 mm pre-RT to 5.4 ± 1.5 mm, 3 months post-RT. The increase in thickness was more pronounced in muscles receiving >50 Gy (Table 2).

**Doses Received by PCM and Associated Functional Changes**

Ricchetti et al\(^{40}\) reported the mean dose to PCM as 61.7 ± 4.3 Gy due to the lack of sparing at the planning (Table 3). At a median follow-up of 13.0 months, 5 from 26 patients were still percutaneous endoscopic gastrostomy-tube dependent. The authors stated that 23% of patients reported dysphagia and a weight loss >10% and estimated that the changes were probably caused by inflammation or edema.

Kumarasiri et al\(^{41}\) calculated the dose of the day for all fractions to estimate the delivered dose to PCM. The mean cumulative dose to the PCM was 63.2 ± 4.7 Gy, which was 0.9 ± 0. Gy (1.4% ± 1.3%) more than planned (Table 3). A strong correlation between the PCM changes mentioned above and the mean dose to PCM was found. Unexpectedly, mid-course adaptive replanning showed only a small decrease in mean dose to PCM, and the authors assumed it to be not large enough to influence clinical outcomes. Regrettably, no relationship between toxicity and dose or changes of PCM was published in this article. It is unclear if more frequent replanning would provide better results.

Eisbruch et al\(^{42}\) also described the results of endoscopies 3 months post-RT. Strictures involving the inferior PCM at the postcriocoid level were identified in 7 of 22 cases. In 3 of these
Table 1. Studies Included in This Review and Risk Assessment of Individual Studies According To Higgins and Green.39

| Author               | No. of patients | Site                        | Prescribed dose | Modality                          | PCM’s parameters                  | Study method                                      | SG | AC | BP | IO | SO | OS |
|----------------------|-----------------|-----------------------------|-----------------|-----------------------------------|------------------------------------|---------------------------------------------------|-----|-----|-----|-----|-----|-----|
| Ricchetti et al40     | 26              | Oropharynx                  | 70 Gy           | kV CT weekly                      | Volume, mean dose                  | Prospective pilot study, consecutive patients     | +  | ?  | ?  | –  | ?  | ?  |
| Kumarasiri et al41    | 23              | Oropharynx                  | 60-70 Gy        | CBCT daily                        | Volume, thickness, mean dose       | Retrospective analysis                           | ?  | ?  | ?  | +  | ?  | ?  |
| Duffy et al44         | 5               | More sites                  | 60-70 Gy        | CBCT weekly                       | Volume, mean dose, V50 Thickness   | Retrospective analysis                           | –  | ?  | ?  | +  | ?  | ?  |
| Eisbruch et al42      | 29              | Base of tongue, larynx, tonsil, hypopharynx | 70 Gy | Endoscopy (3 months after), kV CT (pre, 3 months after) | Thickness                          | Trial phase I, consecutive patients               | +  | ?  | ?  | –  | ?  | ?  |
| Popovtzer et al43     | 12              | Tonsil, base of tongue, unknown, nasopharynx, hypopharynx | 70 Gy | MRI (before and 3 months after) | Signal intensity, mean dose, thickness | Prospective pilot study                           | ?  | ?  | ?  | –  | ?  | ?  |
| Meheissen et al45     | 46              | Oropharynx                  | 70 Gy           | MRI (before, mid, after)          | Signal intensity                   | Randomized trial phase II/III                     | +  | –  | –  | +  | ?  | +  |
| Messer et al46        | 72              | Nasopharynx                 | 70 Gy           | MRI (before, early after, follow up) | Signal intensity, mean dose        | Retrospective analysis                           | –  | ?  | ?  | +  | ?  | ?  |
| Minh Tam Truong et al47| 15             | Nasopharynx, oropharynx, hypopharynx, other | 70 Gy | CT (second, fourth, sixth week and 6 weeks after) | Blood flow, blood volume, mean transit time, capillary permeability | Prospective single arm study                     | ?  | ?  | ?  | –  | ?  | ?  |

Abbreviations: AC, allocation concealment; BP, blinding of participants, personnel, and outcome; CBCT, cone-beam computed tomography; CT, computed tomography; kV CT, kilovolt computed tomography; IO, incomplete outcome data; MRI, magnetic resonance imaging; OS, other sources of bias; PCM, pharyngeal constrictor muscles; SG, sequence generation; SO, selective outcome reporting; V50, volume of the PCM receiving more than 50 Gy.
Table 2. The Thickness of Pharyngeal Constrictor Muscles.

| Author             | Slice of measurement           | Group of patients | PCM thickness, mm |
|--------------------|--------------------------------|------------------|------------------|
| Kumarasiri et al   | Center of the C3               | All patients     | Pre-RT | Post-RT | 3 Months post-RT |
| Eisbruch et al     | Center of the C2               | Gemcitabine (50-150 mg/m²) | 4.3 ± 0.7 | 6.9 ± 1.6 |
| Popovtzer et al    | Middle of the craniocaudal     | All patients     | 2.5 (range, 1-5) | No difference between the pre-RT and post-RT |
|                    | axis of PCM                    | PCM mean dose < 50 Gy | 2.9 ± 0.9 | 5.4 ± 1.5 |
|                    |                                | PCM mean dose >50 Gy | 3.3 ± 1.0 | 5.3 ± 1.7 |
|                    |                                |                  | 2.7 ± 0.8 | 5.7 ± 1.4 |

Abbreviations: PCM, pharyngeal constrictor muscles; RT, radiotherapy.

Table 3. Mean Doses of Pharyngeal Constrictor Muscles Reviewed in This Study.

| Author             | PCM mean dose, Gy | Note                                      |
|--------------------|------------------|-------------------------------------------|
| Ricchetti et al    | 61.7 ± 4.3       | Cumulative after recalculation—63.2 Gy    |
| Kumarasiri et al   | 62.3             | Superior PCM 59 ± 13 Gy, middle PCM 56 ± 15 Gy, inferior PCM 41 ± 22 Gy |
| Duffy et al        | 37.12            | Cumulative after recalculation—37.83 Gy   |
| Popovtzer et al    | 52 ± 18          | Superior PCM                               |
| Messer et al       | 62.4 ± 8.7       | Superior PCM                               |
| Meheissen et al    | 65               | Deducted from the chart                    |

Abbreviation: PCM, pharyngeal constrictor muscles.

7 cases, the stricture volume received 70 Gy. The lowest dose to most PCM causing stricture was 50 Gy.

Duffy et al recalculated the original plan on weekly performed CBCTs. The PCM mean dose and the volume of PCM receiving more than 50 Gy (V50) were compared against the original plan. They described a statistically significant decrease in V50, unfortunately, without quantification. The greatest decrease in V50 of PCM was described in the oropharyngeal case. The reference value of V50 was 9.30 cm³, while the recalculated V50 was 7.70 ± 0.51 cm³. Different results were obtained in the case of bilateral neck disease, where the mean dose to PCM increased. The reference mean dose was 33.50 Gy, while the recalculated mean dose was 36.50 ± 0.41 Gy. The authors linked this change to nonpredictable differences in laryngeal position and neck flexion. Any toxicity information is missing in this article.

Popovtzer et al reported doses to the superior, middle, and inferior PCM as 59 ± 13 Gy, 56 ± 15 Gy, and 41 ± 22 Gy, respectively (Table 3). All the PCM received 52 ± 18 Gy in total. From the cohort of 12 patients, at 3 months post-RT, 2 patients whose PCM received mean doses >60 Gy were gastric tube-dependent, 2 other patients required liquid food, and 8 patients had no or mild dysphagia.

Meheissen et al evaluated doses in PCM only in a chart available in Supplement data. It seems that PCM received doses from 45 to 72 Gy with the mean dose of approximately 65 Gy (Table 3). The authors provided detailed information about dysphagia distribution pre-RT “and post-RT (median follow-up was 7.8 months): 54% patients grade 0, 39% grade 1, 7% grade 2, 0% grade >2 at pre-RT; 17% grade 0, 44% grade 1, 27% grade 2, and 12% grade 3 at post-RT.

Messer et al described the mean dose to the superior PCM as 62.4 ± 8.7 Gy (Table 3) without any reference to dysphagia or another side effect.

Non-negligible anatomic changes in PCM lead to the question: How does the delivered dose differ from the planned one? Several authors reported mean planned doses received by PCM (Table 3). Ricchetti et al, Kumarasiri et al, and Messer et al measured doses around 62 Gy, while Popovtzer et al measured 52 Gy and Duffy et al only 37 Gy. Besides, 2 studies dealt with recalculation of the PCM cumulative dose based on daily or weekly performed CBCT. Both of them reported only a slight discrepancy between planned and delivered doses.

**Magnetic Resonance Imaging Signal and CT Perfusion Parameter Changes**

Popovtzer et al measured and compared the signal intensities of the PCM in pre-RT and 3 months post-RT MRI scans. The signal in T1W scans decreased significantly in each of the 3 PCM (superior, middle, and inferior) receiving a dose higher than 50 Gy. No signal changes were observed in PCM with doses lower than 50 Gy. A significant increase in the T2W signal was described in PCM irradiated throughout the dose range (Table 4). The increase correlated linearly with dose.

Meheissen et al collected data from 3 MRIs at pre-RT, mid-RT, and post-RT. The MRI signal intensities in the superior and middle constrictors were evaluated in the same way as did Popovtzer et al. Percentage signal changes of each muscle were calculated for pre-RT, mid-RT, and post-RT scans. A significant increase in signal intensity in T1W with contrast
was discovered for the superior and middle PCM (Table 4). The T2W signal increase was significant only for the middle PCM. The received dose correlated weakly, albeit still significantly with both T1W with contrast and T2W signal changes for PCM. The percentage signal intensity change was significantly higher in the group of patients with radiation-induced dysphagia than in other patients. The strength of the association of MRI signal changes was calculated not only for the received dose but also for dysphagia grade. Patients with dysphagia grade >2 showed significantly higher changes in T2 signal intensity relative to patients with no or mild dysphagia.

Messer et al characterized MRI signal changes of the superior PCM. T1W and T2W MRI scans were obtained pre-RT, early post-RT, and late post-RT after treatment. The median time to post-RT and late post-RT was 4 months and 41 months, respectively. Data analysis showed the T1W signal decrease in the superior PCM, probably caused by late scarring and fibrosis (Table 3). Patients whose superior PCM received more than 62.25 Gy were associated with a significant fall of the T1W signal. Post-RT T2W scans revealed a signal increase associated with acute edema developed around the superior PCM. The signal at late post-RT on T2W scans had returned to the level at pre-RT. The dose–response relationship of the MRI signal change was obtained.

Not only MRI signal but also CT parameters can contribute to a better understanding of PCM alteration during RT and related dysphagia. Truong et al measured changes in CT perfusion parameters. The spot dose in the area of PCM perfusion measurement was 70 Gy. Patients underwent CT perfusion imaging 4 times in total (second, fourth, and sixth week during treatment, and 6 weeks after). The authors reported the development of dysphagia grade 3 in 7 of 15 patients and grade 0 to 2 in 8 patients during and after chemo-RT (grade 4 was not observed). In 7 patients, grades 1, 2, or 3 (2, 2, and 3 patients, respectively) were present as a baseline before treatment. The values of BF and BV increased substantially during the first 2 weeks of treatment in patients associated with dysphagia development. The CP decreased during chemo-RT relative to baseline in patients with dysphagia grade 3, whereas CP increased in patients with a lower grade. No trend was identified in mean transit time in relation to dysphagia.

**Discussion**

In this review, we summarized the current knowledge about volumetric, dosimetric, and other changes in PCM related to head and neck RT. In general, there are significant PCM volume and thickness alterations caused by inflammation and edema during RT. Moreover, other factors such as concurrent chemotherapy can contribute to PCM volume change, as demonstrated by Eisbruch et al. Furthermore, MRI signal changes are also commonly observed, and they correlate with dose, typically higher than 50 Gy. Importantly, it is not only the dose–response relationship that is associated with MRI changes but also the grade of dysphagia. Cumulative dose recalculation based on daily or weekly performed CBCT showed a slight discrepancy between the planned and delivered dose.

It is known that skeletal muscles are relatively resistant to RT. However, Eisbruch et al stated that evidence of fibrosis

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**Table 4. MRI Signal Intensity Changes.**

| Author          | Group of patients | Pre-RT  | Mid-RT   | Post-RT | 3 Months post-RT | Late post-RT |
|-----------------|-------------------|---------|----------|---------|-----------------|--------------|
| Popovtzer et al | All patients      | 0.87 ± 0.15 | 0.80 ± 0.19 |        |                 |              |
| PCM mean dose   | ≤ 50 Gy           | 0.85 ± 0.12 | 0.86 ± 0.16 |        |                 |              |
| PCM mean dose   | > 50 Gy           | 0.88 ± 0.16 | 0.77 ± 0.20 |        |                 |              |
| Messer et al    | All patients      | 1.5 ± 0.4  | 1.4 ± 0.4  |         |                 |              |
| PCM mean dose   | ≤ 62.25 Gy        | 1.3 ± 0.4  | 1.6 ± 0.4  |         |                 |              |
| PCM mean dose   | > 62.25 Gy        | 1.6 ± 0.4  | 1.3 ± 0.4  |         |                 |              |
| Popovtzer et al | All patients      | 0.62 ± 0.5  | 1.14 ± 0.9  |        |                 |              |
| PCM mean dose   | ≤ 50 Gy           | 0.42 ± 0.07 | 0.60 ± 0.18 |        |                 |              |
| PCM mean dose   | > 50 Gy           | 0.71 ± 0.57 | 1.38 ± 1.00 |        |                 |              |
| Meheissen et al | All patients      | 0.6 ± 0.8  | 0.9 ± 0.9  |         |                 |              |
| Messer et al    | All patients      | 0.48 ± 0.1  | 0.73 ± 0.2  |         | 0.52 ± 0.2      |              |
| PCM mean dose   | ≤ 62.25 Gy        | 0.48 ± 0.2  | 0.71 ± 0.2  |         |                 |              |
| PCM mean dose   | > 62.25 Gy        | 0.48 ± 0.1  | 0.74 ± 0.2  |         |                 |              |
| Meheissen et al | All patients      | 0.9 ± 1.2  | 1.4 ± 1.4  |         |                 |              |

Abbreviations: PCM, pharyngeal constrictor muscles; RT, radiotherapy.
of the submucosa and muscle layers of the esophagus and pharynx were shown in patients having RT-induced dysphagia. Pharyngeal constrictor muscles are located very close to the submucosa and are affected by submucosal inflammation by the increase in proinflammatory cytokines. The presence of the cytokines causes secondary edema and fibrosis of underlying muscles such as PCM. These findings could explain volumetric and other changes in PCM summarized in this review.

Although the number of studies concerning ART of head and neck cancer is continuously increasing, only a few studies have been published so far dealing with PCM changes and we tried to summarize them in this review. Each one is focused on a different aspect of volume increase after RT. On the other hand, the data regarding PCM changes are not contradictory, and the conclusions of individual studies support each other.

The greatest limitation of the studies included in this review is the low number of patients involved in the studies. Firstly due to low statistical significance and secondly due to increased heterogeneity of the cohort as most of the articles describe various treated sites with the different prescribed dose. Thus, the relation of PCM changes to the tumor location, and the dose is not obvious. For instance, Duffy et al described a significant decrease in V50 Gy but without quantification and, unfortunately, only on 5 patients with different tumor location. Another drawback of the currently available studies is the low methodological rigor stemming from incomplete information about patient selection, binding, and outcome data, or other sources of bias (Table 1).

Three of the 9 studies included in this review evaluated thickness changes of PCM during RT. Unfortunately, each team selected a different PCM level for its measurement: C2 vertebra, C3 vertebra, and the middle of the craniocaudal axis. It makes the mutual comparison of the results more demanding. It seems that reference to a position associated with a vertebral body could be more reproducible and less subjective than referring to the middle of the craniocaudal axis. That said, it would be beneficial to find a consensus for future research.

It is well known that MRI provides superior tissue contrast resolution and can detect soft tissue disease. Magnetic resonance imaging parameter that could assess post-RT dysphagia even before clinically apparent development would allow radiation oncologists to adjust the treatment and possibly reduce the risk of toxicity. Such a parameter could be useful, especially when the number of ART dedicated machines combining an MRI scanner and linear accelerator is currently increasing. Although both T1 and T2 signal intensity in PCM correlate with dose and grade of dysphagia, further research with a broader set of patients and better methodology is needed.

Recently, the clinical value of ART has been studied intensively. Although it is evident that substantial anatomic variations such as weight loss, tumor shrinkage, edema, or inflammation are a natural part of head and neck RT, it is still challenging to decide which patients should undergo adaptive replanning and how often. It has been shown that only 20% to 30% of head and neck patients should benefit from ART. Weekly replanning or only 1 early replanning session seems to be suitable ART methods for sparing the parotid glands for locally advanced head and neck patients. The advantage of ART for submandibular glands, oral cavity, and dysphagia-related structures has not yet been sufficiently explored.

Various factors influence tissue behavior during treatment, and many parameters can be monitored. Many radiation oncologists focus their efforts on searching for suitable ones, which could make the replanning strategy decision easier.

**Conclusion**

In summary, this systematic review presents 2 variables, which are suitable for estimation of RT-related PCM changes—PCM thickness measured at the C3 or C2 level and MRI signal intensity. The current literature indicates a significant increase in PCM volume and thickness during RT. In addition, PCM signal intensity changes in MRI scans correlate with the absorbed dose (typically higher than 50 Gy) and also with the grade of dysphagia. Although we assume that PCM changes and functional abnormalities are related to absorbed dose, a generally accepted relationship that has been described in detail is still missing. Obviously, further research in this field is needed. For example, it is still not clear which dosimetric parameter is the most appropriate for the estimation of the development of side effects such as dysphagia, aspiration, or nonoral feeding.

On the other hand, this review contributed to this field of research by a conclusion that PCM thickness and MRI signal intensity could be useful parameters for the estimation of the dysphagia development during or after head and neck RT.

In any case, late pharyngeal toxicity remains a challenge in ART. However, as collaborative research and funding in the field increase, advances that improve the treatment of head and neck cancer are expected to be rapid in the next decade.

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