

## The influence of radiotherapy on swallowing pressure: A study of 10 laryngeal carcinoma patients using high-resolution manometry

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Although dysphagia is a common complication after radiotherapy (RT) for head and neck cancer, its pathogenesis is not completely understood because the swallowing function is affected by complex factors. Appropriate swallowing pressure is an important factor in normal swallowing. When the radiation field includes the pharyngeal segment, intrabolus pressure may be affected. The purpose of this study is to examine the long-term influence of RT on swallowing pressure. Ten patients undergoing treatment for early-stage laryngeal squamous cell carcinoma were included in this study. Sufficient nutritional intake was maintained through oral feeding alone throughout the study period in all of the patients. A high-resolution manometry system with 36 circumferential sensors spaced 1 cm apart was positioned through the nose to record the maximum pressures at the mesopharynx, hypopharynx and the upper esophageal sphincter. The pressures were recorded before and at 6 and 12 months after treatment. There was no statistically significant chronological change in pressures either at meso-, hypopharynx or the upper esophageal sphincter. Even though radiation field includes a part of pharyngeal segment, intrabolus pressure was not found to be affected by the treatment. Despite the disadvantages of RT, the current study did not demonstrate RT had a quantitative influence on swallowing pressure. Further studies are required to clarify the relationship between pharyngeal pressure and the dysphagia induced by RT.

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### Introduction

Cancers of the head and neck account for approximately 5% of all malignancies. The role of concomitant chemoradiotherapy (CRT) in the management of head and neck cancer is currently being established.<sup>1</sup> Major advances in CRT have facilitated organ preservation therapy. Nevertheless, numerous studies have reported on the impairment of various physiological functions after CRT. Dysphagia, which causes weight loss, aspiration pneumonia, and increased meal time, is one of the most serious complications after CRT. A considerable number of patients who undergo CRT

depend on gastrostomy tube feeding for an extended period of time. Dysphagia can therefore be a factor that heavily impairs their quality of life. The pathogenesis of dysphagia after CRT for head and neck cancer is not thoroughly understood. Generally, appropriate pharyngeal pressure is recognized as an important factor in normal swallowing function. It involves both an active component, related to pharyngeal contraction, and a passive component, related to the upper esophageal sphincter (UES). We hypothesized that radiotherapy (RT) to the pharyngeal segment may cause poor pharyngeal contraction, resulting in insufficient pharyngeal pressure.

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To the best of our knowledge, no previous studies have evaluated the pharyngeal pressure changes after RT. In the present study, to clarify the influence of RT in swallowing pressure, we evaluated the pharyngeal pressure of patients following RT using high-resolution manometry (HRM), which can detect even small changes in pharyngeal contraction.

## Subjects and Methods

### Subjects

Ten patients with early-stage glottis cancer who undergoing RT were analyzed. To avoid potential biases caused by the side effects of RT, patients with xerostomia, pain, mucositis, and taste sensation were excluded from the present study. We also excluded patients with advanced cancer to avoid the influence of the volume of primary tumor, which may affect the swallowing function. All of the 10 patients were men (average age, 69 years; range, 56-88 years). The patients had no history of dysphagia, upper gastrointestinal tract surgery, or any other significant medical conditions. Seven patients had stage I (T1N0M0) cancer and only underwent RT. Three patients had stage II (T2N0M0) cancer and underwent RT combined with tegafur/gimeracil/otera-cil potassium. The size of the radiation field, which included part of the middle pharyngeal constrictor muscle and the entire inferior pharyngeal constrictor muscle, was 6 x 6 cm. All of the patients received a total radiation dose of 66 Gy in 33 fractions.

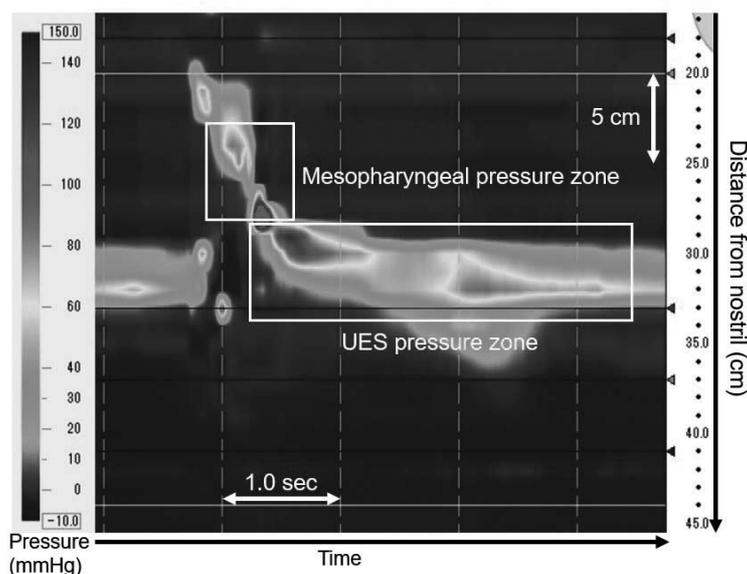
### Measurement Using High-resolution Manometry

A solid-state manometric assembly with 36 circumferential sensors spaced at 1-cm intervals and an exterior diameter of 4.2 mm was used. We have previously described the usage of the HRM system (Manoscan, Sierra Scientific Instruments, Inc, Los Angeles, California) in detail.<sup>2-6</sup>

### Protocol and Analysis

The patients underwent the transnasal placement of the manometric assembly in a natural supine position. Real-time pressure imaging during the insertion of the sensors enabled their accurate placement. The catheter was fixed in place with tape at the nostril. Examinees were asked to swallow 5ml of ice water three or four times, and the mean value of the maximum swallowing pressures were adopted. The parameters measured in this study included the maximum swallowing pressures at the mesopharynx and the UES (Figure 1). We conducted a retrospective analysis of the clinical data; the pressures recorded before and at 6 and 12 months after treatment, and their chronological changes were analyzed.

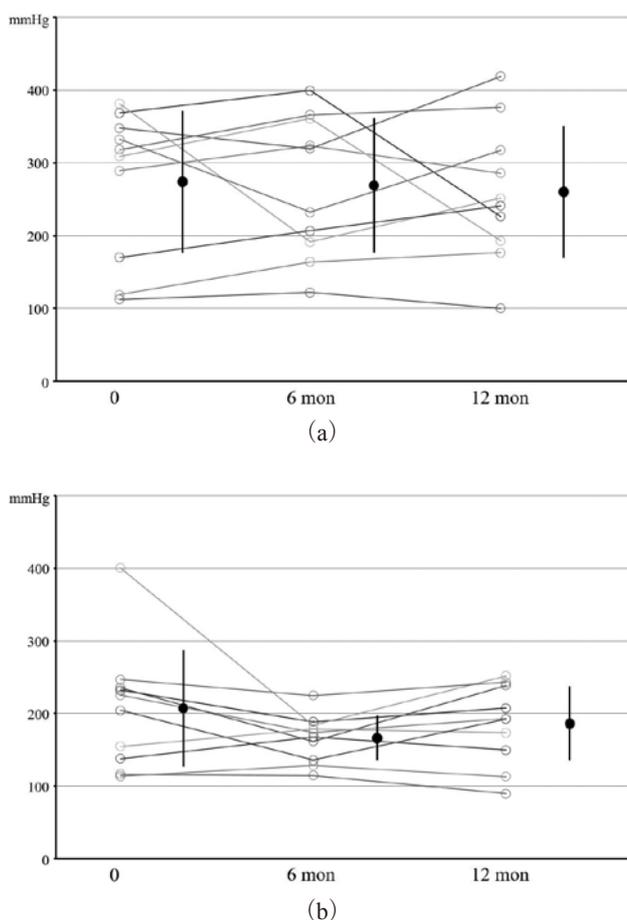
The manometric data were initially analyzed using the Mano View software program (Sierra Scientific Instruments Inc, Los Angeles, CA). A one-way analysis of variance (ANOVA) was used to compare the means among the groups. The study protocol was approved by the Institutional Review Board committee of Nagasaki University Hospital (approval number 15072759).



**Figure 1:** The typical graphic pattern during water swallowing. The two squares demonstrate the zones of pressure measurement.

## Results

All of the examinees maintained sufficient nutritional intake through oral feeding alone without any problems (including dysphagia) throughout the study period. All of the measurements are shown in Figure 2. The mean maximum pressure values in the mesopharynx before and at 6 and 12 months after treatment were  $274.9 \pm 102.0$ ,  $268.7 \pm 96.8$  and  $258.8 \pm 95.1$ , respectively. These values did not differ to a statistically significant extent in any of the three periods ( $F = 0.684$  and  $P = 0.934$ ). The mean maximum pressure values in the UES before and at 6 and 12 months after treatment were  $206.7 \pm 85.2$ ,  $165.8 \pm 32.4$  and  $185.2 \pm 54.7$ , respectively. Again, these values did not differ to a statistically significant extent in any of the three periods ( $F = 1.108$  and  $P=0.345$ ).



**Figure 2:** a) The maximum pressure values in the mesopharynx during water swallowing. b) The maximum pressure values in the UES during water swallowing. The pressures were recorded before (0), and at 6 months (6 mon) and 12 months (12 mon) after RT. The solid circles and bars indicate the mean values and standard deviations, respectively.

## Discussion

Xerostomia, pain, mucositis, taste sensation, and the volume of the primary tumor can affect the swallowing function of head and neck cancer patients undergoing RT. Langmore *et al.* reported that reduced oral intake during RT was associated with poor swallowing function after treatment.<sup>7</sup> Appropriate swallowing pressure is considered to be an important factor in normal swallowing function. We therefore attempted to analyze the changes in swallowing pressure before and after RT. This required a consistent and precise method for measuring swallowing pressure. Several new diagnostic techniques for swallowing disorders have become available in recent years. HRM, which we used in this study, is considered to be easier for the examiner to perform and interpret than conventional manometry. HRM enables various kinematics during swallowing to be observed and analyzed in detail.

Contrary to our hypothesis, no significant chronological changes were observed in the swallowing pressures after RT. The results may indicate that the small field and dose of radiation that are used to treat early-stage laryngeal squamous cell carcinoma may not have much effect on the pharyngeal pressure. Furthermore, these results seem to agree with the fact that all of the 10 patients were able to maintain sufficient oral intake throughout the study period without any particular difficulty. Various morphological changes that occur due to radiation exposure have been reported as possible pathophysiological mechanisms of radiation-induced swallowing dysfunction. In patients with oropharyngeal cancer, the severity of dysphagia is proportional to the dose of radiation to the geniohyoid muscles.<sup>8</sup> Radiation-induced dysphagia is also reported to be caused by the increase in the thickness of the pharyngeal constrictor muscles.<sup>9</sup> In the present study, however, none of the patients developed dysphagia to the extent that it caused problems in daily life. We hypothesize that radiation has little influence on the pharyngeal constrictor muscles in patients with early glottis cancer because the radiation field is smaller than used in the treatment of advanced head and neck cancers. Radiation-induced fibrosis is also known to be a serious late side effect of irradiation.<sup>10</sup> However, Tedla *et al.* reported that they found no significant quantitative increase in muscle fibrosis in the larynx after RT; however, they noted that there was a significant reduction in the number of muscle fibers in the larynx.<sup>11</sup> Given that all 10 patients were able to maintain sufficient oral food intake throughout the study period, it is possible that, in addition to the small area that was exposed to radiation during RT, the frequent use of the reduced swallowing

musculature might have prevented disuse atrophy of the laryngeal muscles, thereby helping to maintain pharyngeal constriction.

Twelve months may have been too short to observe the long-term influence of the RT on swallowing function and pressure; however, considering the ages of the patients, we were concerned about the possible influence of aging on the results if the observation period was too long.

In the future, the evaluation of pharyngeal pressure using HRM is expected to be a useful method for providing objective evidence on the possible pathophysiology associated with dysphagia after RT in patients with advanced head and neck cancer.

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Nothing

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