Investigation of the Optimal Mouthpiece Material for Proton Therapy of Head and Neck Cancer

Masaaki Suzuka
Hokkaido University https://orcid.org/0000-0003-3873-1776
Takashi Mori (tksh.mori@pop.med.hokudai.ac.jp)
Hokkaido University Hospital https://orcid.org/0000-0001-5246-215X
Shigeru Yamano
Hokkaido University
Akiko Takeuchi
Hokkaido University
Tomoka Shima
Hokkaido University
Koichi Yasuda
Hokkaido University
Yurika Kinoshita
Hokkaido University
Hideki Minatogawa
Hokkaido University
Yasuhiro Dekura
Hokkaido University
Masayoshi Tomita
Nikko memorial hospital
Hidefumi Aoyama
Hokkaido University
Kazuyuki Minowa
Hokkaido University

Research

Keywords: proton therapy, head and neck cancer, mouthpiece, CT value, temporary relining resin, vinyl polysiloxane, thermoplastic ethylene vinyl acetate copolymer splint

Posted Date: November 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1069769/v1

Abstract

Purpose: To investigate how the materials of mouthpieces used for proton therapy of head and neck cancer affect the dose distribution in surrounding normal tissue by focusing on the CT values of the materials.

Methods: Six dental materials were used to measure CT values: temporary relining resin, tissue conditioner, vinyl polysiloxane, thermoplastic ethylene vinyl acetate copolymer splint, silicone rubber impression material, and a composite impression material. Among these materials, three of the dental materials were investigated further: one material with the CT value closest to water, and the materials with the highest and lowest CT values. Based on these results, we investigated the effect of the CT value of the mouthpiece on the dose distribution in 17 cases in which a mouthpiece was used during proton therapy for head and neck cancers, the treatment plans were recalculated by changing the CT values of the mouthpiece to that of the three identified dental materials. For each cancer case, the irradiation dose to normal tissue was calculated for the treatment plans. The evaluation indices were set to the mandible max dose (GyE), the mandible mean dose (GyE), the volume of the mandible irradiated above 60 GyE (mandible V-60GyE), the parotid affected side mean dose (GyE), the parotid unaffected side mean dose (GyE), and the oral mean dose (GyE). The Wilcoxon's rank sum test was used to analyze the significance of the differences between treatment plans.

Results: The temporary relining resin with the CT value closest to water was 36.9 HU, the vinyl polysiloxane with the highest CT value was 985 HU, and the thermoplastic ethylene vinyl acetate copolymer splint with the lowest CT value was -89.7 HU. The maximum absolute difference among the treatment plans per case was 4.18 GyE for the oral mean dose. The radiation dose for the evaluation indices did not differ significantly among the treatment plans.

Conclusion: In the range of CT values from -89.7 HU to 985.0 HU covered in this study, the effect of the CT value of the mouthpiece on the dose distribution may be considered to have no clinical impact.

Background

Radiation therapy plays an important role in the therapeutic strategy for head and neck cancers. However, acute and late adverse events are problems in radiation therapy for head and neck cancer. Adverse events of radiation therapy for head and neck cancer include oral mucositis, salivary gland disorders, taste disorders, and osteonecrosis of the jaw. Reducing the dose to normal tissue is expected to reduce the grade and frequency of these adverse events and to maintain the quality of life of the patients. In particular, the average dose to the parotid gland affects salivary gland damage and the volume of the mandible irradiated at above 60 Gy affects osteonecrosis of the jaw[1–3]. Intensity modulated radiation therapy (IMRT) and particle therapy including proton therapy are useful in reducing adverse events of the radiation therapy for head and neck cancer.

In the radiation therapy for head and neck cancer, mouthpieces are sometimes used to protect normal tissue and to improve the accuracy of fixation, and many papers have reported the usefulness of a mouthpiece [4–19]. Most of the mouthpieces were fabricated with dental materials. Though it is considered that different materials may affect the dose distribution of the radiation therapy, there is only one report that has examined the materials used in the mouthpiece in external X-ray irradiation[20]. In addition, there are no reports that have examined the materials used for mouthpieces in proton therapy.

The dose calculation for proton therapy is based on the water equivalent thickness of each kind of tissue on the CT image in the treatment planning. Since the water equivalent thickness is affected by the CT value of the tissue [21–23], it is expected that the dose distribution of the proton therapy will be affected by the CT value of the material used for the mouthpiece.

In our institution, we use temporary relining resin as the material of the mouthpiece for proton therapy, because we know that its CT value is close to that of water, and as we think the effect on the dose distribution is smaller than that of other materials. However it is not known whether the differences are statistically significant.

To investigate how the CT value of the mouthpiece affects the dose distribution to normal tissue in proton therapy, this study measured the CT value of six dental materials and investigated the effect of the CT value on the dose distribution to normal tissue in proton therapy planning.

Methods

Measurement of the CT values of the six dental materials

We selected six dental materials for the measurement of CT values: temporary relining resin (Soft Liner, GC, Tokyo, Japan), tissue conditioner (Tissue Conditioner, Shofu, Kyoto, Japan), vinyl polysiloxane (Exafine putty type, GC, Tokyo, Japan), thermoplastic ethylene vinyl acetate copolymer splint (Dental mouthpiece, Cogit Corporation, Osaka, Japan), silicone rubber impression material (Memosil2, Kulzer Japan, Tokyo, Japan), and a compound impression material (Modelling compound, GC, Tokyo, Japan). As mentioned above, clinically we use temporary relining resin as the material for mouthpieces for proton therapy, but this material tends to include air bubbles. Therefore, we used a vacuum kneading device to make an ideal and uniform material not containing air bubbles for the temporary relining resin for this study. For the other materials, the samples were prepared according to the manufacturer manuals. First, the samples were made with a mold diameter of 32cm and the height 36mm. Next, the samples were embedded in 5 wt% agar with a of 60 mm diameter mold and height 52mm.

The CT images were taken with an Optima CT580w (GE Healthcare, Waukesha, WI, USA). The imaging conditions were set to 120 kV tube voltage and Auto mA tube current. The thickness of the slices was set to 2.5 mm.

The acquired CT data were analyzed using Osirix version 8.5.2 (Pixmeo SARL, Geneva, Switzerland). A region of interest (ROI) with a radius of 10 mm was set at the center of the sample (Figure1), and CT values and standard deviations were measured. Measurements were made with 12 slices for each sample (Figure1), and the mean CT value and the mean standard deviation were determined. Three dental materials were identified: the material with the CT value closest to water, the material with the highest CT value, and the material with the lowest CT value.

Patient selection and simulation

This study was approved by the Institutional Review Board of Hokkaido University Hospital under protocol 018-0061. The subjects were patients who received proton therapy for head and neck cancer at Hokkaido University Hospital from July 2015 to March 2019 and had used a mouthpiece for the purpose of protecting normal tissue during the proton therapy. In all cases, mouthpieces were made from temporary relining resin without employing any vacuum kneading device.

The treatment plan for the proton therapy was created using VQA (Hitachi, Tokyo, Japan). The following treatment plans were prepared: the treatment plan adopted in the actual treatment without changing the CT value of the mouthpiece (plan1), the treatment plan recalculated by changing the CT value of the mouthpiece to the value of the material with the highest CT value (Plan 2), the CT value closest to water (plan 3) and the lowest CT value (plan 4) (Figure 2). When the treatment plan was changed from plan1 to plan2, plan3, and plan 4, the dose prescriptions to the target volume was set in the same manner as with plan1. The proton therapy was performed with PROBEAT-RT (Hitachi, Tokyo, Japan).

Evaluation of the effect of the different CT values of the mouthpiece on normal tissue

We chose the mandible, bilateral parotid glands, and the oral cavity as the organs at risk (OAR). The dose to the OAR for each treatment plan was calculated from the dose volume histogram. The evaluation indices were set to the mandible max dose (GyE), mandible mean dose (GyE), the volume of the mandible irradiated above 60 GyE (V-60GyE) (%), the parotid affected side mean dose (GyE), the parotid unaffected side mean dose (GyE), and the oral mean dose (GyE). The mean, minimum, maximum, and standard deviations of the evaluation indices were calculated for each plan of all cases in order to verify the significance of the changes in the evaluation indices. The absolute differences of the evaluation indices between plan1 and plan2, plan1 and plan3, plan1 and plan4, and plan2 and plan4 per case were calculated, and the mean, minimum, maximum, and standard deviation of the absolute differences were calculated.

Significant differences between treatment plans were determined using the Wilcoxon rank sum test. All statistical analyses were performed using JMP version 14.0.0 (SAS Institute Inc, Cary, NC, USA). A p-value <0.05 was considered statistically significant.

Results

Measurement of CT values of the six dental materials

The mean CT values and mean standard deviations of the six dental materials are shown in Table 1. The CT images of the six dental materials are shown in Figure 3. The mean CT value was 985.0 HU for the vinyl polysiloxane, 587.2 HU for the compound impression material, 302.6 HU for the silicon rubber impression material, 36.9 HU for the temporary relining resin, -41.4 HU for the tissue conditioner, and -89.7 HU for the thermoplastic ethylene vinyl acetate copolymer splint. The vinyl polysiloxane had the highest CT value among the six dental materials. The temporary relining resin had the CT value closest to water among the six dental materials. The thermoplastic ethylene vinyl acetate copolymer splint had the lowest CT value among the six dental materials.

The influence of the CT values of the mouthpiece on the dose distribution in normal tissue in proton therapy planning

The subjects were 17 cases. A list of cases is shown in Table 2. The most common primary site was the nasal cavity, with 10 cases. The histological types were malignant melanoma in 6 cases, adenoid cystic carcinoma in 5 cases, squamous cell carcinoma in two cases, and other types in each of the remaining. Ten cases were treated with proton therapy alone. Four cases were treated with surgery and postoperative proton therapy. Two cases were treated with concurrent chemoradiation therapy. One case was treated with surgery and postoperative chemoradiation therapy. The clinical target volume was expanded on a case-by-case basis based on tumor localization, size, and histology, including subregions adjacent to the primary tumor. In addition to the above, the clinical target volume includes the volume of the primary tumor with a margin of 5-25 mm, depending on the histological type in cases treated without surgery.

Prophylactic irradiation of the cervical lymph node area was not performed. Cervical lymph node metastasis was observed in one case (patient 12). In that case, cervical lymph node dissection was performed followed by proton therapy for the primary tumor. Irradiation doses were 65 GyE in 26 fractions in 6 cases, 60 GyE in 15 fractions in 4 cases, and 70 GyE in 35 fractions in 2 cases; 70.4 GyE in 32 fractions and 66.15 GyE in 35 fractions, 56 GyE in 28 fractions, 50.4 GyE in 28 fractions, and 30 GyE in 6 fractions for one case each.

The purpose of using the mouthpiece was to reduce the dose to the mandible and tongue in 15 cases, dose reduction to the tongue in one case, and dose reduction to the maxilla in one case. As an example, the mouthpiece used in the treatment and the dose distribution diagram of case 14 are shown in Figures 4 and 5. The OAR doses for each case in the treatment plan adopted in the actual treatment (plan1) are shown in Table 3. The mean dose, minimum dose, and maximum dose for each evaluation index for each plan are shown in Table 4. The mean, minimum, and maximum values and standard deviation of each evaluation index remain almost unchanged for all plans even if the CT value of the mouthpiece changes. The mean, minimum, and maximum values and standard deviation for each of the evaluation indices of the absolute differences between plan1 and plan2, plan1 and plan3, plan1 and plan4, and plan2 and plan4 per case are shown in Table5.

There were no significant differences between any of the treatment plans. The difference in maximum values between plans for each evaluation index ranged from 0.05 to 4.18 GyE, with the maximum difference observed for the oral mean dose between plan2 and plan4; the difference in the minimum value between plans for any of the evaluation indices did not change.

Discussion

A variety of materials are used for mouthpieces in clinical applications. However, there are no studies focusing on the CT value of the mouthpieces, not only in particle therapy, but also with X-rays. In this study, we investigated six dental materials. Among these six dental materials, vinyl polysiloxane and thermoplastic ethylene vinyl acetate copolymer splint, have been investigated for particle therapy in the past [4, 5, 15], but there are no previous reports examining the other four materials as mouthpiece materials for particle therapy. Kawamura et al. used vinyl polysiloxane as a stopper in proton therapy, and reported on its safety and accuracy in proton therapy [5]. Ikawa et al. used thermoplastic ethylene vinyl acetate copolymer as a mouthpiece splint in carbon-ion radiation therapy and reported that it helped to protect normal tissue [4, 15]. However, these reports did not investigate multiple materials in proton therapy together. This present study is the first investigation of the effect of different mouthpiece materials on dose distributions in proton therapy. In addition, this study is also the first to report the use of a mouthpiece made of temporary relining resin in proton therapy.

When a mouthpiece is manufactured, air bubbles are introduced into the bulk of the material, resulting in a non-uniform interior. The non-uniformity of the interior may cause variations in CT values and affect the water equivalent thickness, but there is no report on the effect of variations in the uniformity of the material in the interior of the mouthpiece. We used a vacuum kneading device to make ideal and uniform specimens not containing air bubbles inside the temporary relining resin and determined its CT value as 36.9 HU. Compared to the dental materials used in previous reports, this material was the one closest to the CT value of water[4, 5, 15] among the various materials considered, and the mean standard deviation in this specimen was the smallest at 2.0 HU, suggesting it also to be best in terms of uniformity. But clinically used mouthpieces are made without using a vacuum kneading machine. Therefore, they probably contain air bubbles inside, and so their CT values can be assumed to be lower than those of ideal and uniform materials not containing air bubbles inside. In the comparison of plan 1 (the CT used in the actually used plan) and plan 3; there was no clinically significant difference between plans 1 and 3. As above, it seems that there is no significant clinical problem with temporary relining resin mouthpieces when the best possible effort is made to ensure uniformity. This would make it reasonable to use temporary relining resin as the material for mouthpieces when calculating the dose of the proton therapy using the water equivalent thickness. Materials with higher CT values may be affected more by bubble inclusions. Therefore, more careful consideration to air bubbles is required for materials with high CT values. Further, the search for a simpler method to reduce the air bubble content inside the mouthpiece system is a future challenge.

Typical adverse events of radiation therapy for head and neck cancer include oral mucositis, salivary gland disorders, taste disorders, and osteonecrosis of the jaw and more. By reducing the dose to the surrounding normal tissue, it is expected that the degree or frequency of these adverse events will be reduced. Of the above adverse events, late complications of salivary gland disorders and osteonecrosis of the jaw are particularly important. It is known that the average dose to the parotid gland is an index of salivary gland disorders and the volume of the mandible irradiated above 60GyE is the index for osteonecrosis of the jaw[1-3]. From the above, these parameters were set as the evaluation indices.

The main purpose of using the mouthpiece in this study was to reduce the dose to normal tissue by deflecting the position of the mandible and tongue due to the presence of the mouthpiece in the mouth. However, it did not consider the mouthpiece acting as a stopper. The higher CT value tended to lower the mean value of the evaluation indices as shown in table4, considering previous reports[5], the mouthpiece in the present report also functioned as a stopper.

The differences in the mean values between plans for each evaluation index were all small, less than 1 GyE. In addition, no significant difference was found in any of the items between plan1 and plan2, plan1 and plan3, plan1 and plan4, and plan2 and plan4 by the Wilcoxon's rank sum test. Therefore, it may be assumed that the effect of the change in CT values on the dose distribution is adequately small.

Even in the case with the largest difference between treatment plans, the differences in the maximum and mean dose to the mandible were 2.46 GyE and 0.39 GyE, the difference in the percentage of the mandible irradiated with 60 GyE or more was 0.53%, the differences in the mean dose to the parotid affected and unaffected gland were 1.99 GyE and 1.53 GyE, and the difference in the mean dose to the oral cavity was 4.18 GyE. From the above, the difference in the mean dose in the oral cavity was 4.18 GyE, which was somewhat larger than the difference in other parameters. The case with the 4.18 GyE difference was patient 14, who had an oral mean dose of 20.29 GyE in the clinical treatment. The case with the highest oral mean dose in clinical practice was patient 12 with 28.05 GyE, but the difference between plans was 0 GyE.

In considering the several materials for a mouthpiece, some critics may argue that it is necessary to actually make a mouthpiece out of each material, take CT images, and create a treatment plan. While this method may be ideal, it is not practical due to the serious problem of unnecessary radiation exposure to patients, and we believe that the research method employed here is appropriate.

In most of the cases included in this study, the primary site was the nasal cavity or paranasal sinuses. In addition, the irradiation site was only at the primary site, and the area irradiated to the mouthpiece was small, which may have underestimated the effect. In all cases, the beam incidence direction was set so that the proton beam passed through the primary tumor and then through the mouthpiece to reduce uncertainties. In the future, it will be necessary to study cases in which the irradiation dose to the mouthpiece is higher, such as for nasopharyngeal cancer.

Conclusions

In the range of CT values from -89.7 HU to 985.0 HU evaluated in this study, changes in CT values due to the dental materials employed did not cause clinically significant changes in the dose distribution in OAR. Therefore, it would not present problems when selecting dental materials for mouthpieces based on operability, uniformity, and robustness.

Abbreviations

CT: Computed tomography; IMRT: Intensity modulated radiation therapy; OAR: Organs at risk; ROI: Region of interest

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Hokkaido University Hospital under protocol 018-0061.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author upon request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable

Authors’ contributions

All authors participated in the design and plan of the study. MS, TM: The samples were made to measure the CT values. The patient's mouthpiece was fabricated and the OAR values were measured. The measured values were analyzed. SY, AT, TS, YK: The patient's mouthpiece was fabricated. KY, HM, YD: They performed proton therapy on head and neck cancer patients using a mouthpiece. All authors revised the text critically. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

References

1. Nabil S, Samman N. Incidence and prevention of osteoradionecrosis after dental extraction in irradiated patients: a systematic review. Int J Oral Maxillofac Surg. 2011;40:229–43.
2. Costa DA, Costa TP, Netto EC, Joaquim N, Ventura I, Pratas AC, et al. New perspectives on the conservative management of osteoradionecrosis of the mandible: A literature review. Head Neck. 2016;38:1708–16.
3. Kraeima J, Steenbakkers R, Spijkervet FKL, Roodenburg JLN, Witjes MJH. Secondary surgical management of osteoradionecrosis using three-dimensional isodose curve visualization: a report of three cases. Int J Oral Maxillofac Surg. 2018;47:214–19.
4. Ikawa H, Koto M, Ebner DK, Takagi R, Hayashi K, Tsuji H, et al. A custom-made mouthpiece incorporating tongue depressors and elevators to reduce radiation-induced tongue mucositis during carbon-ion radiation therapy for head and neck cancer. Pract Radiat Oncol. 2018;8:e27-e31.
5. Kawamura M, Maeda Y, Takamatsu S, Tameshige Y, Sasaki M, Asahi S, et al. The usefulness of vinyl polysiloxane dental impression material as a proton beam stopper to save normal tissue during irradiation of the oral cavity: basic and clinical verifications. Med Phys. 2013;40:081707.
6. Bodard AG, Racadot S, Salino S, Pommier P, Zrounba P, Montbarbon X. A new, simple maxillary-sparing tongue depressor for external mandibular radiotherapy: a case report. Head Neck. 2009;31:1528–30.
7. Oita M, Ohmori K, Obinata K, Kinoshita R, Onimaru R, Tsuchiya K, et al. Uncertainty in treatment of head-and-neck tumors by use of intraoral mouthpiece and embedded fiducials. Int J Radiat Oncol Biol Phys. 2006;64:1581–8.
8. Johnson B, Sales L, Winston A, Liao J, Laramore G, Parvathaneni U. Fabrication of customized tongue-displacing stents: considerations for use in patients receiving head and neck radiotherapy. J Am Dent Assoc. 2013;144:594–600.
9. Verrone JR, Alves FA, Prado JD, Marcicano A, de Assis Pellizzon AC, Damascena AS, et al. Benefits of an intraoral stent in decreasing the irradiation dose to oral healthy tissue: dosimetric and clinical features. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;118:573–8.
10. Doi H, Tanooka M, Ishida T, Moridera K, Ichimiya K, Tarutani K, et al. Utility of intraoral stents in external beam radiotherapy for head and neck cancer. Rep Pract Oncol Radiother. 2017;22:310–18.
11. Rocha BA, Lima LMC, Paranaiba LMR, Martinez ADS, Pires MBO, de Freitas EM, et al. Intraoral stents in preventing adverse radiotherapeutic effects in lip cancer patients. Rep Pract Oncol Radiother. 2017;22:450–54.
12. Hollows P, Hayter JP, Vasanthan S. The Leicester radiotherapy bite block: an aid to head and neck radiotherapy. Br J Oral Maxillofac Surg. 2001;39:49–51.

13. Feng Z, Wang P, Gong L, Xu L, Zhang J, Zheng J, et al. Construction and clinical evaluation of a new customized bite block used in radiotherapy of head and neck cancer. Cancer Radiother. 2019;23:125–31.
14. Shafai-Erfani G, Willoughby T, Ramakrishna N, Meeks S, Kelly P, Zeidan O. Effectiveness of base-of-skull immobilization system in a compact proton therapy setting. J Appl Clin Med Phys. 2018;19:261–67.
15. Ikawa H, Koto M, Ebner DK, Hayashi K, Takagi R, Tonogi M, et al. The Efficacy of a Custom-Made Mouthpiece With Spacer to Reduce Osteoradionecrosis in Carbon-Ion Radiation Therapy for Tongue-Base Tumor. Adv Radiat Oncol. 2019;4:15–19.
16. Hong CS, Oh D, Ju SG, Ahn YC, Na CH, Kwon DY, et al. Development of a semi-customized tongue displacement device using a 3D printer for head and neck IMRT. Radiat Oncol. 2019;14:79.
17. Zhang L, Garden AS, Lo J, Ang KK, Ahamad A, Morrison WH, et al. Multiple regions-of-interest analysis of setup uncertainties for head-and-neck cancer radiotherapy. Int J Radiat Oncol Biol Phys. 2006;64:1559–69.
18. Wong K, Cheng J, Bowlin K, Olch A. Adaptation of vacuum-assisted mouthpiece head immobilization system for precision infant brain radiation therapy. Pract Radiat Oncol. 2016;6:425–28.
19. Sayer FT, Sherman JH, Yen CP, Schlesinger DJ, Kersh R, Sheehan JP. Initial experience with the eXtend System: a relocatable frame system for multiple-session gamma knife radiosurgery. World Neurosurg. 2011;75:665–72.
20. Katsura K, Utsunomiya S, Abe E, Sakai H, Kushima N, Tanabe S, et al. A study on a dental device for the prevention of mucosal dose enhancement caused by backscatter radiation from dental alloy during external beam radiotherapy. J Radiat Res. 2016;57:709–13.
21. Schneider U, Pedroni E, Lomax A. The calibration of CT Hounsfield units for radiotherapy treatment planning. Phys Med Biol. 1996;41:111–24.
22. Kanematsu N, Matsufuji N, Kohno R, Minohara S, Kanai T. A CT calibration method based on the polybinary tissue model for radiotherapy treatment planning. Phys Med Biol. 2003;48:1053–64.
23. Schaffner B, Pedroni E. The precision of proton range calculations in proton radiotherapy treatment planning: experimental verification of the relation between CT-HU and proton stopping power. Phys Med Biol. 1998;43:1579–92.

Tables

Table 1. Mean CT value and mean SD of the six types of dental materials here

	Vinyl polysiloxane	Compound impression material	Silicon rubber impression material	Temporary relining resin	Tissue conditioner	Thermoplastic ethylene-vinyl acetate copolymer splint
Mean CT value (HU)	985.0	587.2	302.6	36.9	-41.4	-89.7
Mean SD (HU)	4.2	26.5	12.8	2.0	16.6	2.5

Table 2. Patient characteristics

Patient	Gender	Age	Primary site	Histological type	Clinical stage	Treatment	Radiation dose
1	Male	69	Nasal cavity	Squamous cell carcinoma	T4aN0M0	Radiation chemotherapy	70GyE/35Fr
2	Female	75	Nasal cavity	Squamous cell carcinoma	T4aN0M0	Radiation chemotherapy	70GyE/35Fr
3	Male	37	Nasal cavity	Adenoid cystic carcinoma	T4bN0M0	Proton therapy only	65GyE/26Fr
4	Female	35	Nasal cavity	Adenoid cystic carcinoma	T4aN0M0	Proton therapy only	65GyE/26Fr
5	Male	63	Nasal cavity	Malignant melanoma	T3N0M0	Surgery + PostopPT	65GyE/26Fr
6	Female	78	Nasal cavity	Malignant melanoma	T4aN0M0	Proton therapy only	60GyE/15Fr
7	Female	80	Nasal cavity	Malignant melanoma	T3N0M0	Surgery + PostopPT	60GyE/15Fr
8	Female	76	Nasal cavity	Malignant melanoma	T4aN0M0	Proton therapy only	60GyE/15Fr
9	Male	68	Nasal cavity	Malignant melanoma	T3N0M0	Proton therapy only	60GyE/15Fr
10	Female	78	Nasal cavity	Malignant melanoma	T3N0M0	Surgery + PostopPT	30GyE/6Fr
11	Female	80	Maxilla	Osteosarcoma	T3N0M0	Proton therapy only	70.4GyE/32Fr
12	Male	55	Maxillary gingiva	Pleomorphic undifferent tumor	T4aN1M0	Proton therapy only	66.15Gy/35Fr
13	Male	72	Maxillary sinus	Adenoid cystic carcinoma	T4bN0M0	Surgery + PostopPT	65GyE/26Fr
14	Female	70	Buccal mucosa	Adenoid cystic carcinoma	T4bN0M0	Proton therapy only	65GyE/26Fr
15	Female	40	Ethmoidal cell	SMARCB1(INI1)deficient carcinoma	T4bN0M0	Proton therapy only	65GyE/26Fr
16	Female	54	Palatin bone	Adenoid cystic carcinoma	T4aN0M1	Proton therapy only	56GyE/28Fr
17	Female	4	Nasal ala	Rhabdomyosarcoma	T2N0M0	Surgery + Radiation chemotherapy	50.4GyE/28Fr

Table 3. List of clinical values for the OAR items for each patient (plan 1)

Patient	Mandible max(GyE)	Mandible mean(GyE)	Mandible V-60GyE(%)	Parotid affected side mean(GyE)	Parotid unaffected side mean(GyE)	Oral mean(GyE)
1	67.14	2.10	0.06	0.12	0.21	3.30
2	36.96	2.22	0.00	2.94	0.85	16.19
3	60.37	4.65	0.00	7.52	0.19	13.76
4	66.04	4.94	0.83	15.41	0.62	23.26
5	49.89	0.72	0.00	0.01	0.00	4.32
6	45.39	2.70	0.00	2.11	3.57	6.88
7	34.98	6.93	0.00	2.58	1.85	7.53
8	41.66	2.59	0.00	2.91	0.45	15.74
9	18.38	0.46	0.00	0.01	0.02	0.06
10	19.98	1.14	0.00	1.05	0.38	6.55
11	74.83	18.30	21.18	46.48	0.40	11.48
12	70.95	29.78	29.36	6.93	0.02	28.05
13	69.30	18.62	16.47	26.30	0.09	25.37
14	67.67	24.91	29.82	43.56	0.00	20.29
15	62.28	3.90	0.07	2.66	0.81	16.73
16	57.23	1.87	0.00	2.62	0.00	1.74
17	5.12	0.36	0.00	0.00	0.02	1.07

Table 4. Mean, maximum, and minimum values of the evaluation indices of OAR for each plan

		Mean	Minimum	Maximum
Mandible max(GyE)	plan1	49.89 ± 20.30	5.12	74.83
	plan2	50.00 ± 20.10	6.87	74.97
	plan3	50.00 ± 20.10	6.87	74.97
	plan4	50.03 ± 20.00	7.58	74.95
Mandible mean(GyE)	plan1	7.42 ± 9.04	0.36	29.78
	plan2	7.36 ± 9.07	0.31	29.75
	plan3	7.41 ± 9.04	0.36	29.79
	plan4	7.43 ± 9.05	0.38	29.82
Mandible V 60GyE(%)	plan1	5.75 ± 10.60	0.00	29.82
	plan2	5.73 ± 10.58	0.00	29.87
	plan3	5.72 ± 10.56	0.00	29.82
	plan4	5.75 ± 10.60	0.00	29.86
Parotid affected side mean(GyE)	plan1	9.60 ± 14.49	0.00	46.48
	plan2	9.48 ± 14.37	0.00	46.47
	plan3	9.49 ± 14.37	0.00	46.47
	plan4	9.61 ± 14.50	0.00	46.48
Parotid unaffected side mean(GyE)	plan1	0.56 ± 0.88	0.00	3.57
	plan2	0.47 ± 0.63	0.00	2.18
	plan3	0.54 ± 0.83	0.00	3.28
	plan4	0.57 ± 0.91	0.00	3.70
Oral mean(GyE)	plan1	11.90 ± 8.63	0.06	28.05
	plan2	11.40 ± 8.22	0.06	28.04
	plan3	11.64 ± 8.34	0.06	28.06
	plan4	12.01 ± 8.65	0.06	28.04

Table 5. Details of results and differences between plans for each of the evaluation indices

		P value	Absolute difference		
			Mean	Minimum	Maximum
Mandible max(GyE)	between plan1 and plan2	0.97	0.16± 0.40	0.00	1.75
	between plan1 and plan3	0.95	0.15± 0.40	0.00	1.75
	between plan1 and plan4	0.95	0.18± 0.57	0.00	2.46
	between plan2 and plan4	0.97	0.06± 0.17	0.00	0.71
Mandible mean(GyE)	between plan1 and plan2	0.76	0.07± 0.09	0.00	0.37
	between plan1 and plan3	0.86	0.01± 0.02	0.00	0.09
	between plan1 and plan4	0.85	0.01± 0.01	0.00	0.05
	between plan2 and plan4	0.74	0.08± 0.10	0.00	0.39
Mandible V 60GyE(%)	between plan1 and plan2	1.00	0.04± 0.12	0.00	0.53
	between plan1 and plan3	0.97	0.03± 0.10	0.00	0.42
	between plan1 and plan4	0.96	0.01± 0.02	0.00	0.05
	between plan2 and plan4	1.00	0.03± 0.11	0.00	0.48
Parotid affected side mean(GyE)	between plan1 and plan2	0.85	0.12± 0.43	0.00	1.84
	between plan1 and plan3	0.97	0.11± 0.43	0.00	1.84
	between plan1 and plan4	0.93	0.01± 0.04	0.00	0.16
	between plan2 and plan4	0.80	0.13± 0.47	0.00	1.99
Parotid unaffected side mean(GyE)	between plan1 and plan2	0.96	0.09± 0.33	0.00	1.40
	between plan1 and plan3	0.99	0.02± 0.07	0.00	0.29
	between plan1 and plan4	0.90	0.01± 0.03	0.00	0.13
	between plan2 and plan4	0.84	0.10± 0.36	0.00	1.53
Oral mean(GyE)	between plan1 and plan2	0.84	0.61± 0.90	0.00	3.69
	between plan1 and plan3	1.00	0.33± 0.87	0.00	3.69
	between plan1 and plan4	0.95	0.12± 0.18	0.00	0.61
	between plan2 and plan4	0.84	0.74± 1.03	0.00	4.18

Figures

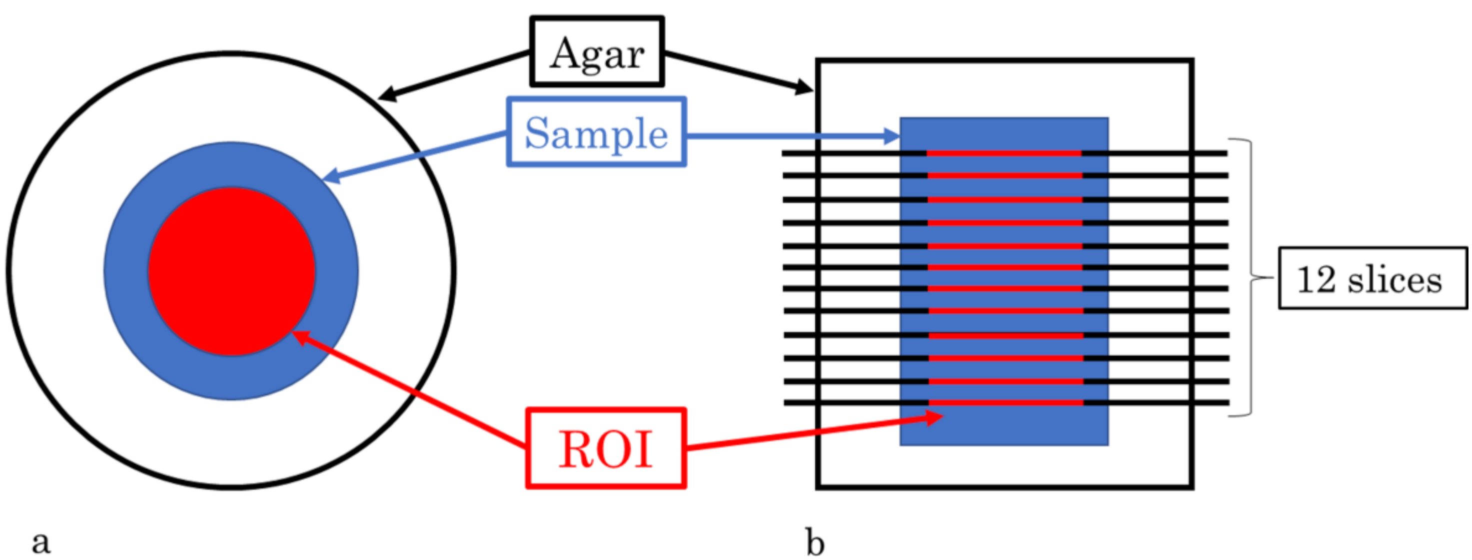

Figure 1

Diagram of a sample for CT value measurements Cylindrical samples, 32 mm in diameter and 36 mm high, were made from three different dental materials and each were embedded in agar. After the CT, a region of interest with a diameter of 10 mm was set in the center of the sample and CT values and standard deviations were measured.

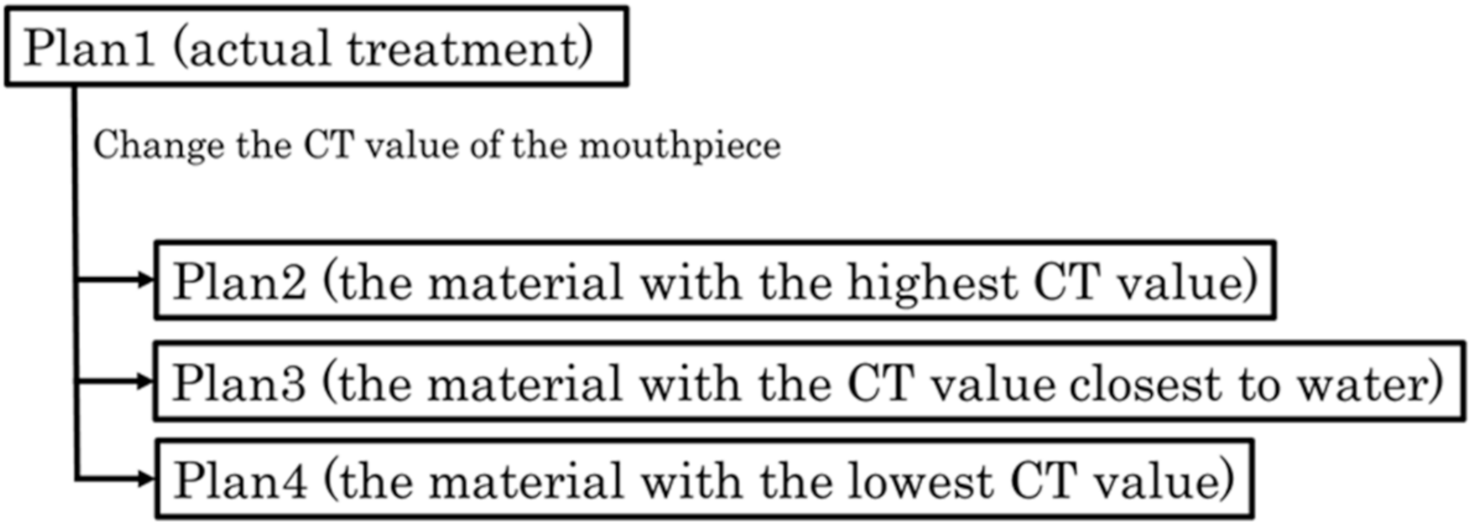

Figure 2

Flow of changing CT value of mouthpiece The CT values of the mouthpieces in the actual treatment were changed to the value of the material with the highest CT value, the value of the material closest to water, and the value of the material with the lowest CT value.

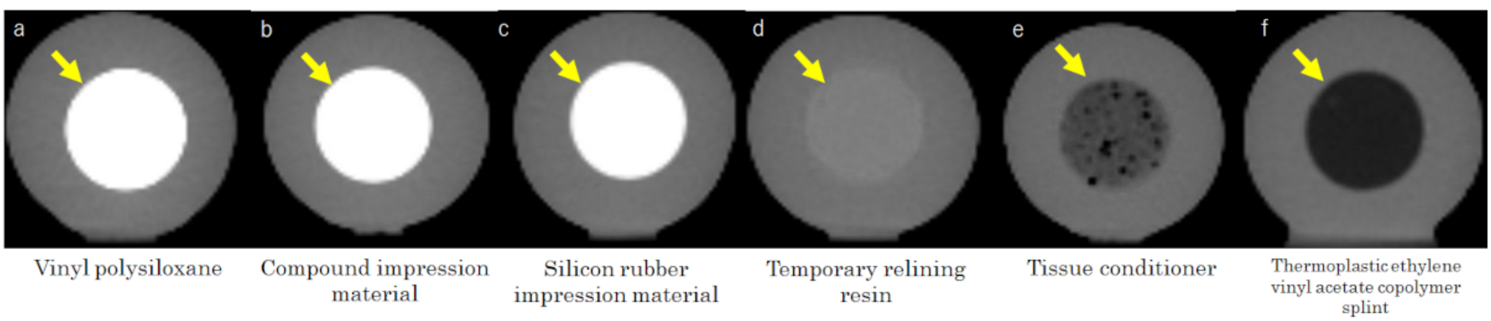

Figure 3

CT images of each sample The yellow arrow indicates the sample. The first from the left image is vinyl polysiloxane (a). The second from the left is the compound impression material (b). The third sample from the left is the silicon rubber impression material (c). The third sample from the right is the temporary relining resin (d). The sample from the right is a tissue conditioner (e). The first sample from the right is a thermoplastic ethylene vinyl acetate copolymer splint (f).

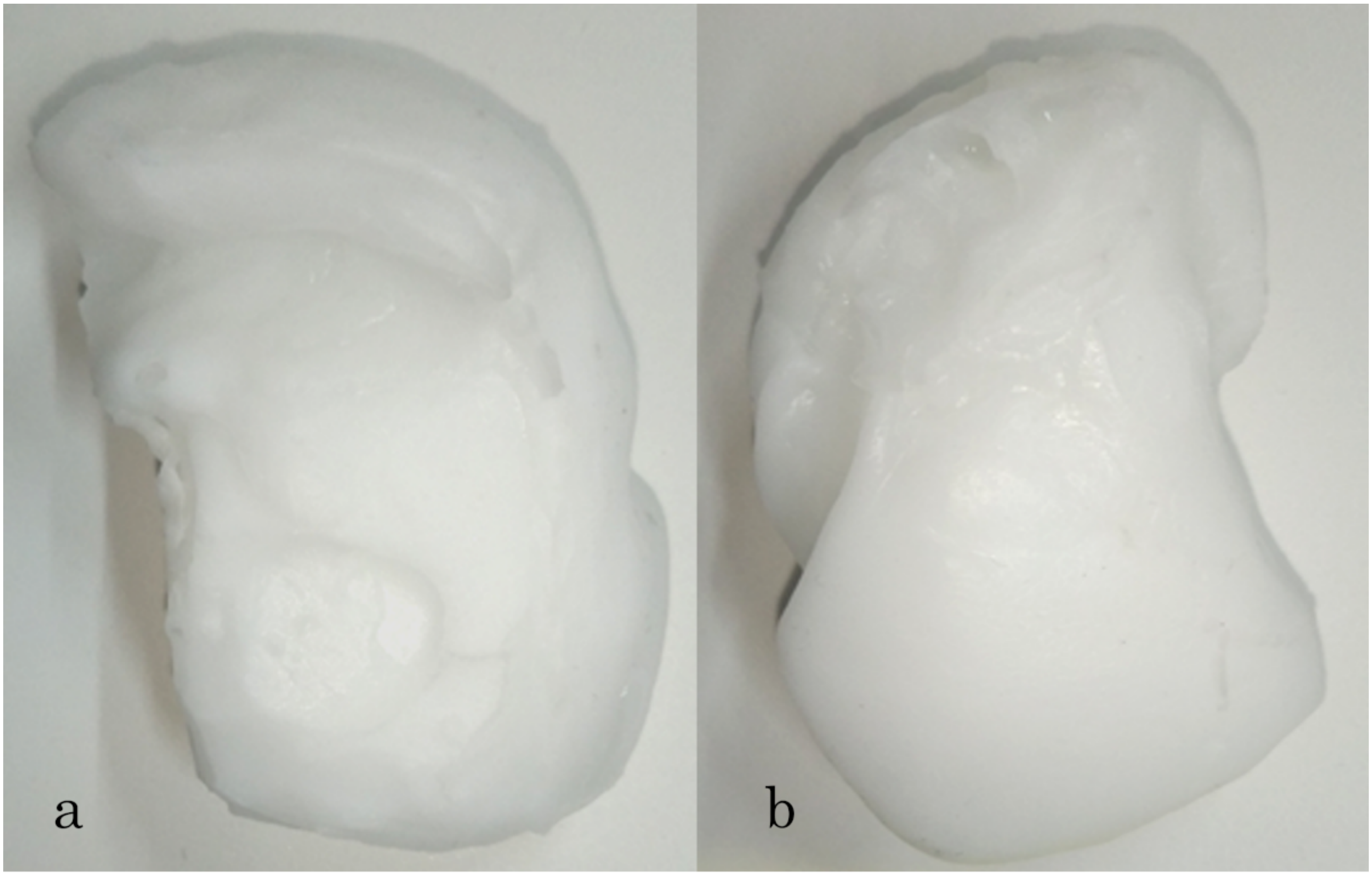

Figure 4

Mouthpiece used in the proton therapy A mouthpiece used in the treatment of right buccal mucosal cancer is shown. The left figure shows the head side of the mouthpiece (a). The right image shows the caudal side of the mouthpiece (b).

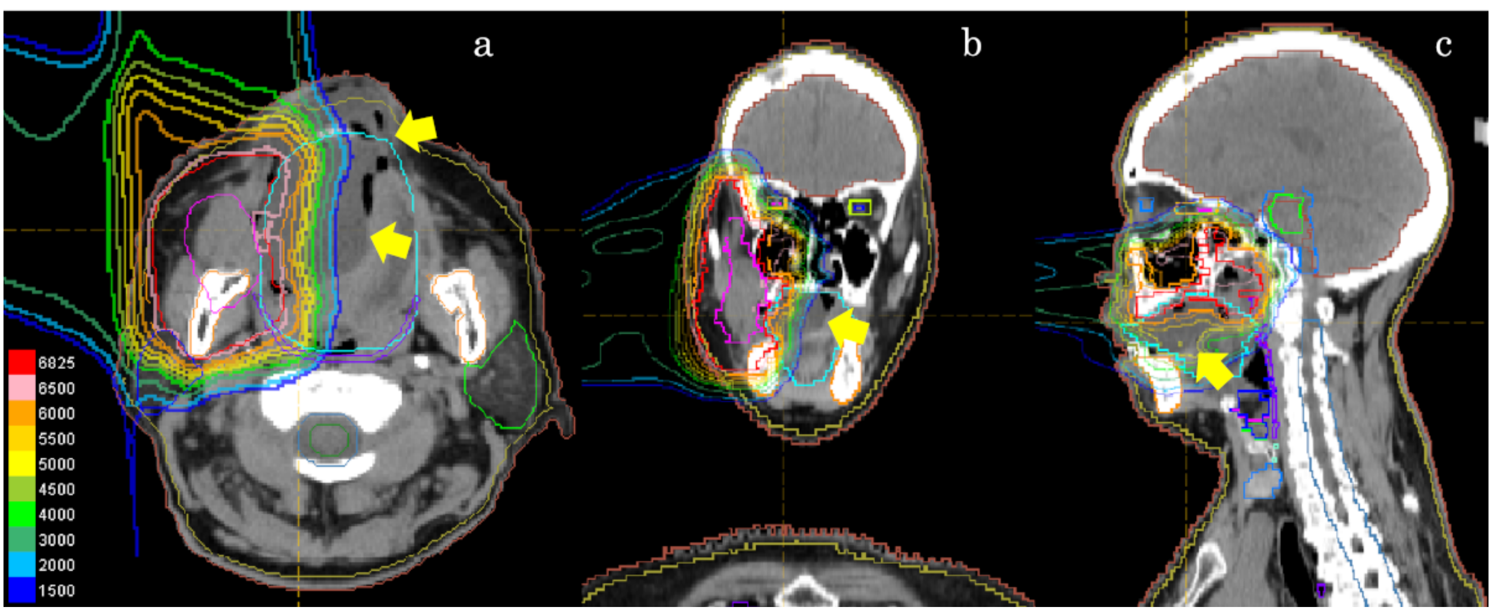

Figure 5

Dose distribution for a patient with right buccal mucosal carcinoma The yellow arrows indicate the mouthpiece.