

Stopping-power ratio of mouthpiece materials for charged-particle therapy in head and neck cancer

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Research

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Abstract

Background: In charged-particle therapy treatment planning, CT numbers of a patient's body are converted into stopping power ratios (SPRs) using a CT-number-to-SPR conversion table constructed for standard human tissues. Since artificial devices used in treatments of head and neck cancer, such as mouthpieces, do not fit into the CT-number-to-SPR conversion table, they may deteriorate treatment accuracy. In this study, the SPRs of five mouthpiece materials were measured, and the error in predicted SPRs based on the conversion table was investigated.

Methods: SPRs of five mouthpiece materials were predicted from their CT numbers using a calibrated conversion table. Independently, the SPRs of the materials were measured by the Bragg-peak shift of a carbon-ion beam passing through the materials. The errors in SPR of the materials were determined as the difference between the predicted and measured SPRs.

Results: The SPRs (error) of the ethylene-vinyl acetate copolymers (EVAs), Nipoflex 710TM and BioplastTM, were 0.997 (0.023) and 0.982 (0.007), respectively. The SPRs (error) of the vinyl silicon impression material (Exafine putty typeTM), the light curable resin (Clear Photoreactive Resin for Formlabs 3D printersTM), and the bis-acrylic resin (TempsmartTM) were 1.517 (0.134), 1.161 (0.068), and 1.26 (0.101), respectively.

Conclusions: The EVA BioplastTM had the minimum SPR error among the five tested materials, indicating the highest human-tissue equivalency. If other artificial materials such as Exafine putty typeTM are used as mouthpieces, it is recommended that their SPRs be overwritten by the correct values in treatment planning processes.

Introduction

In external beam radiation therapy (RT) for head and neck cancer, a mouthpiece has been used to improve positional accuracy and obtain better reproducibility [1, 2]. Doi et al. [1] reported that the use of a mouthpiece in photon-based RT for head and neck cancer patients resulted in a significant reduction in setup errors. The mouthpiece should be effective to reduce the setup errors also in head and neck cancer treatments of charged-particle therapy [3, 4]. Moreover, the mouthpiece can be used to reduce side effects [5–10]. Verrone et al. [7] reported that the use of a mouthpiece during intensity modulated radiation therapy (IMRT) for oral cancer was effective in reducing the dose to normal tissues such as the maxilla and parotid gland. The reduced side effects with custom-made mouthpieces have also been reported in proton [11] and carbon-ion (C-ion) RT [3, 4, 12].

Particle beams have unique physical characteristics distinct from those of photons. The superiority of particle beams is attributed to their low entrance dose, finite range and extremely steep increase in dose in the range of the beams known as the Bragg peak enabling improved target coverage and better sparing of organs at risk (OAR) in close proximity to the target [13, 14]. The range in a patient is, however,

associated with considerable uncertainties due to imaging, patient setup, beam delivery and dose calculation. This range error may cause underdose to the target and overdose to OARs leading to decreased local control and unexpected side effects. Hence accuracy of the beam range in patients is of utmost importance and needs to be calculated as accurately as possible in the treatment planning to utilize the full potential of particle therapy.

In charged-particle therapy, CT images are used for treatment planning and patient dose calculations. For CT-based planning, the CT number is converted to stopping power ratio (SPR) of tissues with respect to water using a CT-number-to-SPR conversion table constructed for standard human tissues [15]. In charged-particle therapy for head and neck cancer, particles can traverse through the mouthpiece in some cases. As the mouthpiece is made of artificial materials, the SPR of the mouthpiece is not necessarily determined correctly from its CT number via the conversion table. Therefore, the mouthpiece may cause range errors of particle beams in patients.

At the QST Hospital, in routine dose calculation of C-ion RT for head and neck cancer with a mouthpiece, the SPR of the mouthpiece is directly determined from its CT number using the calibrated CT-number-to-SPR conversion table. To the best of our knowledge, the dose-calculation procedure for mouthpieces has never been reported so far. In addition, the effects of the mouthpiece material on range of particle beams have never been investigated.

The purpose of this study was to measure the SPRs of five materials clinically used as mouthpieces in charged-particle therapy, and to investigate the SPR error of the materials caused by the CT number-to-SPR conversion. Moreover, to evaluate the effects of SPR error of a mouthpiece made of an ethylene-vinyl acetate copolymer (EVA) on patient dose distribution, we compared the dose distribution calculated from the SPR of the mouthpiece using the CT-number-to-SPR conversion table with the re-calculated dose distribution using the SPR obtained from the present study.

Materials And Methods

Mouthpiece materials used

We investigated five mouthpiece materials used in particle therapy for head and neck cancer to evaluate SPR error and its impact on dose distribution. The characteristics of the materials used in this study are summarized in Table 1. We have been routinely using Nipoflex 710™ (NIP) (Tosoh Corporation, Tokyo, Japan), which is an EVA resin. NIP and Bioplast™ clear soft plate (BIO) (SCHEU-DENTAL GmbH, Iserlohn, Germany) are thermoplastic EVA resins used in dentistry in the treatment of temporomandibular disorders and as protective mouth guards in contact sports. Exafine Putty Type™ (EXA) (GC Corporation, Tokyo, Japan) is a vinyl polysiloxane, and used as an impression material when making dentures. Clear Photoreactive Resin for Formlabs 3D printers™ (3DP) (Formlabs Inc., MA, USA) is a light-cured resin, and used in making 3D printed-oral stents for RT from diagnostic CT images. Tempsmart™ (TEM) (GC

Corporation, Tokyo Japan) is a dual-cured bis-acrylic composite material, and used for temporary crowns and bridges in dental procedures.

Measurement of the stopping power ratio

The SPRs of the mouthpiece materials were measured using 292.3 MeV/u monoenergetic carbon beams at a fixed horizontal port and at a rotating gantry port with 90-degree angulation. 1-mm-width ripple filters made of polymethyl-methacrylate and aluminum were used to mitigate the effect of range straggling due to intervening mouthpiece material at the fixed and rotating gantry ports, respectively. The SPRs of NIP and BIO were measured at the fixed port whereas SPRs of EXA, 3DP and TEM were measured at the rotating gantry port. An in-house parallel plate ionization chamber with a circular sensitive area of 150 mm in diameter was inserted into a motor-driven water tank, and one mouthpiece material was introduced at its upstream surface. The integral depth dose (IDD) of the C-ion beam was measured with and without the mouthpiece material.

The SPR (ρ_s) of the material was determined from the change in the water equivalent path length of C-ion beam due to insertion of the mouthpiece material. It is the ratio of t_w (water equivalent thickness of mouthpiece material) and the geometrical thickness (t_g) of the mouthpiece material, expressed as

$$\rho_s = t_w/t_g. \quad (1)$$

The t was measured at five locations with Vernier calipers and the average was calculated as the thickness of the material. The t_w was determined by the shift of the measured IDD with and without the mouthpiece material by the least squares regression with spline interpolation. The uncertainty of the SPR was calculated on the assumption that the uncertainties of t_g and t_w were 0.5 mm and 0.1 mm, respectively.

Measurement of CT numbers

We measured CT numbers of five mouthpiece materials. In order to adapt the effect of beam hardening on CT imaging of actual head and neck cancer cases, CT imaging was performed in a water-filled cylindrical container with an outer diameter of 20 cm (inside diameter of 18 cm). All CT images were obtained with the CT scanner Aquilion ONE (Canon Medical Systems Corporation, Otawara, Japan). CT imaging parameters were matched to those usually used for head and neck planning (tube voltage, 120 kV; tube current 50 mA; field-of-view [FOV], 500 mm; reconstruction kernels [FC13], Adaptive Iterative Dose Reduction Three-Dimensional [AIDR3D], with a single-energy metal artifact reduction [SEMAR] algorithm).

The CT images were imported to the radiotherapy planning support software (MIM software TM, ver 6.8.4; MIM Software Inc., Cleveland, OH), and the mouthpiece material in the CT image was contoured as the region of interest (ROI). The CT number of the material was determined as the average of the CT number in the ROI. The error of CT numbers was calculated from the standard deviation of CT numbers in the mouthpiece.

CT-number-to-SPR conversion table

A CT-number-to-SPR conversion table was constructed for the CT scanner based on a stoichiometric calibration method developed by Kanematsu et al. [15], in which 11 ICRP body tissues were assumed as representative tissues for the human body [16]. The validity of the conversion method was demonstrated elsewhere [15], and has been clinically used in our institution.

Error in SPR

The SPRs of the mouthpiece materials were measured with a C-ion beam. Independently, the SPRs of the materials were predicted from their CT numbers via the CT-number-to-SPR conversion table. The errors in the SPR were determined as the difference between the predicted and measured SPRs.

Clinical evaluation

We evaluated the effect of mouthpiece-induced range error on dose distribution for clinical cases of head and neck cancer patients treated previously with C-ion RT at the QST Hospital using the NIP mouthpiece. We selected a hard palate mucosal malignant melanoma case treated with C-ion RT of four beams passing through thick mouthpiece materials.

In the patient dose calculation of C-ion RT, the SPR of the mouthpiece material has not been overwritten by either measured or nominal values, but directly derived from its CT number using a calibrated conversion table. The planned dose distribution was recalculated by overwriting the SPR of the mouthpiece by the measured SPR of the NIP in this study. The recalculated dose distribution was compared with the corresponding planned dose distribution, and analyzed by the differential dose distribution and a dose volume histogram (DVH). The original treatment plan and patient dose recalculation were made using the Xio -N™ treatment planning system (ELEKTA; Stockholm, Sweden; Mitsubishi Electric, Tokyo, Japan).

Results

The IDD_s measured with and without the mouthpiece were compared to obtain the water equivalent thickness of each mouthpiece material (t_w). CT numbers, SPRs measured with t_w and t_g , SPRs predicted from the CT numbers using the CT-number-to-SPR conversion table, and the errors of SPR for the five measured materials are shown in Table 2. Additionally, the SPRs of the five materials are plotted on the CT-number-to-SPR conversion table to evaluate their tissue equivalencies in Fig. 1. The measured CT values of both EVA resins were less than 0 and the measured SPRs were less than 1. All other materials had measured CT values greater than 0 and SPRs greater than 1. The SPR errors were 0.023 and 0.007 for the EVA resins of NIP and BIO, respectively. For EXA, 3DP and TEM, the SPR errors were 0.134, 0.068 and 0.101, respectively. EVA-based materials had smaller SPR errors than other materials.

Table 1. Characteristics of mouthpiece materials.

Material	Classification of material	Composition	Thickness (mm)	Mass (g/cm ³)
Nipoflex 710 (NIP)	Thermoplastic resin	Ethylene-vinyl acetate copolymer	37.1 ± 0.1	0.949
Bioplast (BIO)	Thermoplastic resin	Ethylene-vinyl acetate copolymer	35.3 ± 0	0.96
Exafine Putty Type (EXA)	Addition curing silicone impression material	Vinyl polysiloxane, silicon dioxide, and platinum catalysts	47.4 ± 0.1	1.80
Clear Photoreactive Resin for Formlabs 3D printers (3DP)	Light-cured resin	Methacrylated oligomer and methacrylated monomer	40.0 ± 0	1.09 – 1.12
Tempsmart (TEM)	Dual-cured bis-acrylic composite material	Silica filler and methacrylic acid ester	32.9 ± 0.1	Base: 1.2 Catalyst: 1.3

Table 2. CT numbers and stopping power ratios (SPRs) for each material.

Materials	CT numbers (HU)*	Measured SPRs	Predicted SPRs	Error
Nipoflex 710 (NIP)	-66.85 ± 11.91	0.997 ± 0.014	0.974	0.023
Bioplast (BIO)	-65.45 ± 10.35	0.982 ± 0.014	0.975	0.007
GC Exafine Putty Type (EXA)	879.79 ± 31.16	1.517 ± 0.016	1.383	0.134
Clear Photoreactive Resin for Formlabs 3D printers (3DP)	131.94 ± 11.82	1.161 ± 0.015	1.093	0.068
Tempsmart (TEM)	324.15 ± 17.46	1.260 ± 0.019	1.159	0.101

* HU, Hounsfield Unit

In Fig. 2, the planned dose distribution is compared with the recalculated dose distribution determined in the present experiment by assigning the SPR of NIP as 1.00 (because the assignment function of Xio-N™ limits the resolution of the SPR to two decimal places, 0.997 was rounded to 1.00). The isodose line of the recalculated dose distribution was shifted by 1 mm proximal to the area where the particle beam passed through a distance of 5 cm or more of the mouthpiece. There was little difference in planning

target volume (PTV) dose coverage between the planned and recalculated dose distributions and DVHs of PTV in both distributions were almost overlapped with each other.

Discussion

In the photon and charged-particle therapy for head and neck cancer, the effectiveness of the mouthpiece as a spacer to reduce the dose to normal tissues has been reported [3–10, 12]. In charged-particle therapy, the beam may unavoidably pass through the mouthpiece or be stopped on the mouthpiece to spare surrounding normal tissue. However, the CT-number-to-SPR conversion table used in particle therapy has been constructed for standard human tissues [15]. It is not possible to calculate the accurate SPR of the artificial materials, e.g., mouthpieces, from their CT numbers using the CT-number-to-SPR conversion table. Therefore, the use of the beam passing through the artificial material may result in a range error and affect the treatment accuracy. Nevertheless, the SPR of the mouthpiece material has yet to be discussed. In this study, the SPR of five mouthpiece materials were measured. Materials other than EVA-based materials had low equivalence to human tissues. Among the materials evaluated, the EVA resins had high equivalence to human tissue, with the SPR error of within 2% as shown in Fig. 1 and Table 2. Therefore, the SPR of the EVA mouthpiece may acceptably be determined directly from its CT numbers using the CT-number-to-SPR conversion table in charged-particle therapy treatment planning, even if the particle beam passes through the EVA mouthpiece.

In order to evaluate the effect of the range error due to the insertion of the EVA mouthpiece on the patient dose distribution, we compared the planned dose distribution with the SPR of the mouthpiece directly predicted from the conversion table with the recalculated dose distribution with the SPR overwritten to the measured SPR value, i.e., $\rho_s = 1.0$. We confirmed that the dose difference was extremely small. Until now, there have been few reports on use of mouthpiece materials for charged-particle therapy, and the SPR of the mouthpiece material has not been reported. In C-ion RT, we have already reported the efficacy of a mouthpiece made of EVA to reduce the dose of surrounding normal tissues in patients with head and neck cancer [3, 4]. For proton beam therapy at MD Anderson Cancer Center, Aponte et al. [18] reported the effectiveness of a bolus-type stent for a combined intraoral/extraoral defect using heat-polymerized acrylic resin. At the same cancer center, the efficacy of the light-cured resin that can be shaped with a 3DP in the hospital without a professional dentist has been reported for head and neck radiotherapy [19]. Kawamura et al. [11] reported the usefulness of vinyl polysiloxane dental impression material as a proton beam stopper to save normal tissue such as the tongue during irradiation of the oral cavity. In the present study, we found that EVA had relatively high equivalence to human tissues, while the vinyl polysiloxane and the light-cured resin have low equivalence to human tissues, and there was a possible range error from 7 to 13% when particle beam passed through those mouthpiece materials. Dose heterogeneity within the PTV should be kept within -5 to $+7\%$ of the prescribed dose, as recommended by the International Commission on Radiation Units and Measurements (ICRU) Reports 50 [20] and 62 [21]. In order to achieve this, the range error of the mouthpiece materials should be as low as possible. EVA resins are one of the most suitable mouthpiece materials for charged-particle therapy to fulfill the recommended

dose accuracy. When materials other than EVA are used for a mouthpiece, a beam direction passing through the mouthpiece should be avoided. Alternatively, although the number of processes may increase, the SPR of the mouthpiece material should be overwritten by its correct value in treatment planning.

Limitation

The present study had a limitation. There are various types of EVA resins that differ according to the content of vinyl acetate and the CT-number-to-SPR conversion table may not be suitable for all of them. We conducted this study using two kinds of EVA resins. Analysis using various types of EVA resins is required in the future.

Conclusion

This study showed a high tissue equivalency of the EVA mouthpieces. We could directly determine the SPR of the EVA mouthpiece from its CT numbers using the CT-number-to-SPR conversion table, even if the particle beam passed through the EVA mouthpiece. We judged EVA was a suitable mouthpiece material for use in charged-particle therapy.

Abbreviations

3DP: Clear Photoreactive Resin for Formlabs 3D printers™

AIDR3D: Adaptive Iterative Dose Reduction Three-Dimensional

BIO: Bioplast™

C-ion: Carbon-ion

CT: Computed tomography

DVH: Dose volume histogram

EVA: Ethylene-vinyl acetate copolymer

EXA: Exafine Putty Type™

FOV: Field-of-view

HU: Hounsfield Unit

ICRP: International Commission on Radiological Protection

ICRU: International Commission on Radiation Units and Measurements

IDD: Integral depth dose

NIP: Nipoflex 710™

OAR: Organs at risk

PTV: Planning target volume

ROI: Region of interest

RT: Radiation therapy

SEMAR: Single-energy metal artifact reduction

SPR: Stopping power ratio

TEM: Tempsmart™

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HI, TI and MK designed the study. HI and TI collected and analyzed the data, and TI performed the statistical analyses. HI, TI, MK and TB drafted the manuscript. TK, HT, MS, SY, and HT were involved in the general supervision of this study. All authors revised the manuscript and approved the final version.

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Figures

Figure 1

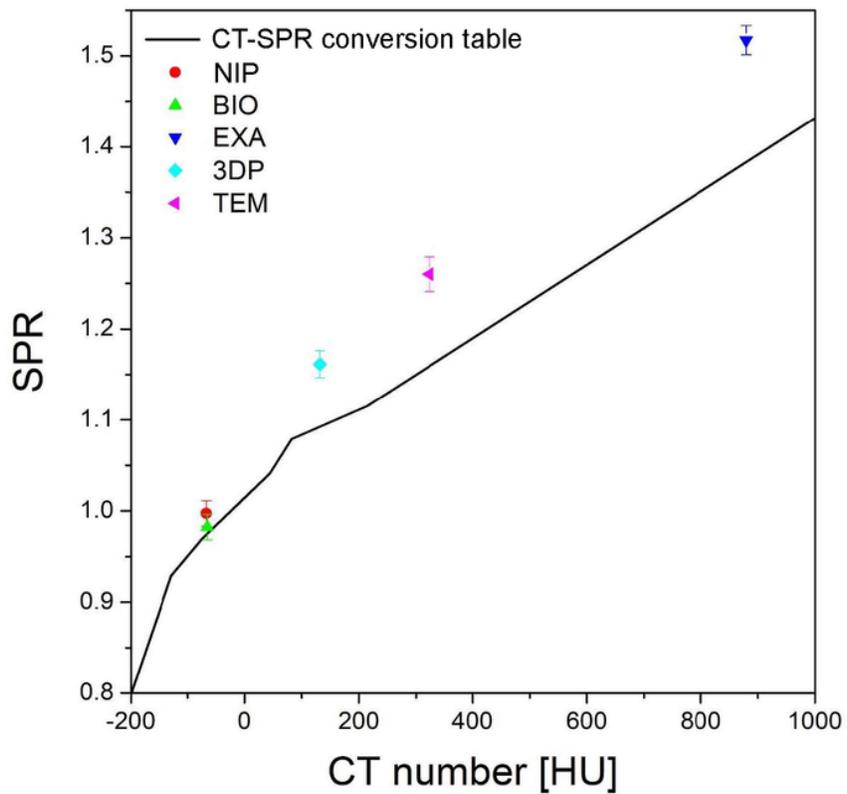


Figure 1

CT-number-to-SPR conversion table (solid line) and SPR measured for five mouthpiece materials.

Figure 2

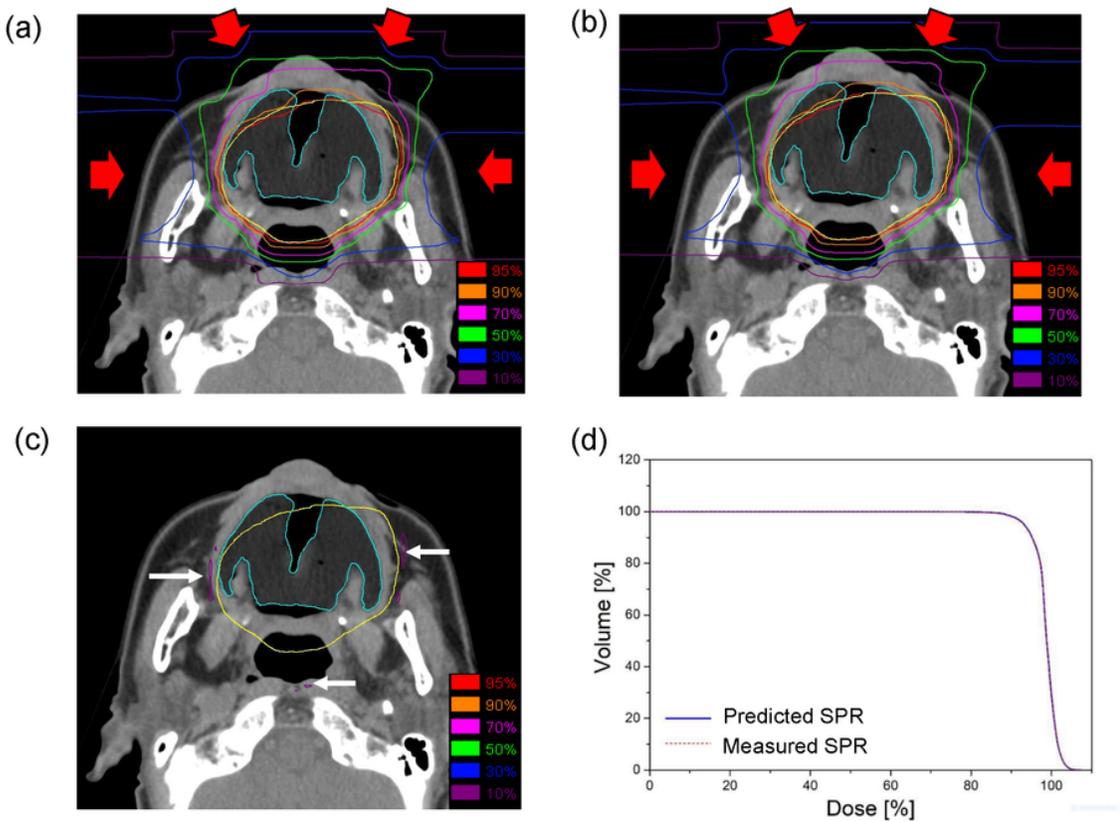


Figure 2

Axial CT images with dose distribution and dose-volume histogram in head and neck cases irradiated by a passive irradiation method with a beam passed through the mouthpiece. Carbon-ion radiation therapy was delivered at 57.6 Gy (relative biological effectiveness) using 4 ports. The shown isodose lines correspond to 95%, 90%, 70%, 50%, 30%, and 10% dose areas. The planning target volume and mouthpiece are demarcated by yellow and cyan lines, respectively. (a) Dose distribution from predicted SPR, calculated from the CT numbers of mouthpiece using CT-number-to-SPR conversion table. (b) Dose distribution recalculated by assigning the SPR of the mouthpiece with the SPR of 1.00 obtained in the present study. (c) The differential dose distribution. There was a dose difference around the distal end of the beam in the dose distribution between the planned and recalculated dose distributions (arrows). (d) Dose-volume histograms of the planning target volume. Dose-volume histogram calculated from the CT number of the mouthpiece with the SPR determined by the CT-number-SPR conversion table (blue solid line). Dose-volume histogram recalculated by assigning the SPR of the mouthpiece with the SPR 1.00 calculated in this study (red dotted line).