Estimation of whole-body radiation exposure from brachytherapy for oral cancer using a Monte Carlo simulation

Y. Ozaki1, H. Watanabe1,*, A. Kaida2, M. Miura2, K. Nakagawa3, K. Toda3, R. Yoshimura3, Y. Sumi4 and T. Kurabayashi1

1Department of Oral and Maxillofacial Radiology, Graduate School, Tokyo Medical and Dental University, Yushima 1-5-45, Bunkyo-ku, Tokyo, 113-8549, Japan
2Department of Oral Radiation Oncology, Graduate School, Tokyo Medical and Dental University, Yushima 1-5-45, Bunkyo-ku, Tokyo, 113-8549, Japan
3Department of Radiation Therapeutics and Oncology, Graduate School, Tokyo Medical and Dental University, Yushima 1-5-45, Bunkyo-ku, Tokyo, 113-8549, Japan
4Center of Advanced Medicine for Dental and Oral Diseases, National Center for Geriatrics and Gerontology, Morio-kacho 7-430, Obu-shi, Aichi, Obu, 474-8511, Japan

*Corresponding author. Department of Oral and Maxillofacial Radiology, Graduate School, Tokyo Medical and Dental University, Yushima 1-5-45, Bunkyo-ku, Tokyo, 113-8549, Japan. Tel: +81-3-5803-5545; Fax: +81-3-5803-0205; Email: hiro.orad@tmd.ac.jp.

ABSTRACT

Early stage oral cancer can be cured with oral brachytherapy, but whole-body radiation exposure status has not been previously studied. Recently, the International Commission on Radiological Protection Committee (ICRP) recommended the use of ICRP phantoms to estimate radiation exposure from external and internal radiation sources. In this study, we used a Monte Carlo simulation with ICRP phantoms to estimate whole-body exposure from oral brachytherapy. We used a Particle and Heavy Ion Transport code System (PHITS) to model oral brachytherapy with 192Ir hairpins and 198Au grains and to perform a Monte Carlo simulation on the ICRP adult reference computational phantoms. To confirm the simulations, we also computed local dose distributions from these small sources, and compared them with the results from Oncentra manual Low Dose Rate Treatment Planning (mLDR) software which is used in day-to-day clinical practice. We successfully obtained data on absorbed dose for each organ in males and females. Sex-averaged equivalent doses were 0.547 and 0.710 Sv with 192Ir hairpins and 198Au grains, respectively. Simulation with PHITS was reliable when compared with an alternative computational technique using mLDR software. We concluded that the absorbed dose for each organ and whole-body exposure from oral brachytherapy can be estimated with Monte Carlo simulation using PHITS on ICRP reference phantoms. Effective doses for patients with oral cancer were obtained.

KEYWORDS: brachytherapy, oral cancer, exposure, estimation, Monte Carlo simulation

INTRODUCTION

Early stage oral cancer can be effectively cured with oral brachytherapy, which can preserve patient quality of life [1, 2]. Our institution started offering this therapy in 1962. The high rate of control with this treatment has been achieved by inserting small radiation sources such as 192Ir hairpins or 198Au grains directly into lesions, which enables us to deliver high doses of radiation, up to 70 Gy per week, on a continuous basis [1]. However, there have been several reports that such interstitial radiotherapy inevitably causes whole-body exposure [3]. Matsubara et al. reported that in brachytherapy patients the equivalent whole-body dose is 0.5 Gy, based on the frequency of dicentrics and rings using data from the peripheral blood of actual patients [4]. There is a concern that such chromosomal changes might cause future radiation-induced malignancies [5, 6]. Thus, it would be important to ascertain whole-body radiation exposure status during oral brachytherapy treatment.

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Physical models of the human body, such as the RANDO phantom [7], with thermoluminescence dosimeters inside have been commonly used for evaluating radiation sources. However, it would be difficult to actually insert radiation sources into the phantom. Recently, the International Commission on Radiological Protection Committee (ICRP) developed reference computational phantoms, which are based on medical imaging data from actual people and made compatible with data from previous ICRP publications. ICRP has recommended using these phantoms to estimate radiation exposure from internal and external radiation sources [8].

In this study, we used the Adult Reference Computational Phantoms and code for Monte Carlo simulation from the Particle and Heavy Ion Transport code System (PHITS) to estimate whole-body radiation exposure from oral cancer brachytherapy [9, 10].

**METHODS**

**Treatment settings**

In this study, we modeled two types of treatment that correspond to two kinds of small radiation sources under the assumption that they are being used to treat early-stage tongue cancer. Early-stage tongue carcinoma corresponds to T1–2 N0 disease in the Union for International Cancer Control classification; the size of the largest local lesion is <4 cm. We usually select either 192Ir hairpins or 198Au grains (Fig. 1a and b, Chiyoda Technol Corp., Bunkyo-ku, Japan), depending on the thickness of the local lesion or patient performance status [2]. Typical placement of 192Ir hairpins and 198Au grains are shown in Fig. 1c and d, which can accommodate lesions with diameters up to 3 cm. 192Ir hairpins are provided by the manufacturer three times per year; thus, the dose rate might differ depending on the time when the sources are implanted into patients. However, the prescribed dose for cancer control is ~70 Gy/5 days. This simulation was carried out using two 500 MBq 192Ir hairpins for 120 h (equivalent to 24 h over 5 days; total of $4.2 \times 10^8$ disintegrations). 198Au grains, which are used in permanent implants, are provided monthly. When used in patients, they are usually adjusted to 185 MBq each, and we aimed for a prescription dose of 80–90 Gy/oo, which corresponds to ~70 Gy over 7 days. The half-life of 198Au grains is short, 2.695 days, and the cumulative dose was calculated to the decay of all sources. There were $6.2 \times 10^8$ MBq disintegrations.

**Monte Carlo simulation using PHITS**

We employed PHITS version 2.52 as the Monte Carlo simulation code, running on the Windows 7 64-bit operating system [9]. PHITS has been used in simulations of therapeutic X-rays, particle radiation therapy, and Boron neutron capture therapy [10, 11]. In this study, we did not use the Electron Gamma Shower computational mode. The CPU was an Intel Core i5 unit (4 cores) with a clock speed of 2.80 GHz. The simulations were performed with the male and female ICRP adult reference computational phantoms [8]. The simulation computations were repeated $10^8$ times per decay by PHITS. The cut-off energy in photons was set to 1 keV. The ICRP phantom is based on computed tomography voxel data, which are composed of 1.9 and 3.9 million voxels for the male and female phantoms, respectively. The dimension of each voxel was $2.1 \times 2.1 \times 8 \text{ mm}^3$ for a male who is 176 cm in height and 73 kg in weight, and $1.8 \times 1.8 \times 4.8 \text{ mm}^3$ for a female who is 163 cm in height and 60 kg in weight. Both phantoms contained 28 target organs. We made source models based on the schematic illustrations shown in Fig. 1a and b. For the 192Ir hairpin source, we set the shape as shown in Fig. 1c, with a diameter of 0.45 mm. For the 198Au grain source, the shape was set to 2.5 mm in length, with a diameter of 0.5 mm. The 192Ir hairpins and 198Au grains were located on the right border and dorsum of the tongue, respectively. The exact coordinates of the center of the 192Ir hairpins in male and females were $(x = 2, y = -5.6, z = 70.97 \text{ (cm)})$ and $(x = 2, y = -4.6, z = 65.97 \text{ (cm)})$, respectively. Similarly, the coordinates of the 198Au grains were $(x = 0, y = -5, z = 72.388 \text{ (cm)})$ and $(x = 2, y = -5, z = 67.875 \text{ (cm)})$, respectively. The photon radiation emitted was set according to the parameters shown in Table 1 [12]. 192Ir undergoes electron capture and β decay, and 198Au only
PHITS could successfully execute the programs, taking ~26 h for one series. The obtained data are shown in Table 2, in which male and female absorbed doses for each organ are listed in gray, and sex-averaged equivalent doses are given in sievert units. In most organs, absorbed doses were determined with relative statistical uncertainties of <1%. For organs distant from the head (e.g., colon, gonads, prostate/uterus, and urinary bladder wall), statistical uncertainties were as high as 10%. Effective doses for each source were calculated and shown on the bottom line in sievert. 192Ir hairpins and 198Au grains delivered effective doses of 0.547 Sv and 0.710 Sv, respectively. To confirm the computational reliability of PHITS, we also computed local dose distributions for both sources using PHITS (Fig. 2a and b) and compared them with the results from the mLDR software (Fig. 2c and d). In Fig. 2, the dose distributions are expressed in heat units [MeV/cm³/source], which could be converted to Gy (J/kg), by multiplying them by 1.602 × 10⁻¹⁰ and the total number of disintegrations. In Fig. 2a, the dose distributions from the 192Ir hairpins are shown, and the line for 10⁻³ heat [MeV/cm³/source] corresponds to 68 Gy (calculated as 10⁻³ × 1.602 × 10⁻¹⁰ × 4.2 × 10⁸). This line is equivalent to the 70 Gy line in Fig. 2c. Similarly, a 10⁻¹³ heat distribution line from the 198Au grains corresponds to 99 Gy (calculated as 10⁻¹³ × 1.602 × 10⁻¹⁰ × 6.2 × 10⁸), which is equivalent to the 90 Gy line in Fig. 2d. Representative points, A and B, were selected (Fig. 2c and d). The absorbed doses at these points were calculated using PHITS (Fig. 2c).

**RESULTS**

**DISCUSSION**

Whole-body exposure from oral brachytherapy

PHITS could successfully execute the programs, taking ~26 h for one series. The obtained data are shown in Table 2, in which male and female absorbed doses for each organ are listed in gray, and sex-averaged equivalent doses are given in sievert units. In most organs, absorbed doses were determined with relative statistical uncertainties of <1%. For organs distant from the head (e.g., colon, gonads, prostate/uterus, and urinary bladder wall), statistical uncertainties were as high as 10%. Effective doses for each source were calculated and shown on the bottom line in sievert. 192Ir hairpins and 198Au grains delivered effective doses of 0.547 Sv and 0.710 Sv, respectively. To confirm the computational reliability of PHITS, we also computed local dose distributions for both sources using PHITS (Fig. 2a and b) and compared them with the results from the mLDR software (Fig. 2c and d). In Fig. 2, the dose distributions are expressed in heat units [MeV/cm³/source], which could be converted to Gy (J/kg), by multiplying them by 1.602 × 10⁻¹⁰ and the total number of disintegrations. In Fig. 2a, the dose distributions from the 192Ir hairpins are shown, and the line for 10⁻³ heat [MeV/cm³/source] corresponds to 68 Gy (calculated as 10⁻³ × 1.602 × 10⁻¹⁰ × 4.2 × 10⁸). This line is equivalent to the 70 Gy line in Fig. 2c. Similarly, a 10⁻¹³ heat distribution line from the 198Au grains corresponds to 99 Gy (calculated as 10⁻¹³ × 1.602 × 10⁻¹⁰ × 6.2 × 10⁸), which is equivalent to the 90 Gy line in Fig. 2d. Representative points, A and B, were selected (Fig. 2c and d). The absorbed doses at these points were calculated using PHITS (Fig. 2c).

**DISCUSSION**

Although oral brachytherapy is associated with a high rate of local control in patients with oral cancer, it presumably results in some whole-body irradiation, based on studies of peripheral blood chromosomal aberrations [3, 4, 17]. This is a biological dosimetry counting method, which is believed to have high sensitivity and reliability. However, this method might be influenced by factors such as neoadjuvant chemotherapy, and it requires technical expertise for analysis. It is customary to use a Rando phantom to estimate radiation exposure from therapeutic and diagnostic radiation. However, this phantom is not suitable for estimating radiation exposure from transient internal radiation sources because this phantom is for an universal use, but it would be
Table 2. Each organ absorbed dose, sex-averaged equivalent doses, and effective doses from oral brachytherapy

| Organ               | Tissue weighting factor | $^{192}$Ir needle | $^{198}$Au grain |
|---------------------|-------------------------|-------------------|------------------|
|                     |                         | Absorbed dose     | Sex-averaged     | Absorbed dose   | Sex-averaged     |
|                     |                         | (Gy)              | equivalent doses (mSv) | (Gy)            | equivalent doses (mSv) |
|                     |                         | male              | female           | male            | female           |
| Bone marrow         | 0.12                    | 0.287             | 0.423            | 0.278           | 0.432            |
|                     |                         | 355.04            |                  | 354.75          |                  |
| Breast              | 0.12                    | 0.103             | 0.255            | 0.082           | 0.202            |
|                     |                         | 179.02            |                  | 141.64          |                  |
| Colon               | 0.12                    | 0.014             | 0.009            | 0.010           | 0.006            |
|                     |                         | 11.71             |                  | 7.88            |                  |
| Lungs               | 0.12                    | 0.120             | 0.206            | 0.099           | 0.160            |
|                     |                         | 163.24            |                  | 129.39          |                  |
| Stomach             | 0.12                    | 0.039             | 0.043            | 0.029           | 0.035            |
|                     |                         | 41.14             |                  | 31.99           |                  |
| Gonads              | 0.08                    | 0.004             | 0.005            | 0.000           | 0.001            |
|                     |                         | 4.32              |                  | 0.65            |                  |
| Liver               | 0.04                    | 0.040             | 0.057            | 0.035           | 0.050            |
|                     |                         | 48.41             |                  | 42.40           |                  |
| Oesophagus          | 0.04                    | 0.398             | 0.716            | 0.305           | 0.506            |
|                     |                         | 556.77            |                  | 405.46          |                  |
| Thyroid             | 0.04                    | 0.704             | 1.510            | 0.525           | 1.005            |
|                     |                         | 1107.29           |                  | 765.22          |                  |
| Urinary bladder wall| 0.04                    | 0.005             | 0.006            | 0.001           | 0.001            |
|                     |                         | 5.19              |                  | 1.24            |                  |
| Endosteum           | 0.01                    | 0.279             | 0.395            | 0.272           | 0.416            |
|                     |                         | 336.91            |                  | 344.01          |                  |
| Brain               | 0.01                    | 0.722             | 0.769            | 1.168           | 1.184            |
|                     |                         | 745.50            |                  | 1175.86         |                  |
| Salivary            | 0.01                    | 3.005             | 6.685            | 2.269           | 4.007            |
|                     |                         | 4845.01           |                  | 3138.06         |                  |
| Skin                | 0.01                    | 0.105             | 0.136            | 0.102           | 0.126            |
|                     |                         | 120.22            |                  | 114.22          |                  |
| Adrenals            | 0.01                    | 0.023             | 0.036            | 0.019           | 0.031            |
|                     |                         | 29.30             |                  | 25.36           |                  |
| Extrathoracic region| 0.01                    | 4.208             | 6.903            | 8.571           | 9.738            |
|                     |                         | 5555.67           |                  | 9154.32         |                  |
| Gall bladder wall   | 0.01                    | 0.030             | 0.041            | 0.024           | 0.038            |
|                     |                         | 35.14             |                  | 31.03           |                  |
| Heart               | 0.01                    | 0.102             | 0.180            | 0.080           | 0.137            |
|                     |                         | 140.77            |                  | 108.10          |                  |
| Kidneys             | 0.01                    | 0.016             | 0.024            | 0.013           | 0.020            |
|                     |                         | 20.20             |                  | 16.79           |                  |
| Lymphatic nodes     | 0.01                    | 0.151             | 0.211            | 0.118           | 0.170            |
|                     |                         | 180.82            |                  | 143.68          |                  |
| Muscle              | 0.01                    | 0.171             | 0.172            | 0.178           | 0.153            |
|                     |                         | 171.40            |                  | 165.56          |                  |
| Oral mucosa         | 0.01                    | 29.584            | 27.942           | 39.616          | 56.025           |
|                     |                         | 28763.05          |                  | 47820.11        |                  |
| Pancreas            | 0.01                    | 0.024             | 0.029            | 0.019           | 0.024            |
|                     |                         | 26.70             |                  | 21.52           |                  |
| Prostate/Uterus     | 0.01                    | 0.004             | 0.004            | 0.000           | 0.002            |
|                     |                         | 4.15              |                  | 1.02            |                  |
| Small intestine     | 0.01                    | 0.011             | 0.013            | 0.007           | 0.009            |
|                     |                         | 12.21             |                  | 8.21            |                  |
| Spleen              | 0.01                    | 0.037             | 0.052            | 0.029           | 0.039            |
|                     |                         | 44.56             |                  | 33.63           |                  |
| Thymus              | 0.01                    | 0.331             | 0.591            | 0.249           | 0.419            |
|                     |                         | 461.21            |                  | 333.69          |                  |
| Lenses of eye       | -                       | 1.542             | 1.586            | 2.362           | 2.763            |
|                     |                         | 1563.80           |                  | 2562.18         |                  |
| Effective dose (mSv)|                         |                   |                  | 546.73          |                  |
|                     |                         |                   |                  | 710.35          |                  |
impossible to be milled if the real sources would be implanted in it. In addition, it would be difficult to purchase small sources for the purpose of such a study. Nowadays, we can perform Monte Carlo simulation on ordinary personal computers with ICRP computational phantoms.

In this study, we used PHITS for Monte Carlo simulation code. We computed the local dose distributions and doses for each organ using small source models. We evaluated the computational reliability of PHITS by comparing the results with those from mLDR, which is based on AAPM-TG43U1 [15, 16]. TG43U1 offers an easy method for computing the dose distribution, but it requires a situation in which radiation equilibrium scatter conditions, and is weak to interseed attenuation [18]. Therefore, it cannot be used for estimating whole-body exposure. On the other hand, Monte Carlo simulation using PHITS can be used for local or whole-body exposure, but it is computationally intensive. We were not certain whether it was executed as designed. Therefore, we compared the results from PHITS with those from mLDR. The dose distributions from PHITS and mLDR were similar, but dose comparisons at representative points showed that there were slight differences (Fig. 2e). However, the difference was ~2.6% for 192Ir hairpins and ~1.4% for 198Au grains, indicating that the results for each organ in the whole-body model would be accurate in the range of several percentage differences.

As a result, we could successfully obtain absorption dose values for each organ in the male and female phantoms, as well as sex-averaged equivalent dose values, as shown in Table 2. In general, the absorbed doses in each organ were higher in females, possibly due to smaller body size. Turning our attention to the radiation sources, the values for areas such as oral mucosa, extrathoracic region, lens of the eye, and brain were higher for 198Au grains than for 192Ir hairpins. For the other organs, absorbed doses were higher for 192Ir hairpins than for 198Au grains, despite sex differences, mainly because the source locations for 198Au grains are more compact and slightly more cranially located than the locations for 192Ir hairpins, but the 192Ir hairpins were longer (4.06 cm) in the cephalocaudal axis, as shown in Fig. 1.

The effective dose of the 192Ir hairpins and 198Au grains were 0.547 and 0.710 Sv, respectively, which are equivalent to the results for 0.5 Gy obtained by Matsubara et al. [4]. These doses may depress hematological function [19]. Matsubara et al. reported that the peripheral lymphocyte count of their patients temporarily decreased by 50% or more, but no bone marrow death was observed. As for other deterministic effects, the absorbed dose for the lens of the eye reached the threshold dose of 0.5–2.0 Gy [20], which is associated with a 1% incidence of lens opacity, but at this dose it is unlikely to progress to cataracts. We have not previously taken a clinical interest in this possibility, but for recurrent cases, we sometimes repeat this treatment two or three times [21]. In this scenario, the cumulative dose could possibly reach the threshold value of 5 Gy for cataracts, and it is necessary for us to inform patients of this possibility in advance. Oral mucosa was exposed to doses of 28–56 Gy, which always causes acute mucositis after brachytherapy. However, this therapy is not associated with other deterministic effects such as infecundity or teratogeny. Stochastic effects from exposure are also of concern. In brachytherapy, photon radiation from small sources is used to treat cancer. It rarely induces another neoplasm in the future. The ICRP committee indicated a risk coefficient of 0.055 events per Sv on the basis of cancer risk [14], resulting in a 0.3% or 0.39% risk of cancer-related death. We previously published data about radiation-induced cancers, and concluded that the crude incidence of them is 1.4–1.8%, which corresponds to a handful of cases [6]. Hence, it would be difficult to work out a reliable number of cancer-related deaths from our

![Image](image.png)
experience only. Concerning hereditary risk, most oral cancers occur in persons in their sixties in Japan, and hereditary effects might be of little consequence, but we can calculate it by multiplying the effective doses by 0.002, which results in 0.001% \[14\]. However, these values for cancer risk and hereditary risk might be acceptable, because patients could obtain a higher quality of life from oral brachytherapy for treatment of oral cancer \[2\]. In this study, we estimated the absorbed dose for each organ and whole-body exposure from brachytherapy in patients with oral cancer. The estimated effective dose was 0.547 Sv from \(^{192}\text{Ir}\) hairpins and 0.710 Sv from \(^{198}\text{Au}\) grains. We can apply this knowledge to clinical situation.

**CONFLICT OF INTEREST**

All authors declare that they have no conflicts of interest.

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