in vivo *35*: 579-584 (2021)
doi:10.21873/invivo.12294

Customized 3D Bolus Applied to the Oral Cavity and Supraclavicular Area for Head and Neck Cancer

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Abstract. *Background/Aim: In this study, a new method to create a customized three-dimensional (3D) bolus by accurately considering the anatomy of an individual patient is demonstrated. Patients and Methods: A 3D bolus structure was created from an extended planning target volume (PTV) to reduce an inevitable skin reaction. In addition, during computed tomography simulation in patients with oral cavity cancers, a balloon was inserted into the mouth of a patient to secure space, and then the area surrounding the balloon was designed into a 3D bolus structure. Results: For patients with head and neck cancers, a customized 3D bolus can reduce the unnecessary skin dose by 14.4% compared to a commercial bolus. For patients with oral cavity cancer, the PTV and tongue doses were 93.8% and 8% of the prescribed dose, respectively. Conclusion: The customized 3D bolus enables effective skin sparing and full coverage of the target area.*

In addition to surgery and chemotherapy, radiation therapy (RT) is one of the key treatments of cancer. Considering the size, location, and extent of metastasis, the RT is used alone or in combination with other treatments. Although the purpose of RT is to control tumors, there is a possibility of adverse effects on normal tissues, which makes it a limiting factor when deciding the radiation dose.

Following RT, the side effects frequently experienced by patients with head and neck (H&N) cancers are lethargy and body weakness. In particular, if the treatment site is oral, side effects such as mucositis and sore throat owing to toxic doses of irradiation to the mucous membrane, dry mouth and oral mucosa disease owing to tongue irradiation, loss of saliva, change in taste sensation, and others may occur. According to Rose-ped *et al*., the most common side effects of RT experienced by the patients with H&N cancers are pharyngitis, oral mucosal disease, and dry mouth, which account for 20, 18, and 14% of the total number of side effects encountered, respectively. Furthermore, in the case where the treatment site was the oral cavity, approximately 90% of the patients experienced a change in taste function and 75% of them experienced a change in their oral health (1).

Another side effect of RT is skin reactions, mainly in the form of sunburn and can be classified into grades 1-4 depending on the severity of the damage (2). In the RTOG 90-03 study, toxicities according to the RT techniques were divided into grades 1-4 for locoregionally advanced H&N cancer patients. Further, the symptoms corresponding to grades 1 and 2 were commonly observed among the patients; some patients exhibited the symptoms corresponding to grades 3 and 4 (3).

Fe *et al*. have evaluated the skin dose in intensity-modulated radiotherapy (IMRT) using a thermoluminescence dosimeter (TLD) and an EBT2 film (4). They observed skin reactions corresponding to grade 3 when the skin doses were higher than 40 Gy for 30 fractions.

Skin reactions in patients with H&N cancers is one of the more important side effects, and efforts to reduce them are currently being investigated in the medical field.

The limit of recoverable dose varies depending on the irradiated area. Zopate *et al*. have reported that the smaller the irradiation area the higher the recoverable dose to the skin, and the wider the irradiation area the lower the recoverable dose (5). This indicates that by narrowing the area of the skin to which the high dose is irradiated, the recoverable dose of the skin is increased, thereby reducing the probability of skin damage by radiation.

The use of bolus for superficial lesion treatment is a significantly useful method since it creates an appropriate dose buildup. However, when a commercial bolus is used on areas of the body with irregular skin, *e.g*., H&N, the bolus

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Key Words: Customized 3D bolus, head and neck cancer, skin reaction, radiation therapy, *in vivo* dosimetry, tongue immobilization.

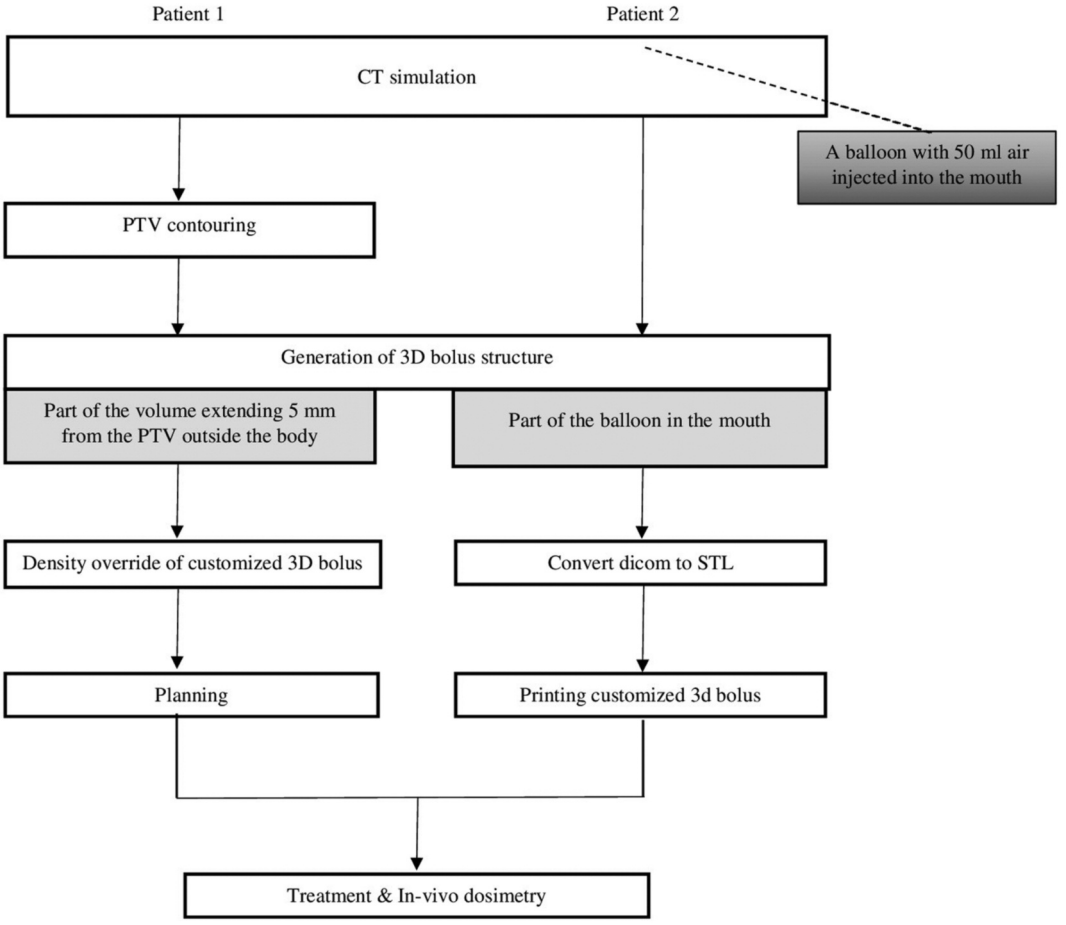

Figure 1. *Workflow for manufacturing a customized 3D bolus.*

Table I. *Basic and treatment information of patient 1 and patient 2.*

Patient characteristic and treatment	Patient 1	Patient 2
Gender	Male	Female
Age	61 y	69 y
Prescribed dose	66 Gy/30 fx	45 Gy/10 fx
Treatment site	Larynx-bilateral neck	Oral cavity (Hard palate)
Treatment technique	2 full arcs, 6 MV	2 full arcs, 6 MV
Year of treatment	04/2020	05/2020
Purpose of RT	Curative treatment	Curative treatment

Table II. *Relative dose comparison with commercial and customized 3D boluses.*

	Relative dose compared to 10-mm commercial bolus [%] (Measurement)
w/o bolus	20.7
3 mm commercial bolus	75.9
5 mm commercial bolus	96.1
Customized 3D bolus	88.5

does not exactly match the skin, resulting in an air gap between the bolus and the skin. Owing to this air gap, the dose buildup does not occur effectively, for not only it does not irradiate the required dose to the specified treatment site, but it also increases the risk of damage due to excess doses reaching areas of the skin outside the treatment site.

In addition, there is a problem of position reproducibility due to changes in the location of the air gap during repeated treatments. For helical tomotherapy (HT) and direct tomotherapy (DT), Akasaka *et al.* have shown through a focused plan study that the air gap between the bolus and the skin may vary with each treatment, and DT has a more serious air gap effect than HT (6). Therefore, there is a need for a new type of bolus that prevents the formation of an air

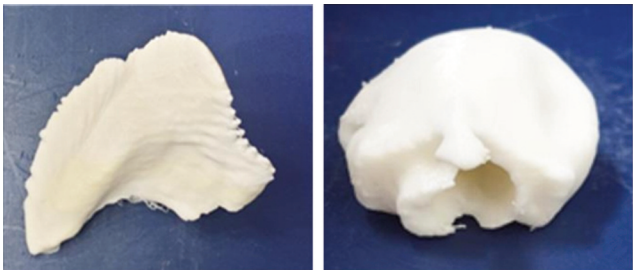

Figure 2. *Customized 3D bolus for (a) patient 1 and (b) patient 2. The 3D bolus in (a) is generated from the extended tumor in CT of patient 1 to provide a sufficient dose to the tumor located in the shallow area of the skin. (b) The 3D bolus of a 50 ml balloon inserted into the mouth patient 2 during CT scan. An air cavity was created in the middle of the bolus for the patient to breathe comfortably.*

Table III. *Relative dose comparison of in vivo dosimetry for patient 1.*

Area	Relative dose compared to prescribed dose [%]			
	w/o bolus (Plan)	0.5 cm bolus (Plan)	Customized 3D bolus (Plan)	Customized 3D bolus (Measurement)
Skin sparing area	34.8	73.0	41.6	58.6
Tumor area	41.3	82.7	67.5	83.2

gap, *i.e.,* a customized patient-specific bolus designed to match the irregular surface of a specific patient.

The 3D printing technology is employed in various medical fields, *e.g.*, for making artificial bones or organs (7, 8), and it has also been used in several institutions in the field of RT. Furthermore, Asfia *et al*. have made immobilizers using 3D printers to minimize patient movement, and reviewed various studies that have used these immobilizers (9).

Park *et al*. applied a 3D bolus, produced from 3D printing, on a breast–one of the irregular skin areas in the human body–along with the H&N. Further, the calculated dose distribution and the measured dose were compared with the commercial bolus. They have reported that the patient-specific 3D bolus can reduce the air gap between the skin and the bolus, thereby reducing the inaccuracies caused by changing daily clinical setups (10).

Canters *et al*. have reported that applying a 3D printed bolus in electron beam treatment can increase target coverage compared to a commercial bolus (11). Chiu *et al*. have reported that a patient-specific 3D bolus can be applied clinically, even when considering the efficiency of time and cost (12).

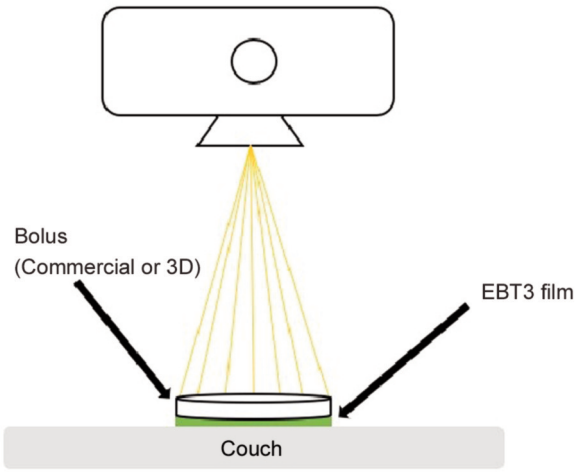

Figure 3. *Experiment to compare the dose buildup effect of a 3D bolus and a commercial bolus in standard conditions. Standard condition: 6 MV X-ray beam with a field size and source-to-surface distance (SSD) of 10×10 cm^2 and 100 cm, respectively. The doses of 3-, 5-, and 10-mm thick commercial boluses and the customized 3D bolus were compared under standard conditions. An EBT3 film was used for the dose measurement.*

In this study, we propose a new method of producing a customized 3D bolus, with the purpose of improving the target coverage and positioning reproducibility.

Patients and Methods

Patients. The patient's dose was evaluated in two patients with H&N cancers. Each of the two patients were treated with a customized 3D bolus. Furthermore, these two patients were selected from the patients who received RT at Kangwon national University Hospital in 2020 (Table I). Patients 1 and 2 received curative treatment with 66 Gy/30 fx and 45 Gy/10 fx for the larynx-bilateral necks and oral cavity (hard palate), respectively. Both the patients were treated with VMAT (2 full arcs, 6 MV) using a linear accelerator (Clinac iX, Varian Medical Systems, Palo Alto, CA, USA).

Manufacturing workflow for a customized 3D bolus. Figure 1 shows the workflow of manufacturing a customized 3D bolus. Since X-ray has a characteristic that the dose is delivered after passing through a buildup section of several millimeters, it must be located at least 5 mm inside the skin to sufficiently deliver the prescribed dose to the tumor. However, if the tumor is located very close to the skin, a bolus that can serve as a buildup must be produced.

For patient 1, after the radiation oncologist contoured the gross tumor volume and planning target volume (PTV) in the computed tomography (CT) image, the PTV was uniformly extended by 5 mm to allow the application of the customized 3D bolus only to the part that satisfies the target coverage, when dose buildup was performed using a bolus located close to the surface. Among the extended PTVs, the area outside the body, *i.e.*, the area where the PTV is close to the skin surface, was set as a customized 3D bolus structure.

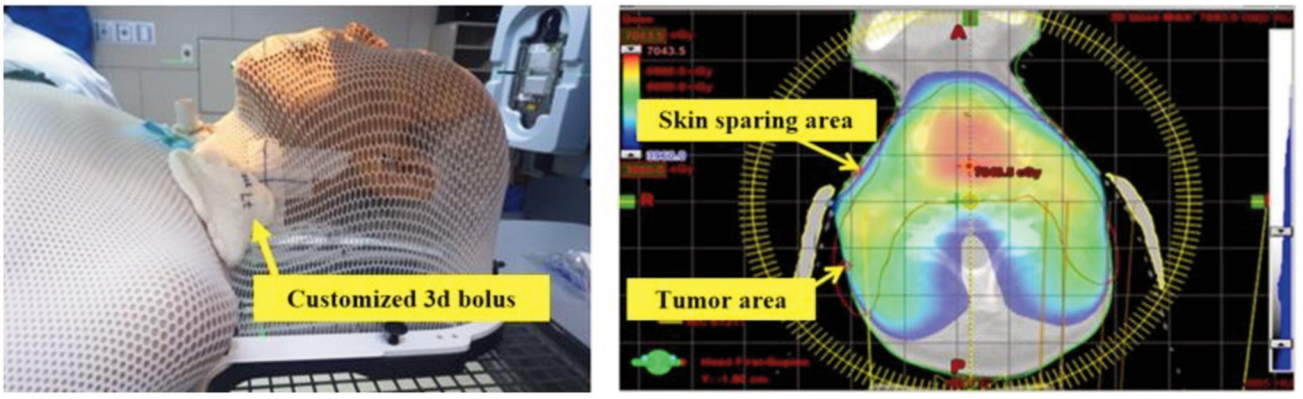

Figure 4. *Treatment setup and dose distribution in the treatment planning for patient 1. (a) Patient 1 is an H&N cancer patient. A customized 3D bolus was created for dose buildup in the area where the tumor was adjacent to the skin and attached to the mask for immobilization during the treatment. Since the customized 3D bolus was created based on the patient's CT, it fits well with the patient's body. The same area viewed as an axial image in the treatment plan is shown in (b). The region below the customized 3D bolus is the buildup area in the axial image, and the area without the bolus is the skin sparing area.*

Table IV. *Relative dose comparison of in vivo dosimetry for patient 2.*

Area	Relative dose compared to prescribed dose [%]	
	Customized 3D bolus (Plan)	Customized 3D bolus (Measurement)
PTV	92.4	93.8
Tongue	22.5	8.0

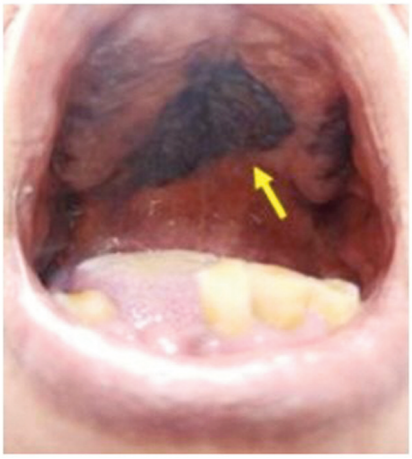

Figure 5. *Treatment site of patient. The tumor lesion of patient 2 is located in the hard palate area; hence, dose buildup is required. Simultaneously, the tongue can be fixed as far as possible from the lesion to reduce unnecessary dose exposure.*

For patient 2, when performing a CT simulation, a balloon was inserted into the patient's mouth, 50 ml of air was injected in the balloon to fix the position of the tongue, and an image was acquired. In the CT image, the volume of the balloon was defined as a customized 3D bolus.

During the treatment planning, the dose was calculated by overriding the density of the bolus to the density of polylactic acid, which was 1.24 g/cm^3. The generated 3D bolus structure was saved in a dicom file format and converted into Standard Triangle Language (STL) file to create a customized 3D bolus using a 3D printer (3DWOX eco, Sindoh, Seoul, South Korea).

The customized 3D boluses for patients 1 and 2 are shown in Figure 2.

Dose evaluation. In vivo dosimetry was performed to verify the dose coverage of tumor lesions and spare effects on normal tissue. In the case of patient 1, to verify the sufficient dose buildup in the skin near the tumor due to the customized 3D bolus, an EBT3 film for dose measurement was placed under the customized 3D bolus. Further, the performance of skin sparing for dose in the skin irrelevant to tumor was evaluated. In addition, to evaluate the buildup effect on the customized 3D bolus produced for patient 1, compared to the commercial bolus, the dose was evaluated under the same conditions (6 MV, 100 MU, 10×10 cm^2 field size, SSD 100 cm) as the commercial bolus with 3, 5, and 10 mm thicknesses. The experimental setup is shown in Figure 3. In the case of patient 2, the target coverage was evaluated between the hard palate and the customized 3D bolus, which is the treatment site, and the dose was also evaluated between the tongue and the customized 3D bolus.

Results

Patient 1. The comparison of the dose between the commercial bolus and the customized 3D bolus of patient 1 showed that the customized 3D bolus was equivalent in terms of the dose to the commercial bolus of approximately 4.3 mm thickness,

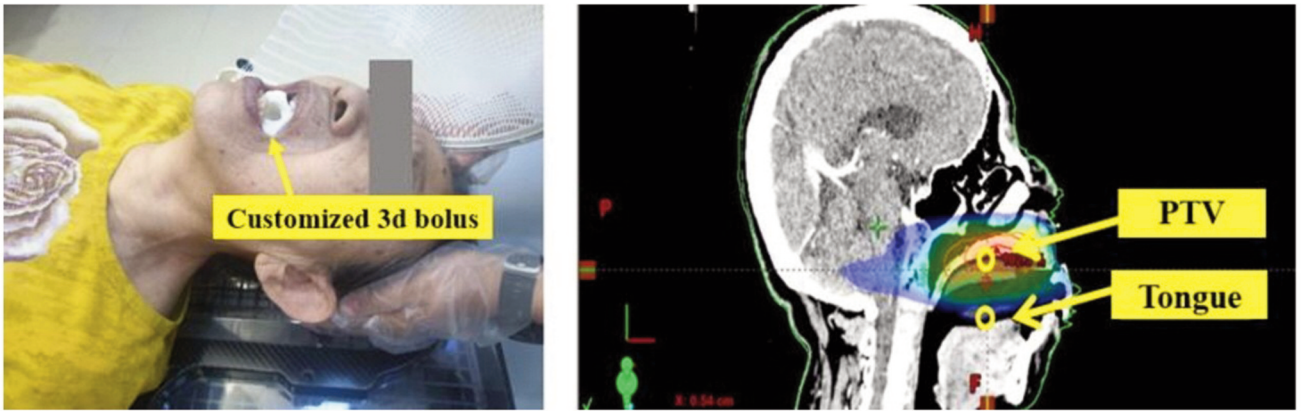

Figure 6. *Treatment setup and planning for patient 2. (a) Treatment setup and applying the customized 3D bolus made to patient 2, (b) a sagittal CT image taken with a balloon injected with 50 ml air in the mouth.*

and it allowed approximately 7.6% lower dose than that of the 5-mm thick bolus (Table II). Figure 4a illustrates how the customized 3D bolus was applied during the treatment of patient 1, and Figure 4b shows the axial dose distribution of the dose-calculated plan including the density override 3D bolus. In Figure 4b, the skin sparing area is the area where the tumor is located deep from the skin; hence, the skin does not receive a large dose, equivalent to the prescribed dose. In contrast, the tumor area is the area where the PTV is located close to the skin and requires dose buildup, and the area where the bolus structure is created from the extended PTV.

The dose distributions at these two points are shown in Table III. The doses at the skin sparing area were 34.8% and 73.0% without and with commercial bolus, respectively. Further, when a customized 3D bolus was applied at the skin sparing area, the dose value was 41.6%, which is similar to the dose value without a bolus.

For the tumor area, the dose was 41.3% without any bolus, 82.7% for the 5-mm thick commercial bolus, and 67.5% for the customized 3D bolus. When patient 1 treated with the customized 3D bolus, the *in vivo* measurements showed 58.6% and 83.2% of the prescribed dose at skin sparing area and tumor area, respectively.

Patient 2. The treatment site of patient 2 is shown in Figure 5. Moreover, the treatment setup and the axial dose distribution of the dose-calculated plan, including density override 3D bolus, is shown in Figure 6a and b, respectively. In Figure 6b, the PTV region is the area that requires dose buildup and the tongue region is the area where the dose buildup is not required. The treatment plan dose and the measured dose in the tumor area of the hard palate were 92.4% and 93.8%, respectively. The dose to the tongue in the treatment plan and *in vivo* measurement were 22.5% and 8.0%, respectively (Table IV).

Discussion

In RT, improving patient outcomes while reducing side effects is always a major concern. All medical staff involved in the patient's treatment discussed together the proper treatment and application of a customized 3D bolus, and performed *in vivo* dosimetry. As a result, the patient-specific treatment was well progressed.

In the case of patient 1, unlike producing the 3D boluses using previously reported methods, the benefit of the production of 3D boluses by expanding the PTV, which is the method proposed in this study, is that they can be made for specific areas of the human body. This method can be applied in the future to other sites such as breasts, hands, and feet.

As a result of the dose measurement for patient 1, if a 5-mm thick bolus was used for the entire area, it can be expected that 48.2 Gy/30 fx would be irradiated in the area where the dose buildup was unnecessary (Figure 4). According to Fu *et al*. (3), the skin reactions corresponding to grade 2 will occur in the skin exposed to this dose. Alternatively, owing to the use of the 3D bolus only in the local area, the dose to the area where the dose buildup is not required is reduced to 24.9 Gy/30fx, and a skin reaction corresponding to grade 1 or less is expected. Therefore, it is obvious that the method used in this study is useful for skin sparing.

In the case of patient 2, applying a 3D bolus to the oral cavity not only produces a better buildup effect, but also has the advantage of immobilizing the tongue; hence, the patient may feel less discomfort during the IMRT treatment. In addition, a hole in the middle of the bolus was created to allow the patient to breathe comfortably, and the shape of the 3D bolus was carefully made to match the mouthpiece worn by the patient and to improve reproducibility during daily repetitive treatment. The 3D bolus production is difficult to

apply to many patients because it requires large production time and work force. However, through this study, the possibility of the customized treatment was confirmed through the cooperation among the members of the department.

Conclusion

In this study, we found that creating a local 3D bolus structure using an extended PTV can improve target coverage and reduce unnecessary skin dose for an irregular skin. In addition, when an oral cavity is treated, the space created in advance using a balloon in the CT simulation step can be made into a 3D bolus structure, so that even when the patients are treated with the 3D bolus inserted in the oral cavity, they can be treated naturally and comfortably. This not only improves target coverage, but also achieves a tongue immobilization effect.

Conflicts of Interest

The Authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Authors' Contributions

All Authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each Author certifies that this material or a similar material has not been submitted to or published in any other journal.

Acknowledgements

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2019R1A2C108912912).

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Received October 21, 2020
Revised November 9, 2020
Accepted November 10, 2020