

# Comparison of Osteoradionecrosis of the Jaw After Superselective Intra-arterial Chemoradiotherapy Versus Conventional Concurrent Chemoradiotherapy of Oral Cancer

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**Purpose:** The purpose of the present study was to compare the incidence of osteoradionecrosis between superselective intra-arterial chemoradiotherapy and intravenous chemoradiotherapy and to verify the risk factors for osteoradionecrosis.

**Materials and Methods:** Of the 79 patients with oral cancer, 40 were treated with intra-venous chemoradiotherapy and 39 were treated with superselective intra-arterial chemoradiotherapy. The incidence of, and risk factors for, osteoradionecrosis were evaluated using statistical analysis.

**Results:** Of the 79 patients, 4 (10%) of 40 in the intravenous chemoradiotherapy and 7 (17.9%) of 39 in the superselective intra-arterial chemoradiotherapy group developed osteoradionecrosis of the jaw. No significant difference was found between the 2 groups. Although the chemoradiotherapy methods, anatomic tumor location, smoking behavior, alcohol consumption, condition of teeth, teeth extraction before radiation, and progression of dental caries were considered predisposing factors for the occurrence of osteoradionecrosis, only progressive dental caries resulted in a significant difference for osteoradionecrosis.

**Conclusions:** The present study is the first report comparing the incidence of osteoradionecrosis between superselective intra-arterial chemoradiotherapy and intravenous chemoradiotherapy. The administration methods of anticancer drugs were not related to the incidence of osteoradionecrosis in our study. From our study, dental caries is the most important risk factor for osteoradionecrosis; therefore, a radiation caries prevention program is crucial to control osteoradionecrosis.

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Osteoradionecrosis (ORN) of the jaw is a severe complication of radiotherapy for head and neck cancer. With the current advances in radiation technologies and the introduction of dental care protocols, the risk of developing ORN has been assumed to have declined, but the incidence is in fact unknown.<sup>1</sup> The most recent incidence of ORN was reported to range from 2.4 to 12%.<sup>1-5</sup> Chemoradiotherapy is the standard treatment of advanced unresectable head and neck carcinoma. A large meta-analysis showed a survival benefit with concurrent intravenous chemoradiotherapy (IVCRT) rather than sequential chemoradiotherapy.<sup>6</sup> Recently, cisplatin-based superselective intra-arterial chemoradiotherapy (SSIACRT) has gained wide acceptance as a common and curative treatment of advanced head and neck cancer. In some reports, no difference was found in the incidence of ORN between IVCRT and radiotherapy alone for head and neck cancer.<sup>7-9</sup> However, only a few reports have referred to ORN of the jaws after SSIACRT.<sup>10</sup> We have treated cases of advanced oral cancer with SSIACRT since 2003, and the results have been encouraging. However, ORN developed in some patients, and the incidence seemed to be more frequent than that after IVCRT. The purpose of the present study was to compare the incidence of ORN between patients undergoing SSIACRT and IVCRT and to verify the risk factors for ORN.

## Materials and Methods

### PATIENT ELIGIBILITY

The medical records of a consecutive series of patients with oral cancer who had been treated at the Department of Oral and Maxillofacial Surgery, Radiology, and Otorhinolaryngology, Hirosaki University Hospital from 2003 to 2011 were reviewed retrospectively. The study group included 79 patients (53 men and 26 women). All patients who had received radiotherapy at a dose of greater than 60 Gy, not only to the tumor, but also to the maxilla or mandible, or both, were included in the present study. For carcinoma of the tongue, lower gingiva, oral base, and upper gingiva, the radiation dose to the tumor, mandible, and maxilla was the same. For carcinoma of the buccal mucosa, the radiation dose to the tumor, maxilla, and mandible was also the same. For patients with neck recurrence, the radiation dose to the tumor and mandible was the same because the recurrence sites were level I and II. Patients with oropharyngeal carcinoma did not undergo SSIACRT in our department and, therefore, were excluded from the present study.

The distribution of patients stratified by the T and N classification for both the IVCRT and SSIACRT groups is listed in Tables 1 and 2, respectively. Of the 79 patients, 40 were treated with IVCRT. Of these 40 patients, 21 had undergone surgery followed by IVCRT, and 19

**Table 1. DISTRIBUTION BY T AND N CLASSIFICATION IN IVCRT GROUP**

T Stage	N Stage (n)						Total (n)
	N0	N1	N2a	N2b	N2c	N3	
T1	3	0	0	0	1	0	4
T2	4	3	1	2	1	2	13
T3	1	0	1	2	2	1	7
T4	5	3	0	5	3	0	16
Total	13	6	2	9	7	3	40

*Kobayashi et al. Comparison of ORN After Different Chemoradiotherapy Regimens. J Oral Maxillofac Surg 2015.*

had undergone only IVCRT. The remaining 39 patients received SSIACRT. Of the 39 patients, 22 had been previously reported on by Kobayashi et al.<sup>11</sup> Of the 79 patients, 3 in the IVCRT group had distant metastasis, but none did so in the SSIACRT group at the first medical consultation. Both groups were suitable for comparison of the incidence of ORN because no statistically significant differences were found in patient age, gender, T and N classification, or the primary sites (Table 3).

### METHODS

The background factors that resulted in the development of ORN and the differences in the frequency of ORN between the IVCRT and SSIACRT groups were analyzed. The grade of ORN was evaluated according to the Common Terminology Criteria for Adverse Events, version 4.0 (2009). The appropriate ethical committees of Hirosaki University Hospital, Hirosaki, Japan, approved the present study. We have read the Declaration of Helsinki and followed those guidelines in the present study.

### TREATMENT OPTIONS

Patients with oral cancer are free to consult with either the oral and maxillofacial surgery or

**Table 2. DISTRIBUTION BY T AND N CLASSIFICATION IN SSIACRT GROUP**

T Stage	N Stage (n)					Total
	N0	N1	N2a	N2b	N2c	
T0	0	0	0	2*	0	2
T1	1	0	0	0	0	1
T2	1	1	1	1	3	7
T3	3	2	0	1	1	7
T4	6	7	1	4	4	22
Total	11	10	2	8	8	39

\* Neck recurrence after surgical treatment.

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