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## Salvage operations for patients with persistent or recurrent cancer of the maxillary sinus after superselective intra-arterial infusion of cisplatin with concurrent radiotherapy

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## Abstract

Our aim was to evaluate the feasibility of salvage operations for patients with persistent or recurrent cancer of the maxillary sinus after superselective intra-arterial infusion of cisplatin with concurrent radiotherapy. We retrospectively analysed the records of 61 patients with cancer of the maxillary sinus who were treated in this way. Chemotherapy comprised  $100-120 \text{ mg/m}^2$  superselective intra-arterial infusions of cisplatin given a median of 4 times weekly (range 2–5). Concurrent radiotherapy was given in a median dose of 65 Gy (range 24–70 Gy). Persistent or recurrent cancer of the maxillary sinus was found in 17 patients, of whom 11 had salvage surgery. The disease was controlled in 8 of the 11, and 7 of the 11 survived with no evidence of disease. Their 5-year overall survival was 61%. Two of the 11 developed serious operative complications. Salvage surgery for patients with persistent or recurrent cancer of the maxillary sinus treated by superselective chemoradiotherapy is both safe and successful. Salvage surgery is a good option when this sort of persistent or recurrent cancer is followed up after the regimen of chemoradiotherapy described.

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Keywords: Maxillary sinus cancer; Salvage surgery; Squamous cell carcinoma; Chemotherapy; Radiotherapy; Intra-arterial

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## Introduction

Cancer of the maxillary sinus is rare. It comprises only about 3% of cancers of the head and neck and about 0.5% of all malignant disease.<sup>1</sup> The annual incidence is 0.5-1.0/100,000 population, and squamous cell carcinoma is the most common histological type, being found in over half of all patients with the disease.<sup>1-3</sup>

Many authors have recommended combined treatments consisting of en bloc radical resection together with irradiation.<sup>4–6</sup> However, the cosmetic problems for patients who have en bloc resection are considerable, so multiple treatments have been introduced to avoid cosmetic problems and to preserve ocular function and improve outcomes. In Japan, superselective intra-arterial cisplatin infusion with concurrent radiotherapy has been introduced to preserve the orbital contents and ocular function in patients with advanced cancers of the maxillary sinus.<sup>7,8</sup> This non-surgical treatment is both safe and highly effective.

Salvage surgery is generally attempted when localised persistent or recurrent primary tumours are found after initial chemoradiotherapy.<sup>9–12</sup> However, we know of no reports of salvage surgery for patients with persistent or recurrent cancer of the maxillary sinus after intensive chemoradiotherapy to date. The purpose of this study was to evaluate the feasibility of salvage surgery and to assess its efficacy for patients with persistent or recurrent cancer of the maxillary sinus after chemoradiotherapy.

## Method

#### Patients

We retrospectively analysed the records of 61 patients with squamous cell carcinoma of the maxillary sinus who had superselective intra-arterial infusion of cisplatin with concurrent radiotherapy at Hokkaido University Hospital, Japan between September 1999 and July 2012. T and N stages were classified according to the American Joint Committee on Cancer (AJCC) staging system 2010. Details of patients are shown in Table 1.

#### Radiotherapy

The irradiation plan during the period 2006–2012 was 40 Gy in 20 fractions of 2 Gy over four weeks for the primary site and involved nodal areas, immediately followed by a boost of 30 Gy in 15 fractions to the primary cancer over an additional three weeks (total dose 70 Gy). Between 1999 and 2005, involved nodal areas and the primary site were irradiated with 40 Gy in 16 fractions of 2.5 Gy over four weeks, with a boost irradiation of 25 Gy in 10 fractions to the primary tumour over an additional 2.5 weeks (total dose 65 Gy).

| Table 1   |
|---|
| Details of the 61 patients. Data are expressed as number (%) unless otherwise |
| stated  |

| Variable                       |            |
|--------------------------------|------------|
| Sex                            |            |
| Male                           | 50 (82)    |
| Female                         | 11 (18)    |
| Age (years)                    |            |
| Median (range)                 | 61 (34–74) |
| Duration of follow up (months) |            |
| Median (range)                 | 64 (9–143) |
| T classification               |            |
| T2                             | 1 (1)      |
| T3                             | 17 (28)    |
| T4a                            | 30 (49)    |
| T4b                            | 13 (21)    |
| N classification               |            |
| N0                             | 49 (80)    |
| N1                             | 7 (11)     |
| N2b                            | 5 (9)      |

## Chemotherapy

Chemotherapy comprised  $100-120 \text{ mg/m}^2$  superselective intra-arterial cisplatin given a median of 4 times weekly (range 2–5). At the same time, sodium thiosulphate was given intravenously (24 g/body weight) to effectively neutralise the cisplatin.

## Salvage surgery

Patients who were not given a full course of irradiation (<65 Gy) were referred for salvage surgery at the end of the course of radiotherapy. Patients given a full course of irradiation (>65 Gy), had a computed tomographic (CT) or magnetic resonance (MR) scan, or both, taken within 3 months of the completion of treatment. If there was persistent primary disease we attempted to biopsy it, and salvage surgery was recommended if viable tumour cells were found.

Patients were usually monitored monthly for recurrence during the first year, every 2 months during the second year, and every 6 or 12 months thereafter until death or the data were censored. CT or MR scans were taken routinely every 3 months during the first year, and every 6 or 12 months thereafter. Surgical complications were graded using the Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 4.0.(from National Cancer Institute web site http://evs.nci.nih.gov/ ftp1/CTCAE/CTCAE\_4.03\_2010-06- 14\_QuickReference 5x7.pdf, National Cancer Institute, US)

## **Statistics**

The Kaplan–Meier test was used to compare survival and local control from the start of treatment to death or failure. Probabilities of less than 0.05 were accepted as significant. The software JMP Pro 10.0.2 statistical software (SAS Institute, Cary, NC) was used to aid the statistical analysis.

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