Chapter 5
ICG Fluorescent Image-Guided Surgery in Head and Neck Cancer

Junkichi Yokoyama and Shinich Ohba

Abstract Neck lymph node metastasis is the most significant prognostic factor of head and neck cancer; however, there remains debate as to the most effective treatment of clinical N0 neck metastasis. Sentinel lymph node (SLN) navigation surgery decreases morbidity associated with neck dissections and reduces the potential of recurrences. While radiocolloids have been previously used to detect SLN, disadvantages of radiocolloids are not only the lack of real-time intraoperative visual information but also the phenomena of "shine-through" radioactivity due to scattering from the primary site. This is especially problematic in cases of cancer located at the floor of the mouth. Additionally, radiocolloids may expose patients and medical staff to irradiation.

To negotiate these problems, ICG (indocyanine green) fluorescence imaging has been used for the detection of SLN, translymphatic chemotherapy, and intra-arterial chemotherapy in cases of head and neck cancer. The advantages of ICG fluorescence imaging include access to real-time intraoperative visual information and little affections of "shine through" even in cases of the floor of the mouth.

Keywords ICG (indocyanine green) fluorescence imaging • Sentinel lymph node (SLN) • Head and neck cancer • Translymphatic chemotherapy • Intra-arterial chemotherapy

5.1 Introduction

The sentinel lymph node (SLN) is defined as the lymph node that first receives lymphatic drainage from the primary cancer [1]. The SLN is thought to be the foremost possible micrometastatic site via lymphatic drainage from the primary

J. Yokoyama (✉)
Department of Otolaryngology Head and Neck Surgery, Juntendo University, Tokyo, Japan

Department of Otolaryngology Head and Neck Surgery, Moriyama Memorial Hospital, 7-12-7 Nishikasai, Edogawa-ku, Tokyo 134-0088, Japan
e-mail: jyokoya@juntendo.ac.jp

S. Ohba
Department of Otolaryngology Head and Neck Surgery, Juntendo University, Tokyo, Japan

M. Kusano et al. (eds.), *ICG Fluorescence Imaging and Navigation Surgery*,
DOI 10.1007/978-4-431-55528-5_5

cancer. Consequently, the pathological status of the SLN can be examined to predict the status of all regional lymph nodes. For this reason, if the SLN is recognized as being negative for cancer metastasis, unnecessary dissection can be avoided and a positive prognosis achieved. This SLN concept is well established in the treatment of patients with several types of solid carcinomas, such as melanoma and breast cancer [2–4]. The SLN concept has revolutionized surgical strategies and modern techniques benefit patients by preventing a range of complications associated with unnecessary prophylactic dissection in cases when the SLN is negative for cancer metastasis. Recently, this highly advantageous SLN concept has been applied to the examination of head and neck cancers [5, 6].

5.2 Sentinel Lymph Node (SLN) Navigation Surgery

In clinically negative neck (cN0) of oral cancer, 20 to 30 % of patients have occult nodal metastases [7]. Neck metastasis is the most significant prognostic factor in oral cancer. However, to date there is no effective noninvasive diagnostic modality for the identification of occult regional disease in patients with cN0. As a result, prophylactic neck dissection in patients with T1/T2 oral cancer with cN0 neck is the procedure typically conducted. This is a significant concern given that approximately 70 to 80 % of neck dissection specimens are found to be negative for regional metastatic disease. In addition, prophylactic neck dissection is associated with severe postoperative complications such as swallowing and shoulder dysfunction.

Due to the critical need for an accurate noninvasive diagnostic approach to cN0 neck, SLN navigation surgery has been applied to patients with oral cancer of the cN0 neck.

Paleri et al. [8] performed a meta-analysis on 19 of these studies in order to examine a larger combined body of data. They reviewed 367 patients, including 301 patients with oral cavity lesions, and found a 97.7 % sentinel node identification rate. The combined sensitivity of SLN biopsy was 92.6 % with a false-negative rate of 3 %. The pooled data provides compelling evidence that there is no statistical difference between SND (selective neck dissection) and SLN biopsy in terms of recurrence, disease-free survival, and mortality.

In 2004, Ross et al. [9] performed a prospective randomized study of 134 patients with T1/T2 oral cavity cancer. They randomized 79 patients to receive SLN biopsy alone and 55 patients to receive SLN biopsy plus elective neck dissection. Sentinel node detection rates were 93 %, and 42 (34 %) patients were upstaged as a result of SLN biopsy.

Overall sensitivity was 93 % with an average follow-up of 2 years. However, sensitivity for floor-of-mouth (FOM) lesions proved to be only 80 % due to “shine through,” which was significantly lower than the results of other subsites in whose sensitivity was 100 %. Of those patients treated with SLN biopsy, only 3.8 % experienced recurrences of disease within 24 months. Those treated with SLN biopsy plus elective neck dissection recorded a 4 % false-negative rate. This study clearly demonstrates that SLN biopsy is as good as elective neck dissection with regard to identifying metastatic disease. However, the study also identified the FOM as a site prone to failure with SLN biopsy.

The obvious pitfall of SLN biopsy is its poor performance in identifying true sentinel nodes in patients with FOM tumors. Many researchers believe that the close proximity of level I nodes to the primary tumor leads to "shine-through" radioactivity, thus masking signals from the relevant SLN [8, 9]. This is a considerable problem associated not only with anatomy but also the properties of the radiolabeled agent.

To overcome the disadvantages of radioactive agents, ICG fluorescence imaging has been applied for detection of SLN of head and neck cancer. SLN around the submandibular lymph nodes can be clearly identified by ICG fluorescence imaging [10, 11]. Additionally, the cost of ICG fluorescence imaging is minimal and does not result in exposure to irradiation as is the case in conventional procedures using technesium 99 m-labeled sulfur colloid.

5.3 ICG Fluorescence Imaging-Guided Surgery for Parapharyngeal Space Tumors

5.3.1 Introduction

In the narrow parapharyngeal space, it is exceedingly difficult to resect tumors without complications such as dysphagia and carotid artery rupture [12]. In order to minimize surgical complications and preserve organs, endoscopic or robotic surgery is often executed when performing head and neck surgery. While highly effective, a disadvantage of these procedures is that it is not possible for the surgeon to physically touch tumors or to directly observe diffusely invaded deep organs. As a result, we have proposed using ICG florescence method for navigation surgery and have demonstrated the advantageous and effectiveness of ICG fluorescent image-guided surgery for the safe resection of parapharyngeal space tumors [13].

5.3.2 Methods

0.5 mg/kg of ICG was injected via the cephalic vein. Observation of the fluorescent image was conducted with HEMS (Hyper Eye Medical System) at 10–30 min after injection. At first, the position of the tumor was marked over pharyngeal mucosa through the use of ICG fluorescence imaging with HEMS. We could confirm the submucosal tumor although obscured by fascia under HEMS imaging and then carried out resection.

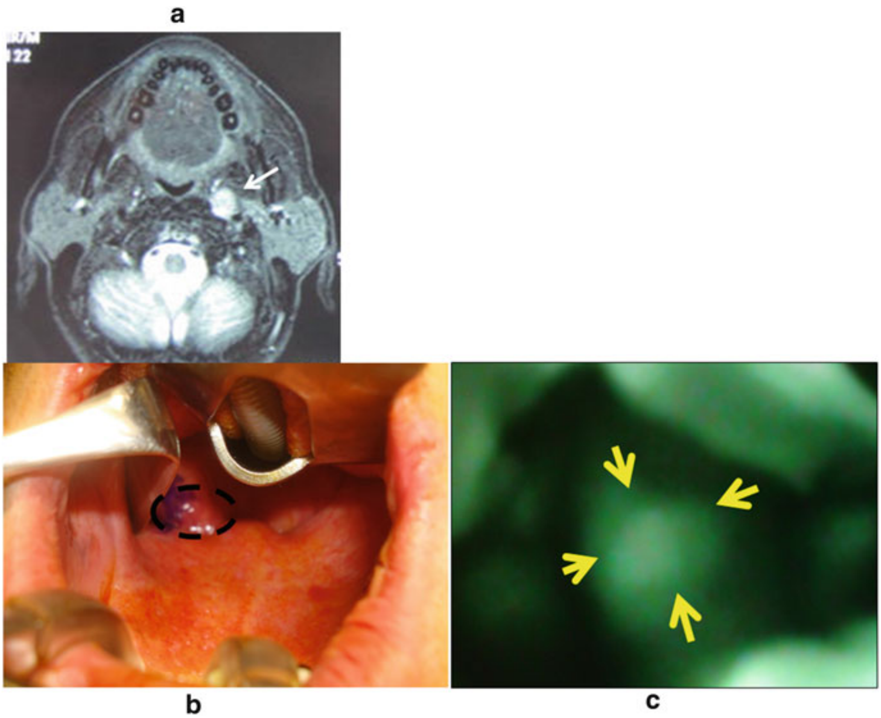

Fig. 5.1 Operative findings of metastatic parapharyngeal space from hypopharyngeal cancer
(**a**): Arrow represents a metastatic lymph node
(**b**): Dotted circle demonstrates the metastatic lymph node detected by ICG fluorescence Imaging over soft plate
(**c**): ICG fluorescence Imaging detects the metastatic lymph node (*arrows*)

5.3.3 Results

All tumors displayed bright fluorescence emissions which clearly contrasted with the surrounding normal structures. Even with the submucosal tumor covered with and obscured by fascia, we could observe the tumor clearly under HEMS imaging (Fig. 5.1). Tumors behind the carotid artery and lower cranial nerves also displayed bright fluorescence emissions and could therefore be clearly detected. Accordingly, we could remove the tumor safely and noninvasively which enabled successful preservation of pharyngeal functions.

5.3.4 Discussion

The handheld HEMS can significantly aid in the detection and visual confirmation of pharyngeal tumors located behind the oral cavity or nasal cavity by

ICG-enhanced imaging with vivid color. Of note is that it can be freely operated intraoperatively by surgeons. Because of the high sensitivity of ICG fluorescence imaging, ICG fluorescence imaging under HEMS can assist surgeons in the identification and resection of tumors which have invaded the parapharyngeal space behind the internal carotid artery, internal jugular vein, and lower cranial nerves.

We have demonstrated a successful method of distinguishing cancer from healthy tissue and the optimum surgical time with HEMS in animal models [14]. Application of endoscopic and robotic surgery for the parapharyngeal space lesions enables surgeons to perform minimally invasive surgery with superior results [15]. However, we need to be able to detect parapharyngeal tumors in deeper and invisible areas when palpation is not possible. This is required in order to resect tumors safely and can be aided through effective tumor detection carried out with ICG fluorescent imaging.

5.3.5 Conclusion

ICG fluorescence imaging is effective for the detection and resection of the parapharyngeal space tumors which enables greater preservation of functions.

5.4 Lymphatic Chemotherapy for Head and Neck Cancer

According to the sentinel theory, metastatic lymph nodes are directly connected with primary tumors via lymphatic canals. Lymphatic chemotherapy is defined as chemotherapy using lymphatic canals between metastatic lymph nodes and primary tumors. This therapy is viewed as an ultimate cancer treatment which is both highly effective and noninvasive.

(a) **Clinical N0 Cases (Occult Neck Metastasis)**

In the following, we consider a newly developed lymphatic chemotherapy procedure targeting the SLN using intra-arterial (I-A) chemotherapy for oral cancer in order to improve prognosis and to preserve organs while avoiding surgical complications [11, 16–18]. Our concept of lymphatic chemotherapy is shown in Fig. 5.2. Namely, the schema of lymphatic chemotherapy demonstrates an anticancer drug administered to the primary cancer which moves selectively to SLNs via lymphatic canals. As a result, the anticancer drug is accumulated in the SLNs and results in a higher anticancer drug concentration in the SLNs than non-SLNs. Because cis-diamminedichloroplatinum (CDDP) is the most promising drug for the treatment of head and neck cancers, we have adopted intra-arterial chemotherapy administered to the primary cancer so as to increase the CDDP concentration. To examine the potential advantages, we compared the CDDP concentration of SLNs with that of non-SLNs. The mean CDDP concentrations in the SLNs and

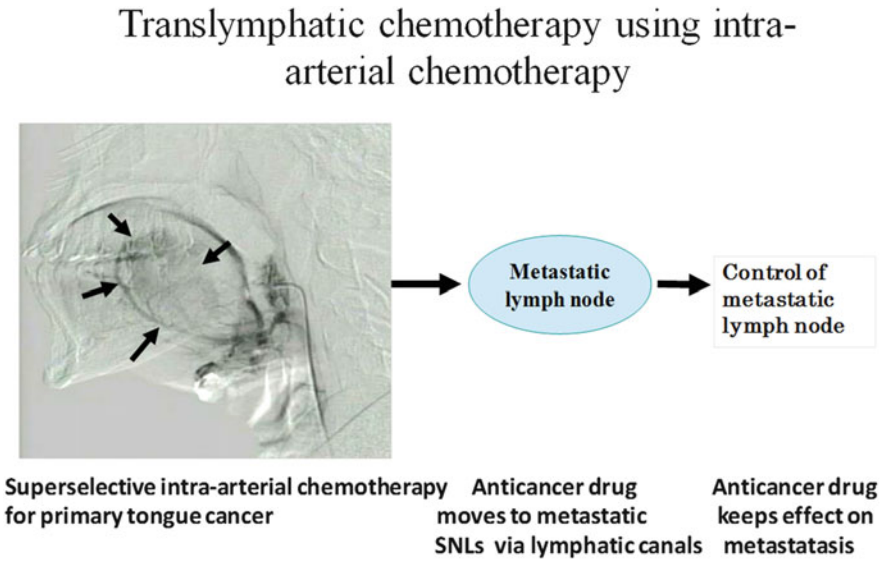

Fig. 5.2 Schema of lymphatic chemotherapy using intra-arterial chemotherapy

non-SLNs were 1.2 μg/g and 0.35 μg/g, respectively. Our ICG fluorescence procedure revealed that all metastatic lymph nodes, including SLNs, were without false-negative SLNs. However, of 7 metastatic lymph nodes, one was not identified by means of the conventional radiocolloid method [11]. Detection of SLNs was clearly demonstrated by ICG fluorescence imaging (Fig. 5.3). The mean number of SLNs was 5.6 (3–8). ICG fluorescence imaging showed a greater number of SLNs than seen when injecting radiocolloid intratumor (mean 3.4). SLNs detected by ICG fluorescence imaging included all of the SLNs detected by the conventional radioactive method.

(b) **Clinical Neck Metastasis Cases**

In the case of oral cancer with neck metastasis, modified radical neck dissection is often conducted to prevent cancer recurrence. However, this procedure can be the cause of severe postoperative complications. Instead of neck dissection and the associated surgical complications, minimally invasive lymphatic chemotherapy targeting neck metastasis based on the sentinel concept may contribute to the development of a revolutionary cancer treatment. This could potentially provide a superior method for the treatment of head and neck cancer which has been a key objective for researchers over many years. In our research, we consider I-A chemotherapy administered to primary oral cancers as not only organ preservation therapy but also a newly developed lymphatic chemotherapy targeting neck metastasis in order to improve prognosis.

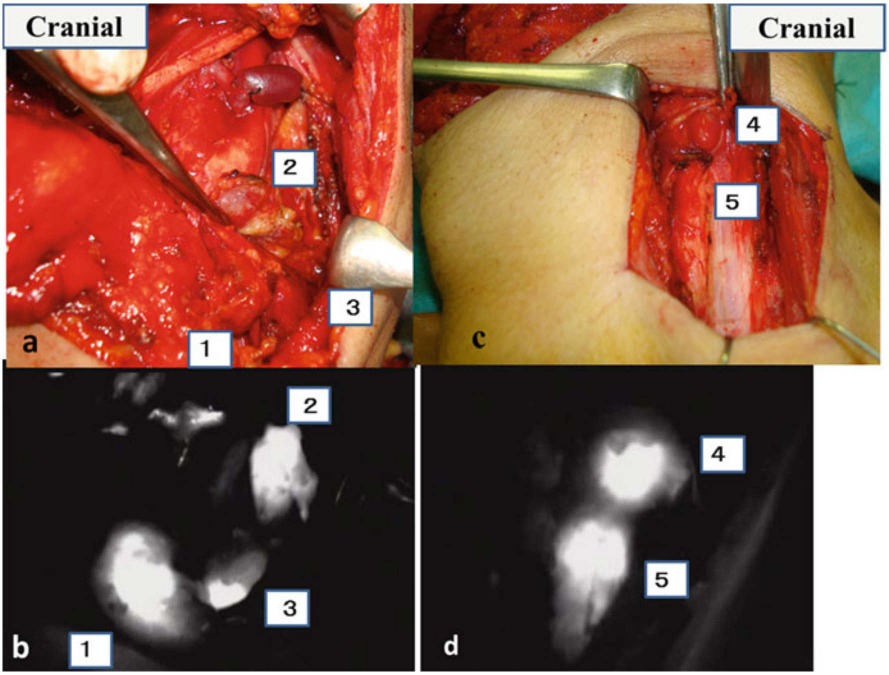

Fig. 5.3 Intraoperative navigation surgery using ICG fluorescence imaging
Upper figures (**a**, **c**) illustrate intraoperative navigation surgery by natural light; lower figures (**b**, **d**) illustrate intraoperative navigation surgery by ICG fluorescence imaging.
Number (1–5) means SLNs. (**a**) and (**b**) represent level II and III dissection. (**c**) and (**d**) represent level III and IV dissection

In our examination we evaluate the effect of lymphatic chemotherapy targeting neck metastases in patients with oral cancer (T3N2bM0) by measuring CDDP concentrations in metastatic lymph nodes and pathological effects [19].

5.4.1 Methods

Seven patients with tongue cancer (cT3N2bM0) were treated by intra-arterial chemotherapy as neoadjuvant chemotherapy. After a week of chemotherapy, patients underwent surgical treatment. Intra-arterial chemotherapy was administered at 75 mg/m^2 of CDDP two times weekly. At the beginning of surgery, 5 mg of ICG was administered to the lingual artery. SLNs were detected using ICG fluorescence imaging and a conventional radioactive method. The effect of lymphatic chemotherapy was evaluated based on the Ohboshi and Shimosato classification using the surgical specimens [20] and apoptosis using Trevigen's apoptosis detection kit.

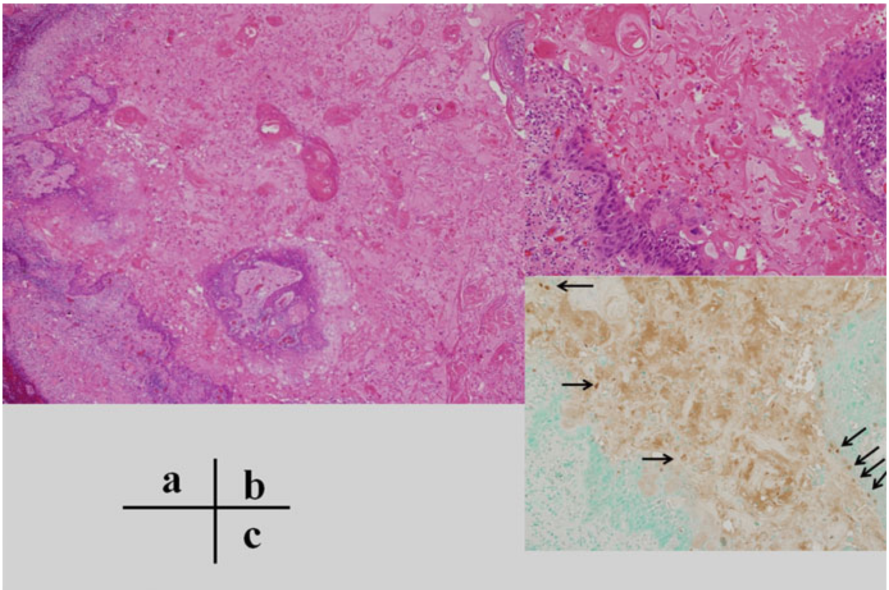

Fig. 5.4 Pathological findings of metastatic lymph nodes after chemotherapy
(**a**) Most of the metastatic cancer resulted in scar tissue; however, small cancer nests were residual (low-power magnification). (**b**) Cancer cells appeared to survive within small cancer nests (high-power magnification). (**c**) Many apoptotic bodies were detected within small cancer nests. *Arrows* indicate apoptotic cells

5.4.2 Results

The mean CDDP concentrations in the metastatic lymph nodes and non-SLNs were 2.35 μg/g and 1.08 μg/g, respectively ($p = 0.034$). Of 27 metastatic nodes, 24 (89 %) were identified by ICG fluorescence imaging; however, only 18 (67 %) were identified by the conventional method ($p = 0.043$). Of 22 measurable metastatic nodes, eight responded (partial response) and 14 did not respond (stable disease). Vast metastatic cancer was almost entirely diminished and resulted in scar tissue. Apoptosis was detected in all 27 metastatic lymph nodes and a pathological effect was achieved (Fig. 5.4).

5.4.3 Discussion

We have recently demonstrated that intra-arterial chemotherapy for the treatment of primary tongue cancers is also effective as a means of lymphatic chemotherapy as it aids in the control of the subclinical metastatic tumors in SLNs (11). All SLNs were detected by ICG fluorescence imaging infused via the lingual artery in cT3N0M0

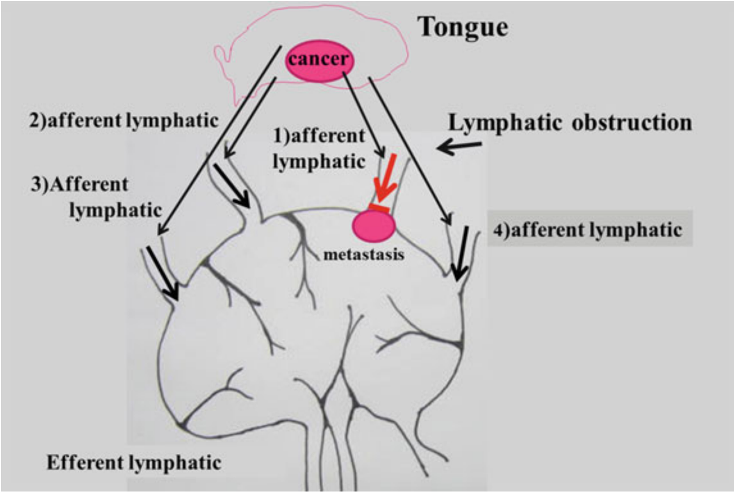

Fig. 5.5 Schema of increasing CDDP concentration of metastatic lymph nodes
Despite occlusion of afferent lymphatics from the tongue cancer, each lymph node has several afferent lymphatics, and ICG or CDDP could move to metastatic lymph nodes via several other afferent lymphatics in the case of intra-arterial infusion. (*1*) Occluded afferent lymphatics (*red arrow*). (*2–4*) Open afferent lymphatics (*black arrows*)

tongue cancer patients. However, of 27 metastatic lymph nodes, 24 (89 %) were detected by ICG fluorescence imaging infused via the lingual artery in seven cT3N2bM0 tongue cancer patients. The number of SLNs including metastatic lymph nodes resulting from I-A infusion was greater than that observed by means of a conventional injection into the tumor. Even in the case of micrometastatic SLNs, an afferent lymphatic canal was sometimes occluded by micrometastatic cancer based on sentinel navigation or CT lymphography [21]. In the current study, we also did not detect 9 (33 %) metastatic lymph nodes by conventional methods due to occlusion of afferent lymphatics from the tongue cancer (Fig. 5.5). However, the lymph nodes contained CDDP concentrations as high as 4.65 μg/g. This was because each lymph node has several afferent lymphatics and ICG or CDDP could move to metastatic lymph nodes via several other afferent lymphatics in the case of intra-arterial infusion. CDDP was released continuously from the primary tongue cancer via the lymphatic canal for a period of over more than 1 week. CDDP was selectively accumulated in metastatic lymph nodes and continued to affect metastatic lymph nodes over a long period.

Our intra-arterial chemotherapy is expected to contribute not only to primary organ preservation but also to positive prognosis by controlling the metastatic SLNs. Preservation of patients' quality of life in advanced cT3N2bM0 tongue cancer can be effectively achieved by intra-arterial chemotherapy and targeting metastatic lymph nodes with lymphatic chemotherapy.

As for ICG fluorescence imaging, metastatic SLNs were clearly detected even in close proximity to the primary tumor and “shine through” could be avoided. The ICG fluorescence imaging procedure demonstrated higher success rates for the detection of SLNs in patients with tumors located in the tongue than the radioactivity method.

5.4.4 Conclusion

CDDP concentrations in metastatic nodes were significantly higher than those in non-SLNs. This novel drug delivery system is feasible for lymphatic chemotherapy targeting metastatic nodes in patients with cT-3N2bM0 tongue cancer.

5.5 Significant Contribution to Superselective Intra-arterial Chemotherapy for Advanced Head and Neck Cancer

5.5.1 Introduction

For advanced paranasal sinus cancer, which is resistant to conventional systemic chemotherapy, superselective intra-arterial chemotherapy is believed to increase the concentration of anticancer drugs in the tumor [11, 22–24]. It is most important for I-A chemotherapy to obtain precise information about the blood supply to tumors. In 1998, we conducted CT angiography in order to accurately determine the blood supply to tumors in cases of head and neck cancer. This was the first time such a study had ever been conducted [25]. Our procedure can provide accurate and detailed information about the vascular supply to head and neck cancers [22, 26-29]. At the same time, it is difficult to confirm the drug distribution areas when the tumor is superficially invasive or the patient has undergone dental treatment involving metal fillings.

Recent advances in ICG fluorescence imaging have enabled visualization of the blood flow in tissues [11, 30, 31]. To date, the only report in which the ICG technique has been applied with intra-arterial chemotherapy was in a case involving oral cancer [32]. We have also utilized ICG fluorescence technique in combination with CT angiography in cases of advanced paranasal sinus cancer [33].

The purpose of this investigation was to assess the feasibility of the ICG fluorescence technique during intra-arterial chemotherapy for advanced paranasal sinus cancer.

Patients: Thirty-six patients with paranasal sinus cancer who were treated by intra-arterial chemotherapy were included in the study. Conventional CT angiography followed by 5 mg of ICG injection was performed to confirm the areas in which the drug had dispersed.

5.5.2 Results

Out of 36 cases, in 17 (47 %) the blood supply to the cancer was clearly detected by CT angiography (Fig. 5.6). By means of adding the infrared ICG evaluation, the blood supply to tumors could be easily confirmed in all cases without exposure to radiation. The information obtained from fluorescence imaging was advantageous when making decisions concerning the administration of chemo-agents for paranasal sinus cancers in cases involving dental metal fillings or skin invasion.

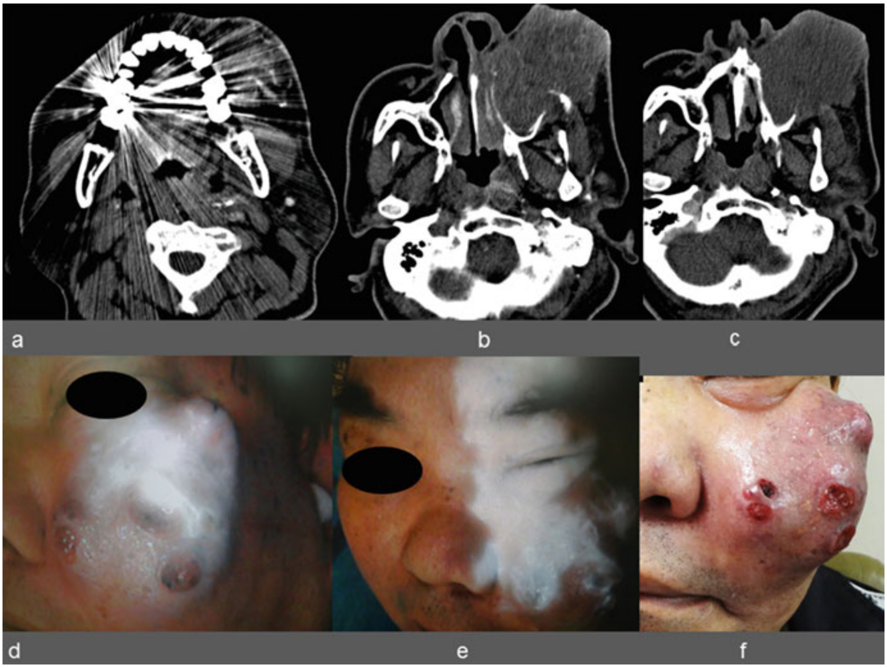

Fig. 5.6 CT angiography and ICG fluorescence imaging of maxillary cancer
(**a**) CT angiography obtained in the selected left side maxillary artery. It was difficult to confirm the vascular territory due to the presence of dental metals. (**b**) CT angiography obtained in the selected left side maxillary artery. It was difficult to confirm the vascular territory due to obstacle enhancement. (**c**) CT angiography obtained in the selected left side internal carotid artery. It was difficult to confirm the vascular territory due to obstacle enhancement. (**d**) ICG fluorescence imaging of the left maxillary artery. It was sufficiently clear to confirm the vascular territory. (**e**) ICG fluorescence imaging of the left internal carotid artery. Cancer involving the facial skin was clearly visible under fluorescent imaging of each vascular area. (**f**) Maxillary cancer invading the face before treatment

ICG fluorescence imaging combined with I-A chemotherapy compensated for the deficiencies of CT angiography for paranasal sinus cancer. ICG fluorescence provided greater clarity and more constructive information concerning the feeders to cancers (Fig. 5.6).

5.5.3 Discussion

Chemoradiotherapy for head and neck cancer plays an important role in organ preservation; nevertheless there are many cases, such as paranasal sinus cancer, for which conventional systemic chemotherapy does not work at all. For such chemo-resistant cancers including paranasal sinus cancer, superselective I-A chemotherapy is considered the most effective method by which to overcome these cancers due to increased concentrations of anticancer drugs in the cancer [11, 22–24]. To achieve effective therapeutic results for paranasal sinus cancer with I-A chemotherapy, precise evaluation of the tumor-feeding artery and drug distribution territories is required. CT angiography provides more precise identification of the blood supply to the tumor than digital subtraction angiography (DSA) [22, 25, 26, 32]. However, we are sometimes unable to confirm the tumor-feeding artery in paranasal sinus cancer patients with dental metal fillings or when the tumor has spread to oral cavities or superficially to the facial skin.

Recently the ICG fluorescence technique has been developed and applied to various fields [11, 30, 31]. We have reported that the ICG fluorescence technique can be a very useful method for treating oral cancers with I-A chemotherapy in patients with dental metal fillings [32]. We also reported our success in identifying the tumor-feeding arteries in paranasal sinus cancer by means of ICG fluorescence imaging. We found that the ICG fluorescence technique was a very useful method even in patients with dental metal fillings.

One of most problematic issues involving the application of I-A chemotherapy for advanced paranasal sinus cancers is that the tumors are often supplied by the internal carotid artery, and consequently, to prevent brain complications, I-A chemotherapies were previously not employed for such cases. However, tumors are often recurrences at the regions where CDDP is not administered by the internal carotid artery. These recurrent tumors in the skull base cannot be resected, and consequently, patient's prognosis is very poor. The development of ICG fluorescent image has enabled us to clearly detect tumor staining and evaluate the contribution to blood supplying for the tumor by the internal carotid artery. Minimal dose of CDDP via the internal carotid artery has enabled us to safely treat advanced paranasal sinus cancer, while improving patient prognosis and preserving organs.

5.6 Conclusion

ICG fluorescence imaging for intra-arterial chemotherapy reveals the blood supplies to paranasal sinus cancers more accurately than CT angiography, especially in cases of superficial spread or those involving dental metal. The application of ICG fluorescence together with CT angiography provides more accurate information about the feeding arteries to tumors and enables effective intra-arterial chemotherapy, while avoiding complications.

References

1. Morton DL, Wen DR, Wong JH et al (1992) Technical details of intraoperative lymphatic mapping for early stage melanoma. Arch Surg 127:392–399
2. Giuliano AE, Kirgan DM, Guenther JM et al (1994) Lymphatic mapping and sentinel Lymphadenectomy for breast cancer. Ann Surg 220:391–401
3. Morton DL, Thompson JF, Essner R et al (1999) Validation of the accuracy of intraoperative lymphatic mapping and sentinel lymphadenectomy for early-stage melanoma: a multicenter trial. Multicenter Selective Lymphadenectomy Trial Group. Ann Surg 230:453–463
4. Krag D, Weaver D, Ashikaga T et al (1998) The sentinel node in breast cancer – a multicenter validation study. N Engl J Med 339:941–946
5. Rinaldo A, Devaney KO, Ferlito A et al (2004) Immunohistochemical studies in the identification of lymph node micrometastases in patients with squamous cell carcinoma of the head and neck. ORL J Otorhinolaryngol Relat Spec 66:38–41
6. De Cicco C, Trifirò G, Calabrese L et al (2006) Lymphatic mapping to tailor selective lymphadenectomy in cN0 tongue carcinoma: beyond the sentinel node concept. Eur J Nucl Med Mol Imaging 33:900–905
7. Shah JP (1990) Patterns of cervical lymph node metastasis from squamous carcinomas of the upper aerodigestive tract. Am J Surg 160:405–409
8. Paleri V, Rees G, Arullendran P et al (2005) Sentinel node biopsy in squamous cell cancer of the oral cavity and oral pharynx: a diagnostic meta-analysis. Head Neck 27:739–747
9. Ross GL, Soutar DS, MacDonald DG et al (2004) Sentinel node biopsy in head and neck cancer: preliminary results of a multicenter trial. Ann Surg Oncol 11:690–696
10. Bredell MG (2010) Sentinel lymph node mapping by indocyanin green fluorescence imaging in oropharyngeal cancer – preliminary experience. Head Neck Oncol 2:31. doi:10.1186/1758-3284-2-31
11. Yokoyama J, Ito S, Ohba S et al (2011) A novel approach to translymphatic chemotherapy targeting sentinel lymph nodes of patients with oral cancer using intra-arterial chemotherapy-preliminary study. Head Neck Oncol 3:42
12. Carrau RL, Myers E, Johnson J (1990) Management of tumors arising in the parapharyngeal space. Laryngoscope 100:583–589
13. Yokoyama J, Ooba S, Fujimaki M et al (2014) Impact of indocyanine green fluorescent image-guided surgery for parapharyngeal space tumors. J Cranio-Maxillofacial Surg 42:835–838
14. Fujimaki M, Yokoyama J, Ohba S et al (2012) Dynamic imaging in determining the optimum surgical time for NIR fluorescent image-guided surgery. Head Neck Oncol 4:50
15. Desai SC, Sung CK, Genden EM (2008) Transoral robotic surgery using an image guidance system. Laryngoscope 118:2003e2005

16. Yokoyama J, Ohba S, Fujimaki M et al (2014) Impact of intra-arterial chemotherapy including internal carotid artery for advanced paranasal sinus cancers involving the skull base. Br J Cancer 1. doi: 10.1038/bjc.2014.501
17. Shiga K, Yokoyama J, Hashimoto S et al (2007) Combined therapy after superselective arterial cisplatin infusion to treat maxillary squamous cell carcinoma. Otolaryngol Head Neck Surg 136:1003–1009
18. Robbins KT (2000) The evolving role of combined modality therapy in head and neck cancer. Arch Otolaryngol Head Neck Surg 126:265–269
19. Yokoyama J, Ohba S, Ito S et al (2012) Impact of lymphatic chemotherapy targeting metastatic lymph nodes in patients with tongue cancer (T3, N2b, M0) using intra-arterial chemotherapy. Head Neck Oncol 4(2):64
20. Shimosato Y, Oboshi S, Baba K (1971) Histological evaluation of effects of radiotherapy and chemotherapy for carcinomas. Jpn J Clin Oncol 1:19–35
21. Matsuzuka T, Kano M, Ogawa H et al (2008) Sentinel node mapping for node positive oral cancer: potential to predict multiple metastasis. Laryngoscope 118(4):646–649
22. Kaketa S, Korogi Y, Miyaguni Y et al (2007) A cone-beam volume CT using a 3D angiography system with a flat panel detector of direct conversion type: usefulness for superselective intra-arterial chemotherapy for head and neck tumors. AJNR Am J Neuroradiol 28:1783–1788
23. Korogi Y, Hirai T, Nishimura R et al (1995) Superselective intraarterial infusion of cisplatin for squamous cell carcinoma of the mouth: preliminary clinical experience. AJR Am J Roentgenol 165:1269–1272
24. Bertino G, Benazzo M, Gatti P et al (2007) Curative and organ-preserving treatment with intra-arterial carboplatin induction followed by surgery and/or radiotherapy for advanced head and neck cancer: single-center five-year results. BMC Cancer 7:62
25. Yokoyama J (2002) Usefulness of CT-angiography for superselective intra-arterial chemotherapy for advanced head and neck cancers. Gan To Kagaku Ryoho 29:2302–2306
26. Miyayama S, Yamashiro M, Hattori Y et al (2002) Usefulness of C-arm CT during superselective infusion chemotherapy for advanced head and neck carcinoma. J Med Imaging Radiat Oncol 55:368–372
27. Hirai T, Korogi Y, Ono K et al (2001) Intra-arterial chemotherapy for locally advanced and/or recurrent hepatic tumors: evaluation of the feeding artery with an interventional CT system. Cardiovasc Intervent Radiol 24:176–179
28. Tomura N, Hashimoto M, Sashi R et al (1996) Superselective angio-CT of brain tumors. AJNR Am J Neuroradiol 17:1073–1080
29. Hirai T, Korogi Y, Ono K et al (2004) Preoperative embolization for meningeal tumors: evaluation of vascular supply with angio-CT. AJNR Am J Neuroradiol 25:74–76
30. Litvack ZN, Zada G, Laws ER Jr (2012) Indocyanine green fluorescence endoscopy for visual differentiation of pituitary tumor from surrounding structures. J Neurosurg 116:935–941
31. Shimada Y, Okumura T, Nagata T et al (2011) Usefulness of blood supply visualization by indocyanine green fluorescence during esophagectomy. Esophagus 8:259–266
32. Ohba S, Yokoyama J, Fujimaki M et al (2012) Significant improvement in superselective intra-arterial chemotherapy for oral cancer by using indocyanine green fluorescence. Oral Oncol 48:1101–1105
33. Yokoyama J, Ohba S, Fujimaki M et al (2012) Significant improvement in superselective intra-arterial chemotherapy for advanced paranasal sinus cancer by using Indocyanine green fluorescence. Eur Arch Otorhinolaryngol 271(10):2795–2801