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Protocol for a multicentre, prospective observational study of elective neck dissection for clinically node-negative oral tongue squamous cell carcinoma (END-TC study)

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ABSTRACT

Introduction In early-stage oral tongue squamous cell carcinoma (OTSCC), elective neck dissection (END) is recommended when occult lymph node metastasis is suspected; however, there is no unanimous consensus on the risks and benefits of END in such cases. The management of clinically node-negative (cN0) OTSCC remains controversial. This study, therefore, aimed to evaluate the efficacy of END and its impact on the quality of life (QoL) of patients with cN0 OTSCC.

Methods and analysis This is a prospective, multicentre, nonrandomised observational study. The choice of whether to perform END at the same time as resection of the primary tumour is based on institutional policy and patient preference. The primary endpoint of this study is 3-year overall survival. The secondary endpoints are 3-year disease-specific survival, 3-year relapse-free survival and the impact on patient QoL. Propensity score-matching analysis will be performed to reduce selection bias.

Ethics and dissemination This study was approved by the Clinical Research Review Board of the Nagasaki University. The protocol of this study was registered at the University Hospital Medical Information Network Clinical Trials Registry. The datasets generated during the current study will be available from the corresponding author on reasonable request. The results will be disseminated internationally, through scientific and professional conferences and in peer-reviewed medical journals.

Trial registration number UMIN000027875.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The strength of this study is the ability to evaluate the efficacy of elective neck dissection for clinically node-negative oral tongue squamous cell carcinoma in a large multicentre nationwide prospective observational study.
⇒ This study is being conducted by the joint research committee of the Japanese Society of Oral Oncology and involves institutions throughout Japan.
⇒ The limitation of this study is that it may not provide stronger evidence due to participants not being randomly assigned to an intervention or control group.
⇒ This prospective observational study is more relevant to clinical practice and more pragmatic to deliver without changing standard of care or ignoring clinician/patient preference.
⇒ Potential confounding differences at baseline due to non-randomisation and the selection biases associated with institutional policy and patient preferences are corrected for with a statistical technique called propensity score matching.

INTRODUCTION

Head and neck cancer is the seventh most common cancer worldwide, accounting for an estimated 888 000 new cases in 2018.[1] Almost 50% of head and neck cancers arise in the oral cavity.[1] Most oral cancers are squamous cell carcinoma, and regional lymph node metastasis of oral squamous

cell carcinoma is a useful prognostic factor of treatment outcomes.[2 3] Early detection of regional lymph node metastases in early-stage oral squamous cell carcinoma contributes to improved survival rates. Occult lymph node metastases are relatively common, even when the pretreatment diagnosis is negative for lymph node metastasis, with a varying frequency between institutions.[4 5] In cases where no involvement of the cervical lymph nodes is observed either clinically or via imaging, elective neck dissection (END) is recommended when occult lymph node metastasis is suspected. However, there is no unanimous consensus on the risks and benefits of END in such cases. Patients who undergo neck dissection have a low risk of spinal accessory-nerve injury, trapezius-muscle dysfunction and upper-limb elevation problems; therefore, unnecessary neck dissection should be avoided to improve patients' quality of life (QoL). Hence, reliable predictors are needed to identify patients with a true node-negative neck.

The depth of invasion (DOI) of the tumour is a predictor of cervical regional lymph node metastasis.[6] Many researchers have examined tumour DOI as a prognostic factor in oral squamous cell carcinoma.[6–8] A large, randomised phase III trial conducted by D'Cruz *et al*[9] revealed that the addition of END to partial glossectomy significantly improved overall survival (OS) in patients with early-stage oral squamous cell carcinoma, regardless of the degree of DOI. Furthermore, subgroup analysis revealed that patients with a pathological DOI of 3 mm or less benefited from END in addition to partial glossectomy.[9] However, there is some scepticism regarding the generalisability of this randomised control trial (RCT) to clinical practice. In general, most cases of lymph node recurrence are curatively operable if detected early; however, in that RCT,[9] 18% of the enrolled patients were deemed inoperable, which does not eliminate the impact of problems with medical resources or diagnostic systems at a single institution.

Previous meta-analyses of RCTs only incorporated RCTs with OS or disease-specific survival (DSS) as outcomes; hence, it is not surprising that END was deemed clinically significant in all of them.[4 10–12] However, several questions remain. Does neck dissection decrease QoL in truly node-negative patients? In addition, is it acceptable to generalise the results of an RCT of a patient population with low generalisability that participates in an RCT? The appropriate neck management for clinically node-negative (cN0) oral tongue squamous cell carcinoma (OTSCC) remains controversial.

Therefore, we conceived a prospective observational study to determine the efficacy of END in cN0 OTSCC, relevant to clinical practice and relatively unrestrictive, by performing curative treatment without randomisation after enrollment and with uniform follow-up. Furthermore, the results of this study may provide new outcome-oriented insights into the efficacy of END for cN0 OTSCC, by focussing on patient QoL.

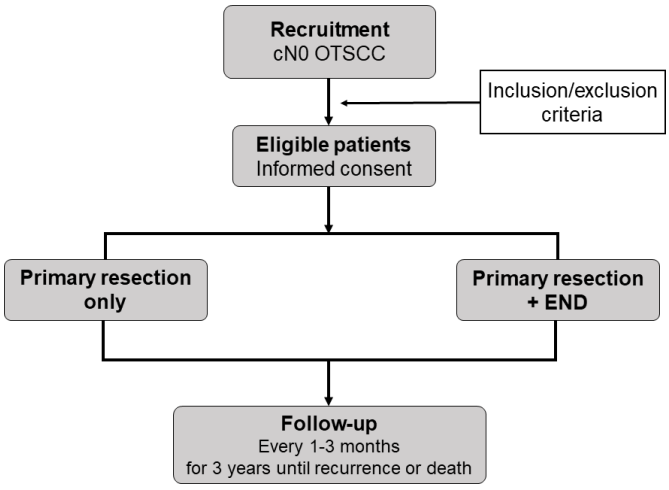

Figure 1 Flow diagram for the trial participants. cN0, clinically node-negative; OTSCC, oral tongue squamous cell carcinoma; END, elective neck dissection.

Objectives

The objective of this study is to evaluate the efficacy of END and its impact on QoL in patients with cN0 OTSCC.

METHODS AND ANALYSIS

Study design

This prospective study was designed as a multicentre, nonrandomised observational study for evaluation of the efficacy of END for patients with cN0 OTSCC. The methodology was developed according to the Strengthening the Reporting of Observational Studies in Epidemiology and standards for reporting diagnostic accuracy statements. The protocol was written based on the Standard Protocol Items: Recommendations for Interventional Trials checklist. Figure 1 contains the study flow chart.

Study setting

This multicentre study is being conducted by the joint research committee of the Japanese Society of Oral Oncology (JSOO). The participating institutions are JSOO-certified high-level clinical facilities in the provision of treatment for oral cancer and accept compliance with the study protocol. The research secretariat solicited the participation of such facilities. The participating facilities are Nagasaki University, Tokyo Medical and Dental University, Kumamoto University, Nippon Dental University, Tokyo Dental College, Kobe University, Tokushima University, Shinshu University, Kurume University, Nara Medical University, Tokyo Medical University, Hokkaido Cancer Center, Hokkaido University, Fukuoka Dental College, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Hirosaki University, Keio University, Nagaoka Red Cross Hospital, Yamagata University, Akita University, Tsukuba University, Tsurumi University, Saga University, Hyogo Medical University, Saiseikai Matsusaka General Hospital, Kagoshima University, Wakayama Medical University, Saitama Prefectural Cancer Centre, NTT Medical Centre Tokyo, Tokai

University, Sapporo Medical University, Osaka University, Dokkyo Medical University, Kanagawa Dental College and Yamaguchi University. The coordinating centre is located at Nagasaki University, and the data coordinating centre is located at the Centre for Clinical Research, Shinshu University Hospital.

Eligibility criteria

Inclusion criteria

- Histologically confirmed OTSCC.
- cN0 OTSCC based on the Union for International Caner Control eighth edition TNM classification.
- No apparent distant metastasis.
- Aged ≥20 years at the time of informed consent acquisition.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
- Patient operable.
- Signed informed consent.

Exclusion criteria

- History of treatment for malignant tumours of the head and neck area.
- History of multiple cancers with a disease-free period of less than 5 years at the date of registration.
- Psychosis or psychiatric symptoms that complicate participation in the study.

Interventions

All patients are diagnosed with enhanced CT or MRI at the minimum. Surgical treatment is performed with the patient under general anaesthesia. Resection of the primary tumour was performed to ensure adequate histopathological margins (>5 mm) in all planes. The choice of whether to perform END at the same time as resection of the primary tumour is based on institutional policy and patient preference. For the END procedure, dissection of at least levels I–III is recommended; however, the type of neck dissection is at the surgeon's discretion. In the group that undergo resection of the primary tumour alone, comprehensive neck dissection (dissection of levels I–V) is indicated when cervical lymph node metastases are detected during follow-up. If there are high-risk factors for postoperative recurrence, such as positive margins and/or extranodal extension, additional resection of the primary tumour, postoperative radiation therapy (RT) or chemoradiation therapy (CRT) may be recommended.

Outcomes

The primary endpoint of this study is OS. The OS will be calculated from the date of curative treatment (the date of surgery or the end date of postoperative RT/CRT) to the date of death from any cause and censored at the last follow-up day at which the patient is alive.

The secondary endpoints are DSS, relapse-free survival (RFS) and the impact on QoL. The DSS will be calculated from the date of curative treatment to the date of death from OTSCC and censored at the time of death from other diseases or the last follow-up day at which the patient is alive. The RFS will be calculated from the date of curative treatment to the date of any relapse or death from any cause and censored at the last follow-up day at which the patient is alive and relapse-free. The impact of QoL is assessed by using the Functional Assessment of Cancer Therapy-Head and Neck (Version 4; FACT-H&N)[13] and the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire.[14] The FACT-H&N consists of 11 items specific to head and neck cancer, an addition to the FACT-General, a QoL questionnaire for cancer in general.

Follow-up and assessment schedule

Participants will be followed up for 3 years after the date of curative treatment. The date of curative treatment is the date of surgery or the end date of postoperative RT/CRT. Patients will be followed up every month for the first year, every 2 months in the second year, and every 3 months thereafter. Palpation with/without ultrasonography will be performed at each follow-up visit. In addition, enhanced CT or MRI of the head and neck will be performed every 3 months after curative treatment and chest X-ray examination or CT every 6 months thereafter. Furthermore, the FACT-H&N questionnaire will be used for assessment 1, 3, 6, 12, 24 and 36 months after curative treatment. Simultaneously, the DASH questionnaire will be used for assessment 36 months after curative treatment. The data collection schedule is presented in table 1.

Sample size

The primary endpoint of this study is 3-year OS, which was used to calculate the required sample size. According to a previous RCT,[9] the 3-year OS rate of patients who underwent resection of the primary tumour alone was 67.5%, and the 3-year OS rate of patients who underwent END was 80.0%. The sample size required to detect differences between two independent proportions was calculated by using the SWOG statistical tool (https://statstools.crab.org/), with 80% power and a two-sided significance level of α=0.05. Accordingly, 199 participants are required in each group. As the rate of END for early-stage tongue cancer in Japan is approximately 25%,[15] the total sample size should be 800. Since this study is a prospective observational study, the sample size should be acceptable in actual clinical practice, but the sample size was set to be statistically advantageous by referring to previous prospective studies. In addition, the drop-out rate was not taken into account.

Recruitment

Participant recruitment started at the participating facilities in November 2017 and will continue to October 2022. The planned study period is November 2017 to October 2026. All patients with cN0 OTSCC are screened for eligibility and asked to provide written informed consent (see online supplemental file). Principal investigator of the participant institutions will train the participants to

Table 1 Schedule of events

	Pretreatment (–4 to 0 weeks)	After curative treatment (months)												
		1	3	6	9	12	15	18	21	24	27	30	33	36
Informed consent	●													
Patient information	●													
Physical examination	●													
Medical history	●													
CT or MRI	●		●	●	●	●	●	●	●	●	●	●	●	●
Chest X-ray or CT				●		●		●		●		●		●
Fact-H&N	●	●	●	●		●				●				●
DASH														●
Palpation or US		At follow-up every month ⟷					At follow-up every 2 months ⟷				●	●	●	●

DASH, Disabilities of the Arm, Shoulder, and Hand questionnaire; Fact-H&N, Functional Assessment of Cancer Therapy-Head and Neck scale; US, ultrasonography.

explain the purpose and details of the study in the local language, obtain written informed consent, and record relevant information on QoL questionnaire. Participants are informed that they have the right to withdraw from the study at any time without having to give a reason.

Patient and public involvement

No patient involved.

Data collection and management

Data collection will be performed by using the Alliance Clinical Research Support System Electronic Data Capture (EDC) software of the University Hospital Clinical Trial Alliance. Data entry into the case report forms will be performed by investigators using the EDC software at each participating facility. Following the completion of the study, the fixed data will be exported, deleted from the EDC, and stored in a public data repository.

Statistical analysis

Clinicopathological characteristics of participants will be compared between the primary resection-only group and the primary resection with END group by using the χ^2 or Fisher's exact test for categorical variables and the t-test or Mann-Whitney U test for continuous variables. Cumulative OS, DSS and RFS rates will be estimated with the Kaplan-Meier method and compared with the log-rank test, followed by multivariate Cox proportional hazards analyses.

Propensity score-matching analysis will be performed to reduce selection biases associated with the institutional policy and patient preferences. The propensity score will be computed via logistic regression for each patient based on the presumed covariates, which includes age, sex, ECOG performance status, smoking status, alcohol consumption, clinical T stage, clinical DOI and oral care management. Propensity score matching will be performed with 1:1 nearest-neighbour matching and a calliper value equal to a width of 0.25 for the SD of the propensity score.

All data analyses will be performed by using IBM SPSS Statistics for Windows V.24.0 (Japan IBM). Two-tailed p values <0.05 will be defined as statistically significant throughout the analyses.

Data sharing

The study investigators will have full access to and ownership of all data. Deidentified data will be made available to interested outside investigators for additional analyses on reasonable request, following reports of primary outcomes, and with an appropriate data use agreement. Anonymised patient data will be made available via the data coordinating centre (Centre for Clinical Research, Shinshu University Hospital; tcend-project@umin.org) to qualified investigators who submit an approved research proposal. The anonymity, reliability and process of the data collected will be explained in the consent form, explaining that the data will be used only for the purpose of the specific study and will be destroyed after completion. To maintain the confidentiality and anonymity of the participants, the identities of the participants will not be mentioned at all. Participants will be coded so that no one but the principal investigator will know whose data are being used. Only the principal investigator will have access to the data.

Perspective/conclusion

Although the superiority of END over primary resection alone in early-stage tongue cancer has been demonstrated by several meta-analyses or systematic reviews,[10–12] there is resistance to generalising and interpreting the results of only a few RCTs. In fact, several problems have been pointed out. First, there is the issue of the difference in the significance of DOI according to the primary site of oral cavity, in other words, whether a DOI of 3 mm

for tongue cancer and 3 mm for oral floor cancer can be considered in the same way. In addition, the issue of the high rate of neck recurrence, in the RCT by India,[9] 43% of the primary resection-only group had neck recurrence, and 18% of them were inoperable. Furthermore, the randomisation of END or not may result in a limited number of study participants, which may lead to a study with low external validity, low generalisability, which is the most feared aspect of RCTs. Therefore, a prospective observational study was conceived to see what would happen if the patients were treated without randomisation and uniformly followed up.

Perspectives of this study may clarify the incidence of occult neck metastases in Japan. It may be possible to set a cut-off value for DOI to determine the superiority of END in tongue cancer. It may be possible to clarify the impact of END on QoL. Ultimately, our results will contribute to determining clear criteria for END.

ETHICS AND DISSEMINATION

This study was approved by the Clinical Research Review Board of Nagasaki University (No. 17061944) in 21 June 2017. At the same time, the protocol of this study was registered at the University Hospital Medical Information Network Clinical Trials Registry (UMIN000027875). Details are available at the following address: https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000031938.

Any protocol changes that impact the study conduct and/or participant risk–benefit profile, including changes in the objectives, design, sample size, participant characteristics, staff or important administrative aspects, require approval from the relevant institutional review board. Minor protocol corrections and/or clarifications that do not affect study conduct or the participant risk–benefit profile are viewed as unimportant administrative changes and documented internally. This protocol was revised to a V.2 on 8 June 2020, to extend the case enrolment period.

The findings of this study will be disseminated internationally through scientific and professional conferences and in peer-reviewed medical journals.

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Contributors MU is the principal investigator of this study. The idea and concept were developed by SY, MU, HK and TK. Data collection was performed by YM, MO, TI, HN, TN, TH, YY, SY, JK, NY, OH, MU, YK, AH, TH, YO, WK, SA, TK, MI, MF, NI-K, KK, RA, KN, MO, AT, TS, YS, KY, MY, YO, AM, AT, HK, IH and KU. Data analysis was performed by SY and HK. The first draft of the manuscript was written by SY, and all authors commented on the previous versions of the manuscript. All authors contributed to the study conception and design and have read and approved the final manuscript.

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Disclaimer The funder will have no role in study design, data collection and analysis, manuscript preparation, or decision to publish.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s)

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Participation in Clinical Research

Prospective observational study of elective neck dissection for clinical N0 tongue cancer

Created: June 21, 2017, ver. 1.0
Revised: June 8, 2020, ver. 2.0

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Introduction

This research is clinical research conducted to improve the cure rate of oral cancer. Clinical research is medical research conducted on human subjects for the purpose of improving methods of disease prevention, diagnosis and treatment, understanding the causes of disease, and improving the quality of life of patients. Nagasaki University Hospital has established the "Nagasaki University Hospital Clinical Research Ethics Committee" to conduct rigorous review of each clinical research. This clinical research is conducted with the approval of the Ethics Committee and the hospital director.

Please note that this clinical research is not a so-called "clinical trial," a clinical study conducted by a pharmaceutical company or other organization to investigate the safety and efficacy of a new drug and obtain approval from the Ministry of Health, Labor and Welfare. You are free to decide whether or not to participate in this study. If you choose not to participate in the study, we will continue to provide the best treatment for your situation.

This study is to determine whether prophylactic neck dissection is effective during resection of tongue cancer that is clinically free of cervical lymph node metastasis (this is called cN0).

1. Description of the Study

In this study, we will prospectively observe the postoperative course of patients who have undergone surgery for tongue cancer with clinically no cervical lymph node metastasis (this is called cN0), with or without prophylactic neck dissection, for 3 years, and examine changes in their general condition in a multicenter setting.

Cervical dissection is a surgical procedure in which cervical lymph nodes suspected of cancer metastasis are removed in one lump with surrounding tissues to thoroughly dissect the neck. Tongue cancer tends to metastasize to cervical lymph nodes, and it is known that 30-40% of patients with early-stage tongue cancer have latent lymph node metastases that are not clinically evident at the time of initial diagnosis but become evident later. In such cases, prophylactic cervical dissection has been reported to improve outcomes (specifically, the 3-year survival rate increased from 67.5% to 80%), but it is not known whether cervical dissection is performed only when it is truly necessary. Unnecessarily performing this surgery can lead to difficulty in lifting the hand, skin hypoesthesia, and a decreased quality of life (QOL). Currently, it is difficult to accurately predict potential cervical lymph node metastases, and the decision to perform prophylactic neck dissection is still unclear.

This study is a clinical research study in a form that is consistent with actual clinical practice, in which prophylactic cervical dissection will be indicated and curative treatment will be performed using the same judgment as before after enrollment in the clinical research study, followed by a uniform follow-up.

2. Research Methods

Research will be conducted at our hospital on patients 20 years of age or older who have undergone surgery for tongue cancer without cervical metastasis from the date of approval by the hospital director of Nagasaki University Hospital to October 31, 2022.

Clinical data necessary for this study will be extracted from medical records and laboratory findings, anonymized so that individuals cannot be identified, and registered at the Data Center (Clinical Research Support System, Clinical Research Center, Shinshu University Hospital). Data collected from the designated training facilities of the Japanese Society of Oral Oncology and others (69 facilities) participating in this study will be compiled. Endpoints will include postoperative survival, postoperative recurrence-free period, and changes in quality of life (QOL) before and after surgery.

3. Consent Form

If you are willing to participate in this clinical study, you will be asked to sign a "Consent Form" in person. We will provide you with this form, and we hope that you will read it carefully and consider it carefully.

4. Anticipated Research Outcomes

In tongue cancer without cervical metastases, it may be possible to identify patients with potential lymph node metastases who truly need prophylactic neck dissection. It may also clarify the extent to which prophylactic cervical dissection results in a decreased quality of life.

5. Expected benefits of this research

It allows prophylactic neck dissection to be performed only in patients with tongue cancer who really need it with latent lymph node metastasis, eliminating the need for unnecessary neck dissection.

6. Study duration and number of expected participants

This study will run from the date of approval by the hospital director of Nagasaki University Hospital until October 31, 2026. A total of approximately 800 people are expected to cooperate in this study from the designated training facilities of the Japanese Society of Oral Oncology and others that are participating in the study.

Of these, Nagasaki University Hospital plans to cooperate with 40 patients.

The study may be terminated when the objective of the study has been achieved before the planned number of patients or the planned period is reached, or when there are instructions to change the implementation plan, etc., and it is deemed difficult to accept these instructions.

7. Disclosure of Research Results

If you wish to see the results of the study, please contact your doctor or the principal investigator. Depending on the time of the research, we may not be able to show you the results. Basically, we will only show the results to you. If a person other than the patient himself/herself requests to see the results, we will show them only to a "surrogate or immediate family member" as necessary.

8. The cost of treatment must be co-paid in accordance with the insurance system.

Patients will not be asked to pay for any special testing or other costs themselves. Therefore, although some co-payment will be incurred, as in the case of regular treatment, including consultations and examinations, participation in this study will not result in higher costs.

9. Conflicts of Interest

This clinical research is being conducted as a physician-led independent study. There are no problems regarding financial benefits or other related interests from companies or organizations that may have a potential conflict of interest, as the principal investigator and research assistants of this research have been reviewed by the Conflict of Interest Review Committee of Nagasaki University Hospital.

10. Response to Serious Health Hazards

This clinical study has been carefully planned based on reports to date. However, in the unlikely event that a serious health hazard occurs as a result of participation in this clinical research, appropriate measures, including necessary treatment, will be taken immediately.

Such treatment will be provided by insurance in accordance with general medical treatment. No compensation will be paid for participation in this clinical study.

11. Protection of your human rights and privacy

The following considerations are made to protect your human rights.

1) This clinical research will be conducted in accordance with the "Guidelines for Conducting Clinical Trials (Japanese Association for Cancer Therapy)," which are designed to protect your human rights. These guidelines are almost the same as the "Standards for Conducting Clinical Trials" that must be followed when conducting clinical trials for new drugs that have not been

approved by the Ministry of Health, Labor and Welfare (the purpose is to "ensure the scientific quality and reliability of the results of clinical research while protecting the human rights, safety and welfare of the subjects"). guidelines for the development of new treatments for cancer.

2) You are free to decide whether or not to participate in this clinical research. If you do not consent, you will not be treated unfavorably.

3) Even if you agree to participate in this clinical study, you are free to withdraw your consent to participate in this clinical study at any time during the treatment period without any prejudice. If you wish to do so, please submit a withdrawal of consent form signed by you to the research staff, or notify us orally. You will not be treated unfavorably in any way if you do not participate in the clinical research.

4) The content of this clinical research plan is subject to scientific and ethical review and approval by the Nagasaki University Hospital Clinical Research Ethics Committee, which was established to protect your human rights, and will be conducted with the permission of the hospital director.

5) We will promptly inform you of any new information that we think is important for you to know about this clinical research.

6) We will take great care to protect your privacy. Your medical records may be accessed by parties involved in this clinical study (including outside parties) to ensure that the clinical study is being conducted properly, but all personal information will be kept confidential. In addition, some of the results of this clinical research and test results may be published in medical papers or as part of materials submitted to the Ministry of Health, Labor and Welfare, but your personal information, including your address, name, and telephone number, will be kept confidential.

7) If you have any questions about this clinical research or your rights, please contact your attending physician or the responsible physician.

12. Handling of information obtained in this study

(1) Handling of information

Since this is a multicenter collaborative study, your information obtained in this study will be provided to the Clinical Research Support Center of Shinshu University Hospital, which is the data center. Your information will be provided to the Center's clinical research support system via the Internet with an identification number attached.

(2) Storage of information

Information obtained in this research will be stored in the Clinical Research Support System of the Clinical Research Support Center of Shinshu University Hospital until at least the end of the research, but will be kept as long as possible after this period.

When disposing of the information, sufficient care will be taken to ensure that personal information is not leaked to outside parties.

13. Clinical Research Results and Presentations

The results of this clinical research will be made public in the form of presentations at scientific meetings and publications in specialized journals, but will never be presented in a way that identifies individuals..

14. Study implementation system

Research Organization
Principal Investigator: Masahiro Umeda (Professor, Department of Oral Oncology, Nagasaki University)

Principal Investigator (Data Management): Hiroshi Kurita (Professor, Department of Dental and Oral Surgery, Shinshu University School of Medicine)

Research Secretariat: Soichi Yanagimoto (Lecturer, Department of Oral Oncology, Nagasaki University)

Data Center: Clinical Research Support Center, Shinshu University Hospital

Research participating facilities: Training facilities designated by the Japanese Oral Tumor Society

To be kept by the hospital, (copy) for patients
ver. 2.0

Consent form

Prospective observational study of elective neck dissection for clinical N0 tongue cancer

Items to be explained

1. **Description of the Study**
2. **Research Methods**
3. **Consent Form**
4. **Anticipated Research Outcomes**
5. **Expected benefits of this research**
6. **Study duration and number of expected participants**
7. **Disclosure of Research Results**
8. **The cost of treatment must be co-paid in accordance with the insurance system.**
9. **Conflicts of Interest**
10. **Response to Serious Health Hazards**
11. **Protection of your human rights and privacy**
12. **Handling of information obtained in this study**
13. **Clinical Research Results and Presentations**
14. **Study implementation system**

[Signature of researcher] I explained the study to the patient.

Date of explanation:
Name of explainer: (signature)

[Patient's signature]

I have received an explanation of and understand the above items, and agree to participate in this study of my own free will and accord. I will receive a copy of the patient handbook and this consent form.

Consent Date:
Patient's name: (signature)