1. Introduction

This informational document describes a clinical study being conducted for patients with early gastric cancer. Clinical research refers to studies that investigate the effectiveness and safety of treatment methods and diagnostic techniques with the participation and cooperation of patients. Clinical research may involve procedures and tests that are not typically part of routine medical care and have a research-oriented aspect. Even the treatment methods currently considered standard have been derived from the results of numerous past clinical studies, highlighting the essential role of clinical research in advancing better treatments and healthcare.

Your attending physician will now explain this clinical study to you and provide you with this informational document. Please take the time to understand its contents thoroughly and decide freely whether to participate in this clinical study after being fully informed and satisfied. If you have any questions or concerns about the research, please feel free to ask your attending physician at any time.

2. Implementation of the Study

This clinical study will be conducted in compliance with the 'Clinical Trial Act' established by the government to protect the rights and safety of participants. The study has been reviewed and approved by a Certified Review Board (comprised of medical experts, legal professionals, and members of the general public) to ensure the protection of participants' rights and ethical and scientific scrutiny. Subsequently, it will be implemented with the approval of the administrators of each participating medical institution.

Even after the commencement of the study, the Certificated Review Board will continuously review whether human rights are being respected, the study is being conducted safely, and compliance with the Clinical Trial Act is maintained.

The name of the Certified Review Board: Kobe University Clinical Research Ethical Committee
Certification number: CRB5180009
7-5-2 Kusunoki-cho, Chuo-ku, Kobe, Hyogo 650-0017, Japan
URL: http://www.hosp.kobe-u.ac.jp/ctrc/cerb/

In conducting this clinical study, an overview of the research plan and its progress is registered and made publicly available on the jRCT (Japan Registry of Clinical Trials) system, established by the Ministry of Health, Labour and Welfare. The results of this clinical study will also be published on the jRCT after the completion of the research.

3. Participation in Clinical Research

Participation in Clinical Research by Voluntary Consent:

In this clinical study, consent from the patients themselves is necessary to allow participation in the research. The attending physician will provide explanations about the study using this informational document. After fully understanding the clinical study being explained, if you feel it is appropriate to participate, please sign and date the consent form at the end of this informational document. Participation in this clinical study is entirely voluntary, so please feel free to discuss with trusted individuals and ultimately decide based on your own will. Additionally, if you have any concerns or uncertainties, please feel free to consult with the attending physician at any time. If you choose not to participate in this clinical study, you will still have access to other appropriate treatments, and there will be no disadvantages or inconveniences in subsequent treatments.

Withdrawal of Consent during Participation in Clinical Research:

If you wish to withdraw from participating in this clinical study for any reason after initially agreeing to participate, you have the right to do so at any time. Please inform your attending physician if you wish to withdraw your consent to participate. Even if you decide to withdraw from the clinical study midway, you will still have access to other appropriate treatments, and there will be no inconvenience or disadvantage in subsequent treatments. However, any specimens, data, or information collected before the withdrawal of consent may be used for the evaluation of the clinical study. If you do not wish for these specimens or data to be used, please inform us so that we can respect your decision.

Please note that if research findings have already been published, such as in scientific papers, at the time consent is withdrawn, it may not be possible to retract those results. We appreciate your understanding in this matter.

4. Patient Condition and Treatment for This Clinical Study

Your condition is early gastric cancer. For cases with an extremely low risk of lymph node metastasis within this condition, endoscopic submucosal dissection (ESD) has become the standard treatment. However, while ESD is a minimally invasive and effective treatment, it requires a high level of technical skill due to the intricate endoscopic manoeuvres involved, resulting in its limited global adoption. To alleviate the technical complexity associated with ESD, the concurrent use of traction devices, which use threads, rubber, or springs to retract lesions, is expected to simplify the procedure.

There are several types of traction devices available. Devices like spring clips or multi-loop traction devices, which allow freedom in setting the direction of traction, have been proven to aid in simplifying treatment. However, devices like thread-attached clips, which restrict traction direction to a single direction towards the cardia, have only shown effectiveness in specific areas with vertical

traction and have not demonstrated overall simplification of treatment for early gastric cancer.

The EndoTrac, a new traction device to be used in this clinical study, offers the advantage of being able to freely set the direction of traction while maintaining the traction force. In a retrospective study conducted at a single facility on the safety of EndoTrac, no device malfunctions or device-related adverse events were observed during its use in 44 cases with lesions in the oesophagus, stomach, duodenum, and colon.

While EndoTrac is expected to simplify treatment, its actual contribution to shortening treatment time has not been proven, and a thorough investigation has not been conducted at this stage.

5. Significance and Objectives of This Clinical Study

Objective:

The objective of this clinical study is to investigate the efficacy of reducing treatment time in Endoscopic Submucosal Dissection (ESD) by comparing it with conventional ESD, either with or without the concurrent use of EndoTrac, in patients with early gastric cancer.

Significance:

Conducting this clinical study may lead to the proposal of a new ESD technique that mitigates technical challenges, potentially aiding in the global adoption of ESDs.

By assessing the efficacy of EndoTrac in shortening treatment times, this study could contribute to improving the standard of care for patients with early gastric cancer.

6. Methodology (Treatment Protocol) of This Clinical Study

Criteria for Participation:

The main criteria for participation are as follows, although there may be additional criteria determined by the attending physician and patients deemed appropriate for participation in this clinical study:

Eligibility Criteria (Participants must meet all of the following criteria to be eligible):

(1) Individuals aged 18 years or older at the time of consent.

(2) Capable of providing informed consent themselves.

(3) Diagnosed with indications for endoscopic treatment based on preoperative endoscopic examination.

(4) No evidence of metastasis on CT scans.

(5) Diagnosed with gastric cancer or suspected gastric cancer based on preoperative tissue biopsy.
(6) Performance status ※1 ranging from 0 to 2, which is an indicator of overall physical condition.
※1 Performance status: A measure of an individual's general well-being and ability to perform activities of daily living, with 0 representing fully active, 1 representing restricted in strenuous activity but ambulatory, and 2 representing ambulatory and capable of self-care but unable to work.

Exclusion Criteria (Individuals who meet any of the following criteria are not eligible to participate):
(1) Individuals for whom ESD without the use of traction devices is expected to be difficult.
(2) Individuals who have undergone surgical resection of the stomach.
(3) Individuals with recurrent or residual lesions after previous endoscopic treatment.
(4) Individuals who have previously participated in this clinical study.
(5) Individuals who are unable to discontinue antithrombotic therapy as prescribed.
(6) Individuals with abnormal haemostasis or coagulation.
(7) Individuals with critical organ dysfunction.
(8) Individuals who require treatment for two or more lesions on the same day.
(9) Individuals who are pregnant or breastfeeding.
(10) Any other individuals deemed unsuitable by the investigators of this trial.

Description of the Medical Device:
The EndoTrac is a device consisting of a slender resinous sheath and a loop-shaped traction thread at the tip, integrated into one unit. A clip is attached to the tip of the loop-shaped traction thread, allowing it to be affixed to the lesion and used to retract the lesion during ESD. This medical device is used under insurance coverage, and there is no additional burden on patients.
On the day of ESD, an overtube with an inner diameter of 16 mm or larger (the portion through which the scope and EndoTrac pass during the procedure) is used as much as possible to avoid interference between the EndoTrac and the endoscope. The overtube facilitates insertion of the endoscope into the body and is used as an adjunctive tool in endoscopic treatment. However, it is not used if there is deemed to be a risk of airway pressure or oesophageal injury during insertion.

Treatment Groups:
There are two treatment groups in this study: the EndoTrac group, which undergoes ESD using the EndoTrac, and the conventional method group, which does not include the use of traction devices like EndoTrac. Each group is randomly assigned with a probability of one in two. You will be randomly and fairly assigned to one of the two groups, similar to drawing lots, and neither you nor your attending physician can choose the treatment group.
Participants are assigned randomly in a 1:1 ratio to the EndoTrac group and the conventional method

group.

Regarding Unawareness of Treatment Method:

This clinical study aims to compare the effectiveness of the conventional treatment group and the EndoTrac group. To ensure an unbiased comparison, it is important to minimise factors other than the treatment method that could influence the results. If you were aware of which treatment method you were receiving, it might affect your interpretation of subjective effects such as abdominal pain. To avoid this influence and enhance the reliability of the research results, you will not be informed about which treatment method you are receiving during the study. However, in case of an emergency, you will be informed about your treatment method.

Instructions for Medical Device Use:

In the EndoTrac group, treatment will be performed using the EndoTrac during ESD. Retraction of the lesion during ESD facilitates the excision and dissection of the lesion. Additionally, the direction of traction can be manipulated by adjusting the length of the thread and pushing or pulling the sheath. In the conventional treatment group, ESD will be performed without using the EndoTrac. After treatment, both groups will receive antacid medication starting from the treatment day, and the resumption of drinking water and meals will be decided by the attending physician.

Specifically, omeprazole 20 mg may be administered intravenously 1–2 times per day, or lansoprazole 30 mg may be administered intravenously 1–2 times per day. Alternatively, one of the following medications may be taken orally once daily: omeprazole 20 mg, rabeprazole 10 mg, esomeprazole 20 mg, lansoprazole 30 mg, or vonoprazan 20 mg. Antacid medication will be continued for 4 weeks from the treatment day. Reduction of dosage according to the patient's physique is possible based on the attending physician's judgment. In unavoidable circumstances such as drug allergies, the attending physician may decide to discontinue oral administration or switch to other antacid medications such as H2 receptor antagonists. If a dose is missed, it should be resumed from the following day.

7. Schedule and Procedures

Schedule:

Once you have agreed to participate in the clinical trial, we will assess your symptoms. If you meet the eligibility criteria, you will be enrolled as a patient in the clinical trial. If you participate in this study, you will undergo four examinations: the pre-observation period, treatment day, the day after treatment, and the post-observation period.

Please refer to the schedule table below for details.

Any tests or procedures listed in the schedule that can be conducted before obtaining consent will use

the results obtained.

Table 1. Participant timeline

Study phase	Screening phase	Treatment phase		Observation phase	Termination
Approval range	Day 0–7 d	Day 1	Day 2+3 d	Day 28±14 d	
Informed consent	X				
Baseline characteristics [a]	X				
Vital sign		X	X		
Complete blood count [b]	X		X		
Serum biochemistry [b]	X		X		
Coagulation test [b]	X				
Electrocardiograph [b]	X				
Abdominal X-ray			X		
Computed tomography [c]	X				
Endoscopy [c]	X				
Pathological diagnosis on biopsy sample [c]	X				
Assessment of the technical difficulty [d]	X				
Procedure time		X			X
Efficacy-related outcomes		X		X	X
Safety-related outcomes		X	X	X	X
Device-related outcomes		X			X

a: Age, performance status, pregnant or lactating, history of critical organ (liver/renal/heart) failure, history of bleeding disorders, registration history for the present trial, the possibility of discontinuing antithrombotic drugs in accordance with guidelines will be interviewed.

b: all assessments must be completed within 4
weeks prior to consent
c: all assessments must be completed within 12
weeks prior to consent
d: based on the information regarding the operator, endoknife, and injectional solution, technical difficulty will be assessed.

Procedures:

We will provide detailed explanations about the procedures to be conducted in the clinical trial below.

✓ Screening phase (Day 0–7 d)

The following items ① to ⑦ will be evaluated:

① Patient background:
- Age
- Sex
- Performance status
- Pregnant or lactating
- History of critical organ (liver, kidney, heart) failure
- History of bleeding disorders
- Registration history for the present trial
- The possibility of discontinuing antithrombotic drugs
- Use of anticoagulants

② Blood test findings:
- Haematological tests
- Biochemical tests
- Coagulation tests

③ Chest and abdominal CT:
- Presence of lymph node metastasis
- Presence of distant metastasis

④ Endoscopy:
- Date of endoscopic examination
- Site of lesion
- Estimated tumour depth
- Estimated tumour size
- Presence of ulcers

History of gastrectomy

Recurrence or residue after endoscopic treatment

Presence of other lesions treated on the same day

⑤ Electrocardiogram:

Presence of electrocardiographic changes associated with acute coronary ischemia

⑥ Histopathological diagnosis of biopsy tissue

⑦ Assessment of anticipated difficulties in planned treatment or lesion treatment:

Planned operator

Type of planned endoknife

Type of planned injection solution

Presence of treatment difficulty (whether treatment can be performed without using traction devices such as an EndoTrac and relying solely on manual techniques)

✓ Treatment phase Day 1 (±0 days)

The following items ① to ⑥ will be evaluated:

① Vital signs (heart rate, blood pressure, body temperature)

② Procedure time

③ Handover (indicating a change of operator)

④ Number of bleeding events during the procedure

⑤ Device-related outcomes:

Direction of treatment

EndoTrac attachment time

EndoTrac attachment site

Number of EndoTracs used

Number of EndoTracs detached

Timing of EndoTrac attachment

Timing of EndoTrac detachment

Presence of tissue damage during surgery due to EndoTracs

Presence of postoperative tissue damage due to EndoTracs

⑥ Safety-related outcomes:

Presence of adverse events

Type of adverse events

Severity of adverse events

✓ Treatment period Day 2 (+3 d)

The following items ① to ⑦ will be evaluated:

① Subjective and objective symptoms (focus on upper abdominal pain, hematemesis)

② Vital signs

③ Haematological tests

④ Biochemical tests

⑤ Abdominal X-ray

⑥ Safety-related outcomes:

Presence of adverse events

Type of adverse events

Severity of adverse events

✓ Observation phase (Day 28) (±14 d)

The following items, ① and ②, will be evaluated:

① Safety-related outcomes:

Presence of adverse events

Type of adverse events

Severity of adverse events

② Histopathological diagnosis

Duration of the Clinical Trial:

This clinical trial will be conducted from the date of publication of the implementation plan (or 1 January 2023) until 31 July 2024. If you participate in this study, your scheduled participation period will be five weeks in total, including one week for the screening period before treatment initiation and four weeks for the observation period after treatment completion.

8. Participating Hospitals and Expected Number of Participants for This Clinical Trial

This clinical trial will be conducted at 11 medical institutions in Hyogo Prefecture and Osaka Prefecture. Below is the list of planned medical institutions for implementation. Approximately 142 patients are expected to participate in total.

Participating hospitals

- Kobe University Hospital
- Kobe University Hospital International Clinical Cancer Research Center
- Hyogo Cancer Center
- Akashi Medical Center
- Osaka Saiseikai Nakatsu Hospital
- Kobe Red Cross Hospital
- Kita-harima Medical Center
- Yodogawa Christian Hospital

- Sanda City Hospital
- Konan Medical Center
- Hyogo Prefectural Harima-Himeji General Medical Center

9. Post-Trial Management

After the clinical trial concludes, appropriate medication will be selected based on your symptoms, and the best possible treatment will be administered.

10. Expected Benefits and Potential Risks

Benefits:

By participating in this clinical trial and using the EndoTracs, there is a potential for contributing to shorter treatment times compared to conventional treatment methods. However, this potential benefit is currently uncertain. There will be no direct benefit to you if conventional treatment is administered.

Risks:

Participation in this clinical trial may entail risks such as mucosal damage due to the insertion or removal of EndoTracs, as well as damage to lesions during clip removal or EndoTrac detachment during the procedure. The use of EndoTracs may not align with the preferences of the operator due to randomisation. There is a possibility of prolonged treatment times if assigned to the conventional treatment group. Participation in this clinical trial may result in more detailed and potentially inconvenient scheduling of clinic visits and tests compared to standard medical care.

Expected Adverse Events and Risks:

You may experience adverse events (equivalent to side effects in pharmaceuticals) such as those listed below. If you experience any concerning symptoms after participating in the clinical trial, please do not hesitate to seek advice.

Mucosal damage (due to the forcible insertion/removal of the device)

Lesion damage (during clip removal from the lesion or EndoTracs detachment during the procedure)

Device damage (due to excessive force)

11. Regarding the Occurrence of Health Impacts During the Clinical Trial

While this clinical trial is scientifically and meticulously planned based on previous reports, if you experience any symptoms that you have not had before, during, or after the trial, please promptly contact your attending physician and discuss treatment options. Please refer to the contact information provided in section 23, "Inquiry Contact for the Clinical Study".

In the event that you experience any health impacts as a result of this clinical trial, you will receive appropriate treatment and compensation. This clinical trial is covered by clinical research insurance, and compensation within the scope of clinical research insurance can be provided if severe health impacts occur as a result of this clinical trial. However, if the health impact is entirely unrelated to this clinical trial or if it occurred due to your failure to follow the instructions of your attending physician (for example, failure to adhere to the items outlined in section 22, " Responsibilities of the Participant "), or if it is deemed to be your own responsibility (intentional or gross negligence), compensation may be denied or reduced.

12. New Information Regarding the Clinical Trial

While you are participating in this clinical trial, new information, such as adverse events, may arise. If new information arises that may affect your willingness to continue participating in the clinical trial, it will be communicated to you verbally or through the informed consent document, and your attending physician will confirm your willingness to continue participating in the clinical trial.

13. Alternative Treatment Methods

If you choose not to participate in this study, you may receive treatment without the use of traction or by using some form of traction device.

14. Termination of the Clinical Trial

Even if you wish to continue participating in the clinical trial, the principal investigator may decide to terminate your participation in the study for reasons such as:

・If it is determined that you do not meet the inclusion criteria after participating in the clinical trial.
・If your condition worsens and the attending physician deems it appropriate to discontinue your participation.
・If you become pregnant.
・If the clinical trial itself is discontinued.

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15. Costs and Compensation Related to the Clinical Trial

Medical Expenses:

The medical equipment used in this clinical trial will be used within the scope of regular medical care, so participating in this study will not incur additional costs.

Compensation:

Participating in this clinical trial will not increase the number of visits compared to regular medical care. Therefore, there is no compensation or financial relief associated with participating in this clinical trial.

16. Storage and Disposal of Samples

Your research data related to this clinical trial will be stored for a period of five years after publication of the results in the jRCT or for a period determined by each implementing medical institution, whichever is longer. After this period, any identifiable information about you (such as medical record numbers or names) will be permanently anonymised before disposal. Clinical data extracted from medical records will be shredded or deleted completely. Additionally, if you choose to withdraw your consent for participation in this clinical trial, the information obtained up to the point of withdrawal will still be utilised as clinical research data. However, if you do not wish for your information to be used, you have the right to refuse its use. In such cases, any information related to this study will be irreversibly destroyed at the time of consent withdrawal. However, if information has already been used for publication purposes, it may not be possible to discard it.

17. Viewing of Medical Records and Protection of Personal Information

Viewing of Medical Records:

In order to ensure that this clinical trial is conducted properly while protecting your rights, personnel involved in the clinical trial (such as monitors, certified review board members, officials from the Ministry of Health, Labour and Welfare, etc.) may directly access your medical records, including your medical charts, to verify the conduct of the clinical trial. These individuals are legally bound by confidentiality obligations and handle your privacy with utmost care. By signing the consent form, you authorise the personnel involved in the clinical trial to access your medical records.

Protection of Personal Information:

In this clinical trial, all personal information, such as your name, will be managed using code numbers (referred to as anonymisation). As this study is a multicentre collaborative research, information related to the clinical trial will be sent to Kobe University Hospital, but it will be sent in a form where you cannot be identified. Therefore, data obtained from you will not include any information that could identify you, and your name or other privacy-related information will not be used in the analysis, reporting to conferences or journals or publication in the jRCT, ensuring that you remain anonymous. Additionally, if you feel that your personal information is not being used appropriately, you have the right to request disclosure, correction, or cessation of use of your personal information.

18. Disclosure of Information Related to the Clinical Trial

If you wish to have access to the study protocol and related documents of this clinical trial, except for

personal information of other patients and matters that may adversely affect the entire study, such information can be provided upon request. If you are interested, please do not hesitate to contact the clinical trial inquiry desk at section 23. Additionally, an overview of this clinical trial is registered on the jRCT (https://jrct.niph.go.jp/), and the study results will be published after the completion of the clinical trial, so please refer to it.

19. Handling of Research Data

19.1 Research Data:

All data obtained in this clinical study will be used solely for the purpose of conducting and analysing the results of this clinical study and will not be used for any other purpose. The data from this clinical study will be submitted to Kobe University Hospital, with some personal information removed, and will be used for interpreting the results. However, these data may be used for future studies targeting the same disease, but individual explanations will not be provided. Additionally, it is possible to refuse the use of data when new studies are planned. Currently, there are no planned studies.

19.2 Genetic Information:

This clinical study does not have the potential to provide important information about genetic characteristics that could be inherited by you or your descendants.

20. Ownership of Intellectual Property Rights

Any intellectual property rights arising from new insights gained in this clinical study will be owned by Kobe University Hospital or the researchers and will not be attributed to you.

21. Funding Source and Conflict of Interest Related to the Clinical Study

Funding Source:

This clinical study will be conducted using research funds from the Department of Gastroenterology, Kobe University Hospital.

Conflict of Interest:

In this clinical study, individuals who have a conflict of interest with Top Corporation, the manufacturer of the medical device used in the study, are involved. Conflict of interest management is overseen by the principal investigator, who establishes management criteria, and the responsible physician at each participating medical institution develops a management plan based on these criteria. These management criteria and plans are reviewed by the Certified Review Board.

22. Responsibilities of the Participant

If you choose to participate in this clinical study, please cooperate with the following:

Be sure to attend appointments on scheduled dates.

Inform us if you are receiving treatment from other departments or hospitals.
Inform us if you are taking any medications.
Contact your attending physician immediately if you experience any unusual symptoms.

23. Inquiry Contact for the Clinical Study

For questions, concerns, or complaints regarding this clinical study, please contact the participating physician or the patient consultation office at Kobe University Hospital. For inquiries related to treatment or your health condition, please contact the respective participating medical institution (the hospital you are visiting).

-Patient consultation office at Kobe University Hospital-
7-5-2 Kusunoki-cho, Chuo-ku, Kobe, Hyogo 650-0017, Japan
Tel: +81-78-6667 Email: soudanct@med.kobe-u.ac.jp

Consent Form

Name of the Study: Randomised controlled, patient-blinded, multicentre, superiority trial to evaluate the efficacy of the line-attached sheath-type traction device for endoscopic submucosal dissection in patients with superficial gastric neoplasms

I have received sufficient explanation from the physician regarding the above-mentioned study, have been given the opportunity to consider it, and have understood it. Therefore, I consent to participate in this clinical study of my own free will. Additionally, I have received the explanatory document and consent form for this consent.

Signature of the Participant
Name of the Participant (Signature) _____
Date of Consent: ____/____/____

Signature of the Explanatory Person
[Name of the Principal Investigator (or Co-Investigator)] (Signature) _____
Date of Explanation: ____/____/____