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## Developing a magnetic-assisted-POCUS guided bronchoscopy among patients with suspected difficult endotracheal intubation: protocol for a randomized controlled study

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Developing a magnetic-assisted-POCUS guided bronchoscopy among patients with suspected difficult endotracheal intubation: protocol for a randomized controlled study

Tian Yuan¹, Fei Yuda¹, Bai Bing¹, Cui Xulei¹, Zhang Yuelun², Wang Chunrong¹, Yu Chunhua¹*, Huang Yuguang¹

Author affiliations
¹ Department of Anesthesiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China.
² Medical Research Center, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China.

*Corresponding author: Chunhua Yu, Yu.chunhua@aliyun.com

ABSTRACT

Introduction Endotracheal intubation (ETI) is a crucial but risky procedure, especially among patients suspected of difficult endotracheal intubation (DTI). Bronchoscopy, as an improved technique commonly used in DTI, might encounter visualization difficulties. The magnetic point-of-care ultrasound (MGPOCUS) not only provides a novel visualization from the outside but also enables the estimation of the relative position and trajectory of bronchoscopy. The study aims to evaluate the efficiency of MGPOCUS-guided bronchoscopy in time taken to the first-attempt success, the first-attempt and overall success of ETI, complications, and satisfaction of visualization among patients suspected of DTI.

Methods and analysis The study is a randomized, parallel-group, single-blinded, single-center study. Participants (n=350) will be recruited by the primary anesthesiologist and randomized to groups of ETI with bronchoscopy or MGPOCUS-guided bronchoscopy. The primary outcome is the time taken to the first-attempt success ETI. Secondary outcomes include procedure time, the first-attempt and overall success, complications, and satisfaction of visualization. Cox regression with the Bonferroni correction and the linear mixed regression will be used to analyze the outcomes.

Ethics and dissemination The trial protocol were approved by the institution of the Ethics Committee of the Peking Union Medical College Hospital. Findings will be disseminated through conference presentations and peer-reviewed journals.

Trial registration number NCT05647174.

Keywords Difficult airway, endotracheal intubation, POCUS, magnetic ultrasound

Word counts 3228

Article summary

Strength 1: This is a pioneer study regarding the application of magnetic-assisted
point-of-care-ultrasound-guided bronchoscopy among patients suspected of difficult intubation based on randomized controlled, two-arm, single-center evidence.

**Strength 2:** The magnetic-assisted point-of-care-ultrasound-guided bronchoscopy was designed based on the principle of magnetic guided puncture embedded in the application of ultrasound in the airway.

**Strength 3:** The study data will be independently processed by an independent data and safety monitoring committee.

**Limitation 1:** Blinding of investigators won’t be possible, though the estimation of outcomes is objective.

**Limitation 2:** The experienced physician will perform both interventions, thus limiting transferability to other less-experienced individuals.

**INTRODUCTION**

Endotracheal intubation (ETI) is crucial as a fundamental method to secure the airway\(^1\), yet the leading cause of death or vegetative state among healthy participants undergoing elective surgery\(^2\)\(^,\)\(^3\). It is consistently shown that difficult endotracheal intubation (DTI) majorly contributed to adverse events\(^4\)\(^\)\(^5\)\(^6\). Though the advent of flexible bronchoscopy has brought revolutionary innovations for DTI, there are still worrisome, just as the closed-claims analysis of the United States has yielded\(^7\). Most often, intubation by flexible bronchoscopy is performed via the oral route\(^8\), the procedure can be tricky or delayed as the difficulty of the visualization. Dealing methods, such as keeping the tip in the midline, or withdrawing until the location can be identified, remain widely variable in terms of rapidness\(^9\)\(^10\). The active research to improve visualization and movement confirms that this issue continues to challenge many physicians\(^11\)\(^12\).

Point-of-care ultrasound (POCUS) has broadened the horizons for airway management since it allows visualization of the upper airway from the outside\(^13\). The American Heart Association updated the Guidelines on Adult Advanced Cardiovascular Life Support (ACLS), which recommended using ultrasound as a confirmation method for a tracheal tube\(^14\). Several studies provide promising results about the high pooled sensitivity (about 98%) and specificity (about 97%) of POCUS in confirming ETI\(^15\)\(^16\)\(^17\). Real-time POCUS further extends to assist ETI\(^18\)\(^19\). Notably, POCUS provides a view independent from the laryngoscopy or bronchoscopy, making it possible to combine the outside with the inside visualization\(^13\). Also, magnetically guided ultrasound has improved regional anesthesia and vascular catheterization procedure\(^20\). The technology of magnetic POCUS (MGPOCUS) collects magnetic signals and calculates the trajectory modeled by corresponding software. It enables the possibility of estimating the relative position and the advanced trajectory, guiding bronchoscopy when encountering a difficulty of laryngeal exposure. To date, there has been little conclusive evidence to seek the application of MGPOCUS-guided bronchoscopy in anticipated difficult intubation.

The study is designed to estimate the application of MGPOCUS-guided bronchoscopy within anticipated DTI on the procedure time, the success rate, the number of attempts, the complications, and the visual satisfaction of performers. Compared with flexible bronchoscopy alone, we seek to estimate the significance of
the combined visualization with MGPOCUS-guided bronchoscopy.

METHODS AND ANALYSIS

Study design and setting
This is a randomized, parallel-group, single-blinded, single-center study. The study will be conducted in the anesthesia department and operating room of the Chinese Academy of Medical Sciences Peking Union Medical College Hospital (Beijing, China), a tertiary academic hospital with an annual operation census of above 80,000 participants. The protocol is structured based on the Standard Protocol Items for Randomized Trials (SPIRIT) Statement: defining standard protocol items for a clinical study.

Participant recruitment
After assessing the eligibility and obtaining informed consent, the primary anesthesiologist will recruit the participants while performing the preoperative evaluation. The research team will confirm the eligibility.

Inclusion criteria
Participants will be eligible for inclusion if they meet all of the following items:
- Aged between 18 and 85 years old.
- Requiring ETI.
- Anticipated DTI meets one or more positive findings in the airway evaluation, including history, examination, and appropriate investigations of anatomy (Table 1).
- Signed written informed consent.
- Willingness for the primary anesthesia team to participate.

Table 1 Airway assessment

<table>
<thead>
<tr>
<th>Specific Predictors</th>
<th>Positive findings</th>
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<tr>
<td>Morbid obesity</td>
<td>BMI ≥ 40</td>
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<tr>
<td>Adverse dentition</td>
<td>Presence</td>
</tr>
<tr>
<td>The prior difficulty of endotracheal intubation</td>
<td>Presence</td>
</tr>
<tr>
<td>Mouth opening</td>
<td>&lt; 4 cm</td>
</tr>
<tr>
<td>Head and upper neck extension</td>
<td>&lt; 30 degrees from neutral</td>
</tr>
<tr>
<td>Mandibular protrusion (Lip bite test)</td>
<td>Inability to prognath</td>
</tr>
<tr>
<td>Modified Mallampati class</td>
<td>III or IV</td>
</tr>
<tr>
<td>Thyromental distance</td>
<td>&lt; 6 cm</td>
</tr>
<tr>
<td>Sternomental distance</td>
<td>&lt; 12 cm</td>
</tr>
<tr>
<td>Neck circumference</td>
<td>&gt; 40 cm</td>
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</table>

Exclusion criteria
Participants will be excluded if they meet at least one of the following items:
- Anterior neck lesions (masses, lacerations, or subcutaneous emphysema).
- A history of neck operation or tracheotomy.
- Allergies to ultrasound coupling gel.
- At the risk of pulmonary or cardiovascular complications during intubation with flexible bronchoscopy, including severe hypoxemia, severe pulmonary hypertension, and unstable or intense obstructive airway disease.
- At the risk of bleeding during bronchoscopy, including anticoagulants or coagulopathy, renal insufficiency, and superior vena cava syndrome.
- High risk of aspiration.
- Current pregnancy.
- The patient is unable to cooperate (for awake intubation).

**Randomization and concealment**

Participants will be randomized in a 1:1 ratio to an intervention group (MGPOCUS-guided bronchoscopy) or a control group (bronchoscopy). The random number sequence will be generated by the “if” package of R software by delegated research staff and uploaded to our institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Ltd., Beijing, China). The primary care anesthesiologist will be informed of the database account information before performing ETI to guarantee allocation concealment.

**Blinding**

Trial participants and data analysts will be blinded to the assignment of interventions. Blinding of the investigator is generally impossible, yet the evaluation of outcomes is objective.

**Study interventions**

This study compares two interventions of performing DTI, a novel MGPOCUS-guided bronchoscopy and standard bronchoscopy. Participants in each group will accept standard perioperative interventions, including the essential monitoring of physiological parameters, sufficient preoxygenation, effective airway topicalization of local anesthetic for awake intubation or general anesthesia for post-induction intubation, and confirmation of ETI position by capnography. Essential monitoring will be performed before, during, and after ETI, with at least echocardiography, non-invasive blood pressure, and pulse oximetry. Preoxygenation will be administered with a mask to ensure end-tidal carbon dioxide is more than 93%.

ETI in both groups will be performed by a senior anesthesiologist with more than five years of experience in flexible bronchoscopy. MGPOCUS-guided bronchoscopy-guided intubation will be performed in collaboration with a senior anesthesiologist with more than five years of experience in POCUS and who has fulfilled more than 50 cases of ultrasound-guided airway management. An additional experienced airway manager will stand by in the operating room.

Patients that plan to intubate awake will accept topical airway anesthesia and sedation if required. An atomizer will apply 2% lidocaine with a maximum total dose of 5-7 mg/kg to the base of the tongue, the oropharynx, the hypopharynx, and the laryngeal structures. If required, sedation regimens will be applied, including midazolam 1-2 mg with repeated as necessary to a total dose of 0.025-0.1 mg/kg.
fentanyl 25-200 mcg titrated to effect in divided doses at 5-minute intervals, or
dexmedetomidine bolus one mcg/kg over 10 minutes followed by an infusion of 0.2-1
mcg/kg/hr. Patients intubated after induction will be anesthetized with propofol 1.5-2.5
mg/kg, fentanyl 25-100 mcg/kg, lidocaine 0.5-1.5mg/kg, midazolam 1-2 mg, and
rocuronium 0.6-1.2 mg/kg as required. The position of the tracheal tube will be
confirmed by capnography with at least four consistent waves and bilateral auscultation
of breath sounds.

**Bronchoscopy-guided ETI**
After clear suctioning of oropharyngeal secretions, the tip of a bronchoscopy will be
put through the middle of the incisors. The bronchoscopy will be appropriately oriented
and flexed to move along the oral midline and achieve a satisfactory view of airway
structures. Once the epiglottis and glottis are located, the tip of a bronchoscopy will be
advanced through the glottis to the level above the carina, followed by the advancement
of a tracheal tube already loaded. If required, a supplemental application of 2%
lidocaine with a maximum total dose of 5-7mg/kg will be applied to the larynx via the
working channel of the bronchoscopy. According to the operators’ will, approaches can
be used to improve visualization, including jaw thrust, tongue pulling forward, cervical
extension when not contraindicated, and bronchoscopy withdrawal.

**MGPOCUS-assisted bronchoscopy-guided ETI**
The system of MGPOCUS was derived and adapted from a previously described model
used in vascular catheterization. It consists of an ultrasonic machine (Piloter US
scanner, Wisonic, Inc., Shenzhen, Guangdong, China), a 4-15MHz linear transducer
with integrated ultrasonic and magnetic sensing capabilities (Wisonic, Inc., Shenzhen,
Guangdong, China), a magnetizing box (Wisonic, Inc., Shenzhen, Guangdong, China),
and a magnetized metal needle fixed near the tip of the bronchoscopy (Figure 1).

The MGPOCUS system uses several display features to enable the 3-dimensional
positioning of the bronchoscopy tip to be displayed in a 2-dimensional ultrasonic image.
Figure 2 shows an example of how the trajectory of the magnetizing needle fixed on a
bronchoscopy is displayed when it does or not overlap with the ultrasound beam.
Specifically, the trajectory of a magnetized bronchoscopy is indicated by a solid line
when it is within the ultrasonic beam. Otherwise, when it is positioned either anterior
or posterior to the ultrasonic beam, its trajectory is shown as a dashed line.

While clear suctioning of oropharyngeal secretions, the transducer is positioned
transversely at the level of the patient’s thyroid cartilage. Moving the transducer
cephalad or caudal, a view of vocal folds is visualized as an isosceles triangle with a
central tracheal shadow (Figure 3). The line connecting the vocal cords’ anterior and
posterior commissure is marked as the midline of the ultrasonography. The midline is
maintained and directed cephalad to visualize the tongue and epiglottis. The second
provider will perform intubation with a bronchoscopy, as described above. The
performer will adjust the direction of advancement according to the relative position of
the magnetized bronchoscopy to the midline of the ultrasonography. Once the solid line
displaying the magnetized bronchoscopy is within the trachea, the pre-loaded tracheal
tube will be advanced. Once the solid line is displayed posterolateral to the airway, the bronchoscopy will be withdrawn and adjusted according to the MGPOCUS image.

**Discontinuing interventions**
Desaturation below 90% will be considered a failed attempt of ETI. If desaturation is encountered, face mask ventilation will be performed with 100% oxygen for 2 min, and the attempt will be repeated. The procedure will be considered a failure with more than two attempts or 600 seconds, and the airway manager will proceed with the following strategy or technique. If emergencies arise, such as oxygen desaturation or hemodynamic instability, challenging to correct, the primary anesthesia team will determine whether to continue or terminate the trial.

**Outcomes**
Baseline assessments will be collected while preoperative evaluation, including demographic characteristics (age, sex, height, weight, body mass index, American Society of Anesthesiologists physical status score, procedure performer) and airway assessment (Table 1).

The primary outcome is the time taken to successful ETI at the first attempt. Time will be recorded in real-time from bronchoscopic first-passage through teeth to tube well placed. The first-attempt success is defined as a successful ETI with no more than 180 seconds and without reinsertion of bronchoscopy through teeth. Successful ETI is confirmed by capnography with at least four consistent waves.

The secondary outcomes are to detect the procedure time, the first-attempt and overall success, the number of attempts, complications, and satisfaction with visualization. Complications will be recorded, including desaturation, obvious trauma, bloody secretions, post-extubation hoarseness, and sore throat. The 5-point Likert scale assesses satisfaction with visualization.

**Data management and statistics**

**Sample size calculation**
Based on the preliminary study, the hypothesis is that MGPOCUS-guided bronchoscopy will achieve an improvement of 22 seconds to succeed in ETI at the first attempt, compared with 50 seconds performed with bronchoscopy alone. Hence, it is estimated that a sample size of 318 subjects will achieve a power of 90% (type II error 0.1) to detect a statistically significant difference between the two groups with a confidence of 95% (type I error 0.05). Considering the 10% possibility of dropouts, 350 subjects in each group will be recruited.

**Data collection and protection**
All data will be collected on the institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Ltd, Beijing, China) by an investigator independently. Data entry and processing will be performed before unblinding of investigators. The database will be centralized and managed by the leading researchers. A unique research identification data (ID) code will be used to
ensure confidentiality and anonymity. The ID will be used to identify participants and
the allocation. The recorded data in the study will not be linked to the participant’s
personal information. The data will be transferred securely and will be stored
confidentially on password-protected computers that the researchers can only access by
General Data Protection Regulation.

Data statistics plan
Demographic characteristics and airway assessment variables will be presented using
descriptive statistics for the overall sample. Continuous data will be described using
mean (standard deviation [SD]) or median (interquartile range [IQR]), depending on
the distribution of the data. Categorical data will be described using numbers and
proportions.
For the primary outcome, the time taken to the first-attempt success will be analyzed
using a Cox proportional hazards model with the Bonferroni correction as a
multiplicity adjustment that treats failed ETI at the first attempt as censored. For
secondary outcomes, procedure time for successful ETI will be analyzed using a
linear mixed model that treats ETI success or failure as the outcome and procedure
performer as a random effect. The first attempt and overall success will be analyzed
using mixed-effects logistic regression. Any two-sided P-value <0.05 will be
considered statistically significant. Statistical analyses will be performed on

Termination of the study
An independent statistician will conduct the interim analysis of the primary outcome
when 50% of participants have been enrolled. The results will be reported to the
independent data and safety monitoring committee and discussed with the steering
committee. The Peto approach is used to terminate the study when the intervention
group greatly benefits from the control group using symmetric stopping boundaries at
P<0.001. The study will not be stopped in case of futility unless the independent data
and safety monitoring committee advises otherwise. In this case, the potential stopping
for futility will be discussed with the steering committee.

Data monitoring
A steering committee will manage the study. Screening and recruitment will be
reviewed at monthly meetings. An independent data and safety monitoring committee
will meet every three months to ensure patient safety and data quality.

Safety
The independent data and safety monitoring committee will supervise the study’s
progress by examining safety variables monthly. Adverse events are defined as “any
undesirable experience occurring to a subject during the study, whether or not
considered related to the intervention.” Any potential adverse events must be monitored,
recorded, and discussed with the independent data and safety monitoring committee.
Patient and public involvement
The study protocol was developed in collaboration with anesthesiologists with extensive experience managing difficult airways or POCUS. Their feedback and expectations regarding research questions and outcome measures were discussed and applied for adjustment. Since the absence of experimental knowledge and subjective feeling, participants were not involved in our research's design, conduct, reporting, or dissemination plans.

DISCUSSION
The study answers whether the assistance of MGPOCUS will improve the efficiency of bronchoscopy in DTI through real-time detection of relative positions from outside visualization. Despite innovations in technique, bronchoscopy can encounter difficulties in visualization. MGPOCUS, an airway management strategy independent of inside view [14], has suspected the superiority of real-time ETI confirmation during the procedure [15,16]. POCUS-guided style intubation has been reported as a remedial measure in DTI [19,20]. However, it has yet to be well established the application of MGPOCUS-guided bronchoscopy in DTI. This study will provide vital information to inform DTI management in the future.

Ethics approval and study registration
Ethical approval has been granted by the respective ethics committees at the Peking Union Medical College Hospital (Institutional Review Board #ZS-3428), and written informed consent will be obtained from all participants. The study was registered online (clinicaltrials.gov; NCT05647174; Sponsor; date of registration: 12/03/2022).

Acknowledgment

Dissemination of findings
The findings will be disseminated and published through conference presentations and peer-reviewed manuscripts. Each manuscript will be submitted to all co-investigators for review of its appropriateness and scientific quality before submission.

Data statement
Data is available upon request from the corresponding author after the completion of the study.

Author contributions
TY has contributed to the conception and design of the study protocol and to drafting and revising the manuscript. FYD has contributed to both the concept and design of the study protocol. CXL and BB have guided the US implementation. ZYL and WCR have assisted in the statistical improvement. YCH and HYG have aided the methodological improvement and critically revised the draft. All authors have read, provided feedback, and approved the final manuscript.

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Competing interest statement None declared.

Patient consent for publication Not required.

References


12 Lim WY, Wong P. Awake supraglottic airway guided flexible bronchoscopic intubation in patients with anticipated difficult airways: a case series and narrative review. Korean J


Figure legends

Figure 1. The schematic diagram shows the transducer, magnetizing box, and bronchoscopy fixed with a magnetized metal needle used in the MGPOCUS system. The magnetized needle is located on the anterior side of the bronchoscopy in the same direction as its forward flexion. The needle is fixed near the tip of the bronchoscopy and fixed by a non-magnetizable plastic ring.

Figure 2. This figure is a virtual display of a magnetized bronchoscopy not within the ultrasound beam and deviated the midline of the probe, showing the position of the magnetized bronchoscopy relative to the midpoint of the ultrasound probe (upper) and the estimated line of advance of the bronchoscopy (lower). The solid red line indicates that the magnetized bronchoscopy is not within the ultrasound beam. The estimated path of its advancement based on the magnetic signal is between the two blue solid lines and will reach the position marked by the red box. TC thyroid cartilage. VC vocal cords. AC anterior commissure. T trachea.

Figure 3. This figure is a virtual display of the magnetized bronchoscopy within the ultrasound beam and probe midline, showing the position of the magnetized bronchoscopy relative to the ultrasound probe midpoint (upper) and the estimated path of advancement of the bronchoscopy (lower). The solid green line indicates that the magnetized bronchoscopy is within the ultrasound beam and that its estimated trajectory of progress based on the magnetic signal is between the two solid blue lines and will reach the position indicated by the green box. At the same time, hyperechoic points are shown between the vocal cords based on the ultrasonic signals. TC thyroid cartilage. VC vocal cords. AC anterior commissure. T trachea.
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334x284mm (96 x 96 DPI)
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Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:


<table>
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<tr>
<th>Reporting Item</th>
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Administrative information

Title #1 Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym
Trial registration: All items from the World Health Organization Trial Registration Data Set

Protocol version: Date and version identifier

Funding: Sources and types of financial, material, and other support

Roles and responsibilities: Names, affiliations, and roles of protocol contributors

Roles and responsibilities: Name and contact information for the trial sponsor

Roles and responsibilities: Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities

Roles and responsibilities: Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and
other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)

Introduction

Background and rationale

Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention

Background and rationale: choice of comparators

Explanation for choice of comparators

Objectives

Specific objectives or hypotheses

Trial design

Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)

Methods:

Participants, interventions, and outcomes

Study setting

Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained
Eligibility criteria

#10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)

Interventions:

#11a Interventions for each group with sufficient detail to allow description replications, including how and when they will be administered

Interventions:

#11b Criteria for discontinuing or modifying allocated modifications interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)

Interventions:

#11c Strategies to improve adherence to intervention protocols, adherance and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)

Interventions:

#11d Relevant concomitant care and interventions that are permitted or prohibited during the trial

Outcomes

#12 Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended
Participant timeline

#13 Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)

Sample size

#14 Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations

Recruitment

#15 Strategies for achieving adequate participant enrolment to reach target sample size

Methods:

Assignment of interventions (for controlled trials)

Allocation: sequence generation

#16a Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions

Allocation concealment mechanism

#16b Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque,
sealed envelopes), describing any steps to conceal the sequence until interventions are assigned

Allocation: #16c Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions

Blinding (masking) #17a Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how

Blinding (masking): #17b If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial

Methods: Data collection, management, and analysis

Data collection plan #18a Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol
Data collection plan: #18b Plans to promote participant retention and complete retention follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

Data management #19 Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol

Statistics: outcomes #20a Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol

Statistics: additional analyses #20b Methods for any additional analyses (eg, subgroup and adjusted analyses)

Statistics: analysis population and missing data #20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)

Methods: Monitoring

Data monitoring: formal committee #21a Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further
details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

Data monitoring: \#21b Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial

Harms \#22 Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct

Auditing \#23 Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor

Ethics and dissemination

Research ethics approval \#24 Plans for seeking research ethics committee / institutional review board (REC / IRB) approval

Protocol amendments \#25 Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)
Consent or assent: Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)

Consent or assent: Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable

Confidentiality: How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial

Declaration of interests: Financial and other competing interests for principal investigators for the overall trial and each study site

Data access: Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators

Ancillary and post trial care: Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation

Dissemination policy: Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions
Dissemination policy: **#31b** Authorship eligibility guidelines and any intended use of professional writers

Dissemination policy: **#31c** Plans, if any, for granting public access to the full reproducible research protocol, participant-level dataset, and statistical code

**Appendices**

Informed consent **#32** Model consent form and other related documentation given to participants and authorised surrogates

Biological specimens **#33** Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

None The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist can be completed online using [https://www.goodreports.org/](https://www.goodreports.org/), a tool made by the EQUATOR Network in collaboration with Penelope.ai
Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation in a general tertiary hospital: protocol for a randomized controlled study

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Complete List of Authors:
Tian, Yuan; Peking Union Medical College Hospital, Anesthesiology
Fei, Yuda; Peking Union Medical College Hospital, Department of Anesthesiology
Bing, Bai; Peking Union Medical College Hospital
Cui, Xulei; Peking Union Medical College Hospital, Department of Anesthesiology
Zhang, Yuelun; Peking Union Medical College Hospital
Wang, Chunrong; Peking Union Medical College Hospital, Department of Anesthesiology
Chunhua, Yu; Peking Union Medical College Hospital, Anesthesiology
Huang, Yuguang; Peking Union Medical College Hospital

Primary Subject Heading: Anaesthesia
Secondary Subject Heading: Anaesthesia, Emergency medicine, Radiology and imaging, Surgery
Keywords: ANAESTHETICS, Bronchoscopy < THORACIC MEDICINE, Ultrasound < RADIOLOGY & IMAGING
Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation in a general tertiary hospital: protocol for a randomized controlled study

Tian Yuan¹, Fei Yuda¹, Bai Bing¹, Cui Xulei¹, Zhang Yuelun², Wang Chunrong¹, Yu Chunhua¹*, Huang Yuguang¹

Author affiliations
¹ Department of Anesthesiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China.
² Medical Research Center, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China.

*Corresponding author: Chunhua Yu, Yu.chunhua@aliyun.com

ABSTRACT

Introduction Endotracheal intubation (ETI) is a crucial but risky procedure, especially among patients suspected of difficult endotracheal intubation (DTI). Bronchoscope, as an improved technique commonly used in DTI, might encounter visualization difficulties. The magnetic point-of-care ultrasound (MGPOCUS) provides a novel visualization from the outside and enables the estimation of the relative position and trajectory of the bronchoscope. The study aims to evaluate the efficiency of MGPOCUS-guided bronchoscope in time taken to the first-attempt success, the first-attempt and overall success of ETI, complications, and satisfaction of visualization among patients suspected of DTI.

Methods and analysis The study is a randomized, parallel-group, single-blinded, single-center study. Participants (n=350) will be recruited by the primary anesthesiologist and randomized to groups of ETI with bronchoscope or MGPOCUS-guided bronchoscope. The primary outcome is the time taken to the first-attempt success ETI. Secondary outcomes include procedure time, the first-attempt and overall success, complications, and satisfaction of visualization. Cox regression with the Bonferroni correction and the linear mixed regression will be used to analyze the outcomes.

Ethics and dissemination The trial protocol were approved by the institution of the Ethics Committee of the Peking Union Medical College Hospital. Findings will be disseminated through conference presentations and peer-reviewed journals.

Trial registration number NCT05647174.

Keywords Difficult airway, endotracheal intubation, POCUS, magnetic ultrasound

Word counts 3228

Article summary

Strength 1: This is a pioneer study regarding applying magnetic-assisted point-of-care-
ultrasound-guided bronchoscope among patients suspected of difficult intubation based on randomized controlled, two-arm, single-center evidence.

**Strength 2:** The magnetic-assisted point-of-care-ultrasound-guided bronchoscope was designed based on the principle of magnetically guided puncture embedded in the application of ultrasound in the airway.

**Strength 3:** An independent data and safety monitoring committee will independently process the study data.

**Limitation 1:** Blinding of investigators won’t be possible, though the estimation of outcomes is objective.

**Limitation 2:** The experienced physician will perform both interventions, thus limiting transferability to other less-experienced individuals.

**INTRODUCTION**

Endotracheal intubation (ETI) is crucial as a fundamental method to secure the airway\(^1\), yet the leading cause of death or vegetative state among healthy participants undergoing elective surgery\(^2\,^3\). It is consistently shown that difficult endotracheal intubation (DTI) majorly contributed to adverse events\(^4\,^5\,^6\). Though the advent of flexible bronchoscope has brought revolutionary innovations for DTI, there are still worrisome, just as the closed-claims analysis of the United States has yielded\(^7\). Most often, intubation by flexible bronchoscope is performed via the oral route\(^8\). The procedure can be tricky or delayed as the difficulty of the visualization. Visibility impaired by blood or secretions is supposed to predict difficult bronchoscope intubation. Dealing methods, such as clearance of secretions, keeping the tip in the midline, or withdrawing until the location can be identified, remain widely Vary in rapidity and uncertainty about maintaining the proper orientation\(^9\,^10\). The active research to improve visualization and movement confirms that this issue continues to challenge many physics\(^11\,^12\).

Point-of-care ultrasound (POCUS) has broadened the horizons for airway management since it allows visualization of the upper airway from the outside\(^13\). The American Heart Association updated the Guidelines on Adult Advanced Cardiovascular Life Support (ACLS), which recommended using ultrasound as a confirmation method for a tracheal tube\(^14\). Several studies provide promising results about the high pooled sensitivity (about 98%) and specificity (about 97%) of POCUS in confirming ETI\(^15\,^16\,^17\). Real-time POCUS further extends to assist ETI\(^18\,^19\). Notably, POCUS provides a view independent from the laryngoscopy or bronchoscope, making it possible to combine the outside with the inside visualization\(^13\). Also, magnetically guided ultrasound has improved regional anesthesia and vascular catheterization procedure\(^20\). The magnetic POCUS (MGPOCUS) technology collects magnetic signals and calculates the trajectory modeled by corresponding software. It enables the possibility of estimating the relative position and the advanced trajectory, guiding bronchoscope when encountering a difficulty of laryngeal exposure. To date, there has been little conclusive evidence to seek the application of MGPOCUS-guided bronchoscope in anticipated difficult intubation.

The study is designed to estimate the application of MGPOCUS-guided bronchoscope within anticipated DTI on the procedure time, the success rate, the
number of attempts, the complications, and the visual satisfaction of performers. Compared with flexible bronchoscope alone, we seek to estimate the significance of the combined visualization with MGPOCUS-guided bronchoscope.

METHODS AND ANALYSIS

Study design and setting
This is a randomized, parallel-group, single-blinded, single-center study. The study will be conducted in the anesthesia department and operating room of the Chinese Academy of Medical Sciences Peking Union Medical College Hospital (Beijing, China), a tertiary academic hospital with an annual operation census of above 80,000 participants. The protocol is structured based on the Standard Protocol Items for Randomized Trials (SPIRIT) Statement: defining standard protocol items for a clinical study.

Participant recruitment
After assessing the eligibility and obtaining informed consent (See supplementary file 1), the primary anesthesiologist will recruit the participants while performing the preoperative evaluation. The research team will confirm the eligibility.

Inclusion criteria
Participants will be eligible for inclusion if they meet all of the following items:

- Aged between 18 and 85 years old.
- Requiring ETI and without known indicators for awake tracheal intubation.
- Anticipated DTI meets one or more positive findings in the airway evaluation, including history, examination, and appropriate investigations of anatomy (Table 1).
- The primary anesthesia team, independent from the study team, considers bronchoscope intubation after induction the first choice.
- Signed written informed consent.

Table 1 Airway assessment

<table>
<thead>
<tr>
<th>Specific Predictors</th>
<th>Positive findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbid obesity</td>
<td>BMI ≥ 40</td>
</tr>
<tr>
<td>Adverse dentition</td>
<td>Presence</td>
</tr>
<tr>
<td>The prior difficulty of endotracheal intubation</td>
<td>Presence</td>
</tr>
<tr>
<td>Mouth opening</td>
<td>&lt; 4 cm</td>
</tr>
<tr>
<td>Head and upper neck extension</td>
<td>&lt; 30 degrees from neutral</td>
</tr>
<tr>
<td>Mandibular protrusion (Lip bite test)</td>
<td>Inability to prognath</td>
</tr>
<tr>
<td>Modified Mallampati class</td>
<td>III or IV</td>
</tr>
<tr>
<td>Thyromental distance</td>
<td>&lt; 6 cm</td>
</tr>
<tr>
<td>Sternomental distance</td>
<td>&lt; 12 cm</td>
</tr>
<tr>
<td>Neck circumference</td>
<td>&gt; 40 cm</td>
</tr>
</tbody>
</table>

Exclusion criteria
Participants will be excluded if they meet at least one of the following items:
Anterior neck lesions (masses, lacerations, or subcutaneous emphysema).

- A history of neck operation or tracheotomy.
- Allergies to ultrasound coupling gel.
- At the risk of pulmonary or cardiovascular complications during intubation with flexible bronchoscope, including severe hypoxemia, severe pulmonary hypertension, and unstable or intense obstructive airway disease.
- The high risk of bleeding during bronchoscope intubation, including anticoagulants or coagulopathy, renal insufficiency, and superior vena cava syndrome.
- High risk of aspiration.
- Current pregnancy.

Randomization and concealment
Participants will be randomized in a 1:1 ratio to an intervention group (MGPOCUS-guided bronchoscope) or a control group (bronchoscope). The random number sequence will be generated by the “if” package of R software by delegated research staff and uploaded to our institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Ltd., Beijing, China). The primary care anesthesiologist will be informed of the database account information before performing ETI to guarantee allocation concealment.

Blinding
Trial participants and data analysts will be blinded to the assignment of interventions. Blinding of the investigator is generally impossible, yet evaluating outcomes is objective.

Study interventions
This study compares two interventions of performing DTI, a novel MGPOCUS-guided bronchoscope, and a standard bronchoscope. Participants in each group will accept common perioperative interventions, including the essential monitoring of physiological parameters, sufficient preoxygenation, or institutional standard general anesthesia, and confirmation of ETI position by capnography. Essential monitoring will be performed before, during, and after ETI, with at least echocardiography, non-invasive blood pressure, and pulse oximetry. Preoxygenation will be administered with a mask to ensure pulse oximetry saturation of more than 93%.

ETI in both groups will be performed by a senior anesthesiologist with more than five years of experience in flexible bronchoscope. MGPOCUS-guided bronchoscope-guided intubation will be performed in collaboration with a senior anesthesiologist with more than five years of experience in POCUS and who has fulfilled more than 50 cases of ultrasound-guided airway management. An additional experienced airway manager will stand by in the operating room.

Institutional standard general anesthesia will include propofol 1.5-2.5 mg/kg, fentanyl 25-100 mcg/kg, lidocaine 0.5-1.5 mg/kg, midazolam 1-2 mg, and rocuronium 0.6-1.2 mg/kg. The position of the tracheal tube will be confirmed by capnography with at least four consistent waves and bilateral auscultation of breath sounds.
Bronchoscope-guided ETI

After clear suctioning of oropharyngeal secretions, the tip of a bronchoscope will be put through the middle of the incisors. The bronchoscope will be appropriately oriented and flexed to move along the oral midline and achieve a satisfactory view of airway structures. Once the epiglottis and glottis are located, the tip of a bronchoscope will be advanced through the glottis to the level above the carina, followed by the advancement of a tracheal tube already loaded. According to the operators’ will, approaches can be used to improve visualization, including jaw thrust, tongue pulling forward, cervical extension when not contraindicated, and bronchoscope withdrawal.

MGPOCUS-assisted bronchoscope-guided ETI

The system of MGPOCUS was derived and adapted from a previously described model used in vascular catheterization\(^2^4\). It consists of an ultrasonic machine (Piloter US scanner, Wisonic, Inc., Shenzhen, Guangdong, China), a 4-15MHz linear transducer with integrated ultrasonic and magnetic sensing capabilities (Wisonic, Inc., Shenzhen, Guangdong, China), a magnetizing box (Wisonic, Inc., Shenzhen, Guangdong, China), and a magnetized metal needle fixed near the tip of the bronchoscope (Figure 1).

The MGPOCUS system uses several display features to enable the 3-dimensional positioning of the bronchoscope tip to be displayed in a 2-dimensional ultrasonic image. Figure 2 shows an example of how the trajectory of the magnetizing needle fixed on a bronchoscope is displayed when it does or not overlap with the ultrasound beam. Specifically, the trajectory of a magnetized bronchoscope is indicated by a solid line when it is within the ultrasonic beam. Otherwise, when positioned anterior or posterior to the ultrasonic beam, its trajectory is shown as a dashed line.

While clear suctioning of oropharyngeal secretions, the transducer is positioned transversely at the patient’s thyroid cartilage level. Moving the transducer cephalad or caudal, a view of vocal folds is visualized as an isosceles triangle with a central tracheal shadow (Figure 3). The line connecting the vocal cords' anterior and posterior commissure is marked as the midline of the ultrasonography. The midline is maintained, and directed cephalad to visualize the tongue and epiglottis. The second provider will perform intubation with a The bronchoscope, as described above. When the view of the bronchoscope is unclear, MGPOCUS can provide an assisted view to locate the relative position of the bronchoscope and the vocal folds. Suppose the two lines locating the bilateral vocal cord midline and the bronchoscope do not partially overlap. In that case, the performer will adjust the direction of advancement according to the relative position of the magnetized bronchoscope to the midline of the vocal cords. Once the solid line displaying the magnetized bronchoscope is within the trachea, the pre-loaded tracheal tube will be advanced. Once the solid line is displayed posterolateral to the airway, the bronchoscope will be withdrawn and adjusted according to the MGPOCUS image. Similar to adjusting the direction of the needle to achieve the puncture target, the magnetized needle on the bronchoscope is guided to the trachea according to the ultrasonography with magnetic signals.
Discontinuing interventions
Desaturation below 90% will be considered a failed attempt of ETI. If desaturation is encountered, face mask ventilation will be performed with 100% oxygen for 2 min, and the attempt will be repeated. The procedure will be considered a failure with more than two attempts or 600 seconds, and the airway manager will proceed with the following strategy or technique. If emergencies arise, such as oxygen desaturation or hemodynamic instability, challenging to correct, the primary anesthesia team will determine whether to continue or terminate the trial.

Outcomes
Baseline assessments will be collected while preoperative evaluation, including demographic characteristics (age, sex, height, weight, body mass index, American Society of Anesthesiologists physical status score, procedure performer) and airway assessment (Table 1).

The primary outcome is the time to successful ETI at the first attempt. Time will be recorded in real-time from bronchoscopic first-passage through teeth to tube well placed. The first-attempt success is a successful ETI with no more than 180 seconds and without reinsertion of bronchoscope through teeth. Successful ETI is confirmed by capnography with at least four consistent waves.

The secondary outcomes are to detect the procedure time, the first attempt and overall success, the number of attempts, complications, and satisfaction with visualization. Complications, including desaturation, obvious trauma, bloody secretions, post-extubation hoarseness, and sore throat, will be recorded. The 5-point Likert scale assesses satisfaction with visualization.

Data management and statistics
Sample size calculation
Based on the preliminary study, it is supposed that MGPOCUS-assisted bronchoscope-guided ETI will achieve the first-attempt success with $28 \pm 22$ seconds, and bronchoscope-guided ETI with $50 \pm 41$ seconds. Hence, it is estimated that a sample size of 98 subjects will achieve a power of 90% (type II error 0.1) to detect a statistically significant difference between the two groups with a two-sided type I error of 0.05. Assuming the potentially skewed distribution of the time of first-attempt success would lead 10% statistical power loss, 54 subjects in each group will be recruited.

Data collection and protection
All data will be collected on the institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Ltd, Beijing, China) by an investigator independently. Data entry and processing will be performed before unblinding of investigators. The database will be centralized and managed by the leading researchers. A unique research identification data (ID) code will be used to ensure confidentiality and anonymity. The ID will be used to identify participants and
the allocation. The recorded data in the study will not be linked to the participant’s personal information. The data will be transferred securely and stored confidentially on password-protected computers that the researchers can only access by General Data Protection Regulation.

**Data statistics plan**

Demographic characteristics and airway assessment variables will be presented using descriptive statistics for the overall sample. Continuous data will be described using mean (standard deviation [SD]) or median (interquartile range [IQR]), depending on the distribution of the data. Categorical data will be described using numbers and proportions.

For the primary outcome, the time taken to the first-attempt success will be analyzed using a Cox proportional hazards model with the Bonferroni correction as a multiplicity adjustment that treats failed ETI at the first attempt as censored. For secondary outcomes, procedure time for successful ETI will be analyzed using a linear mixed model that treats ETI success or failure as the outcome and procedure performer as a random effect. The first attempt and overall success will be analyzed using mixed-effects logistic regression. Any two-sided P-value <0.05 will be considered statistically significant. Statistical analyses will be performed on R software version 3.5.1 (R Foundation for Statistical Computing).

**Termination of the study**

An independent statistician will conduct the interim analysis of the primary outcome when 50% of participants have been enrolled. The results will be reported to the independent data and safety monitoring committee and discussed with the steering committee. The Peto approach is used to terminate the study when the intervention group greatly benefits from the control group using symmetric stopping boundaries at P<0.001. The study will contained only be stopped in case of futility if the independent data and The potential stopping for futility will be discussed with the steering committee in this case.

**Data monitoring**

A steering committee will manage the study. Screening and recruitment will be reviewed at monthly meetings. An independent data and safety monitoring committee will meet every three months to ensure patient safety and data quality.

**Safety**

The independent data and safety monitoring committee will supervise the study’s progress by examining safety variables monthly. Adverse events are defined as “any undesirable experience occurring to a subject during the study, whether or not considered related to the intervention.” Any potential adverse events must be monitored, recorded, and discussed with the independent data and safety monitoring committee.

**Patient and public involvement**
The study protocol was developed in collaboration with anesthesiologists with extensive experience managing difficult airways or POCUS. Their feedback and expectations regarding research questions and outcome measures were discussed and applied for adjustment. Since the absence of experimental knowledge and subjective feeling, participants were not involved in our research's design, conduct, reporting, or dissemination plans.

Ethics approval and study registration
Ethical approval has been granted by the respective ethics committees at the Peking Union Medical College Hospital (Institutional Review Board #ZS-3428), and written informed consent will be obtained from all participants. The study was registered online (clinicaltrials.gov; NCT05647174; Sponsor; date of registration: 12/03/2022).

Acknowledgment
Dissemination of findings
The findings will be disseminated and published through conference presentations and peer-reviewed manuscripts. Each manuscript will be submitted to all co-investigators for review of its appropriateness and scientific quality before submission.

Data statement
Data is available upon request from the corresponding author after the completion of the study.

Author contributions
TY has contributed to the conception and design of the study protocol and to drafting and revising the manuscript. FYD has contributed to both the concept and design of the study protocol. CXL and BB have guided the US implementation. ZYL and WCR have assisted in the statistical improvement. YCH and HYG have aided the methodological improvement and critically revised the draft. All authors have read, provided feedback, and approved the final manuscript.

Funding statement
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Competing interest statement
None declared.

Patient consent for publication
Not required.

References


**Figure legends**
Figure 1. The schematic diagram shows the transducer, magnetizing box, and bronchoscope fixed with a magnetized metal needle used in the MGPOCUS system. The magnetized needle is located on the anterior side of the bronchoscope in the same direction as its forward flexion. The needle is fixed near the tip of the bronchoscope and fixed by a non-magnetizable plastic ring.

Figure 2. This figure is a virtual display of a magnetized bronchoscope not within the ultrasound beam and deviated the midline of the probe, showing the position of the magnetized bronchoscope relative to the midpoint of the ultrasound probe (upper) and the estimated line of advance of the bronchoscope (lower). The solid red line indicates that the magnetized bronchoscope is not within the ultrasound beam. The estimated path of its advancement based on the magnetic signal is between the two blue solid lines and will reach the position marked by the red box. TC thyroid cartilage. VC vocal cords. AC anterior commissure. T trachea.

Figure 3. This figure is a virtual display of the magnetized bronchoscope within the ultrasound beam and probe midline, showing the position of the magnetized bronchoscope relative to the ultrasound probe midpoint (upper) and the estimated path of advancement of the bronchoscope (lower). The solid green line indicates that the magnetized bronchoscope is within the ultrasound beam and that its estimated trajectory of progress based on the magnetic signal is between the two solid blue lines and will reach the position indicated by the green box. At the same time, hyperechoic points are shown between the vocal cords based on the ultrasonic signals. TC thyroid cartilage. VC vocal cords. AC anterior commissure. T trachea.
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293x284mm (96 x 96 DPI)
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334x275mm (96 x 96 DPI)
Participant Consent Form

Project: Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation

Contact Address:

<table>
<thead>
<tr>
<th>Dr Yuan Tian</th>
<th>Dr Chunhua Yu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesiology Department, Peking Union Medical College Hospital, Dongcheng District, Beijing, China</td>
<td>Anesthesiology Department, Peking Union Medical College Hospital, Dongcheng District, Beijing, China</td>
</tr>
<tr>
<td>Email: <a href="mailto:tianyuan95@pumch.cn">tianyuan95@pumch.cn</a></td>
<td>Email: <a href="mailto:Yu.chunhua@aliyun.com">Yu.chunhua@aliyun.com</a></td>
</tr>
<tr>
<td>Contact number: 008617611356059</td>
<td>Contact number: 00861069152001</td>
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</table>

Date: Mar, 2022

Background information

General anesthesia tracheal intubation is the primary anesthetic method to ensure the completion of surgery and patient safety. Detection of unintended tracheal intubation is an important step in this method and is an important factor in reducing anesthetic accidents and ensuring postoperative regression. Real-time ultrasound is a rapid, non-invasive detection method that potentially benefits patients with difficult intubation.

In our study, patients willing to participate in this study and at risk for difficult intubation were randomly assigned to either the ultrasound-assisted laryngoscopic view or the laryngoscopic view group, and the location of tracheal intubation was detected using noninvasive cervical ultrasound-assisted intubation with laryngoscopic view or laryngoscopic view at the same time as tracheal intubation to assess the difference in the effectiveness of the two methods. In order to obtain data related to the application of ultrasound-assisted methods for detecting the position of intubation in patients with difficult intubation.

Our study can provide more valuable evidence for clinical decision making in the refinement of airway management in patients with difficult tracheal intubation. Your participation will make an important contribution to obtaining such evidence, allowing other patients to benefit from your contribution.

Who should not participate in the study?

There are strict inclusion and exclusion criteria for this study. Any patient who does not meet the inclusion criteria should not participate in this study, in addition to 1) patients who are participating in other clinical studies; 2) those who are considered by the investigators to be unsuitable for clinical studies for other reasons.

What will I need to do if I participate in the study?

1. Before you are enrolled in the study, your doctor will ask questions, record your
general condition, and assess whether you are at risk for difficult intubation. It will be
determined that you are an eligible inclusion, that you are volunteering for the study,
and you will be asked to sign an informed consent form.

2. If you volunteer to participate in the study, we will perform a standard or
ultrasound-assisted protocol for you, depending on the randomization group, and
record the monitoring results.

Possible benefits of participating in the study.
If you participate in the study, the results of the study will have important implications
for clinical decision making in all general anesthesia tracheal intubation populations
and will provide you with the following improved support for evaluation and
consultation during your anesthesia. This includes:
1. better assessment measures: including more detailed and improved airway
assessment. There are no tests outside of the current treatment routine, which will not
increase the cost of your treatment, and if additional tests are incurred as a result of
the study itself, they will be free of charge to you.
2. Specialized visits and consultations: The visits and consultations of this project will
be conducted by specially trained personnel, so that you can receive timely and
comprehensive consultations on the contents related to general anesthesia tracheal
intubation, and your relevant questions will be answered and dealt with in a timely
manner.

Possible risks, adverse reactions and discomfort, inconvenience of participating
in the study.
This project uses laryngoscopic visualization alone and ultrasound-assisted
laryngoscopic visualization; laryngoscopic visualization is a routine clinical method
and ultrasound-assisted method is a non-invasive method, so participation in this
project itself will not increase your risk.
You will be required to participate in airway evaluations during the study, and these
will take up some of your time and may also cause you problems or inconvenience.
If you experience any discomfort after the clinical study, including during the study,
or if there are any new changes in your condition, or any unforeseen circumstances,
whether or not related to the study, you should promptly notify your physician, who
will make a determination and provide appropriate medical treatment.

Related Costs and Compensation
There are no additional anesthetic risks or costs associated with either of the methods
involved in this study, and the patient is responsible for the costs associated with
routine anesthetic management. Treatments and examinations required for your
concurrent medical conditions will also not be covered free of charge. However, if
additional tests are performed as a result of the program itself, they will be free of
charge to you.
The intervention methods involved in this study are non-invasive and routine, and will
not cause damage to the patient, so there is no compensation involved in this project.
Is personal information confidential?
Your medical records (study charts/CRFs, labs, etc.) will be kept intact at the hospital you visit. Your doctor will record the results of laboratory tests and other examinations in your medical record. The investigator, ethics committee and drug regulatory authorities will be given access to your medical records. Records of all your personal information, including name, phone number, email, and address, will not appear in electronic databases, and any public reports of the results of this study will not disclose your personal identity and information. We will make every effort to protect the privacy of your personal medical information to the extent permitted by law.

How can I get more information?
You can ask any questions about this study at any time and get the appropriate answers. For inquiries (investigator contact): 17611356059; and you have the right to ask questions about your rights or related risks, inquiries (ethics review committee contact): 69156874

Your physician will promptly notify you of any important new information during the study that may affect your willingness to continue to participate in the study.
You can voluntarily choose to participate in the study and withdraw from the study Participation in the study is entirely at your discretion. You may refuse to participate in the study or withdraw from the study at any time during the study, and this will not affect the relationship between you and your physician, nor will it affect your medical treatment or any other loss of benefits.

Your physician or investigator may discontinue your participation in this study at any time during the study for reasons of your best interest.
If you withdraw from this study for any reason, you may also be asked to undergo laboratory tests and physical examinations if your doctor deems it clinically necessary.

What should I do now?
It is up to you (and your family) to decide whether to participate in this study.
Please ask your doctor as many questions as possible before you make a decision to participate in the study.
Thank you for reading the above materials. If you decide to participate in this program, please tell your doctor and he/she will make all the arrangements for you to participate in the study. Please keep this information with you.

Statement of Consent
I have read the above description of this study and have had the opportunity to discuss and ask questions about this study with my doctor. All of the questions I have asked have been answered to my satisfaction.
I am aware of the possible risks and benefits of participating in this study. I understand that participation in this study is voluntary, I acknowledge that I have had sufficient time to consider it, and I understand that I can ask my doctor for more information at any time.
I may withdraw from this study at any time without discrimination or reprisal, and without my medical treatment or rights being affected in any way. I am equally aware that if I withdraw from the study in the middle of the study, especially if I withdraw for medication reasons, it would be very beneficial to the study as a whole for me to inform my physician of any changes in my condition and to complete the appropriate physical and physical examinations. If I need to take any other medication due to a change in my condition, I will consult my doctor beforehand or tell him/her truthfully afterwards. I give my consent to the drug regulatory authority, ethics committee or sponsor's representative to access my study data. I will be provided with a signed and dated copy of the informed consent form. Finally, I have decided to give my consent to participate in this study and I promise to follow medical advice as far as possible.

Subject's name

Subject's signature

Date

If the patient has appointed a legal proxy (if applicable, and signed a proxy agreement):

Name of legal attorney (in block letters)

Signature of legal attorney

Date

I confirm that the details of this study, including their rights and possible benefits and risks, have been explained to the patient and that they have been given a copy of the signed informed consent form.

Name of investigator

Signature

Date
# Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:


<table>
<thead>
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<th>Reporting Item</th>
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<td><strong>Administrative information</strong></td>
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<tr>
<td>Title</td>
<td>#1</td>
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<tr>
<td>Trial registration</td>
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<tr>
<td>Trial registration: data set</td>
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<td>Protocol version</td>
<td>#3</td>
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</table>
Funding

#4 Sources and types of financial, material, and other support

Roles and responsibilities:
contributorship

#5a Names, affiliations, and roles of protocol contributors

Roles and responsibilities:
sponsor contact information

#5b Name and contact information for the trial sponsor

Roles and responsibilities:
sponsor and funder

#5c Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities

Roles and responsibilities:
committees

#5d Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)

Introduction

Background and rationale

#6a Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention

Background and rationale: choice of comparators

#6b Explanation for choice of comparators

Objectives

#7 Specific objectives or hypotheses
<table>
<thead>
<tr>
<th>Trial design #8</th>
<th>Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)</th>
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<tr>
<td>Methods: Participants, interventions, and outcomes</td>
<td></td>
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<tr>
<td>Study setting #9</td>
<td>Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained</td>
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<tr>
<td>Eligibility criteria #10</td>
<td>Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)</td>
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<tr>
<td>Interventions: description #11a</td>
<td>Interventions for each group with sufficient detail to allow replication, including how and when they will be administered</td>
</tr>
<tr>
<td>Interventions: modifications #11b</td>
<td>Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)</td>
</tr>
<tr>
<td>Interventions: adherence #11c</td>
<td>Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)</td>
</tr>
<tr>
<td>Interventions: concomitant care #11d</td>
<td>Relevant concomitant care and interventions that are permitted or prohibited during the trial</td>
</tr>
<tr>
<td>Outcomes #12</td>
<td>Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure)</td>
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pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended.

Participant timeline #13  Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure).

Sample size #14  Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations.

Recruitment #15  Strategies for achieving adequate participant enrolment to reach target sample size.

Methods:
Assignment of interventions (for controlled trials)

Allocation: sequence generation #16a  Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions.

Allocation concealment mechanism #16b  Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned.
Allocation: implementation

Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions

Blinding (masking)

Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how

Blinding (masking): emergency unblinding

If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial

Methods: Data collection, management, and analysis

Data collection plan

Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

Data collection plan: retention

Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

Data management

Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol
Statistics: outcomes #20a Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol 6-7

Statistics: additional analyses #20b Methods for any additional analyses (eg, subgroup and adjusted analyses) 6-7

Statistics: analysis population and missing data #20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) 6-7

Methods: Monitoring

Data monitoring: formal committee #21a Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed 7

Data monitoring: interim analysis #21b Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial 7

Harms #22 Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct 7

Auditing #23 Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor 7
<table>
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<tr>
<th>Topic</th>
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<th>Description</th>
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<tr>
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<td>#24</td>
<td>Plans for seeking research ethics committee / institutional review board (REC / IRB) approval</td>
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<tr>
<td>Protocol amendments</td>
<td>#25</td>
<td>Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)</td>
</tr>
<tr>
<td>Consent or assent</td>
<td>#26</td>
<td>Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)</td>
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<tr>
<td>Consent or assent: ancillary studies</td>
<td>#26</td>
<td>Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable</td>
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<tr>
<td>Confidentiality</td>
<td>#27</td>
<td>How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial</td>
</tr>
<tr>
<td>Declaration of interests</td>
<td>#28</td>
<td>Financial and other competing interests for principal investigators for the overall trial and each study site</td>
</tr>
<tr>
<td>Data access</td>
<td>#29</td>
<td>Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators</td>
</tr>
<tr>
<td>Ancillary and post-trial care</td>
<td>#30</td>
<td>Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation</td>
</tr>
</tbody>
</table>
Dissemination policy: trial results
- Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions

Dissemination policy: authorship
- Authorship eligibility guidelines and any intended use of professional writers

Dissemination policy: reproducible research
- Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code

Appendices

Informed consent materials
- Model consent form and other related documentation given to participants and authorized surrogates

Biological specimens
- Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

None

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Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation in a general tertiary hospital: protocol for a randomized controlled study

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<th>BMJ Open</th>
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<tr>
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<td>05-May-2023</td>
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<tr>
<td>Complete List of Authors:</td>
<td>Tian, Yuan; Peking Union Medical College Hospital, Anesthesiology Fei, Yuda; Peking Union Medical College Hospital, Department of Anesthesiology Bing, Bai; Peking Union Medical College Hospital Cui, Xulei; Peking Union Medical College Hospital, Department of Anesthesiology Zhang, Yuelun; Peking Union Medical College Hospital Wang, Chunrong; Peking Union Medical College Hospital, Department of Anesthesiology Chunhua, Yu; Peking Union Medical College Hospital, Anesthesiology Huang, Yuguang; Peking Union Medical College Hospital</td>
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<td>Secondary Subject Heading:</td>
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<tr>
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</table>
Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation in a general tertiary hospital: protocol for a randomized controlled study

Tian Yuan¹, Fei Yuda¹, Bai Bing¹, Cui Xulei¹, Zhang Yuelun², Wang Chunrong¹, Yu Chunhua¹*, Huang Yuguang¹

Author affiliations
¹ Department of Anesthesiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China.
² Medical Research Center, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China.

*Corresponding author: Chunhua Yu, Yu.chunhua@aliyun.com

ABSTRACT

Introduction Endotracheal intubation (ETI) is a crucial but risky procedure, especially among patients suspected of difficult endotracheal intubation (DTI). Bronchoscope, as an improved technique commonly used in DTI, might encounter visualization difficulties. The magnetic point-of-care ultrasound (MGPOCUS) provides a novel visualization from the outside and enables the estimation of the relative position and trajectory of the bronchoscope. The study aims to evaluate the efficiency of MGPOCUS-guided bronchoscope in time taken to the first-attempt success, the first-attempt and overall success of ETI, complications, and satisfaction of visualization among patients suspected of DTI.

Methods and analysis The study is a randomized, parallel-group, single-blinded, single-center study. Participants (n=108) will be recruited by the primary anesthesiologist and randomized to groups of ETI with bronchoscope or MGPOCUS-guided bronchoscope. The primary outcome is the time taken to the first-attempt success ETI. Secondary outcomes include procedure time, the first-attempt and overall success, complications, and satisfaction of visualization. Cox regression with the Bonferroni correction and the linear mixed regression will be used to analyze the outcomes.

Ethics and dissemination The trial protocol were approved by the institution of the Ethics Committee of the Peking Union Medical College Hospital. Findings will be disseminated through conference presentations and peer-reviewed journals.

Trial registration number NCT05647174.

Keywords Difficult airway, endotracheal intubation, POCUS, magnetic ultrasound

Word counts 3228

Strengths and limitations
• This is a pioneer study regarding applying magnetic-assisted point-of-care-
ultrasound-guided bronchoscope among patients suspected of difficult intubation based on randomized controlled, two-arm, single-center evidence.

- The magnetic-assisted point-of-care-ultrasound-guided bronchoscope was designed based on the principle of magnetically guided puncture embedded in the application of ultrasound in the airway.
- An independent data and safety monitoring committee will independently process the study data.
- Blinding of investigators won’t be possible, though the estimation of outcomes is objective.
- The experienced physician will perform both interventions, thus limiting transferability to other less-experienced individuals.

INTRODUCTION

Endotracheal intubation (ETI) is crucial as a fundamental method to secure the airway\(^1\), yet the leading cause of death or vegetative state among healthy participants undergoing elective surgery\(^2,3\). It is consistently shown that difficult endotracheal intubation (DTI) majorly contributed to adverse events\(^4-6\). Though the advent of flexible bronchoscope has brought revolutionary innovations for DTI, there are still worrisome, just as the closed-claims analysis of the United States has yielded\(^7\). Most often, intubation by flexible bronchoscope is performed via the oral route\(^8\). The procedure can be tricky or delayed as the difficulty of the visualization. Visibility impaired by blood or secretions is supposed to predict difficult bronchoscope intubation. Dealing methods, such as clearance of secretions, keeping the tip in the midline, or withdrawing until the location can be identified, remain widely Vary in rapidity and uncertainty about maintaining the proper orientation\(^9,10\). The active research to improve visualization and movement confirms that this issue continues to challenge many physics\(^11,12\).

Point-of-care ultrasound (POCUS) has broadened the horizons for airway management since it allows visualization of the upper airway from the outside\(^13\). The American Heart Association updated the Guidelines on Adult Advanced Cardiovascular Life Support (ACLS), which recommended using ultrasound as a confirmation method for a tracheal tube\(^14\). Several studies provide promising results about the high pooled sensitivity (about 98%) and specificity (about 97%) of POCUS in confirming ETI\(^15-17\). Real-time POCUS further extends to assist ETI\(^18,19\). Notably, POCUS provides a view independent from the laryngoscopy or bronchoscope, making it possible to combine the outside with the inside visualization\(^13\). Also, magnetically guided ultrasound has improved regional anesthesia and vascular catheterization procedure\(^20\). The magnetic POCUS (MGPOCUS) technology collects magnetic signals and calculates the trajectory modeled by corresponding software. It enables the possibility of estimating the relative position and the advanced trajectory, guiding bronchoscope when encountering a difficulty of laryngeal exposure. To date, there has been little conclusive evidence to seek the application of MGPOCUS-guided bronchoscope in anticipated difficult intubation.

The study is designed to estimate the application of MGPOCUS-guided bronchoscope within anticipated DTI on the procedure time, the success rate, the
number of attempts, the complications, and the visual satisfaction of performers. Compared with flexible bronchoscope alone, we seek to estimate the significance of the combined visualization with MGPOCUS-guided bronchoscope.

METHODS AND ANALYSIS

Study design and setting
This is a randomized, parallel-group, single-blinded, single-center study. The study will be conducted in the anesthesia department and operating room of the Chinese Academy of Medical Sciences Peking Union Medical College Hospital (Beijing, China), a tertiary academic hospital with an annual operation census of above 80,000 participants. The protocol is structured based on the Standard Protocol Items for Randomized Trials (SPIRIT) Statement: defining standard protocol items for a clinical study.

Participant recruitment
After assessing the eligibility and obtaining informed consent (See supplementary file 1), the primary anesthesiologist will recruit the participants while performing the preoperative evaluation. The research team will confirm the eligibility.

Inclusion criteria
Participants will be eligible for inclusion if they meet all of the following items:
- Aged between 18 and 85 years old.
- Requiring ETI and without known indicators for awake tracheal intubation.
- Anticipated DTI meets one or more positive findings in the airway evaluation, including history, examination, and appropriate investigations of anatomy (Table 1).
- The primary anesthesia team, independent from the study team, considers bronchoscope intubation after induction the first choice.
- Signed written informed consent.

Table 1  Airway assessment

<table>
<thead>
<tr>
<th>Specific Predictors</th>
<th>Positive findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbid obesity</td>
<td>BMI $\geq 40$</td>
</tr>
<tr>
<td>Adverse dentition</td>
<td>Presence</td>
</tr>
<tr>
<td>The prior difficulty of endotracheal intubation</td>
<td>Presence</td>
</tr>
<tr>
<td>Mouth opening</td>
<td>$&lt; 4$ cm</td>
</tr>
<tr>
<td>Head and upper neck extension</td>
<td>$&lt; 30$ degrees from neutral</td>
</tr>
<tr>
<td>Mandibular protrusion (Lip bite test)</td>
<td>Inability to prognath</td>
</tr>
<tr>
<td>Modified Mallampati class</td>
<td>III or IV</td>
</tr>
<tr>
<td>Thyromental distance</td>
<td>$&lt; 6$ cm</td>
</tr>
<tr>
<td>Sternomental distance</td>
<td>$&lt; 12$ cm</td>
</tr>
<tr>
<td>Neck circumference</td>
<td>$&gt; 40$ cm</td>
</tr>
</tbody>
</table>

Exclusion criteria
Participants will be excluded if they meet at least one of the following items:
• Anterior neck lesions (masses, lacerations, or subcutaneous emphysema).
• A history of neck operation or tracheotomy.
• Allergies to ultrasound coupling gel.
• At the risk of pulmonary or cardiovascular complications during intubation with flexible bronchoscope, including severe hypoxemia, severe pulmonary hypertension, and unstable or intense obstructive airway disease.
• The high risk of bleeding during bronchoscope intubation, including anticoagulants or coagulopathy, renal insufficiency, and superior vena cava syndrome.
• High risk of aspiration.
• Current pregnancy.

Randomization and concealment
Participants will be randomized in a 1:1 ratio to an intervention group (MGPOCUS-guided bronchoscope) or a control group (bronchoscope). The random number sequence will be generated by the “if” package of R software by delegated research staff and uploaded to our institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Ltd., Beijing, China). The primary care anesthesiologist will be informed of the database account information before performing ETI to guarantee allocation concealment.

Blinding
Trial participants and data analysts will be blinded to the assignment of interventions. Blinding of the investigator is generally impossible, yet evaluating outcomes is objective.

Study interventions
This study compares two interventions of performing DTI, a novel MGPOCUS-guided bronchoscope, and a standard bronchoscope. Participants in each group will accept common perioperative interventions, including the essential monitoring of physiological parameters, sufficient preoxygenation, or institutional standard general anesthesia, and confirmation of ETI position by capnography. Essential monitoring will be performed before, during, and after ETI, with at least echocardiography, non-invasive blood pressure, and pulse oximetry. Preoxygenation will be administered with a mask to ensure pulse oximetry saturation of more than 93%.

ETI in both groups will be performed by a senior anesthesiologist with more than five years of experience in flexible bronchoscope. MGPOCUS-guided bronchoscope-guided intubation will be performed in collaboration with a senior anesthesiologist with more than five years of experience in POCUS and who has fulfilled more than 50 cases of ultrasound-guided airway management. An additional experienced airway manager will stand by in the operating room.

Institutional standard general anesthesia will include propofol 1.5-2.5 mg/kg, fentanyl 25-100 mcg/kg, lidocaine 0.5-1.5mg/kg, midazolam 1-2 mg, and rocuronium 0.6-1.2 mg/kg. The position of the tracheal tube will be confirmed by capnography with at least four consistent waves and bilateral auscultation of breath sounds.
Bronchoscope-guided ETI
After clear suctioning of oropharyngeal secretions, the tip of a bronchoscope will be put through the middle of the incisors. The bronchoscope will be appropriately oriented and flexed to move along the oral midline and achieve a satisfactory view of airway structures. Once the epiglottis and glottis are located, the tip of a bronchoscope will be advanced through the glottis to the level above the carina, followed by the advancement of a tracheal tube already loaded. According to the operators’ will, approaches can be used to improve visualization, including jaw thrust, tongue pulling forward, cervical extension when not contraindicated, and bronchoscope withdrawal.

MGPOCUS-assisted bronchoscope-guided ETI
The system of MGPOCUS was derived and adapted from a previously described model used in vascular catheterization. The system is only used for visualization the needle fixed on the bronchoscope, not moving the bronchoscope. It consists of an ultrasonic machine (Piloter US scanner, Wisonic, Inc., Shenzhen, Guangdong, China), a 4-15 MHz linear transducer with integrated ultrasonic and magnetic sensing capabilities (Wisonic, Inc., Shenzhen, Guangdong, China), a magnetizing box (Wisonic, Inc., Shenzhen, Guangdong, China), and a magnetized metal needle fixed near the tip of the bronchoscope (Figure 1).

The MGPOCUS system uses several display features to enable the 3-dimensional positioning of the bronchoscope tip to be displayed in a 2-dimensional ultrasonic image. Figure 2 shows an example of how the trajectory of the magnetizing needle fixed on a bronchoscope is displayed when it does or not overlap with the ultrasound beam. Specifically, the trajectory of a magnetized bronchoscope is indicated by a solid line when it is within the ultrasonic beam. Otherwise, when positioned anterior or posterior to the ultrasonic beam, its trajectory is shown as a dashed line.

While clear suctioning of oropharyngeal secretions, the transducer is positioned transversely at the patient’s thyroid cartilage level. Moving the transducer cephalad or caudal, a view of vocal folds is visualized as an isosceles triangle with a central tracheal shadow (Figure 3). The line connecting the vocal cords’ anterior and posterior commissure is marked as the midline of the ultrasonography. The midline is maintained, and directed cephalad to visualize the tongue and epiglottis. The second provider will perform intubation with a bronchoscope, as described above. When the view of the bronchoscope is unclear, MGPOCUS can provide an assisted view to locate the relative position of the bronchoscope and the vocal folds. Suppose the two lines locating the bilateral vocal cord midline and the bronchoscope do not partially overlap. In that case, the performer will adjust the direction of advancement according to the relative position of the magnetized bronchoscope to the midline of the vocal cords. Once the solid line displaying the magnetized bronchoscope is within the trachea, the pre-loaded tracheal tube will be advanced. Once the solid line is displayed posterolateral to the airway, the bronchoscope will be withdrawn and adjusted according to the MGPOCUS image. Similar to adjusting the direction of the needle to achieve the puncture target, the magnetized needle on the bronchoscope is guided to
the trachea according to the ultrasonography with magnetic signals.

**Discontinuing interventions**

Desaturation below 90% will be considered a failed attempt of ETI. If desaturation is encountered, face mask ventilation will be performed with 100% oxygen for 2 min, and the attempt will be repeated. The procedure will be considered a failure with more than two attempts or 600 seconds, and the airway manager will proceed with the following strategy or technique. If emergencies arise, such as oxygen desaturation or hemodynamic instability, challenging to correct, the primary anesthesia team will determine whether to continue or terminate the trial.

**Outcomes**

Baseline assessments will be collected while preoperative evaluation, including demographic characteristics (age, sex, height, weight, body mass index, American Society of Anesthesiologists physical status score, procedure performer) and airway assessment (Table 1).

The primary outcome is the time to successful ETI at the first attempt. Time will be recorded in real-time from bronchoscopic first-passage through teeth to tube well placed. The first-attempt success is a successful ETI with no more than 180 seconds and without reinsertion of bronchoscope through teeth. Successful ETI is confirmed by capnography with at least four consistent waves.

The secondary outcomes are to detect the procedure time, the first attempt and overall success, the number of attempts, complications, and satisfaction with visualization. Complications, including desaturation, obvious trauma, bloody secretions, post-extubation hoarseness, and sore throat, will be recorded. The 5-point Likert scale assesses satisfaction with visualization.

**Data management and statistics**

**Sample size calculation**

Based on our preliminary study (unpublished data), it is supposed that MGPOCUS-assisted bronchoscope-guided ETI will achieve the first-attempt success with 28±22 seconds, and bronchoscope-guided ETI with 50±41 seconds. Hence, it is estimated that a sample size of 98 subjects will achieve a power of 90% (type II error 0.1) to detect a statistically significant difference between the two groups with a two-sided type I error of 0.05. Assuming the potentially skewed distribution of the time of first-attempt success would lead 10% statistical power loss, 54 subjects in each group will be recruited.

**Data collection and protection**

All data will be collected on the institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Ltd, Beijing, China) by an investigator independently. Data entry and processing will be performed before
unblinding of investigators. The database will be centralized and managed by the leading researchers. A unique research identification data (ID) code will be used to ensure confidentiality and anonymity. The ID will be used to identify participants and the allocation. The recorded data in the study will not be linked to the participant’s personal information. The data will be transferred securely and stored confidentially on password-protected computers that the researchers can only access by General Data Protection Regulation.

Data statistics plan
Demographic characteristics and airway assessment variables will be presented using descriptive statistics for the overall sample. Continuous data will be described using mean (standard deviation [SD]) or median (interquartile range [IQR]), depending on the distribution of the data. Categorical data will be described using numbers and proportions.

For the primary outcome, the time taken to the first-attempt success will be analyzed using a Cox proportional hazards model with the Bonferroni correction as a multiplicity adjustment that treats failed ETI at the first attempt as censored. For secondary outcomes, procedure time for successful ETI will be analyzed using a linear mixed model that treats ETI success or failure as the outcome and procedure performer as a random effect. The first attempt and overall success will be analyzed using mixed-effects logistic regression. Any two-sided P-value <0.05 will be considered statistically significant. Statistical analyses will be performed on R software version 3.5.1 (R Foundation for Statistical Computing).

Termination of the study
An independent statistician will conduct the interim analysis of the primary outcome when 50% of participants have been enrolled. The results will be reported to the independent data and safety monitoring committee and discussed with the steering committee. The Peto approach is used to terminate the study when the intervention group greatly benefits from the control group using symmetric stopping boundaries at P<0.001. The study will contain only be stopped in case of futility if the independent data and The potential stopping for futility will be discussed with the steering committee in this case y will be discussed with the steering committee.

Data monitoring
A steering committee will manage the study. Screening and recruitment will be reviewed at monthly meetings. An independent data and safety monitoring committee will meet every three months to ensure patient safety and data quality.

Safety
The independent data and safety monitoring committee will supervise the study’s progress by examining safety variables monthly. Adverse events are defined as “any undesirable experience occurring to a subject during the study, whether or not considered related to the intervention.” Any potential adverse events must be monitored,
recorded, and discussed with the independent data and safety monitoring committee.

**Patient and public involvement**

The study protocol was developed in collaboration with anesthesiologists with extensive experience managing difficult airways or POCUS. Their feedback and expectations regarding research questions and outcome measures were discussed and applied for adjustment. Since the absence of experimental knowledge and subjective feeling, participants were not involved in our research's design, conduct, reporting, or dissemination plans.

**Ethics approval and study registration**

Ethical approval has been granted by the respective ethics committees at the Peking Union Medical College Hospital (Institutional Review Board #ZS-3428), and written informed consent will be obtained from all participants. The study was registered online (clinicaltrials.gov; NCT05647174; Sponsor; date of registration: 12/03/2022).

**Acknowledgment**

**Dissemination of findings**

The findings will be disseminated and published through conference presentations and peer-reviewed manuscripts. Each manuscript will be submitted to all co-investigators for review of its appropriateness and scientific quality before submission.

**Data statement**

Data is available upon request from the corresponding author after the completion of the study.

**Author contributions**

All authors contributed to the conception and design of the study protocol. Tian Yuan drafted the manuscript. Fei Yuda, Bai Bing, and Wang Chunrong acquired and analyzed data. Zhang Yuelun interpreted data and methodologically revised the manuscript. Cui Xulei, Yu Chunhua, and Huang Yuguang reviewed and revised the manuscript critically. All authors have read, provided feedback, and approved the final version of the manuscript.

**Funding statement**

This work was supported by Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences (2021-I2M-C&T-B-020) and National High Level Hospital Clinical Research Funding (2022-PUMCH-A-148).

**Competing interest statement** None declared.

**Patient consent for publication** Not required.

**References**


Figure legends

Figure 1. Composition of the MGPOCUS system.
The schematic diagram shows the transducer, magnetizing box, and bronchoscope fixed with a magnetized metal needle used in the MGPOCUS system. The magnetized needle is located on the anterior side of the bronchoscope in the same direction as its forward flexion. The needle is fixed near the tip of the bronchoscope and fixed by a non-magnetizable plastic ring.

Figure 2. The virtual display of MGPOCUS-assisted bronchoscope not within the ultrasound beam.
This figure is a virtual display of a magnetized bronchoscope not within the ultrasound beam and deviated the midline of the probe, showing the position of the magnetized bronchoscope relative to the midpoint of the ultrasound probe (upper) and the estimated line of advance of the bronchoscope (lower). The solid red line indicates that the magnetized bronchoscope is not within the ultrasound beam. The estimated path of its advancement based on the magnetic signal is between the two blue solid lines and will reach the position marked by the red box. *TC* thyroid cartilage. *VC* vocal cords. *AC* anterior commissure. *T* trachea.

Figure 3. The virtual display of MGPOCUS-assisted bronchoscope within the
ultrasound beam.
This figure is a virtual display of the magnetized bronchoscope within the ultrasound beam and probe midline, showing the position of the magnetized bronchoscope relative to the ultrasound probe midpoint (upper) and the estimated path of advancement of the bronchoscope (lower). The solid green line indicates that the magnetized bronchoscope is within the ultrasound beam and that its estimated trajectory of progress based on the magnetic signal is between the two solid blue lines and will reach the position indicated by the green box. At the same time, hyperechoic points are shown between the vocal cords based on the ultrasonic signals. *TC* thyroid cartilage. *VC* vocal cords. *AC* anterior commissure. *T* trachea.
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293x284mm (96 x 96 DPI)
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Participant Consent Form

Project: Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation

Contact Address:

<table>
<thead>
<tr>
<th>Dr Yuan Tian</th>
<th>Dr Chunhua Yu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesiology Department, Peking Union Medical College Hospital, Dongcheng District, Beijing, China</td>
<td>Anesthesiology Department, Peking Union Medical College Hospital, Dongcheng District, Beijing, China</td>
</tr>
<tr>
<td>Email: <a href="mailto:tianyuan95@pumch.cn">tianyuan95@pumch.cn</a></td>
<td>Email: <a href="mailto:Yu.chunhua@aliyun.com">Yu.chunhua@aliyun.com</a></td>
</tr>
<tr>
<td>Contact number: 008617611356059</td>
<td>Contact number: 00861069152001</td>
</tr>
</tbody>
</table>

Date: Mar, 2022

Background information

General anesthesia tracheal intubation is the primary anesthetic method to ensure the completion of surgery and patient safety. Detection of unintended tracheal intubation is an important step in this method and is an important factor in reducing anesthetic accidents and ensuring postoperative regression. Real-time ultrasound is a rapid, non-invasive detection method that potentially benefits patients with difficult intubation.

In our study, patients willing to participate in this study and at risk for difficult intubation were randomly assigned to either the ultrasound-assisted laryngoscopic view or the laryngoscopic view group, and the location of tracheal intubation was detected using noninvasive cervical ultrasound-assisted intubation with laryngoscopic view or laryngoscopic view at the same time as tracheal intubation to assess the difference in the effectiveness of the two methods. In order to obtain data related to the application of ultrasound-assisted methods for detecting the position of intubation in patients with difficult intubation.

Our study can provide more valuable evidence for clinical decision making in the refinement of airway management in patients with difficult tracheal intubation. Your participation will make an important contribution to obtaining such evidence, allowing other patients to benefit from your contribution.

Who should not participate in the study?

There are strict inclusion and exclusion criteria for this study. Any patient who does not meet the inclusion criteria should not participate in this study, in addition to 1) patients who are participating in other clinical studies; 2) those who are considered by the investigators to be unsuitable for clinical studies for other reasons.

What will I need to do if I participate in the study?

1. Before you are enrolled in the study, your doctor will ask questions, record your
general condition, and assess whether you are at risk for difficult intubation. It will be determined that you are an eligible inclusion, that you are volunteering for the study, and you will be asked to sign an informed consent form.

2. If you volunteer to participate in the study, we will perform a standard or ultrasound-assisted protocol for you, depending on the randomization group, and record the monitoring results.

**Possible benefits of participating in the study.**

If you participate in the study, the results of the study will have important implications for clinical decision making in all general anesthesia tracheal intubation populations and will provide you with the following improved support for evaluation and consultation during your anesthesia. This includes:

1. Better assessment measures: including more detailed and improved airway assessment. There are no tests outside of the current treatment routine, which will not increase the cost of your treatment, and if additional tests are incurred as a result of the study itself, they will be free of charge to you.

2. Specialized visits and consultations: The visits and consultations of this project will be conducted by specially trained personnel, so that you can receive timely and comprehensive consultations on the contents related to general anesthesia tracheal intubation, and your relevant questions will be answered and dealt with in a timely manner.

**Possible risks, adverse reactions and discomfort, inconvenience of participating in the study.**

This project uses laryngoscopic visualization alone and ultrasound-assisted laryngoscopic visualization; laryngoscopic visualization is a routine clinical method and ultrasound-assisted method is a non-invasive method, so participation in this project itself will not increase your risk.

You will be required to participate in airway evaluations during the study, and these will take up some of your time and may also cause you problems or inconvenience.

If you experience any discomfort after the clinical study, including during the study, or if there are any new changes in your condition, or any unforeseen circumstances, whether or not related to the study, you should promptly notify your physician, who will make a determination and provide appropriate medical treatment.

**Related Costs and Compensation**

There are no additional anesthetic risks or costs associated with either of the methods involved in this study, and the patient is responsible for the costs associated with routine anesthetic management. Treatments and examinations required for your concurrent medical conditions will also not be covered free of charge. However, if additional tests are performed as a result of the program itself, they will be free of charge to you.

The intervention methods involved in this study are non-invasive and routine, and will not cause damage to the patient, so there is no compensation involved in this project.
Is personal information confidential?
Your medical records (study charts/CRFs, labs, etc.) will be kept intact at the hospital you visit. Your doctor will record the results of laboratory tests and other examinations in your medical record. The investigator, ethics committee and drug regulatory authorities will be given access to your medical records. Records of all your personal information, including name, phone number, email, and address, will not appear in electronic databases, and any public reports of the results of this study will not disclose your personal identity and information. We will make every effort to protect the privacy of your personal medical information to the extent permitted by law.

How can I get more information?
You can ask any questions about this study at any time and get the appropriate answers. For inquiries (investigator contact): 17611356059; and you have the right to ask questions about your rights or related risks, inquiries (ethics review committee contact): 69156874
Your physician will promptly notify you of any important new information during the study that may affect your willingness to continue to participate in the study.
You can voluntarily choose to participate in the study and withdraw from the study Participation in the study is entirely at your discretion. You may refuse to participate in the study or withdraw from the study at any time during the study, and this will not affect the relationship between you and your physician, nor will it affect your medical treatment or any other loss of benefits.
Your physician or investigator may discontinue your participation in this study at any time during the study for reasons of your best interest.
If you withdraw from this study for any reason, you may also be asked to undergo laboratory tests and physical examinations if your doctor deems it clinically necessary.

What should I do now?
It is up to you (and your family) to decide whether to participate in this study.
Please ask your doctor as many questions as possible before you make a decision to participate in the study.
Thank you for reading the above materials. If you decide to participate in this program, please tell your doctor and he/she will make all the arrangements for you to participate in the study. Please keep this information with you.
Statement of Consent
I have read the above description of this study and have had the opportunity to discuss and ask questions about this study with my doctor. All of the questions I have asked have been answered to my satisfaction.
I am aware of the possible risks and benefits of participating in this study. I understand that participation in this study is voluntary, I acknowledge that I have had sufficient time to consider it, and I understand that I can ask my doctor for more information at any time.
I may withdraw from this study at any time without discrimination or reprisal, and
without my medical treatment or rights being affected in any way.
I am equally aware that if I withdraw from the study in the middle of the study,
especially if I withdraw for medication reasons, it would be very beneficial to the
study as a whole for me to inform my physician of any changes in my condition and
to complete the appropriate physical and physical examinations.
If I need to take any other medication due to a change in my condition, I will consult
my doctor beforehand or tell him/her truthfully afterwards.
I give my consent to the drug regulatory authority, ethics committee or sponsor's
representative to access my study data.
I will be provided with a signed and dated copy of the informed consent form.
Finally, I have decided to give my consent to participate in this study and I promise to
follow medical advice as far as possible.

Subject's name

Subject's signature

Date

If the patient has appointed a legal proxy (if applicable, and signed a proxy
agreement):

Name of legal attorney (in block letters)

Signature of legal attorney

Date

I confirm that the details of this study, including their rights and possible benefits and
risks, have been explained to the patient and that they have been given a copy of the
signed informed consent form.

Name of investigator

Signature

Date
Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

**Instructions to authors**

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:


<table>
<thead>
<tr>
<th>Reporting Item</th>
<th>Page Number</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td><strong>Administrative information</strong></td>
<td></td>
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<tr>
<td>Title</td>
<td>#1</td>
<td>Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym</td>
</tr>
<tr>
<td>Trial registration</td>
<td>#2a</td>
<td>Trial identifier and registry name. If not yet registered, name of intended registry</td>
</tr>
<tr>
<td>Trial registration: data set</td>
<td>#2b</td>
<td>All items from the World Health Organization Trial Registration Data Set</td>
</tr>
<tr>
<td>Protocol version</td>
<td>#3</td>
<td>Date and version identifier</td>
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</tbody>
</table>
Funding #4 Sources and types of financial, material, and other support 8

Roles and responsibilities: contributorship #5a Names, affiliations, and roles of protocol contributors 8

Roles and responsibilities: sponsor contact information #5b Name and contact information for the trial sponsor 1,8

Roles and responsibilities: sponsor and funder #5c Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities 8

Roles and responsibilities: committees #5d Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) 8

Introduction

Background and rationale #6a Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention 2

Background and rationale: choice of comparators #6b Explanation for choice of comparators 2

Objectives #7 Specific objectives or hypotheses 2
<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trial design</strong></td>
<td>#8 Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)</td>
</tr>
<tr>
<td><strong>Methods:</strong> Participants, interventions, and outcomes</td>
<td></td>
</tr>
<tr>
<td><strong>Study setting</strong></td>
<td>#9 Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained</td>
</tr>
<tr>
<td><strong>Eligibility criteria</strong></td>
<td>#10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)</td>
</tr>
<tr>
<td><strong>Interventions:</strong> description</td>
<td>#11 Interventions for each group with sufficient detail to allow replication, including how and when they will be administered</td>
</tr>
<tr>
<td><strong>Interventions:</strong> modifications</td>
<td>#11 Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)</td>
</tr>
<tr>
<td><strong>Interventions:</strong> adherance</td>
<td>#11c Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)</td>
</tr>
<tr>
<td><strong>Interventions:</strong> concomitant care</td>
<td>#11d Relevant concomitant care and interventions that are permitted or prohibited during the trial</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>#12 Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood</td>
</tr>
</tbody>
</table>
pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended.

Participant timeline  #13 Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure).

Sample size  #14 Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations.

Recruitment  #15 Strategies for achieving adequate participant enrolment to reach target sample size.

Methods:
Assignment of interventions (for controlled trials)

Allocation: sequence generation  #16a Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions.

Allocation concealment mechanism  #16b Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned.
Allocation:
implementation

Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions

Blinding (masking):

Who will be blinded after assignment to interventions (e.g., trial participants, care providers, outcome assessors, data analysts), and how

Blinding (masking): emergency unblinding

If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial

Methods: Data collection, management, and analysis

Data collection plan

Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) and a description of study instruments (e.g., questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

Data collection plan: retention

Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

Data management

Plans for data entry, coding, security, and storage, including any related processes to promote data quality (e.g., double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol
<table>
<thead>
<tr>
<th>Statistics: outcomes</th>
<th>#20</th>
<th>Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statistics: additional analyses</td>
<td>#20</td>
<td>Methods for any additional analyses (eg, subgroup and adjusted analyses)</td>
</tr>
<tr>
<td>Statistics: analysis population and missing data</td>
<td>#20c</td>
<td>Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)</td>
</tr>
</tbody>
</table>

**Methods:**

### Monitoring

<table>
<thead>
<tr>
<th>Data monitoring: formal committee</th>
<th>#21</th>
<th>Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data monitoring: interim analysis</td>
<td>#21</td>
<td>Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial</td>
</tr>
</tbody>
</table>

**Harms**

| Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct |

**Auditing**

| Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor |

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6-7 | 6-7 | 6-7 | 7 | 7 | 7 | 7
**Ethics and dissemination**

<table>
<thead>
<tr>
<th>Plan</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research ethics approval</strong></td>
<td>Plans for seeking research ethics committee / institutional review board (REC / IRB) approval</td>
</tr>
<tr>
<td><strong>Protocol amendments</strong></td>
<td>Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)</td>
</tr>
<tr>
<td><strong>Consent or assent</strong></td>
<td>Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)</td>
</tr>
<tr>
<td><strong>Consent or assent: ancillary studies</strong></td>
<td>Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable</td>
</tr>
<tr>
<td><strong>Confidentiality</strong></td>
<td>How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial</td>
</tr>
<tr>
<td><strong>Declaration of interests</strong></td>
<td>Financial and other competing interests for principal investigators for the overall trial and each study site</td>
</tr>
<tr>
<td><strong>Data access</strong></td>
<td>Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators</td>
</tr>
<tr>
<td><strong>Ancillary and post trial care</strong></td>
<td>Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation</td>
</tr>
</tbody>
</table>
Dissemination policy: trial results

Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions

Dissemination policy: authorship

Authorship eligibility guidelines and any intended use of professional writers

Dissemination policy: reproducible research

Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code

Appendices

Informed consent materials

Model consent form and other related documentation given to participants and authorised surrogates

Biological specimens

Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

None The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist can be completed online using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai
Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation in a general tertiary hospital: protocol for a randomized controlled study

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<thead>
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<th>Journal:</th>
<th>BMJ Open</th>
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<tr>
<td>Article Type:</td>
<td>Protocol</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>08-Jun-2023</td>
</tr>
<tr>
<td>Complete List of Authors:</td>
<td>Tian, Yuan; Peking Union Medical College Hospital, Anesthesiology Fei, Yuda; Peking Union Medical College Hospital, Department of Anesthesiology Bing, Bai; Peking Union Medical College Hospital Cui, Xulei; Peking Union Medical College Hospital, Department of Anesthesiology Zhang, Yuelun; Peking Union Medical College Hospital Wang, Chunrong; Peking Union Medical College Hospital, Department of Anesthesiology Chunhua, Yu; Peking Union Medical College Hospital, Anesthesiology Huang, Yuguang; Peking Union Medical College Hospital</td>
</tr>
<tr>
<td>Primary Subject Heading:</td>
<td>Anaesthesia</td>
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<tr>
<td>Secondary Subject Heading:</td>
<td>Anaesthesia, Emergency medicine, Radiology and imaging, Surgery</td>
</tr>
<tr>
<td>Keywords:</td>
<td>ANAESTHETICS, Bronchoscopy &lt; THORACIC MEDICINE, Ultrasound &lt; RADIOLOGY &amp; IMAGING</td>
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For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation in a general tertiary hospital: protocol for a randomized controlled study

Tian Yuan¹, Fei Yuda¹, Bai Bing¹, Cui Xulei¹, Zhang Yuelun², Wang Chunrong¹, Yu Chunhua¹*, Huang Yuguang¹

Author affiliations
¹ Department of Anesthesiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China.
² Medical Research Center, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China.

*Corresponding author: Chunhua Yu, Yu.chunhua@aliyun.com

ABSTRACT

Introduction Endotracheal intubation (ETI) is a crucial but risky procedure, especially among patients suspected of difficult endotracheal intubation (DTI). Bronchoscope, as an improved technique commonly used in DTI, might encounter visualization difficulties. The magnetic point-of-care ultrasound (MGPOCUS) provides a novel visualization from the outside and enables the estimation of the relative position and trajectory of the bronchoscope. The study aims to evaluate the efficiency of MGPOCUS-guided bronchoscope in time taken to the first-attempt success, the first-attempt and overall success of ETI, complications, and satisfaction of visualization among patients suspected of DTI.

Methods and Analysis The study is a randomized, parallel-group, single-blinded, single-center study. Participants (n=108) will be recruited by the primary anesthesiologist and randomized to groups of ETI with bronchoscope or MGPOCUS-guided bronchoscope. The primary outcome is the time taken to the first-attempt success ETI. Secondary outcomes include procedure time, the first-attempt and overall success, complications, and satisfaction of visualization. Cox regression with the Bonferroni correction and the linear mixed regression will be used to analyze the outcomes.

Ethics and dissemination The trial protocol were approved by the institution of the Ethics Committee of the Peking Union Medical College Hospital. Findings will be disseminated through conference presentations and peer-reviewed journals.

Trial registration number NCT05647174.

Keywords Difficult airway, endotracheal intubation, POCUS, magnetic ultrasound

Word counts 3228

Article summary

Strength 1: This is a pioneer study regarding applying magnetic-assisted point-of-care-
ultrasound-guided bronchoscope among patients suspected of difficult intubation based on randomized controlled, two-arm, single-center evidence.

**Strength 2:** The magnetic-assisted point-of-care-ultrasound-guided bronchoscope was designed based on the principle of magnetically guided puncture embedded in the application of ultrasound in the airway.

**Strength 3:** An independent data and safety monitoring committee will independently process the study data.

**Limitation 1:** Blinding of investigators won’t be possible, though the estimation of outcomes is objective.

**Limitation 2:** The experienced physician will perform both interventions, thus limiting transferability to other less-experienced individuals.

**INTRODUCTION**

Endotracheal intubation (ETI) is crucial as a fundamental method to secure the airway, yet the leading cause of death or vegetative state among healthy participants undergoing elective surgery. It is consistently shown that difficult endotracheal intubation (DTI) majorly contributed to adverse events. Though the advent of flexible bronchoscope has brought revolutionary innovations for DTI, there are still worrisome, just as the closed-claims analysis of the United States has yielded. Most often, intubation by flexible bronchoscope is performed via the oral route. The procedure can be tricky or delayed as the difficulty of the visualization. Visibility impaired by blood or secretions is supposed to predict difficult bronchoscope intubation. Dealing methods, such as clearance of secretions, keeping the tip in the midline, or withdrawing until the location can be identified, remain widely Varied in rapidity and uncertainty about maintaining the proper orientation. The active research to improve visualization and movement confirms that this issue continues to challenge many physicans.

Point-of-care ultrasound (POCUS) has broadened the horizons for airway management since it allows visualization of the upper airway from the outside. The American Heart Association updated the Guidelines on Adult Advanced Cardiovascular Life Support (ACLS), which recommended using ultrasound as a confirmation method for a tracheal tube. Several studies provide promising results about the high pooled sensitivity (about 98%) and specificity (about 97%) of POCUS in confirming ETI. Real-time POCUS further extends to assist ETI. Notably, POCUS provides a view independent from the laryngoscopy or bronchoscope, making it possible to combine the outside with the inside visualization. Although ultrasound has shown advantages in evaluating soft tissues on the surface of the airway, it is difficult to display the inside of the air-filled airway. The application progress of magnetically assisted ultrasound in the regional block and vascular catheterization suggests that it can be used to visualize the relative position of the targets in the case of poor ultrasonography. The magnetic POCUS (MGPOCUS) technology collects magnetic signals and calculates the trajectory modeled by corresponding software. It enables the possibility of estimating the relative position and the advanced trajectory, guiding the bronchoscope when encountering a difficulty of laryngeal exposure. To date, there has been little conclusive evidence to seek the application of an MGPOCUS-
guided bronchoscope in anticipated difficult intubation.

The study is designed to estimate the application of MGPOCUS-guided bronchoscope within anticipated DTI on the procedure time, the success rate, the number of attempts, the complications, and the visual satisfaction of performers. Compared with the flexible bronchoscope alone, we seek to estimate the significance of the combined visualization with the MGPOCUS-guided bronchoscope.

METHODS AND ANALYSIS

Study design and setting
This is a randomized, parallel-group, single-blinded, single-center study. The study will be conducted in the anesthesia department and operating room of the Chinese Academy of Medical Sciences Peking Union Medical College Hospital (Beijing, China), a tertiary academic hospital with an annual operation census of above 80,000 participants. The protocol is structured based on the Standard Protocol Items for Randomized Trials (SPIRIT) Statement: defining standard protocol items for a clinical study.

Participant recruitment
After assessing the eligibility and obtaining informed consent (See supplementary file 1), the primary anesthesiologist will recruit the participants while performing the preoperative evaluation. The research team will confirm the eligibility.

Inclusion criteria
Participants will be eligible for inclusion if they meet all of the following items:

- Aged between 18 and 85 years old.
- Requiring ETI and without known indicators for awake tracheal intubation.
- Anticipated DTI meets one or more positive findings in the airway evaluation, including history, examination, and appropriate investigations of anatomy (Table 1).
- The primary anesthesia team, independent from the study team, considers bronchoscope intubation after induction the first choice.
- Signed written informed consent.

<table>
<thead>
<tr>
<th>Specific Predictors</th>
<th>Positive findings</th>
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<tr>
<td>Morbid obesity</td>
<td>BMI ≥ 40</td>
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<tr>
<td>Adverse dentition</td>
<td>Presence</td>
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<td>The prior difficulty of endotracheal intubation</td>
<td>Presence</td>
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<tr>
<td>Mouth opening</td>
<td>&lt; 4 cm</td>
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<td>Head and upper neck extension</td>
<td>&lt; 30 degrees from neutral</td>
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<td>Mandibular protrusion (Lip bite test)</td>
<td>Inability to prognath</td>
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<td>Modified Mallampati class</td>
<td>III or IV</td>
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<td>Thyromental distance</td>
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<td>Sternomental distance</td>
<td>&lt; 12 cm</td>
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<tr>
<td>Neck circumference</td>
<td>&gt; 40 cm</td>
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</table>
Exclusion criteria
Participants will be excluded if they meet at least one of the following items:

- Anterior neck lesions (masses, lacerations, or subcutaneous emphysema).
- A history of neck operation or tracheotomy.
- Allergies to ultrasound coupling gel.
- At the risk of pulmonary or cardiovascular complications during intubation with a flexible bronchoscope, including severe hypoxemia, severe pulmonary hypertension, and unstable or intense obstructive airway disease.
- The high risk of bleeding during bronchoscope intubation, including anticoagulants or coagulopathy, renal insufficiency, and superior vena cava syndrome.
- High risk of aspiration.
- Current pregnancy.

Randomization and concealment
Participants will be randomized in a 1:1 ratio to an intervention group (MGPOCUS-guided bronchoscope) or a control group (bronchoscope). The random number sequence will be generated by the “if” package of R software by delegated research staff and uploaded to our institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Ltd., Beijing, China). The primary care anesthesiologist will be informed of the database account information before performing ETI to guarantee allocation concealment.

Blinding
Trial participants and data analysts will be blinded to the assignment of interventions. Blinding of the investigator is generally impossible, yet evaluating outcomes is objective.

Study interventions
This study compares two interventions of performing DTI, a novel MGPOCUS-guided bronchoscope and a standard bronchoscope. Participants in each group will accept common perioperative interventions, including the essential monitoring of physiological parameters, sufficient preoxygenation institutional standard general anesthesia, and confirmation of ETI position by capnography. Critical monitoring will be performed before, during, and after ETI, with at least echocardiography, non-invasive blood pressure, and pulse oximetry. Preoxygenation will be administered with a mask to ensure pulse oximetry saturation of more than 93%.

ETI in both groups will be performed by a senior anesthesiologist with more than five years of experience in flexible bronchoscope. MGPOCUS-guided bronchoscope-guided intubation will be performed in collaboration with a senior anesthesiologist with more than five years of experience in POCUS and who has fulfilled more than 50 cases of ultrasound-guided airway management. An additional experienced airway manager will stand by in the operating room.

Institutional standard general anesthesia will include propofol 1.5-2.5 mg/kg,
fentanyl 25-100 mcg/kg, lidocaine 0.5-1.5mg/kg, midazolam 1-2 mg, and rocuronium 0.6-1.2 mg/kg. The position of the tracheal tube will be confirmed by capnography with at least four consistent waves and bilateral auscultation of breath sounds.

**Bronchoscope-guided ETI**
After clear suctioning of oropharyngeal secretions, the tip of a bronchoscope will be put through the middle of the incisors. The bronchoscope will be appropriately oriented and flexed to move along the oral midline and achieve a satisfactory view of airway structures. Once the epiglottis and glottis are located, the tip of a bronchoscope will be advanced through the glottis to the level above the carina, followed by the advancement of a tracheal tube already loaded. According to the operators’ will, approaches can be used to improve visualization, including jaw thrust, tongue pulling forward, cervical extension when not contraindicated, and bronchoscope withdrawal.

**MGPOCUS-assisted bronchoscope-guided ETI**
The system of MGPOCUS was derived and adapted from a previously described model used in vascular catheterization. The system is only used for visualization of the needle fixed on the bronchoscope, not moving the bronchoscope. It consists of an ultrasonic machine (Piloter US scanner, Wisonic, Inc., Shenzhen, Guangdong, China), a 4-15MHz linear transducer with integrated ultrasonic and magnetic sensing capabilities (Wisonic, Inc., Shenzhen, Guangdong, China), a magnetizing box (Wisonic, Inc., Shenzhen, Guangdong, China), and a magnetized metal needle fixed near the tip of the bronchoscope (Figure 1).

The MGPOCUS system uses several display features to enable the 3-dimensional positioning of the bronchoscope tip to be displayed in a 2-dimensional ultrasonic image. Figure 2 shows an example of how the trajectory of the magnetizing needle fixed on a bronchoscope is displayed when it does or not overlap with the ultrasound beam. Specifically, the trajectory of a magnetized bronchoscope is indicated by a solid line when it is within the ultrasonic beam. Otherwise, its trajectory is shown as a dashed line when positioned anterior or posterior to the ultrasonic beam.

While clear suctioning of oropharyngeal secretions, the transducer is positioned transversely at the patient’s thyroid cartilage level. Moving the transducer cephalad or caudal, a view of vocal folds is visualized as an isosceles triangle with a central tracheal shadow (Figure 3). The line connecting the vocal cords' anterior and posterior commissure is marked as the midline of the ultrasonography. The midline is maintained, and directed cephalad to visualize the tongue and epiglottis. The second provider will perform intubation with a bronchoscope, as described above. When the view of the bronchoscope is unclear, MGPOCUS can provide an assisted view to locate the relative position of the bronchoscope and the vocal folds. Suppose the two lines locating the bilateral vocal cord midline and the bronchoscope do not partially overlap. In that case, the performer will adjust the direction of advancement according to the magnetized bronchoscope's relative position to the vocal cords' midline. Once the solid line displaying the magnetized bronchoscope is within the trachea, the pre-loaded tracheal tube will be advanced. Once the solid line is displayed posterolateral to the
airway, the bronchoscope will be withdrawn and adjusted according to the MGPOCUS image. Similar to adjusting the direction of the needle to achieve the puncture target, the magnetized needle on the bronchoscope is guided to the trachea according to the ultrasonography with magnetic signals.

**Discontinuing interventions**
Desaturation below 90% will be considered a failed attempt of ETI. If desaturation is encountered, face mask ventilation will be performed with 100% oxygen for 2 min, and the attempt will be repeated. The procedure will be considered a failure with more than two attempts or 600 seconds, and the airway manager will proceed with the following strategy or technique. If emergencies arise, such as oxygen desaturation or hemodynamic instability, challenging to correct, the primary anesthesia team will determine whether to continue or terminate the trial.

**Outcomes**
Baseline assessments will be collected while the preoperative evaluation, including demographic characteristics (age, sex, height, weight, body mass index, American Society of Anesthesiologists physical status score, procedure performer) and airway assessment (Table 1).

The primary outcome is the time for successful ETI at the first attempt. Time will be recorded in real-time from bronchoscopic first-passage through teeth to tube well placed. The first-attempt success is a successful ETI with no more than 180 seconds and without reinsertion of the bronchoscope through teeth. Successful ETI is confirmed by capnography with at least four consistent waves.

The secondary outcomes are to detect the procedure time, the first attempt and overall success, the number of attempts, complications, and satisfaction with visualization. Complications will be recorded, including desaturation, obvious trauma, bloody secretions, post-extubation hoarseness, and sore throat. The 5-point Likert scale assesses satisfaction with visualization.

**Data management and statistics**

**Sample size calculation**
Based on our preliminary study (unpublished data), it is supposed that MGPOCUS-assisted bronchoscope-guided ETI will achieve the first-attempt success with 28±22 seconds (N 16) and bronchoscope-guided ETI with 50±41 seconds (N 13). Hence, it is estimated that a sample size of 98 subjects will achieve a power of 90% (type II error 0.1) to detect a statistically significant difference between the two groups with a two-sided type I error of 0.05. Assuming the potentially skewed distribution of the time of first-attempt success would lead 10% statistical power loss, 54 subjects in each group will be recruited.

**Data collection and protection**
All data will be collected on the institutional database (Hospital Clinical Research Database; Beijing Huiren Technology Development Co., Ltd, Beijing, China) by an investigator independently. Data entry and processing will be performed before unblinding of investigators. The database will be centralized and managed by the leading researchers. A unique research identification data (ID) code will be used to ensure confidentiality and anonymity. The ID will be used to identify participants and the allocation. The recorded data in the study will not be linked to the participant’s personal information. The data will be transferred securely and stored confidentially on password-protected computers that the researchers can only access by General Data Protection Regulation.

Data statistics plan
Demographic characteristics and airway assessment variables will be presented using descriptive statistics for the overall sample. Continuous data will be described using mean (standard deviation [SD]) or median (interquartile range [IQR]), depending on the distribution of the data. Categorical data will be described using numbers and proportions.

For the primary outcome, the time taken to the first-attempt success will be analyzed using a Cox proportional hazards model with the Bonferroni correction as a multiplicity adjustment that treats failed ETI at the first attempt as censored. For secondary outcomes, procedure time for successful ETI will be analyzed using a linear mixed model that treats ETI success or failure as the outcome and procedure performer as a random effect. The first attempt and overall success will be analyzed using mixed-effects logistic regression. Any two-sided P-value <0.05 will be considered statistically significant. Statistical analyses will be performed on R software version 3.5.1 (R Foundation for Statistical Computing).

Termination of the study
An independent statistician will conduct the interim analysis of the primary outcome when 50% of participants have been enrolled. The results will be reported to the independent data and safety monitoring committee and discussed with the steering committee. The Peto approach is used to terminate the study when the intervention group greatly benefits from the control group using symmetric stopping boundaries at P<0.001. The study will contain only be stopped in case of futility if the independent data and The potential stopping for futility will be discussed with the steering committee, in this case, y will be discussed with the steering committee.

Data monitoring
A steering committee will manage the study. Screening and recruitment will be reviewed at monthly meetings. An independent data and safety monitoring committee will meet every three months to ensure patient safety and data quality.

Safety
The independent data and safety monitoring committee will supervise the study’s
progress by examining safety variables monthly. Adverse events are defined as “any undesirable experience occurring to a subject during the study, whether or not considered related to the intervention.” Any potential adverse events must be monitored, recorded, and discussed with the independent data and safety monitoring committee.

**Patient and public involvement**
The study protocol was developed in collaboration with anesthesiologists with extensive experience managing difficult airways or POCUS. Their feedback and expectations regarding research questions and outcome measures were discussed and applied for adjustment. Since the absence of experimental knowledge and subjective feeling, participants were not involved in our research’s design, conduct, reporting, or dissemination plans.

**Ethics approval and study registration**
Ethical approval has been granted by the respective ethics committees at the Peking Union Medical College Hospital (Institutional Review Board #ZS-3428), and written informed consent will be obtained from all participants. The study was registered online (clinicaltrials.gov; NCT05647174; Sponsor; date of registration: 12/03/2022).

**Acknowledgment**

**Dissemination of findings**
The findings will be disseminated and published through conference presentations and peer-reviewed manuscripts. Each manuscript will be submitted to all co-investigators for review of its appropriateness and scientific quality before submission.

**Data statement**
Data is available upon request from the corresponding author after the completion of the study.

**Author contributions**
TY has contributed to the conception and design of the study protocol and to drafting and revising the manuscript. FYD has contributed to both the concept and design of the study protocol. CXL and BB have guided the US implementation. ZYL and WCR have assisted in the statistical improvement. YCH and HYG have aided the methodological improvement and critically revised the draft. All authors have read, provided feedback, and approved the final manuscript.

**Funding statement**
This work was supported by the Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences (2021-I2M-C&T-B-020) and National High-Level Hospital Clinical Research Funding (2022-PUMCH-A-148).

**Competing interest statement** None declared.

**Patient consent for publication** Not required.

**References**


Figure legends

Figure 1. The schematic diagram shows the transducer, magnetizing box, and bronchoscope fixed with a magnetized metal needle used in the MGPOCUS system.
The magnetized needle is located on the anterior side of the bronchoscope in the same direction as its forward flexion. The needle is fixed near the tip of the bronchoscope and fixed by a non-magnetizable plastic ring.

Figure 2. This figure is a virtual display of a magnetized bronchoscope not within the ultrasound beam and deviated the midline of the probe, showing the position of the magnetized bronchoscope relative to the midpoint of the ultrasound probe (upper) and the estimated line of advance of the bronchoscope (lower). The solid red line indicates that the magnetized bronchoscope is not within the ultrasound beam. The estimated path of its advancement based on the magnetic signal is between the two blue solid lines and will reach the position marked by the red box. TC thyroid cartilage. VC vocal cords. AC anterior commissure. T trachea.

Figure 3. This figure is a virtual display of the magnetized bronchoscope within the ultrasound beam and probe midline, showing the position of the magnetized bronchoscope relative to the ultrasound probe midpoint (upper) and the estimated path of advancement of the bronchoscope (lower). The solid green line indicates that the magnetized bronchoscope is within the ultrasound beam and that its estimated trajectory of progress based on the magnetic signal is between the two solid blue lines and will reach the position indicated by the green box. At the same time, hyperechoic points are shown between the vocal cords based on the ultrasonic signals. TC thyroid cartilage. VC vocal cords. AC anterior commissure. T trachea.
Figure 1. Composition of the MGPOCUS system.
The schematic diagram shows the transducer, magnetizing box, and bronchoscope fixed with a magnetized metal needle used in the MGPOCUS system. The magnetized needle is located on the anterior side of the bronchoscope in the same direction as its forward flexion. The needle is fixed near the tip of the bronchoscope and fixed by a non-magnetizable plastic ring.

293x284mm (96 x 96 DPI)
Figure 2. The virtual display of MGPOCUS-assisted bronchoscope not within the ultrasound beam. This figure is a virtual display of a magnetized bronchoscope not within the ultrasound beam and deviated the midline of the probe, showing the position of the magnetized bronchoscope relative to the midpoint of the ultrasound probe (upper) and the estimated line of advance of the bronchoscope (lower). The solid red line indicates that the magnetized bronchoscope is not within the ultrasound beam. The estimated path of its advancement based on the magnetic signal is between the two blue solid lines and will reach the position marked by the red box. *TC* thyroid cartilage. *VC* vocal cords. *AC* anterior commissure. *T* trachea.

334x284mm (96 x 96 DPI)
Figure 3. The virtual display of MGPOCUS-assisted bronchoscope within the ultrasound beam.

This figure is a virtual display of the magnetized bronchoscope within the ultrasound beam and probe midline, showing the position of the magnetized bronchoscope relative to the ultrasound probe midpoint (upper) and the estimated path of advancement of the bronchoscope (lower). The solid green line indicates that the magnetized bronchoscope is within the ultrasound beam and that its estimated trajectory of progress based on the magnetic signal is between the two solid blue lines and will reach the position indicated by the green box. At the same time, hyperechoic points are shown between the vocal cords based on the ultrasonic signals. *TC* thyroid cartilage. *VC* vocal cords. *AC* anterior commissure. *T* trachea.

334x275mm (96 x 96 DPI)
Participant Consent Form

Project: Developing a magnetic-assisted-POCUS guided bronchoscope among patients with suspected difficult endotracheal intubation

Contact Address:

<table>
<thead>
<tr>
<th>Dr Yuan Tian</th>
<th>Dr Chunhua Yu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesiology Department, Peking Union Medical College Hospital, Dongcheng District, Beijing, China</td>
<td>Anesthesiology Department, Peking Union Medical College Hospital, Dongcheng District, Beijing, China</td>
</tr>
<tr>
<td>Email: <a href="mailto:tianyuan95@pumch.cn">tianyuan95@pumch.cn</a></td>
<td>Email: <a href="mailto:Yu.chunhua@aliyun.com">Yu.chunhua@aliyun.com</a></td>
</tr>
<tr>
<td>Contact number: 008617611356059</td>
<td>Contact number: 00861069152001</td>
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Date: Mar, 2022

Background information

General anesthesia tracheal intubation is the primary anesthetic method to ensure the completion of surgery and patient safety. Detection of unintended tracheal intubation is an important step in this method and is an important factor in reducing anesthetic accidents and ensuring postoperative regression. Real-time ultrasound is a rapid, non-invasive detection method that potentially benefits patients with difficult intubation.

In our study, patients willing to participate in this study and at risk for difficult intubation were randomly assigned to either the ultrasound-assisted laryngoscopic view or the laryngoscopic view group, and the location of tracheal intubation was detected using noninvasive cervical ultrasound-assisted intubation with laryngoscopic view or laryngoscopic view at the same time as tracheal intubation to assess the difference in the effectiveness of the two methods. In order to obtain data related to the application of ultrasound-assisted methods for detecting the position of intubation in patients with difficult intubation.

Our study can provide more valuable evidence for clinical decision making in the refinement of airway management in patients with difficult tracheal intubation. Your participation will make an important contribution to obtaining such evidence, allowing other patients to benefit from your contribution.

Who should not participate in the study?

There are strict inclusion and exclusion criteria for this study. Any patient who does not meet the inclusion criteria should not participate in this study, in addition to 1) patients who are participating in other clinical studies; 2) those who are considered by the investigators to be unsuitable for clinical studies for other reasons.

What will I need to do if I participate in the study?

1. Before you are enrolled in the study, your doctor will ask questions, record your
general condition, and assess whether you are at risk for difficult intubation. It will be determined that you are an eligible inclusion, that you are volunteering for the study, and you will be asked to sign an informed consent form.

2. If you volunteer to participate in the study, we will perform a standard or ultrasound-assisted protocol for you, depending on the randomization group, and record the monitoring results.

**Possible benefits of participating in the study.**

If you participate in the study, the results of the study will have important implications for clinical decision making in all general anesthesia tracheal intubation populations and will provide you with the following improved support for evaluation and consultation during your anesthesia. This includes:

1. better assessment measures: including more detailed and improved airway assessment. There are no tests outside of the current treatment routine, which will not increase the cost of your treatment, and if additional tests are incurred as a result of the study itself, they will be free of charge to you.

2. Specialized visits and consultations: The visits and consultations of this project will be conducted by specially trained personnel, so that you can receive timely and comprehensive consultations on the contents related to general anesthesia tracheal intubation, and your relevant questions will be answered and dealt with in a timely manner.

**Possible risks, adverse reactions and discomfort, inconvenience of participating in the study.**

This project uses laryngoscopic visualization alone and ultrasound-assisted laryngoscopic visualization; laryngoscopic visualization is a routine clinical method and ultrasound-assisted method is a non-invasive method, so participation in this project itself will not increase your risk.

You will be required to participate in airway evaluations during the study, and these will take up some of your time and may also cause you problems or inconvenience. If you experience any discomfort after the clinical study, including during the study, or if there are any new changes in your condition, or any unforeseen circumstances, whether or not related to the study, you should promptly notify your physician, who will make a determination and provide appropriate medical treatment.

**Related Costs and Compensation**

There are no additional anesthetic risks or costs associated with either of the methods involved in this study, and the patient is responsible for the costs associated with routine anesthetic management. Treatments and examinations required for your concurrent medical conditions will also not be covered free of charge. However, if additional tests are performed as a result of the program itself, they will be free of charge to you.

The intervention methods involved in this study are non-invasive and routine, and will not cause damage to the patient, so there is no compensation involved in this project.
Is personal information confidential?
Your medical records (study charts/CRFs, labs, etc.) will be kept intact at the hospital you visit. Your doctor will record the results of laboratory tests and other examinations in your medical record. The investigator, ethics committee and drug regulatory authorities will be given access to your medical records. Records of all your personal information, including name, phone number, email, and address, will not appear in electronic databases, and any public reports of the results of this study will not disclose your personal identity and information. We will make every effort to protect the privacy of your personal medical information to the extent permitted by law.

How can I get more information?
You can ask any questions about this study at any time and get the appropriate answers. For inquiries (investigator contact): 17611356059; and you have the right to ask questions about your rights or related risks, inquiries (ethics review committee contact): 69156874
Your physician will promptly notify you of any important new information during the study that may affect your willingness to continue to participate in the study.
You can voluntarily choose to participate in the study and withdraw from the study Participation in the study is entirely at your discretion. You may refuse to participate in the study or withdraw from the study at any time during the study, and this will not affect the relationship between you and your physician, nor will it affect your medical treatment or any other loss of benefits.
Your physician or investigator may discontinue your participation in this study at any time during the study for reasons of your best interest.
If you withdraw from this study for any reason, you may also be asked to undergo laboratory tests and physical examinations if your doctor deems it clinically necessary.

What should I do now?
It is up to you (and your family) to decide whether to participate in this study.
Please ask your doctor as many questions as possible before you make a decision to participate in the study.
Thank you for reading the above materials. If you decide to participate in this program, please tell your doctor and he/she will make all the arrangements for you to participate in the study. Please keep this information with you.
Statement of Consent
I have read the above description of this study and have had the opportunity to discuss and ask questions about this study with my doctor. All of the questions I have asked have been answered to my satisfaction.
I am aware of the possible risks and benefits of participating in this study. I understand that participation in this study is voluntary, I acknowledge that I have had sufficient time to consider it, and I understand that I can ask my doctor for more information at any time.
I may withdraw from this study at any time without discrimination or reprisal, and without my medical treatment or rights being affected in any way.

I am equally aware that if I withdraw from the study in the middle of the study, especially if I withdraw for medication reasons, it would be very beneficial to the study as a whole for me to inform my physician of any changes in my condition and to complete the appropriate physical and physical examinations.

If I need to take any other medication due to a change in my condition, I will consult my doctor beforehand or tell him/her truthfully afterwards.

I give my consent to the drug regulatory authority, ethics committee or sponsor's representative to access my study data.

I will be provided with a signed and dated copy of the informed consent form.

Finally, I have decided to give my consent to participate in this study and I promise to follow medical advice as far as possible.

Subject's name

Subject's signature

Date

If the patient has appointed a legal proxy (if applicable, and signed a proxy agreement):

Name of legal attorney (in block letters)

Signature of legal attorney

Date

I confirm that the details of this study, including their rights and possible benefits and risks, have been explained to the patient and that they have been given a copy of the signed informed consent form.

Name of investigator

Signature

Date
Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

**Instructions to authors**

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:


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Funding #4 Sources and types of financial, material, and other support

Roles and responsibilities: contributorship

Roles and responsibilities: sponsor contact information

Roles and responsibilities: sponsor and funder

Introduction

Background and rationale #6a Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention

Background and rationale: choice of comparators #6b Explanation for choice of comparators

Objectives #7 Specific objectives or hypotheses
### Trial design

**Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)**

### Methods:

#### Participants, interventions, and outcomes

<table>
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<tr>
<th>Component</th>
<th>Description</th>
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<tr>
<td><strong>Study setting</strong></td>
<td>Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained</td>
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<td><strong>Eligibility criteria</strong></td>
<td>Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)</td>
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<td><strong>Interventions:</strong></td>
<td>Interventions for each group with sufficient detail to allow replication, including how and when they will be administered</td>
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<td>- <strong>description</strong></td>
<td>Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)</td>
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<td>- <strong>adherance</strong></td>
<td>Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)</td>
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<tr>
<td>- <strong>concomitant care</strong></td>
<td>Relevant concomitant care and interventions that are permitted or prohibited during the trial</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure)</td>
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</table>
pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended.

Participant timeline #13 Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure).

Sample size #14 Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations.

Recruitment #15 Strategies for achieving adequate participant enrolment to reach target sample size N/A

Methods:
Assignment of interventions (for controlled trials)

Allocation: sequence generation #16a Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions.

Allocation concealment mechanism #16b Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned.
Allocation: implementation

Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions

Blinding (masking)

Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how

Blinding (masking): emergency unblinding

If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial

Methods: Data collection, management, and analysis

Data collection plan

Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

Data collection plan: retention

Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

Data management

Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol
<table>
<thead>
<tr>
<th><strong>Statistics: outcomes</strong></th>
<th><strong>Methods:</strong></th>
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<tbody>
<tr>
<td><strong>#20 a</strong> Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol</td>
<td></td>
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<tr>
<td><strong>#20 b</strong> Methods for any additional analyses (eg, subgroup and adjusted analyses)</td>
<td></td>
</tr>
<tr>
<td><strong>#20c</strong> Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)</td>
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### Methods:

#### Monitoring

<table>
<thead>
<tr>
<th><strong>Data monitoring:</strong></th>
<th><strong>Harms</strong></th>
<th><strong>Auditing</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>#21 a</strong> Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed</td>
<td><strong>#22</strong> Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct</td>
<td><strong>#23</strong> Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor</td>
</tr>
<tr>
<td><strong>#21 b</strong> Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial</td>
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<thead>
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<td>Ethics and dissemination</td>
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<td>Plan for seeking research ethics committee / institutional review board (REC / IRB) approval</td>
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<tr>
<td>Protocol amendments</td>
<td>#25</td>
<td>Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)</td>
<td>8</td>
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<tr>
<td>Consent or assent</td>
<td>#26</td>
<td>Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)</td>
<td>3</td>
</tr>
<tr>
<td>Consent or assent: ancillary studies</td>
<td>#26</td>
<td>Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable</td>
<td>N/A</td>
</tr>
<tr>
<td>Confidentiality</td>
<td>#27</td>
<td>How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial</td>
<td>7</td>
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<tr>
<td>Declaration of interests</td>
<td>#28</td>
<td>Financial and other competing interests for principal investigators for the overall trial and each study site</td>
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<tr>
<td>Data access</td>
<td>#29</td>
<td>Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators</td>
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</tr>
<tr>
<td>Ancillary and post trial care</td>
<td>#30</td>
<td>Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation</td>
<td>7</td>
</tr>
</tbody>
</table>
Dissemination policy: trial results | #31a Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions

Dissemination policy: authorship | #31b Authorship eligibility guidelines and any intended use of professional writers

Dissemination policy: reproducible research | #31c Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code

Appendices

Informed consent materials | #32 Model consent form and other related documentation given to participants and authorised surrogates

Biological specimens | #33 Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

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