Platform Construction and Clinical Application of 5G Technology for Remote Operation of the R-One™ Robot in Percutaneous Coronary Intervention

Clinical Trial Protocol

Version No. : 1.0

Date : 2025-03-01

Name of investigated device : Vascular Interventional Navigation Control System
Model/Specification : R-One

Class III devices subject to clinical trial approval	:	Yes ☑	No ☐
Equivalent products in China	:	Yes ☐	No ☑

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CONFIDENTIALITY STATEMENT

Protocol Revision History

Version No.	Date of Revision	Revision Description
1.0	2025-03-01	/

Statistical considerations

1 Sample size calculation

The sample size of this trial was calculated based on the primary endpoint, namely the surgical success indicator. Based on literature analysis[12][13][14][15][16][17][18][19][20][21]and expert expertise, the trial uses the clinical success rate and technical success rate as the primary endpoints. According to the sample size calculated by PASS software, the inclusion of 63 subjects in the pilot study could provide 90% power to detect the difference, but the formal trial should be calculated based on the single group target value method. Subsequently, the enrollment will be expanded to carry out the formal trial, and the sample size will be combined. 63 cases in the pilot study will be included in the intention-to-treat analysis (ITT).

The statistical hypothesis test corresponding to the subsequent formal test is as follows:

The target value of clinical success rate is set at 90.0%. Assuming that the expected clinical success rate of PCI surgery performed by the 5G remote-controlled R-One™ robot could reach 97%, the statistical significance level of the test set at 2.5% one-sided and test assurance (Power) at 90%, each group requires 135 cases. Considering a drop-out rate of about 10%, the total sample size was adjusted to 149 cases.

The target value of technical success rate is set at 90.0%. Assuming that the expected technical success rate of PCI surgery performed by the 5G remote-controlled R-One™ robot could reach 97%, the statistical significance level of the test set at 2.5% one-sided and test assurance (Power) at 90%, each group requires 135 cases. Considering a drop-out rate of about 10%, the total sample size was adjusted to 149 cases.

The formal clinical trial will be regarded as a success if both the primary endpoints, clinical success rate and technical success rate meet the target

value. The total sample size for the formal trial is 149 cases, with a combined test efficacy of 81%.

The formula of estimated sample size is:

$$n = \frac{\left[Z_{1-\alpha/2}\sqrt{P_0(1-P_0)} + Z_{1-\beta}\sqrt{P_T(1-P_T)}\right]^2}{(P_T - P_0)^2}$$

P_T is the expected event rate of the test group, and P_0 is the target value.

Notes: Based on previously published literatures on PCI surgical robots [1][2][3][4][5][6][7][8][9][10], clinical success rate is analyzed using studies with larger sample size (>30 cases) and multicenter [3][5][7]. The random effect values obtained from statistical analysis ranged from 0.875- 0.963, and the lower limit of 0.9 (90%) was selected as the target value based on the conservative principle to reduce the risk of false positives.

2 Minimum and maximum number of subjects each clinical trial site and the rationale

The trial will be conducted at multiple clinical trial sites simultaneously, and in principle, the enrollments shall be distributed as evenly as possible across centers to guarantee sufficient representativeness of each center. However, the feasibility and progress of enrollment should also be considered. Thus, the enrolment will be adjusted according to the actual situation to ensure the relative balance of sample size at each centre, and the final enrollment size of a particular centre shall not exceed 50% of the maximum sample size.

3 Criteria for conformity/non-conformity of clinical trials results

The results of the clinical trial would be considered qualified if the lower limits

of the 95% confidence intervals for 2 primary endpoints exceed the target value of 90%; otherwise, the clinical trial results are not qualified.

4 Criteria and reasons for terminating the trial based on statistical reasons

The trial does not have midterm analysis and will not involve trial termination for statistical reasons.

5 Selection criteria and reasons for subjects included in the analysis

A population to be analyzed need clear definition before the statistical analysis begins. The trial is conducted with three data sets for analysis: full analysis set, per protocol set and safety set.

Full analysis set (FAS): A subjects analysis set is defined based on the principle of Intention To Treat (ITT): refers to the data set consisting of all the subjects who were treated with the investigational device. Subjects may be excluded in very limited circumstances, such as violation of important enrollment criteria and no observational data after enrollment.

Per protocol set (PPS): The per protocol set is a subset of the full analysis set and includes subjects who have received the treatment specified in the protocol, with observational data for the primary endpoints, and without significant violations of the trial protocol. If a subject need to be excluded from the full analysis set and the per protocol set, first of all, the exclusion shall conform to the definition in the protocol, and secondly, the reasons for exclusion need to be fully specified, and be elaborated in the blind review.

Safety analysis set (SS): Subjects who used the investigational device and had

at least one safety evaluation indicator.

FAS population was used for baseline demographics analysis. FAS and PPS were used for efficacy analysis SS was used for the safety analysis.

6 Statistical method

6.1 General Principles

SAS version 9.4 or above was used for statistical analysis.

All statistical tests were performed using two-sided tests, unless otherwise stated.

The measuring indicators are described by the mean, standard deviation, median, minimum, maximum, and quartiles.

Classification and grade indicators are described by frequencies and percentages.

6.2 Case characteristics

6.2.1 Completion of enrollment

Summarize the number of enrollment and cases completed at each center and make a list of cases that were not included in various populations.

6.2.2 General information and baseline characteristics

mainly use descriptive statistics. Age and weight are described according to measurement data; previous medical history and gender are described according to enumeration data. Description of general information and baseline characteristics are based on the FAS population.

6.2.3 Research exposure

Duration of study:

Study duration (days) = date of last follow-up (trial termination date) - date of

signed informed consent + 1

Study duration is described by measurement data.

6.3 Effectiveness Analysis

6.3.1 Primary Evaluation Indicators

The study contained 2 primary endpoints, using single group target value approach, with hypothesis testing:

H0: PT≤P0

H1: PT > P0

α = 0.025 (unilateral)

Clinical success rate: Overall clinical success rate and that of each centre are described by enumeration data, and 95% confidence intervals for the total clinical success rate will be calculated. The study hypothesis is valid if the lower 95% confidence interval exceed target value by comparison.

Technical success rate: Overall technical success rate and that of each centre are described by enumeration data, and 95% confidence intervals for the total technical success rate will be calculated. The study hypothesis is valid if the lower 95% confidence interval exceed target value by comparison.

The trial reaches the target value of single group as long as both the primary endpoints meet the requirements. The primary efficacy evaluation is based on the FAS and PPS populations.

6.3.2 Secondary Evaluation Indicators

Secondary efficacy evaluation is based on FAS and PPS.

Statistical descriptions and hypothesis tests are used to describe operation duration, robot-assisted operation time, patient radiation exposure, surgeon radiation exposure, contrast dose, MACE at discharge and 1-month after surgery. Appropriate statistical descriptions and statistical tests are selected based on the type of indicator (refer to "6.1 General Principles").

6.3.3 Product Performance Evaluation

Evaluation of intraoperative physiological load on surgeons, evaluation of intraoperative psychological load on surgeons and incidence rate of serious system malfunction: use descriptive statistics and appropriate statistical description method will be selected according to the type of indicator (refer to "6.1 General principles").

6.4 Safety set analysis

The number of cases and incidence rate of adverse events, investigational device-related adverse events, and serious adverse events use descriptive statistics, and terminated cases due to adverse events, or due to serious adverse events will be presented in a list.

7 Management of missing, erroneous and irrational data

7.1 Processing of Missing Value

The filling of missing data only applies to missing data of primary endpoint in the FAS dataset. The filling strategy adopts the worst-fill method, and the other missing data are not required to be filled.

7.2 Management of erroneous and irrational data

During the data management process, the data in the database will be verified logically. Any erroneous and irrational data found will raise enquiry to the investigator in the form of a query form (Query), and will be adjusted based on the written responses of the investigator. Database won't be locked-in until all erroneous and irrational data are corrected.

Data of subjects who dropped out or withdrew from the study will be still

included in the final statistical analysis. In the statistical report, the specific reasons for all subjects dropped-out or withdrew were described in detail. And missing data of the primary endpoint due to early withdrawal was supposed to be carried forward according to the above-mentioned missing value treatment strategy.

8 Procedures for reporting deviations from the original statistical plan

It needs to be confirmed by the sponsor and the principal investigator, correspond to the relevant content of the protocol, be specified in more detailed than those in the protocol, and be finalized before data lock. Any deviations from the relevant content of the protocol must be fully discussed in principle, without substantial changes to the main analytical principles, methods and analysis sets, and all modifications should be documented.

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