PHILIPS

Statistical Analysis Plan – Collaboration Live Clinical Study

Protocol Number: US-GIS-Collaboration Live-2019-10649

Protocol Title: Collaboration Live Clinical Study

Author(s):

Jing Wang

Protocol Statistician

Philips Clinical Affairs

PHILIPS

Statistical Analysis Plan – Collaboration Live Clinical Study

TABLE OF CONTENTS

1 LIST OF ABBREVIATIONS

AE	Adverse Event
ADE	Adverse Device Effect
ALARA	As Low As Reasonably Achievable
CRF	Case Report Form
CI	Confidence Interval
DD	Device Deficiency
EDC	Electronic Data Capture
LSAF	Life Science Analytics Framework
OB/GYN	Obstetrics/Gynecology
SAE	Serious Adverse Event
SAS	Statistical Analysis Software
SD	Standard deviation
UADE	Unanticipated Adverse Device Effect

2 INTRODUCTION

The Collaboration Live Clinical Study is intended to evaluate the performance and safety of the Collaboration Live software in a clinical setting.

Ultrasound imaging is a form of medical imaging that involves the use of high frequency sound waves. Typically used to help a physician evaluate, diagnose, and treat patients, ultrasound imaging is minimally invasive and no radiation is involved. Collaboration Live is a software solution integrated into Philips EPIQ Ultrasound Systems that enables remote viewing, conferencing and control of the system. All study scanning (including scanning performed under remote control) will be conducted using the ALARA principle to ensure the safety of the subjects. As ultrasound imaging is based on non-ionizing radiation, it is generally considered safe when used by appropriately trained health care providers.

3 STUDY OBJECTIVES

The study objective is to evaluate the performance and safety of the Collaboration Live software in a clinical setting. The study will assess the use of Collaboration Live in conferencing, sharing, and remote control of the Philips EPIQ 5 and EPIQ 7 Ultrasound Systems (software version 5.0.2) in performing routine OB/GYN ultrasound examination.

4 INVESTIGATIONAL PLAN

4.1 Overall Study Design

This is a prospective, non-randomized, single-arm clinical study.

4.2 Discussion of Study Design

Subjects are scanned using a Philips EPIQ 5 or EPIQ 7 Ultrasound System equipped with Collaboration Live software. The study investigator will evaluate performance of the Collaboration Live tool with regard to performance of conferencing, sharing and control capabilities. No patient follow-up is planned beyond the initial exam. The anticipated study duration is three months.

4.3 Selection of Study Population

4.3.1 Inclusion Criteria

Inclusion criteria for subject selection include,

1. Subject is at least 18 years of age
2. Subject in indicated for a routine OB/GYN ultrasound examination at the site.
3. Subject is willing and capable of providing informed consent and participating in this study.

4.3.2 Exclusion Criteria

Exclusion criteria for subject selection include,

1. A medical condition or co-morbidity that would be unduly affected by study participation, per investigator discretion.

4.4 Treatments

4.4.1 Treatment Groups

All eligible subjects will undergo a routine OB/GYN ultrasound exam at the site. The Philips EPIQ Ultrasound Systems with Collaborative Live feature will be used for the exam.

4.4.2 Randomization

There is no randomization in this study.

4.5 Control to Minimize Bias

This is prospective, non-randomized study. No specific controls are required to minimize bias.

5 EFFICACY AND SAFETY VARIABLES

5.1 Primary Analysis Variables

The primary analysis variable is the clinically acceptable performance of remote control functionality. It consists of two parts.

1. Whether the system responds to the remote input as intended and without a delay interfering with the conduct of the exam (Yes/No) will be collected on CRF.
2. A clinically acceptable exam would result in no adverse events related to the control feature.

If a AE related to use of Collaborative Live or remote control feature is reported, then the primary analysis variable will be No.

5.2 Secondary Analysis Variables

The secondary analysis variables are listed as below:

1. Success of key tasks (Establishing the remote connection, Establishing text chat, Establishing voice call, Establishing webcam feed, Establishing screen share, Establishing remote control) in the collaborative exam will be collected.
2. For the key tasks (Establishing text chat, Establishing voice call, Establishing webcam feed, Establishing screen share), 5-point scale data will be reported by physician and sonographer respectively to assess ease of use.
3. User feedback regarding streaming, image quality and overall experience will also be reported by physician and sonographer respectively.
4. A telemedicine satisfaction questionnaire[1] will be answered by subject following remote consultation to assess patient feedback regarding remote consultation.
5. Distance between the scanning facility and the investigator's location will be recorded (in miles) to assess the travel reduction by using collaboration live.
6. Reimbursement amount received for remote patient consultation will be reported. The difference of reimbursement amount between remote consultation and standard rates for in-person consultation will be evaluated.

5.3 Safety Variables

Variables to assess subject safety will be captured on the Adverse Event CRF. Key variables will include the name of the AE, onset date, resolution date, severity of AE, relationship to use of Collaborative Live or remote control feature, SAE and unanticipated device effects (UADE). Device deficiencies (DD) will be captured on the Device Event/Deficiency CRF.

5.4 Appropriateness of Measurements

The questionnaires designed for capturing the endpoints are based on a paper published in 2003[1]. In addition, reported clinical adverse events are appropriate measures of safety.

6 DATA QUALITY ASSURANCE

After the data are reported and submitted to the EDC system, programmed edit checks are raised to ensure that data collection is consistent and complete. In addition, post data submission, data are remotely reviewed via data listings and edit check. Data queries are then generated in the EDC and discrepancies/concerns are then resolved within the EDC system. A sponsor representative will monitor the completion of the Comparison CRF for quality assurance purposes.

7 STATISTICAL METHODS

7.1 Sample Size

The Primary Endpoint is clinically acceptable performance of remote control functionality. Clinical acceptability of the Collaboration Live software will be evaluated for each subject during remote control of the ultrasound system.

A way to describe the statistical properties of the study design is in terms of 95% confidence interval of the true rate of clinical acceptability based on the observed data. Table 1 provides the two-sided 95% confidence interval (CI) for the true rate of clinical accepatability among 30 enrolled subjects using Clopper-Pearson Exact method[2]. If clinical acceptability is observed in all 30 patients, then the 95% exact two-sided lower confidence bound for the rate of such response in this population would be > 80% (with lower bound of 95% CI = 88.4%). Alternatively, it means if the observed accepatability rate is 100%, then the range of 88.4% - 100% will contain the true acceptability rate, with 95% probability.

Table 1: Ninety-five Percent Confidence Intervals for True Rate of clinical accepatability by Observed Acceptability Rate

N	Observed Acceptability Rate	95% CI for True Acceptability Rate
30	30/30 (100%)	(88.4%, 100%)
	29/30 (96.7%)	(82.8%, 99.9%)
	28/30 (93.3%)	(77.9%, 99.2%)
	27/30 (90.0%)	(73.5%, 97.9%)

	26/30 (86.7%)	(69.3%, 96.3%)
	25/30 (83.3%)	(65.2%, 94.3%)
	24/30 (80.0%)	(61.4%, 92.3%)

All subjects completing the study will be included in the primary endpoint analysis. No follow-up is required beyond the initial study visit and therefore, no loss to follow-up or withdrawal is anticipated. However, if subject withdraw were to occur prior to evaluation of clinical acceptability, additional subjects will be enrolled to compensate for the withdrawn subjects. The study will end when 30 subjects have been enrolled and data collection is complete.

7.2 General Consideration

Data will be summarized by descriptive statistics. Continuous variables will be summarized using the number of non-missing observations, mean, standard deviation (SD), median, minimum, and maximum; categorical variables will be summarized using the frequency count and the percentage of subjects in each category. All analyses will be conducted using SAS Life Science Analytics Framework (LSAF).

7.3 Analysis Population

All analyses will be performed on the enrolled subject population. For this study, subjects will be defined as enrolled if they meet all eligibility criteria and provide informed consent, and enrolment date is documented on enrollment CRF.

7.3.1 Handling of Dropouts or Missing Data

Complete data are expected for all measurements since this is a single visit study. Missing values will be treated as missing. The number of cases with missing values will be reported.

7.3.2 Efficacy Subset

There will be no efficacy subset for this study.

7.4 Patient Disposition

Subject disposition will include the number of screened subjects, screen failures, number of enrolled subjects, completed subjects and discontinuations. The reasons for discontinuations will also be presented.

7.5 Demographics and Baseline Characteristics

Subject demographics (e.g., age, race and ethnicity) and baseline characteristics (e.g., BMI) will be summarized for all enrolled subjects.

7.6 Compliance

All protocol deviations observed during the study will be described. A listing of all deviations will also be presented.

7.7 Concomitant Therapy

None is collected because only subjects without medical condition or co-morbidity will be enrolled.

7.8 Statistical Analysis

7.8.1 Primary Analysis

The proportion of the clinically acceptable performance of remote control functionality will be summarized. In addition, the corresponding 95% Exact Clopper-Pearson CIs[2] will be presented.

7.8.2 Secondary Analysis

For the variables listed in section 5.2, continuous variables will be summarized using the number of non-missing observations, mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized using the frequency count and the percentage of subjects in each category. In addition, 95% CI will be calculated for the mean difference of reimbursement amount between remote consultation and standard rates for in-person. And a paired t-test (α=0.05) will be used to evaluate the mean difference of reimbursement amount between remote consultation and standard rates for in-person consultation.

7.9 Safety Analysis

Safety analyses will present the number and percent of enrolled subjects with each of the following outcomes.

- One or more adverse events (AE)
- One or more AE judged to be either related or possibly related to the test product
- One or more moderate to severe AE
- One or more serious AE
- One or more unanticipated adverse device effect (UADE)

In addition, data listings of all reported adverse events will be presented.

The number and percent of enrolled subjects with device deficiencies will be presented. In addition, data listings of all device deficiencies will be provided.

7.10 Subgroup Analysis

There are no planned subgroup analyses.

7.11 Adjustment for Covariates

There will be no adjustments for covariates.

7.12 Multiple Comparison and Multiplicity

There will be no multiple comparisons.

8 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS

8.1 Changes in the Conduct of the Study

There are no changes in the conduct of the study.

8.2 Changes in the Planned Analysis

There are no changes in the planned analyses.

9 REFERENCES

1. Yip MP, AM Chang, J Chan and AE Mackenzie. Development of the Telemedicine Satisfaction Questionnaire to evaluate patient satisfaction with telemedicince: a preliminary study. Journal of Telemedicine and Telecare 2003; 9: 46-50.
2. Vollset, Stein; “Confidence Intervals for a Binomial Proportion”; Statistics in Medicine, Vol 12, pp. 809-824, 2006.

10 TABLES

Attached in separate document.

11 FIGURES

Attached in separate document.

12 INDIVIDUAL SUBJECT DATA LISTINGS

Data listing will be prepared for all data reported in the CRFs. Data listings will contain subject ID, as the unique identifiers as applicable and will be sorted by subject.

Document Revision History

Version	Date	Author	Description of Change	Reason for Change
1.0	14-Jan-2019	Jing Wang	Initial Release	NA

Document Approval History

Approved by	Role / Function	Signature	Date
Jing Wang	Project Statistician (SAP Author)		
T.J. Battisti	Clinical Development Scientist		
Jeddah Wegerhoff	Clinical Study Manager		
Kevin Najarian	Global Director Biostatistics and Data Management		