STUDY PROTOCOL

Validation study on RENEW's Aingeal at KK Women's and Children's Hospital

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INTRODUCTION

RENEW's Surveillance Monitoring system is made up of two main components: a patient-worn wireless vital signs monitor (Aingeal) that transmits data over Wi-Fi to a central station software platform (Surveillance Station).

The Aingeal device measures single lead ECG, heart rate, respiration waveform and rate, and skin temperature. A snapshot of data is transmitted by the devices intermittently to the Surveillance Station, enabling vital signs trends to be plotted. If any heart, respiration rate or skin temperature values move outside of pre-defined high and low limits (individually set for each patient) an alert is raised. ECG arrhythmia detection algorithms automatically record and send ECG data if the patient is suspected to be experiencing an arrhythmia event (Asystole, Ventricular Fibrillation, Tachycardia or Bradycardia).

This proposal describes the evaluation of RENEW's Aingeal device within a paediatric out-patient setting in KK Women's and Children's Hospital ("KKH"), the main tertiary women and children hospital in Singapore.

In the paediatric population, assessment of RENEW's Aingeal device will include the accuracy of the device at deriving heart rate from single lead ECG and at deriving respiratory rate when compared against a commonly used vital signs monitor.

User acceptance of Aingeal and the Surveillance System will be considered within paediatric settings.

AIMS & OBJECTIVES

The aims of the study are:

- To examine the validity of vital signs recorded from paediatric patients (aged between 3 and 17 years) using the Aingeal device
- To determine user acceptance of Aingeal and the Surveillance system

The study will determine whether:

1. Heart rates calculated by the Aingeal device during paediatric patient monitoring are within clinically acceptable accuracy ranges
2. Respiration rates calculated by the Aingeal device during paediatric patient monitoring are comparable with respiration rates recorded using a portable bedside End Tidal Carbon Dioxide ($ETCO_2$) monitor.
3. The Aingeal device and Surveillance system are acceptable to Healthcare Professionals (HCPs), to paediatric patients, and to paediatric patients' parents or guardian.

STUDY DESIGN

Paediatric Out-patient Population

The Surveillance System will be installed in a paediatric outpatient clinic at KKH. A standalone Wi-Fi network will be set up to facilitate system use for the purposes of the study. Children attending the clinic aged between 3 and 17 years old will be invited to participate. Written consent from the child's parents or guardian will be obtained prior to participation.

Subsequent to obtaining consent, trained personnel will confirm the child's eligibility with their parent or guardian against the following inclusion and exclusion criteria:

Inclusion Criteria

- ✓ Male or female paediatric patients, aged between 3 and 17 years
- ✓ Patients attending outpatient care at KKH Women's and Children's Hospital, Singapore

Exclusion Criteria

- × Patients with active, implantable devices (such as a pacemaker or ICD)
- × Patients with any skin condition or injury affecting the electrode placement site
- × Patients that are pregnant
- × Those patients who, in the opinion of the outpatient clinic staff, are not suitable to participate.

Eligible and willing patients will be set up with an Aingeal electrode and device and Medtronic's Capnostream 35 portable respiratory cannula.

Recording of vital signs will begin at resting phase with the study subjects seated comfortably for 10 minutes. Younger children may be seated on the caregiver's or parents' lap. After the resting phase, the child will be asked to take a short walk around the clinic for 5 minutes. Younger children may be offered the playground instead.

Information on age, height, weight, sex and medical history will be collected from the patients' medical notes or reported by the patient's parent or guardian. At the completion of vital signs recording, feedback from the child and their parents or guardian will be obtained using self-reported questionnaires (Appendix 1).

Patient Identification

A patient enrolment log will be maintained at each investigational site. This enrolment log will link the identifiable patient to a study patient number which will be used on all study data.

Withdrawal and Discontinuation

All patients will have the right to withdraw their participation from the study at any time. Withdrawal will not affect their routine medical care. Patients may be withdrawn if it is thought to be in their best interests. The reason for withdrawal of any patient will be documented and any data gained up to the point of withdrawal may be used in analyses.

DATA ANALYSIS AND STATISTICAL METHODS

Paediatric Out-patient Population

Paediatric patients will be monitored simultaneously using the Aingeal and Capnostream devices for fifteen minutes over two phases (ten minutes at rest and five minutes during walking or playing). Before data collection commences, the time on the Surveillance Station will be verified against the time on the Capnostream device to ensure that respiratory data can be paired as closely as possible.

Heart Rate Comparison

Each of the ECG waveforms recorded by the Aingeal device will have heart rate calculated manually by a trained reviewer that has been blinded to the heart rate derived by the Aingeal device to minimise bias. Ten subjects will provide approximately 100 minutes (or 2 hours) of Aingeal data and approximately 100 heart rates. Both sets of heart rates will be compared using the approach of Bland Altman [1, 2].

Respiratory Rate Comparison

The Aingeal device averages respiration rate over a 30 second window (or a period of 10 breaths, whichever is shorter). The respiration rate is updated each minute at the Surveillance Station. The Capnostream device stores data at resolution of 1 sample per second.

As a result there will be many more data points from the Capnostream device than from the Aingeal device over the same observation period. Ten subjects will provide approximately 100 minutes (or 2 hours) of Aingeal data and approximately 100 respiration rates. Both sets of respiratory rates will be compared using the approach of Bland Altman. Datasets will be stratified by age group as described in Table 1.

A total sample of 10 paediatric outpatients stratified by the age groups of 3 to 5 years old, 6 to 9 years old, 10 to 14 years old and 15 to 17 years old is estimated to provide an accuracy of 5% for respiratory rate, with estimated differences ranging from 0.7 to 1.25 breaths. The sample estimation is calculated based on a minimum of 8 repeated measures per child, having accounted for 20% attrition rate and 20% data loss due to signal loss, noise or time discrepancies.

Bland Altman Analysis

The heart and respiration rate counts from each measurement method will be compared against each other in a pair-wise manner using the approach of Bland & Altman. For each parameter, this involves plotting the difference in the counts against the mean of the two absolute counts. The 95% and 99% limits of agreement, equivalent to 2 times standard deviation (sd) and 3 sd will be plotted. This process will be repeated for each portion of the test (at rest and during activity) and for each age group (3 to 5 years old, 6 to 9 years old, 10 to 14 years old and 15 to 17 years old) for heart rate and respiration rate. Adjustments for age and sex will be considered.

Feedback and Demographic Analysis

Summaries of patient, parent and HCP acceptability, demographics and medical history will be produced. In general, categorical data will be summarised using frequency counts and percentages, and continuous data will be summarised using means, standard deviations, minimums, medians and maximums.

RENEW's AINGEAL PROCESS REQUIREMENTS

A. Application and Registration

No	Step by Step Application
1	Add patient to Central (Surveillance) Station.
2	Assign Aingeal Device to patient. (Pair the RENEW's Aingeal Device identifier code with Subject ID on the Surveillance Station and on the Patient Log. .)
3	Thoroughly clean the skin using alcohol wipes. Poor skin prep may result in poor signal quality.
4	Apply electrodes: Position the electrodes as shown in the figures below. RENEW's Aingeal Device should be placed on the left chest, just left of the centre of the sternum and below the collar bone. The right chest electrode should be placed just right of the centre of the sternum and below the collar bone. Place the electrode on the left side of the patient's body at the 7th rib and on the midline.
5	Connect device & start-up: Turn on RENEW's Aingeal device by pressing the "ON" Button. Check that the device beeps, that the Wi-Fi LED changes from orange to green, and that the Leads LED changes from blue to unlit.
6	Start Monitoring Patients on RENEW's Surveillance Station. Validate waveforms.
7	Check alarm limits.

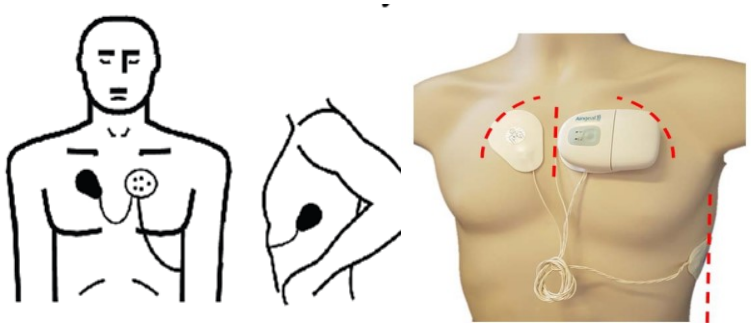

Fig. A. Aingeal Device on adult

B. Data Collection and Validation

The RENEW's Aingeal is a wearable wireless device that measures single lead ECG and impedance pneumography waveforms to derive heart and respiration rates. Skin temperature is measured via a thermistor on the electrode patch. Every minute these parameters and a 25 second snapshot of waveform data are transmitted to the Surveillance Station over Wi-Fi.

The RENEW's Aingeal will be attached onto the Subjects for continuous monitoring during the Study.

i. The Subjects will each be identified by a unique Subject ID assigned at time of recruitment and a Device ID using an agreed format.

ii. Raw vital signs data ie. Readings, will be extracted from Surveillance System and provided to KKH research team for further study data mapping and analysis.

iii. Sampling Rate will be derived using a data averaging method over a period of 60 seconds for the Capnostream data output. KKH requires all raw data points, in additional to per minute.

iv. KKH will extract the averaging data points for further data processing and mapping against the Subject's demographics; e.g age, gender, height, weight etc.

For first week of the trial, Renew is required to extract the daily data files onsite and provide to KKH. This is to ensure that the setup is working well and correct data is collected and verified. There is no contact between the participants and the representative from the study sponsor. Also, the patient's details will not be keyed into the system as we will only put participant's subject ID number, which will not allow sponsor to identify the patients.
Removal and De-Registration

No	Step by Step Application
1	Turn off the RENEW's Aingeal by pressing and holding the "OFF" Button on the RENEW's Aingeal until the green LED is unlit.
2	Remove the RENEW's Aingeal gently from the Subject
3	Slowly and carefully remove the electrodes from the Subject
4	The subject can be discharged from the Surveillance Station after data collection has completed and all required data is collected.
5	Dispose the electrodes appropriately into designated bins.

C. Training Plan

The training program is designed to provide the relevant study team members with sufficient knowledge and skills to configure and use the RENEW Surveillance System. The program will comprise of interactive instructor led clinical demonstration.

Training will take place onsite. The study team members are encouraged to actively participate in the demonstration cum hands-on session. This is to prepare the study team members to understand and identify any potential modifications being made to their existing routines and workflow.

ROLES AND RESPONSIBILITIES

RENEW will provide all necessary Surveillance system equipment and accessories required to facilitate validation of the Aingeal Surveillance system. KKH's involvement includes proposal development and data collection for the paediatric study and for the adult in-patient study, analysis and reporting of study findings will be performed additionally. KKH will also be providing space and technical support necessary for the conduct of the validation study.

TIMELINES AND DELIVERABLES

Stages	**Period**
Planning	July 2017 to October 2017
HSA approval for Aingeal	Dec 2017
IRB submission to approval	Jan 2018
Internal briefing	Jan 2018
Commencement of study	Jan 2018
Mid-study interim report	Apr 2018
Completion of study	June 2018
Data collation and analysis	July/August 2018
Findings (Dissemination)	September 2018
Publication of study	December 2018

CONCLUSION

This study is aimed to test the feasibility of RENEW's Aingeal in a clinical setting, and its findings may be useful in augmenting RENEW's Aingeal system's role in clinical monitoring of vital signs and early warning system for paediatric patients at KK Women's and Children's hospital.

References

1. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet (London, England) 1986;**1**(8476):307-10
2. Bland JM, Altman DG. Comparing methods of measurement: why plotting difference against standard method is misleading. The Lancet 1995;**346**(8982):1085-87 doi: http://dx.doi.org/10.1016/S0140-6736(95)91748-9[published Online First: Epub Date]|.

Appendix 1

Date:_____ Questionnaire for Healthcare Staff

1. Did you receive any briefing in how to use the RENEW's Aingeal device?

☐ Yes ☐ No ☐ Not Sure

2. Was the information given to you adequate?

☐ Yes ☐ No ☐ Not Sure

Please answer all the questions that apply to your duties. If a question does not apply to your responsibilities, please select Not Applicable. Take note that there is no right or wrong answer.

During the test of RENEW's Aingeal Device:	**Strongly Disagree**	**Disagree**	**Neither Agree or Disagree**	**Agree**	**Strongly Agree**	**Not Applicable**
It was easy to set patients up on the **Surveillance Monitoring Central Station**.	1	2	3	4	5	9
RENEW's Aingeal Device was easy to apply onto the patient.	1	2	3	4	5	9
RENEW's Aingeal Device did not appear to increase patient's discomfort.	1	2	3	4	5	9
Loss of readings (vital signs) from RENEW's Aingeal Device was uncommon.	1	2	3	4	5	9
I was able to view and monitor my patient's vital signs on the **Surveillance Monitoring Central Station** easily.	1	2	3	4	5	9
I could have used **RENEW's Aingeal Device** without special training.	1	2	3	4	5	9
RENEW's Aingeal Device meets my clinical needs.	1	2	3	4	5	9
RENEW's Aingeal Device is safe for clinical use.	1	2	3	4	5	9
RENEW's Aingeal Device Surveillance Monitoring is easily integrated with the ward routine.						
RENEW's Aingeal Device Surveillance Monitoring enhances patient care delivered in the ward.	1	2	3	4	5	9

Additional comments

ID TAG

Questionnaire for Participants (Paediatric outpatient clinic)

Date:_____

Ward:_____

Please answer all questions. Parents/Accompanying adults involved may provide assistance to children in responding to this survey. Take note that there is no right or wrong answer.

During the test of RENEW's Aingeal Device:	**Strongly Disagree**	**Disagree**	**Neither Agree or Disagree**	**Agree**	**Strongly Agree**
I was given adequate information on the **RENEW's Aingeal Device** to be used on my child/ward**.**	1	2	3	4	5
My child/ward is comfortable having **RENEW's Aingeal Device** on him/her all the time.	1	2	3	4	5
My child/ward does not have skin irritations from using **RENEW's Aingeal Device**.	1	2	3	4	5
My child/ward is able to continue with his/her daily activities with **RENEW's Aingeal Device.**	1	2	3	4	5
My child/ward is comfortable having his/her heart and respiratory rates monitored using **RENEW's Aingeal Device.**	1	2	3	4	5
If my child's vital signs need to be monitored for medical reasons, I would feel more secure with continuous monitoring of my child's heart and respiratory rates using **RENEW's Aingeal Device** than with periodic checks by hospital staff or nurses.	1	2	3	4	5

Additional comments

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