STUDY PROTOCOL

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

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*Also refer to Page 4 on the statistical analysis details.

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 an adult in-patient setting KK Women's and Children's Hospital ("KKH"), the main tertiary women and children hospital in Singapore.

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

AIMS & OBJECTIVES

The aims of the study are:

- To examine the feasibility of using the Aingeal device within an adult in-patient setting
- To determine user acceptance of Aingeal and the Surveillance system

The study will determine whether:

1. The Surveillance system can be successfully installed and deployed in an adult post-operative in-patient setting
2. The Aingeal device and Surveillance system are acceptable to Healthcare Professionals (HCPs), to adult patients.

STUDY DESIGN

The Surveillance System will be installed in a 32-bed post-operative gynaecology ward in KKH. A standalone Wi-Fi network will be set up to facilitate system use for the purposes of the evaluation.

Fifty post-operative female patients receiving opioid therapy via patient controlled analgesia (PCA) on the ward will be invited to wear an Aingeal device for the duration of their opioid therapy.

Subsequent to obtaining consent, trained personnel will confirm the patient's eligibility against the following inclusion and exclusion criteria:

Inclusion Criteria

- ✓ Adult female patients, aged 21 years or over
- ✓ Patients admitted to post-operative gynaecological ward at KKH Women's and Children's Hospital, Singapore
- ✓ Patients receiving opioid therapy via patient controlled analgesia (PCA)
- ✓ Patients that are on electronic nursing charting

- ✓ Patients that are on acute pain service monitoring

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 (Heart Rate detection algorithm has not been designed to reject foetal heart rate)
- × Those patients who, in the opinion of the ward staff, are not suitable to participate.

HCPs will be trained on system use and asked to use the system as a routine part of care delivery until thirty five patients have been monitored. All information presented by the system will be verified using existing hospital procedures before action is taken. Routine care that is appropriate for the patient at the investigational site will continue unchanged and unaffected by the study activities.

HCPs will be asked to provide feedback on their experiences with the system, which will be reviewed with ward management. Consideration will be given to the clinical utility of the system, ease of use, patient and nurse acceptance and integration with existing workflow. Patients that have worn the device will be invited to complete a feedback questionnaire.

Anonymous data recorded by the Aingeal device during the evaluation will be collected and reviewed to provide information on device performance and system use.

Vital signs data recorded during routine observations taken by nursing staff and associated dates and times will be collected from electronic records, de-identified and compared against vital signs trends recorded by the Aingeal device.

If any interesting clinical scenarios occur, HCPs will be asked to record the patient's Aingeal device Serial Number and the date, time and duration of the clinical scenario.

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

In adults, a total of 35 in-patient post-operative women on opioid therapy will be invited to wear the Aingeal device to facilitate a proof-of-concept evaluation of the Surveillance system as part of an integrated monitoring with opioid delivery system at ward setting.

Each patient will be set up for monitoring on admission. Duration of opioid therapy for post-operative in-patients may range from one day until three days, with patients receiving opioid therapy on average for two days. Once opioid therapy is no longer required Aingeal monitoring will be ended and each patient would be encouraged to have at least 1 day of monitoring on the Aingeal monitoring to be recorded during the study. De-identified log files will be extracted from the Surveillance Station and reprocessed to produce counts of the number of alarms raised during monitoring. A sample of the data will be reviewed to determine whether cardiac and respiratory alarms are defined as True or False, with an overall Alarm Rate per patient per day and False Positive Alarm Rate per patient per day derived. Vital sign trend graphs for each patient will be produced.

Summaries of patient and HCP acceptability, demographics and reason for admission 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. Bland-Altman analyses will be used to compare Aingeal heart and respiration rates with vital signs data recorded in the patient's electronic record. Any time differences between the Surveillance Station software and the devices used by staff for routinely measured vital signs input will be accounted for in the analysis. Adult In-patient Population

The sample size of 35 was based on assumption that the mean difference between two methods as 5 breaths/min, standard deviation (SD) of the difference as 2.45 breaths/min with maximum allowed difference between the methods as 12 breaths/min, level of significance $\alpha = 5\%$ and power as 80% we plan to recruit 35 adult in-patients. Hence a total of 35 in-patient post-operative adult women on opioid therapy will be recruited to wear the Aingeal device to facilitate a proof-of-concept evaluation of the Surveillance system as part of an integrated monitoring with opioid delivery system at ward setting.

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.

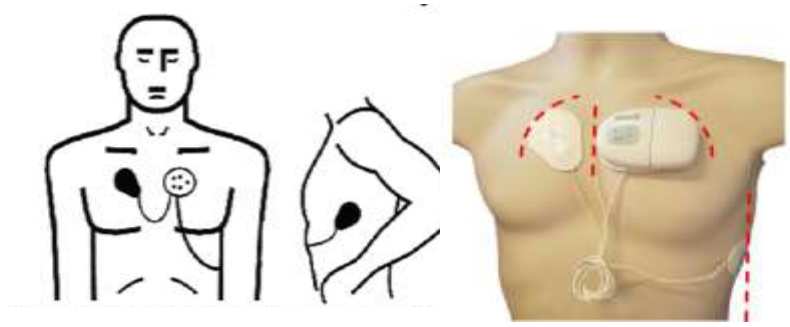

Fig. A. Aingeal Device on adult

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 the 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.

C. 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.

D. Training Plan

The training program is designed to provide the relevant participants 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. Participants are encouraged to actively participate in the demonstration cum hands-on session. This is to prepare the Participants 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 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 (3 months turnaround)
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

Reference

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:_____ Ward:_____ 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
RENEW's Aingeal Device allows early detection of deterioration of condition in significant no of patients	Decrease 5-10%	Decrease 1-5%	Same 0%	Increase 1-5%	Increase 5-10%	Not Applicable

Additional comments

ID TAG

Questionnaire for Participants (Women's ward)

Date:_____

Ward:_____

Please answer all questions. 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.**	1	2	3	4	5
I am comfortable having **RENEW's Aingeal Device** on me all the time.	1	2	3	4	5
I do not have skin irritations from using **RENEW's Aingeal Device**.	1	2	3	4	5
I am able to continue with my daily activities with **RENEW's Aingeal Device.**	1	2	3	4	5
If asked, I am comfortable applying **RENEW's Aingeal Device** on my own.	1	2	3	4	5
I am comfortable having my heart and respiratory rates monitored using **RENEW's Aingeal Device.**	1	2	3	4	5
I am comfortable having my heart and respiratory rates monitored remotely with **RENEW's Aingeal Device**, without having the nurse present at my side.	1	2	3	4	5
I feel more secure with continuous monitoring with **RENEW's Aingeal Device** than with periodic checks of my heart and respiratory rates.	1	2	3	4	5
I am keen to continue with remote monitoring of my heart and respiratory rates in the hospital ward with **RENEW's Aingeal Device** (if I were to be in the hospital ward again).	1	2	3	4	5

Additional comments

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