Submission to Emergency Medicine Australasia:

Accuracy of QT interval measurement on ECGs displayed on electronic 'smart' devices

*Dr Joe-Anthony Rotella, MBBS, BSc, MAICD[1,2]

Professor David McD Taylor, MBBS, MD, MPH, DRCOG, FACEM[2]

Dr Anselm Wong, MBBS, FACEM[1,2]

Dr Shaun L Greene, MBChB, MSc, FACEM[1,2]

[1]Victorian Poisons Information Centre, Austin Health, Heidelberg, Victoria, Australia, 3084

[2]Department of Emergency Medicine, Austin Health, Heidelberg, Victoria, Australia, 3084

Author contributions:

JAR: Study design, data collection, drafting and subsequent editing of manuscript

DT: Study design, statistical analyses, editing of manuscript

AW: Study design, data collection, editing of manuscript

SG: Study design, data collection, editing of manuscript

*Corresponding author

Dr Joe-Anthony Rotella

c/- Emergency Department, Austin Health, Studley Road, Heidelberg, Victoria, Australia 3084

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/1742-6723.12541

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Email: ja.rotella@gmail.com Telephone: +61 409 972 438

WORD COUNT: 2161

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INTRODUCTION

Conduction intervals derived from the electrocardiograph (ECG) are useful in the diagnosis, risk-assessment and management of patients who have taken an overdose of a number of pharmaceuticals. Many drugs, such as amisulpride, sotalol and amitriptyline, have cardiotoxic effects and can cause conduction abnormalities visible on an ECG[1]. Acute poisoning with drugs such as these is associated with significant morbidity and mortality[2].

Management of cardiotoxicity following acute poisoning often requires specialised knowledge accessed through consultation with a clinical toxicologist. Specialised bedside clinical toxicology consultation is not commonly available in all hospitals, and so expertise is often provided via Specialists in Poison Information (SPIs) and clinical toxicologists based in regional Poison Information Centres (PICs). In cases of cardiotoxicity discussed via telephone, SPIs and clinical toxicologists have traditionally relied upon the interpretation of the ECG by the medical staff at the patient's bedside.

One study in the USA found 50% of medical staff reporting ECG findings to a SPI misinterpreted the ECGs and, as a result, management and disposition may have

been clinically affected[4]. The ECG QRS and QT interval durations were most commonly reported in error[4]. Intervals interpreted by computerised ECG machines have also been reported as predisposed to large measurement errors (as large as 20%) and consequently may not provide a reliable substitute[5]. As these intervals provide crucial data in the assessment of patients poisoned with cardiotoxic drugs, erroneous measurement can lead to inappropriate risk assessment, management and disposition. The consequence of decisions made on an incorrect measurement could lead to harm (e.g. failure to anticipate *torsades de pointes* due to an incorrectly interpreted QT interval).

The advent of electronic 'smart' devices that encompass high quality camera technology (e.g. Apple iPhone® or iPad®) may offer a potential solution. These devices are widely available across the globe with approximately fifty million devices sold in the last quarter of 2014[6]. Medical staff at the bedside could use such a device to capture an image of the ECG, subsequently allowing a clinical toxicologist to view and interpret the ECG remotely. This includes remote measurement of the QT interval.

We hypothesise that there is no difference in the accuracy of the QT interval measurement using these modalities, when compared to the original paper ECG. The aim of the study was to compare the accuracy of QT interval measurements from four modalities (iPhone 4G®, iPad 2®, 17-inch computer monitor, ECG facsimile) against the 'gold standard' original bedside ECG.

METHODS

Study design, setting and period

This was a prospective, observational study conducted at a tertiary referral hospital, between November 2012 and May 2014, inclusive. The Emergency Department (ED) has an attendance of approximately 75,000 patients annually. The hospital has an inpatient Clinical Toxicology service and a regional PIC. Approval for the study was obtained from the hospital's Human Research Ethics Committee.

Study ECGs

The study used 12-lead ECGs that were recorded, as part of routine medical care, from adult patients (aged 16 years or more) who presented to the ED. ECGs with an abnormal QT interval (greater than 480 milliseconds measured directly) were used for the study. This is the group of ECGs where accurate measurement of the QT interval is most clinically relevant. Fifteen original ECGs were used in the study. The original ECGs were obtained by the principal investigator and served as the 'gold standard' ECGs against which all other copies/photographs were compared. The ECGs were rendered non-identifiable by removal of all identifiers (name, date of birth, medical record number). A facsimile copy was made using the ED facsimile machine (Phillips PageWriter TC30™). Electronic images of the ECG were captured using an Apple iPhone 4G® and copied to an Apple iPad 2® and a folder on a secure computer with a 17-inch monitor. Images were captured in a clinical area without additional lighting to reproduce usual working conditions in the Emergency Department.

Because this study was purely ECG-based, done with non-identifiable patient ECGs, patient consent was not required. The study did not change any part of the routine clinical management of these patients.

Participant recruitment

An email invitation to ED's Consultants and Trainees invited participation in the study.

Inclusion and Exclusion Criteria

Only Emergency Medicine trainees and consultants practicing in the study ED were included in the study. This included ED Consultants, who were also specialist Toxicologists. There were no exclusion criteria. Informed written consent was obtained from all doctors prior to their participation in the study. The plan for recruitment and subsequent data collection is summarised in Figure 1.

Data Collection

Consenting participants were given a brief, refresher tutorial (<5 minutes) by the principal investigator on the QT interval and its measurement on the ECG (Figure 2). The tutorial included the definition of the QT interval; how it is measured; units of measurement and which ECG leads would be utilised in this study.

Each participant, by themselves, took part in 5 study sessions. In each session, they examined all 15 ECGs using one device only that had been randomly allocated using a pre-prepared randomisation table. They examined the same

ECGs using the other modalities in subsequent sessions, which were at least two weeks apart.

Participants were asked to measure and record the absolute QT intervals, in milliseconds (msec), of leads I, II, V2, V4, V6 and one other lead. The median of these measurements was calculated in the same manner as previous studies evaluating the use of a QT nomogram to determine the QT interval in poisoned patients[7,8]. The QT nomogram method requires manual measurement of the QT interval in six individual leads as listed previously and calculation of the median value; this is subsequently plotted against heart rate on a nomogram. This method was chosen to reflect existing recommended practice for measurement of the QT interval. Single designated smart devices, a single 17-inch computer monitor, and a single fax machine was employed.

Study Endpoints

Primary Endpoint

The primary study endpoint was the QT interval measurement for each modality. The QT interval measured on the bedside ECG served as the 'gold standard'. If the difference between the gold standard QT interval and that measured on an electronic device was more than 40msec (considered a clinically significant difference as this represents more than one small square on an ECG), then the device reading was deemed as inaccurate.

Secondary Endpoints

- Variability of QT interval measurements across the ECG leads. All QT intervals measured for each lead were pooled (all participants and all modalities) and the leads were compared.

- Variability of QT interval measurements across study participants. All QT intervals measured by each participant were pooled and the participants were compared.

Sample Size and Statistical Analyses

An audit of cases with prolonged QT interval durations (measured on an original bedside ECG) revealed that the mean (SD) QT interval was 510 (70) msec. In order to demonstrate that the QT interval measured on one of the four modalities differed by at least 40msec (<470 or >550msec), at least 80 pairs of QT measurements (gold standard-modality pairs) were required for each modality (level of significance 0.05, 2 sided, power 0.95). In total, 13 doctors participated with each examining 15 ECGs. This resulted in 195 pairs for each modality. This number was well in excess of that required, but helped account for the fact that mean (SD) values were used for the sample size calculation while non-parametric tests were used for all analyses.

The QT interval data were found to be non-normally distributed (Kolmogorov-Smirnov test $p<0.001$). **The Chi square test was employed to examine the agreement between each doctor's median gold standard QT interval measurement (for each ECG) and those of the four modalities. There was agreement between a gold standard and modality measurement if they differed by ≤40msec.** Comparisons of **pooled ECG lead** QT intervals **(all doctors' measurements combined)** of the gold standard and the four modalities employed the Kruskal-Wallis test. This test was also employed to compare the QT intervals measured by each doctor. The Friedman's two way

analysis of variance test was employed to compare the QT interval measurements across the various ECG leads. SPSS for Windows statistical software (Version 22.0, SPSS Inc., Chicago, Illinois, USA) was used for all analyses (level of significance 0.05).

RESULTS

Thirteen doctors volunteered in the study and were recruited, measuring the QT intervals on 15 ECGs using the five aforementioned modalities as intended. Of the participants, nine were trainees and four were consultants. Three of the participants were also Consultant Toxicologists.

In total, each participant recorded 975 measurements. All data collection forms were completed with no blank fields identified. Non-parametric analysis was required as the medians attained for leads 1 and v4 were not normally distributed.

The proportions of agreement between each doctor's median gold standard and modality QT intervals (for each ECG) are described in Table 1. The proportions were similar for facsimile, iPhone and computer (~80%) but much less for the iPad (70.3%), (p=0.02).

For each lead examined, there were no significant differences in median QT interval measurements between the modalities and the bedside ECG (**Table 2**). For each lead, the median QT interval was the same across all modalities. The QT

interval for V2 was the same as the other leads (with the exception of lead I) but had the least variability in measurement i.e. smallest interquartile range (Figure 3).

There was a statistically significant difference between the QT interval measurements of the participants ($p<0.001$) (Figure 4). The median QT intervals varied from 480msec to 530msec across the participants.

DISCUSSION

Our study demonstrates that the QT interval can be accurately measured **using an ECG facsimile, iPhone and computer screen but not an iPad. No significant difference was found between the QT intervals of the ECG leads when the intervals were pooled**. This is similar to a previous study that demonstrated that interpretation of acute ST-segment elevation using a mobile phone with camera technology had high reliability similar to that of the same printed ECG[9]. **However, when the intervals were examined at the level of the individual doctor, ECG and modality, the iPad was less accurate than the other three modalities.**

The practice of QT interval measurement in overdose patients and subsequent risk assessment varies in clinical practice[10]. The QT nomogram[11] has been independently shown to be more accurate and produce fewer false positives than formulas such as Bazzett's, which tends to underestimate the QT interval duration at very slow and very fast heart rates[11, 12]. The QT nomogram method

has been validated by the original study investigators for use in risk assessment in overdose with agents implicated in causing drug-induced *torsades des pointes* in overdose[13]. The QT nomogram method requires manual measurement of the QT interval in six individual leads and calculation of the median value; this is subsequently plotted against heart rate on a nomogram. The QT nomogram method relies on accurate manual measurement of the QT interval. Our study demonstrates that this can be done effectively using an ECG displayed on different electronic devices, allowing real-time remote expert risk assessment following overdose of cardiotoxic drugs.

In our study, lead V2 was found to be the most useful for measuring the QT interval. It is possible that measurement of this lead alone could be used as a surrogate for the median value of the six individual lead measurements currently required for accurate interpretation of the the QT nomogram.[13] A single lead measurement may lead to more busy ED clinicians manually measuring the QT interval, rather than relying upon the less accurate ECG calculated value. This requires further evaluation in future research, where the value for lead V2 alone could be compared to the original median derivation on the QT nomogram.

There was a significant difference in QT interval measurement between the participants in this study. Given unequal representation and a small participant group, it was not possible to compare Trainees, ED Consultants and ED Consultants/Specialist Toxicologists. Confounding variables that may also explain the observed variability, but were not accounted for in the study methodology, include visual impairment, age, time of day, and general aptitude

with information technology, prior experience and familiarity with the measurement of the QT interval. Although not specifically examined in this study, the level of experience (trainee, consultant) did not seem to correlate with accuracy of measurement.

This study had several limitations. The study was undertaken at a single centre and the findings may have limited external validity. Selection bias may have been introduced by convenience sampling of participants. However, this is unlikely and was necessary to ensure that those who volunteered were committed to full participation. All participants examined the same ECGs in order to standardise all intervals to be measured. Measurement bias was likely to have been minimised by the time period elapsed between each participant session. Although unlikely, participants may have recalled specific ECGs from previous sessions, thus increasing the accuracy of the measurements. Time spent to undertake measurements were not recorded and this may have contributed to the findings. In addition, a recognised specialist such as an electrophysiologist did not undertake the 'gold standard' measurements, nor were callipers used (which has been recommended by other authors)[12]. The iPhone 4G used to photograph the ECGs was 5 megapixel camera quality so the findings cannot be extrapolated to 'smart' devices with an inferior resolution. Newer models with upgraded camera technology have already superseded the devices used in the study however intuitively; logic would dictate that a higher resolution camera and viewing device would produce the same outcome. All participants undertook the tutorial on QT interval measurement in order to minimise the confounding effect of clinical experience in emergency medicine. Only single

devices/machines were used in order to avoid potential confounding introduced by the use of more than one of each device.

CONCLUSION

The QT interval can be accurately measured using **an ECG facsimile, iPhone and computer screen but not with an iPad.** Absolute measurements vary between doctors. If a single lead is used to measure the QT interval duration then lead V2 is recommended. Research is recommended to determine if a single lead measurement is comparable to the median of six measured leads as recommended when using the QT nomogram.

Competing Interests

The study was not funded. The authors have no conflicts to declare.

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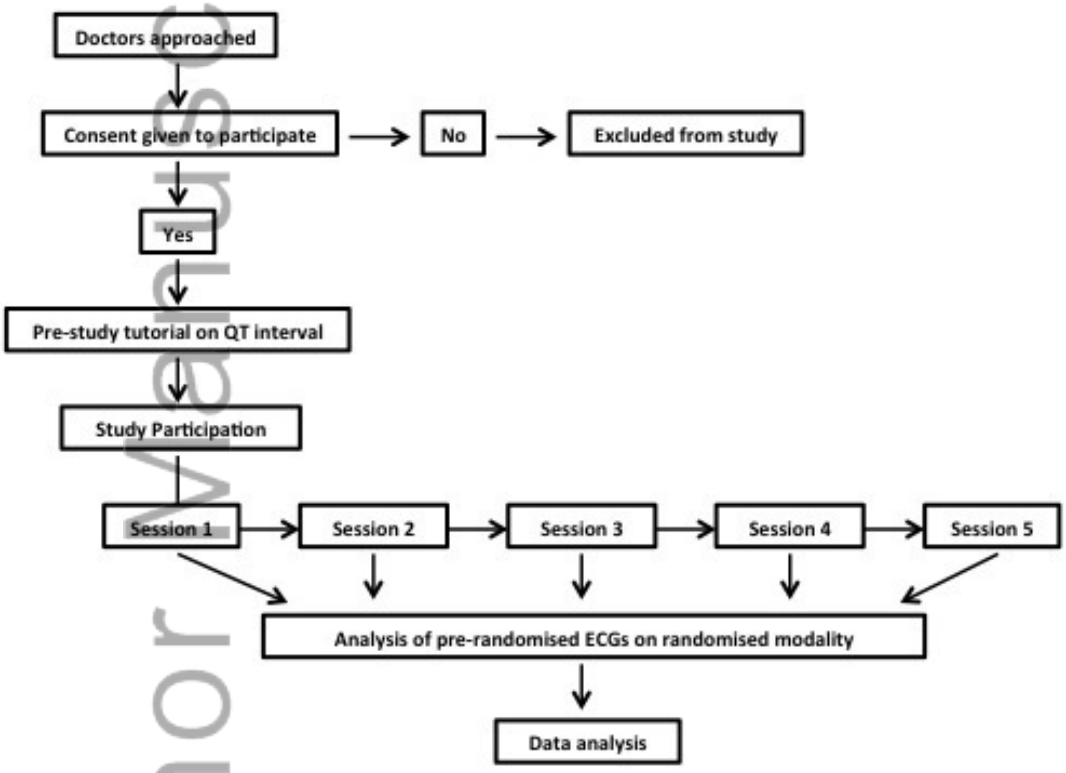

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Accuracy of QT Interval measurements on electronic 'smart' devices

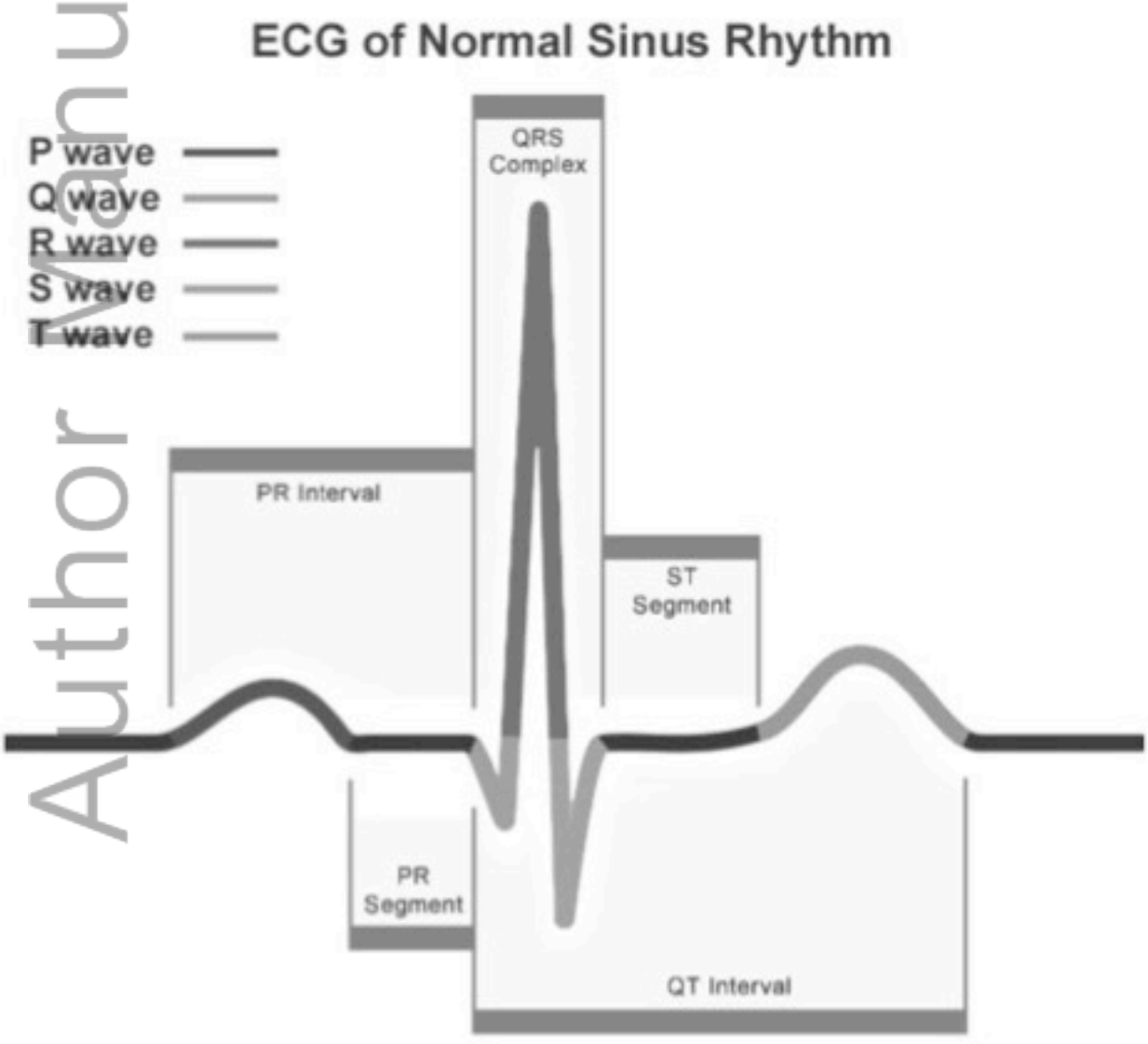
QT Tutorial

QT Interval

- Defined as the interval between the ***start of the Q wave*** and ***the end of the T wave*** (return to isoelectric line)

(NB. If a Q wave is **not** present, the interval is measured from the **start of the QRS complex** to the end of the T wave)

For the purposes of this study, please measure the QT interval (without correction for rate) on **leads I, II, V2, V4, V6 and one other** in milliseconds (1 small ECG square is equal to 40 milliseconds) and record it in the provided data collection form



1 small square on an ECG = 40 milliseconds

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Figure 3. QT interval measurements by lead with median and interquartile ranges

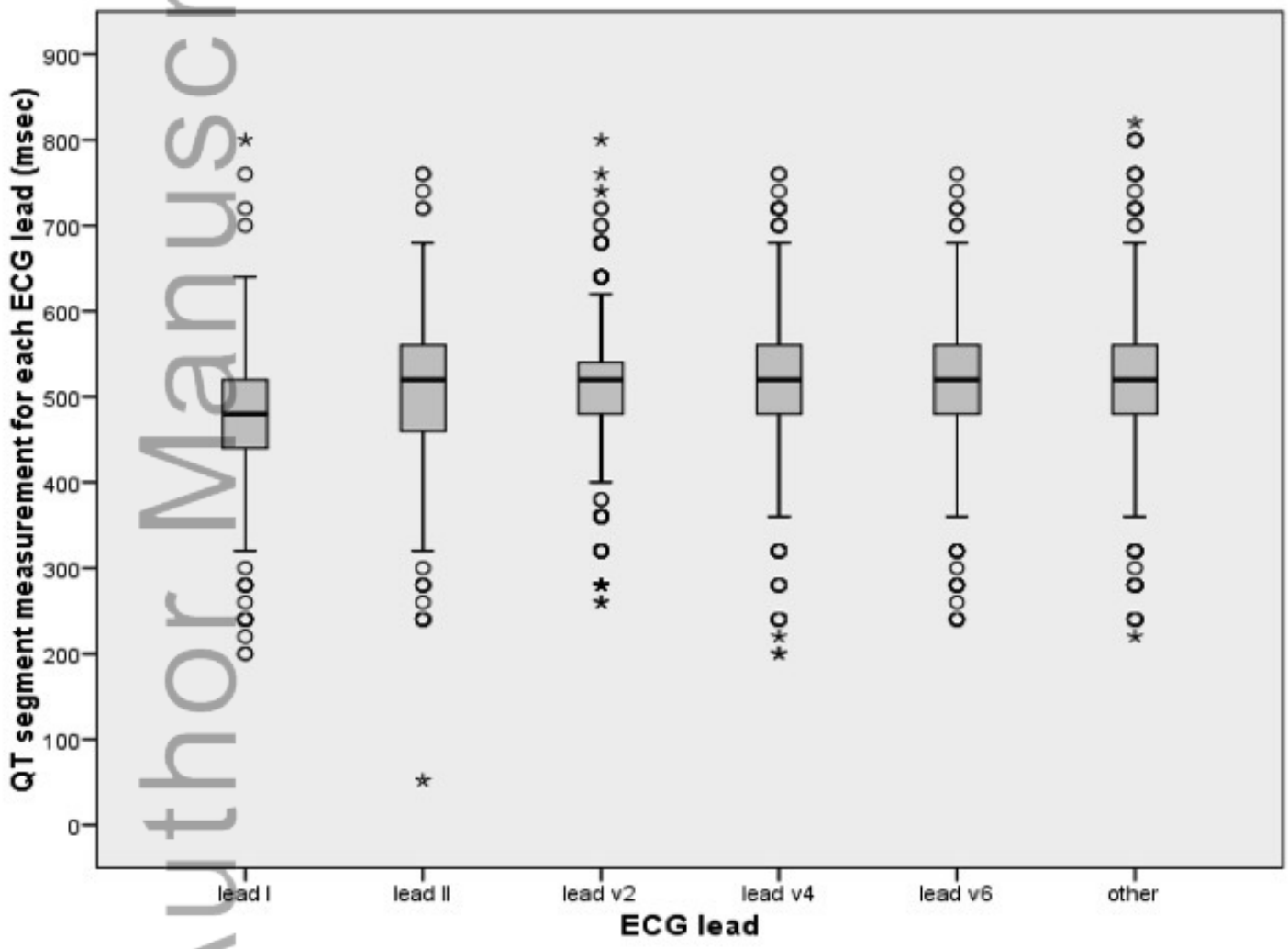

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Figure 4. Range of median measurements for each doctor with median and interquartile ranges

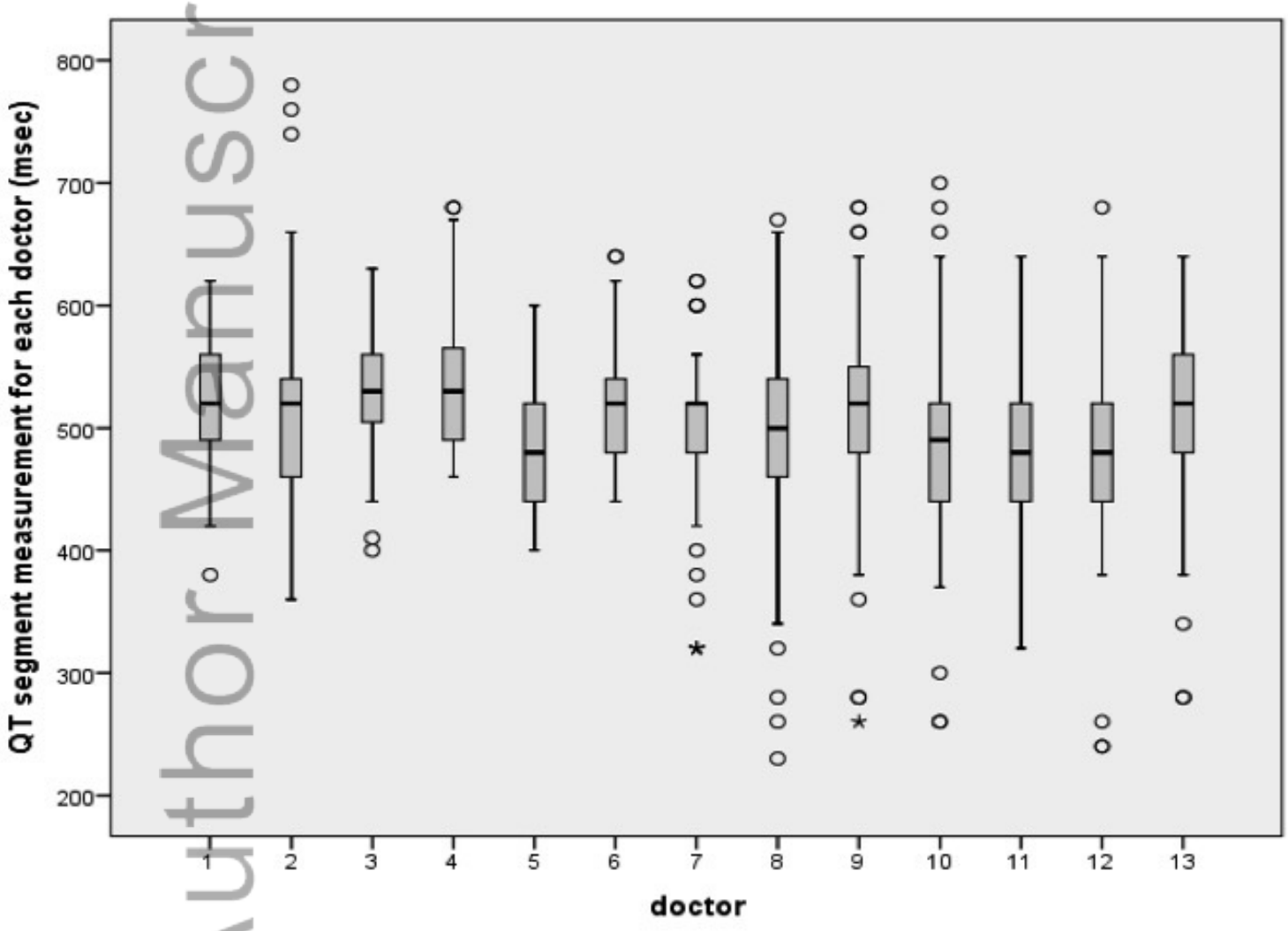

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Table 1. Agreement between each doctor's median gold standard QT interval measurements and the four modality measurements

Modality[†]	Agreement[‡] n (%)	Disagreement n (%)	p value[§]
Facsimile	156 (80.0)	39 (20.0)	
iPhone	161 (82.6)	34 (17.4)	
iPad	137 (70.3)	58 (29.7)	0.02
Computer	154 (79.0)	41 (21.0)	

[†]For each modality, there were 195 QT interval measurements (13 doctors x 15 ECGs)
[‡]Modality and gold standard QT interval measurements ≤40msec
[§]Comparing the proportions of agreements across the four modalities

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Table 2. Median (IQR) QT interval measurements (msec) for each lead and for each modality

ECG Lead	Bedside	Facsimile	iPhone	iPad	17' monitor	p*
I	480 (80)	480 (80)	480 (80)	480 (80)	480 (80)	0.44
II	520 (80)	520 (80)	520 (100)	520 (100)	520 (80)	0.31
V2	520 (80)	520 (80)	520 (40)	520 (60)	520 (40)	0.70
V4	520 (80)	520 (80)	520 (80)	520 (40)	520 (80)	0.41
V6	520 (100)	520 (80)	520 (80)	520 (80)	520 (80)	0.46

*Kruskal-Wallis test

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Figures and Tables

Figure 1. Participant recruitment and data collection

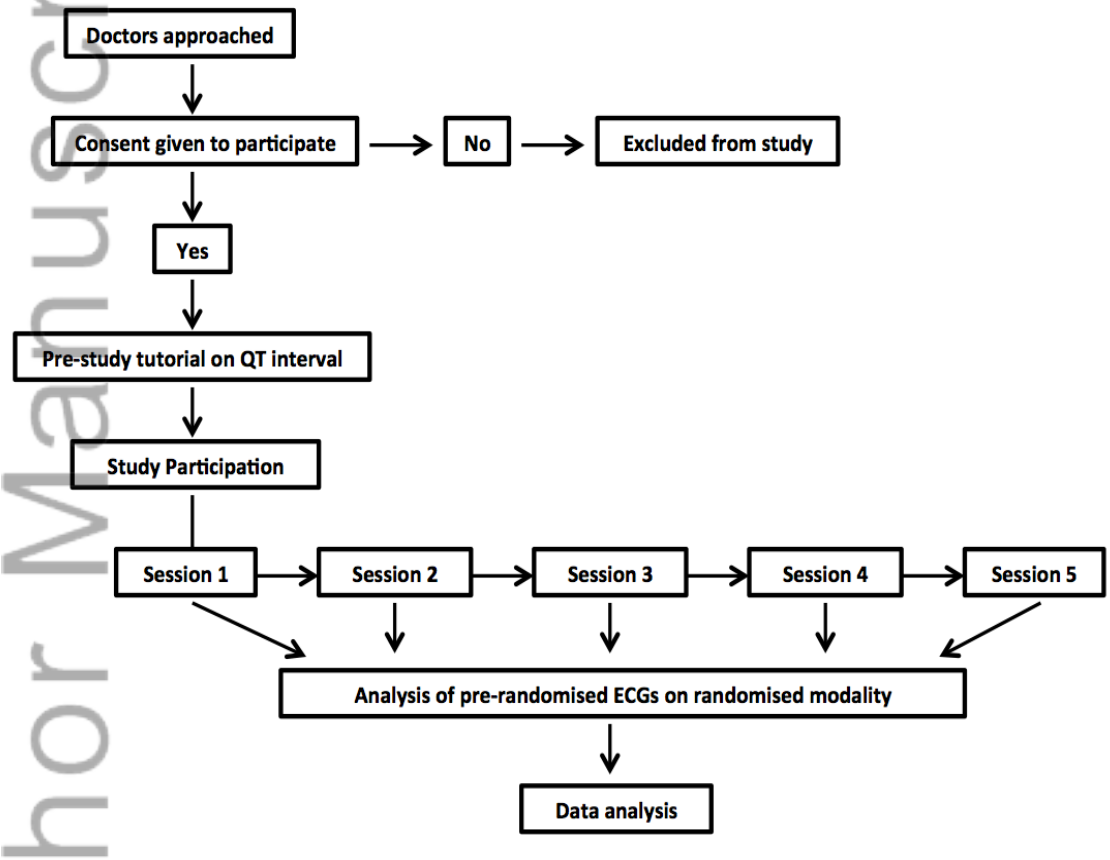
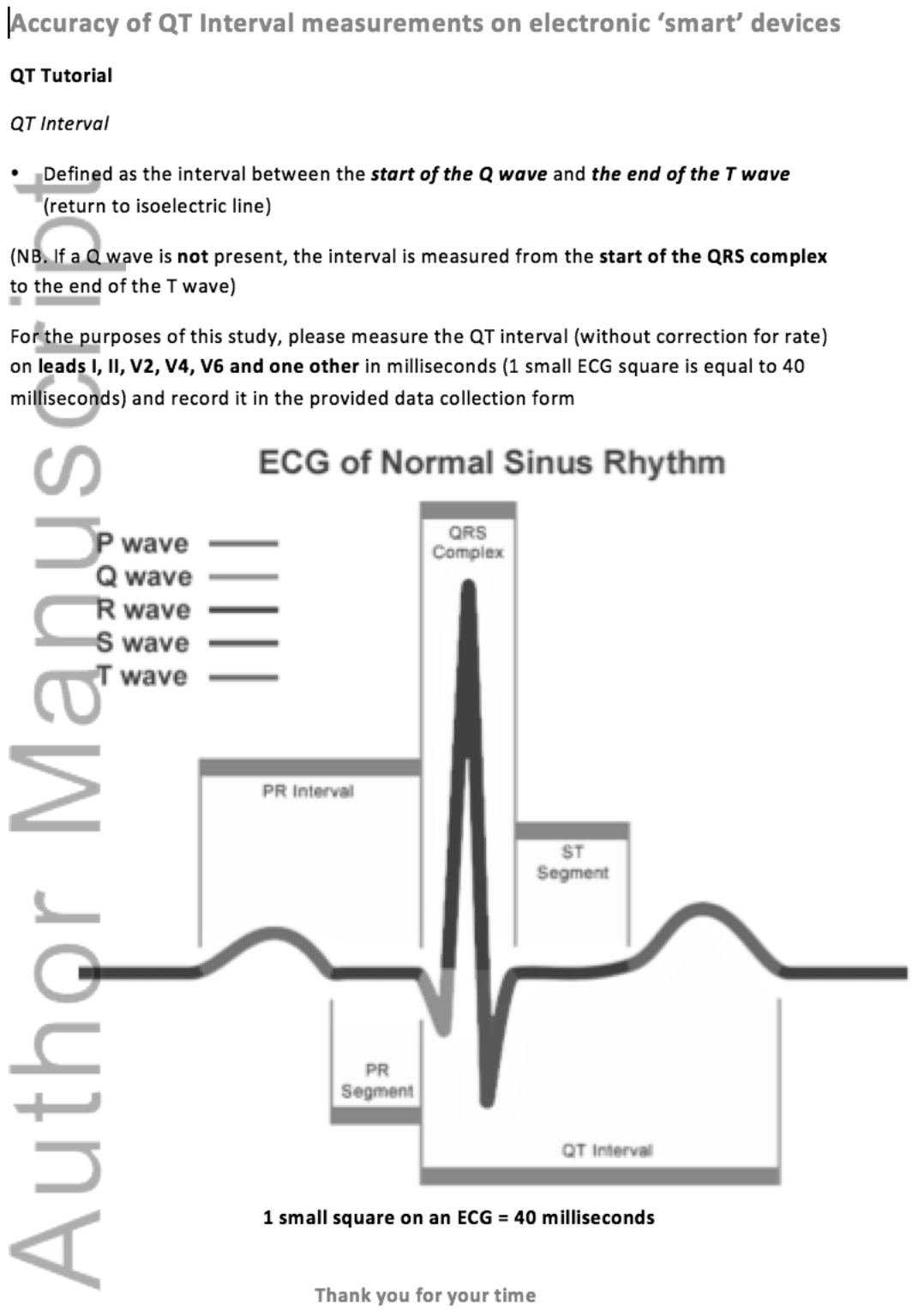


Figure 2. Material used for the QT interval measurement tutorial



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Thank you for your time

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*Kruskal-Wallis test

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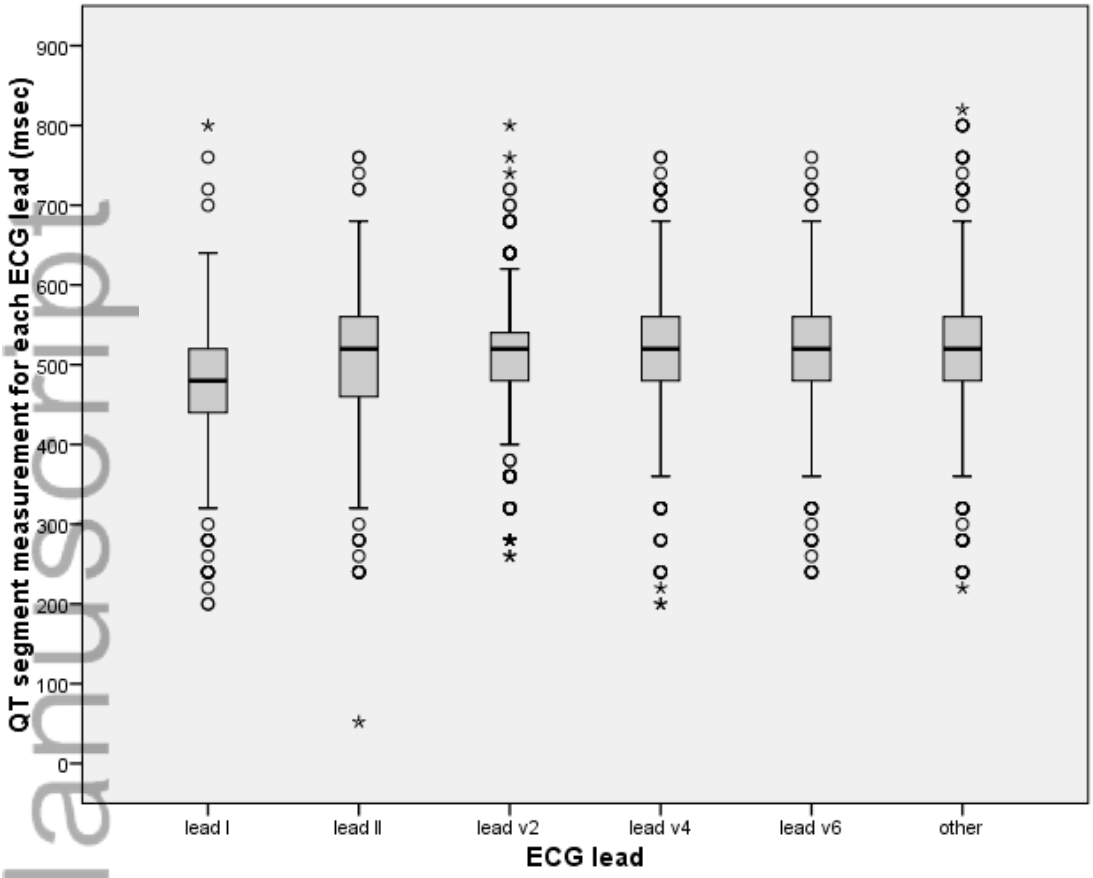

Figure 4. Range of median measurements for each doctor with median and interquartile ranges