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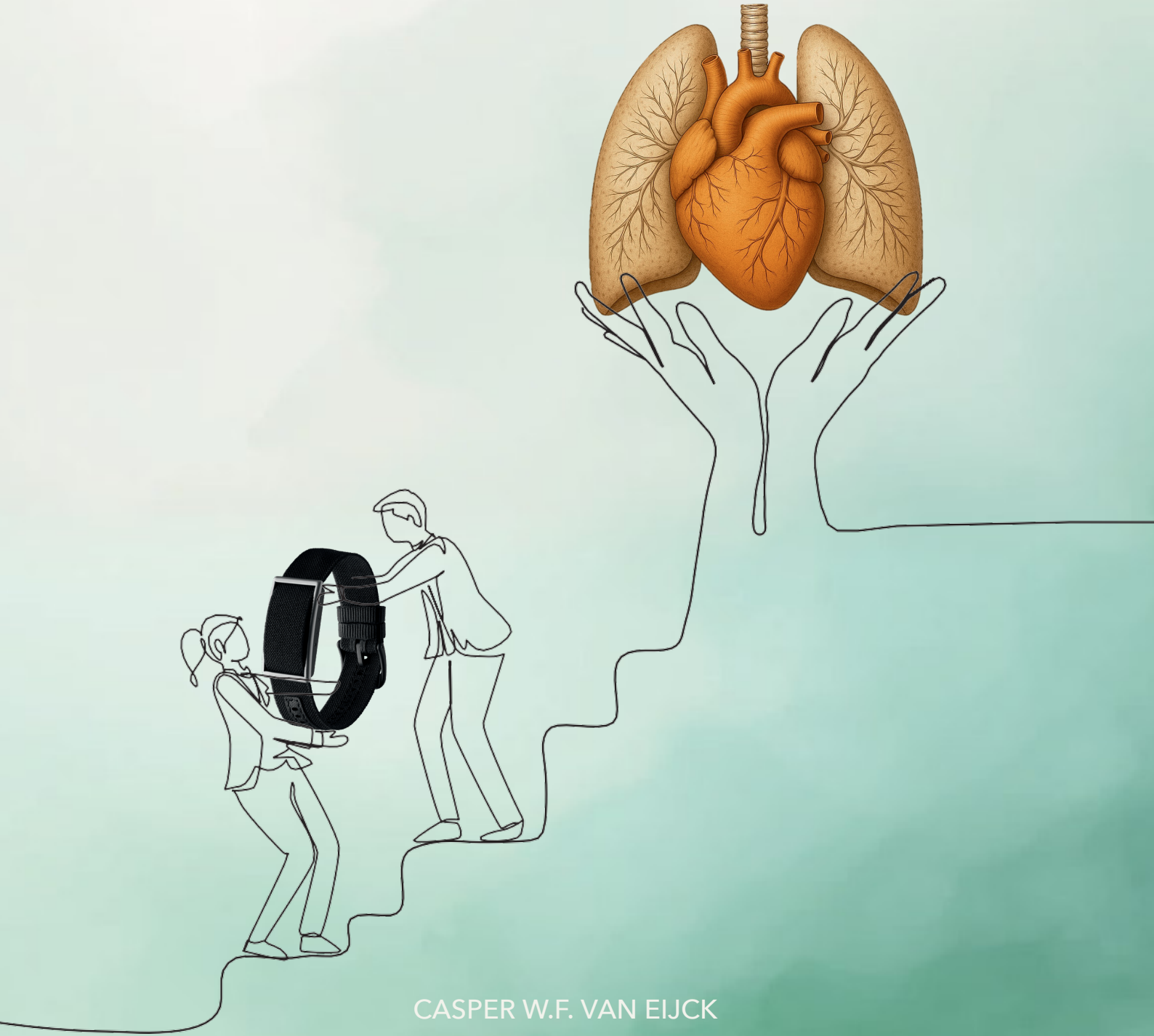

CASPER W.F. VAN EIJCK

INNOVATE TO ELEVATE CARDIAC SURVEILLANCE IN ONCOLOGY CARE

CLINICAL EVALUATION OF A WEARABLE ECG IN TKI-TREATED NSCLC PATIENTS

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VOORWOORD (PREFACE)

Deze thesis is het tastbare eindresultaat van mijn bijzondere traject als student BSc Klinische Technologie & MSc Technical Medicine, een reis die begon met veel nieuwsgierigheid en enthousiasme, maar ook met twijfel. Niet omdat het vakgebied me niet aansprak, maar juist omdat het vakgebied nog relatief jong is, met een beperkte zichtbaarheid in de kliniek en geen concreet vervolg pad. Een toekomstbeeld als klinisch technoloog vond en vind ik moeilijk om voor te stellen.

Mijn bachelor jaren verliepen voorspoedig en boden ruimte voor het studentenleven in Delft, waardoor ik uiteindelijk 3,5 jaar over de bachelor deed in plaats van 3. Aan het einde van mijn eerste masterjaar, waarin we voortbouwden op de medische en technische kennis uit de bachelor, brak de COVID-pandemie uit. Dat leidde tot een periode van onzekerheid, want we konden niet starten aan onze KT-schappen in ons tweede masterjaar. In plaats daarvan begon ik met remote onderzoek op de afdeling Tumor Immunopathologie. Al snel merkte ik dat onderzoek goed aansloot bij de achtergrond van een klinisch technoloog: het combineren van medische inhoud met technische en analytische inzichten. In die periode publiceerde ik zelfs mijn eerste artikel.

Toen ik na deze periode eindelijk mocht starten aan mijn tweede klinische stage, begon ik te twijfelen: 'waarom wil ik geen arts worden?'. Die twijfel leidde ertoe dat ik me aanmeldde voor de premaster Geneeskunde. Ik werd toegelaten en mocht een jaar later starten met mijn coschappen. Precies op dat moment kreeg ik de kans voor een promotietraject, immunotherapie bij alvleesklierkanker, in een oncologisch instituut in Madrid. Hier kon ik verder bouwen aan het onderzoek dat ik in het Erasmus MC was gestart.

Na een periode van 1,5 jaar in Madrid keerde ik terug om mijn coschappen Geneeskunde te hervatten en tegelijkertijd, op een lager pitje, mijn promotieonderzoek in het Erasmus MC af te ronden. Tijdens mijn coschap interne geneeskunde stak de twijfel opnieuw de kop op. Lange tijd had ik gedacht dat ik arts moest worden om écht impact te kunnen maken, maar ik realiseerde me dat dit idee mede was gevormd door de beperkingen en onzekerheden van de COVID-periode. Tijdens mijn promotieonderzoek had ik juist de meerwaarde van de Klinisch Technoloog leren kennen en waarderen. Ik ondervond dat Klinisch Technologen bij uitstek geschikt zijn voor translationeel onderzoek, dankzij hun unieke combinatie van klinische en technische expertise, gekoppeld aan vaardigheden in programmeren, visualisatie, en fysiologie.

Na veel wikken en wegen besloot ik mijn MSc Technical Medicine alsnog af te ronden, een keuze waar ik nog altijd blij mee ben. Zoals gezegd, vormt deze thesis het tastbare eindresultaat van dat besluit. Het schrijven ervan was voor mij bijzonder, niet alleen vanwege de weg die eraan voorafging, maar ook omdat ik deze keer schreef als gepromoveerde onderzoeker. Ik legde de lat hoog voor, misschien soms té hoog. Maar daarnaast heb ik in het afgelopen jaar talloze keren moeten uitleggen hoe het mogelijk was dat ik een PhD had maar geen masterdiploma. Ik ben blij dat ik die vraag komende tijd niet opnieuw hoef te beantwoorden.

Alles bij elkaar was het een ongebruikelijk pad en wat mijn volgende stap wordt, weet ik nog niet. Ik ben iniedergeval dankbaar dat ik mezelf nu Klinisch Technoloog mag noemen, of Technische Geneeskundige, of Technical Physician, of 'een soort technische dokter.' Dat er meerdere benamingen zijn, geeft mooi weer hoe nieuw maar ook onbekend het vakgebied is.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AI	Artificial Intelligence
ANOVA	Analysis of Variance
BMI	Body Mass Index
bpm	beats per minute
CR	Coefficient of Repeatability
CSV	Comma-Separated Values
CV	Coefficient of Variation
EMC	Erasmus MC
EPD	Electronic Patient Dossier
HR	Heart Rate
HR	Heart Rate Variability
ICCs	Intraclass Correlation Coefficients
IQR	Interquartile Ranges
MEANS	Modular ECG Analysis System
NPV	Negative Predictive Value
NSCLC	Non-Small Cell Lung Cancer
OS	Overall Survival
PPV	Positive Predictive Value
QTc	corrected QT
R	Pearson's correlation coefficient
RR	Respiratory Rate
SA	Sinoatrial
SCLC	Small Cell Lung Cancer
SD	Standard Deviations
SpO_2	Oxygen Saturation
SQI	Signal Quality Index
TKI	Tyrosine Kinase Inhibitor
TM	Technical Medicine
κ	Cohen's kappa coefficient
ρ	Spearman's rank correlation coefficient

SUMMARY

Introduction: Osimertinib and alectinib are tyrosine kinase inhibitors (TKIs) used for EGFR- and ALK-mutated non-small cell lung cancer (NSCLC), respectively. While these agents have substantially improved survival in early-stage and metastatic settings, they are associated with clinically relevant cardiac toxicities, QTc prolongation for osimertinib and sinus bradycardia for alectinib. Current guidelines recommend electrocardiographic (ECG) monitoring, yet conventional 12-lead ECGs are impractical for frequent use in ambulatory oncology care. Medically regulated single-lead wearable ECG devices offer a promising alternative for real-time, patient-friendly rhythm surveillance.

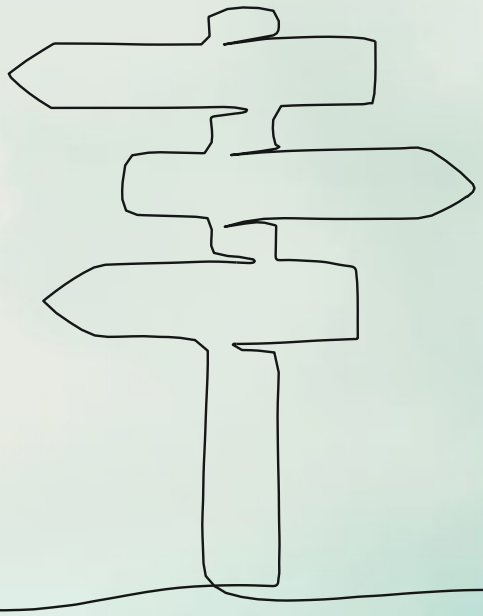
Objectives: This thesis aimed to evaluate the clinical performance, reproducibility, and diagnostic concordance of the single-lead ECG function of the Corsano CardioWatch in NSCLC patients treated with TKIs. Specifically, intra-device reproducibility, intra-device agreement with conventional 12-lead ECGs, and diagnostic classification.

Methods: This study was part of the prospective, non-WMO MOVIS-RESP trial conducted at Erasmus MC, including NSCLC patients treated with osimertinib (n = 39) or alectinib (n = 32). Each patient received three consecutive single-lead ECGs with the Corsano CardioWatch and one conventional 12-lead ECG. Reproducibility of ECG parameters was assessed using coefficients of variation (CV), repeated measures analysis, and intra-class correlation coefficients (ICCs). Agreement between devices was evaluated using Bland–Altman plots, ICCs, and correlation analyses. Diagnostic performance was determined via conventional metrics.

Results: Of 213 Corsano ECGs, 96% met signal quality thresholds. Corsano parameter reproducibility was 'excellent' for HR, RR, and QTc (ICCs ≥ 0.91), 'good' for QT and PR (ICCs 0.78–0.82), and 'moderate' for QRS duration (ICC 0.63). Corsano with EMC ECG agreement was 'excellent' for HR and QTc (ICCs ≥ 0.85), 'good' for QT and RR (ICCs ~0.80), 'poor-to-moderate' for PR and QRS (ICCs ≤ 0.47). Bland–Altman analysis showed 'low' bias for HR, RR, and QT intervals and wider limits of agreement for PR and QRS durations. The CardioWatch accurately classified rhythm abnormalities, achieving 97% overall accuracy and $\kappa = 0.93$ for detecting total abnormal rhythms. Sinus bradycardia ($\kappa = 0.94$) and abnormal sinus rhythm ($\kappa = 0.88$) were reliably detected.

Discussion: The Corsano CardioWatch was well tolerated and enabled rapid ECG acquisition in seated patients, which benefits those with mobility impairments. Its integrated digital platform supported stable data transmission and clinician access. While wearable ECGs are economically favourable and patient-preferred, concerns remain regarding potential false positives, digital literacy, and algorithm transparency. Transitioning to home use introduces further considerations, including adherence, remote triage protocols, and device accessibility. Structured onboarding, patient support, and robust telecardiology systems will be essential for safe deployment.

Conclusion: The Corsano CardioWatch showed strong intra-device parameter reproducibility and high diagnostic concordance for common arrhythmias. Agreement with 12-lead ECGs was excellent for HR and QTc but limited for PR and QRS intervals, aligning with known constraints of single-lead ECGs. The device shows promise as a user-friendly, medically regulated tool for remote ECG monitoring in oncology. Future studies should assess long-term performance in unsupervised, home-based contexts and determine clinical impact on patient safety, treatment continuity, and healthcare resources.



THESIS OBJECTIVES

This thesis aims to evaluate the reproducibility, diagnostic accuracy, and clinical usability of the single-lead ECG functionality of the Corsano CardioWatch 287-2 in patients with NSCLC receiving osimertinib and alectinib TKI treatment. To this end, a prospective, single-centre, non-WMO feasibility study was designed and conducted in a real-world outpatient setting. The findings may inform the integration of wearable ECG monitoring into standard oncological care to facilitate earlier detection and treatment for TKI-induced cardiotoxicities.

Technical Analysis Components

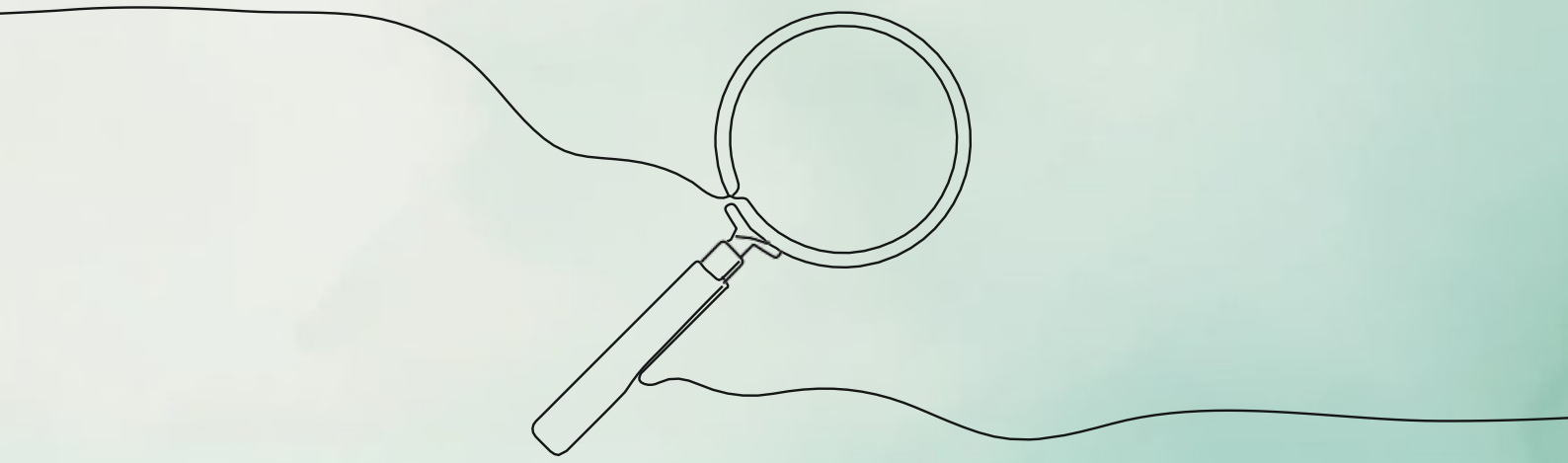
1. Intra-device reproducibility: evaluated across three consecutive Corsano ECG recordings per patient using standard signal quality criteria and test–retest variability measures.
2. Inter-device agreement: evaluated by comparing key rhythm-related ECG parameters (heart rate, RR, PR, QRS, QT, and QTc intervals) between Corsano and conventional EMC ECGs.
3. Rhythm diagnosis concordance: determined by comparing Corsano-based rhythm classifications with those validated by clinicians using EMC ECGs.
4. Impact of clinical characteristics: explored through analyses of how patient factors such as age, BMI, skin type, and forearm hair density influence discrepancies between the two devices.

Clinical Activity Components

The clinical components of this thesis were conducted at the outpatient clinics of Prof. Dingemans and Dr. Paats. As part of the Erasmus MC (EMC) team, I engaged in ethical compliance, patient inclusion, data collection, and communication responsibilities.

These activities contributed to the successful execution of the ECG substudy in the MOVIS-RESP trial:

- *Regulatory and Ethical Procedures*; I prepared and submitted the METC protocol for ethical review and managed subsequent revisions based on committee feedback. I adhered to ethical standards, informed consent, and data confidentiality throughout the study.
- *Patient Recruitment and ECG Acquisition*; Eligible patients were contacted before their outpatient visit to provide information, address concerns, and confirm participation. I obtained written informed consent and guided patients through the study procedures, including three consecutive Corsano ECG recordings per protocol. Post-inclusion, I conducted follow-up calls to address patient questions if needed.
- *Data Collection and Management*; Clinical and ECG data were entered and securely managed in Castor, ensuring structured and standardised collection. I also extracted relevant data from the EPD to facilitate harmonised comparisons with 12-lead ECG outputs.
- *Professional Development and Clinical Familiarisation*: Through direct patient interaction and coordination of study logistics, I developed clinical professionalism and communication skills. I became familiar with patient care pathways and gained insights into outpatient workflows.
- *Research Presentation and Communication*: I delivered two research presentations: an initiation session outlining the study objectives and methodology, and a final presentation communicating the study findings and their clinical relevance to the department



1 INTRODUCTION

1.1 Lung Cancer and Therapy

1.1a Epidemiology and Non-Small Cell Lung Cancer Staging

Lung cancer remains a major contributor to cancer-related morbidity and mortality worldwide. In the Netherlands, around 14,500 new cases are diagnosed annually, making it the third most common cancer by incidence[1]. Strongly linked to smoking behaviours from two to three decades earlier, its prevalence among women is rising due to slower reductions in smoking rates. As a result, female lung cancer cases are expected to increase from 6,532 in 2019 to 8,500 by 2032, while male cases may rise from 7,805 to over 8,100, with most growth projected in those aged ≥75 years[2].

Non-small cell lung cancer (NSCLC) constitutes approximately 69% of all cases, while small cell lung cancer (SCLC) accounts for 12%. The remainder consists of unclassified cases, often due to diagnostic limitations in advanced disease[2]. Prognosis and treatment strongly depend on the stage at diagnosis. For stage I NSCLC (28% of cases), five-year overall survival (OS) reaches 71% following surgery and 41% after stereotactic radiotherapy[3,4]. In stage II (1%), standard surgical resection followed by adjuvant chemotherapy results in an estimated five-year OS of 58%[5,6]. For stage III (24%), standard chemoradiotherapy achieves a five-year OS of around 30%, though immunotherapy has improved three-year OS from 40% to 48% since 2018[6].

Nevertheless, 49% of patients are diagnosed with stage IV disease due to the frequently asymptomatic nature of early-stage NSCLC[1]. At stage IV, patients have metastasised, and the five-year OS is approximately 7%[2]. The most common metastases are found in the bone (41%), lung (29%), and pleura (84%), with 54% of patients exhibiting multi-organ involvement[1,7].

1.1b Molecular Mutation Testing and Targeted Therapy

In stage IV NSCLC, molecular profiling guides therapy by identifying actionable driver mutations. Molecular testing is performed in over 90% of stage IV MSCLC adenocarcinoma cases[8]. KRAS (38%), EGFR (11%), and BRAF (4%) mutations are most prevalent, while 32% lack detectable alterations[8]. Targeted therapies, mainly tyrosine kinase inhibitors (TKIs), have improved survival in patients with actionable mutations[2,9-14]. The median OS for patients with EGFR, ALK, and BRAF mutant disease is 23, 48, and 19 months, respectively, accompanied by five-year OS rates of 11%, 46%, and 22%[8,10,15]. Yet, only 59% of eligible patients receive targeted therapy[8]. For mutation-negative NSCLC, treatment options have evolved significantly since the introduction of immunotherapy in 2019[16].

Osimertinib is a third-generation TKI approved for early and advanced stages of EGFR-mutated NSCLC. In resected stages Ib–IIIa, the ADAURA trial demonstrated an 88% five-year OS with osimertinib versus 78% with placebo[13]. In metastatic disease, the FLAURA trial showed that first-line osimertinib extended median OS to 39 months compared to 32 months with earlier-generation EGFR-TKIs[10].

Alectinib, a second-generation TKI, is similarly approved in early-stage and advanced-stage ALK-mutated NSCLC. In resected stages Ib–IIIa, the ALINA trial showed that adjuvant alectinib significantly prolonged disease-free survival compared to platinum-based chemotherapy, with a two-year DFS

rate of 94% versus 63%[14]. In metastatic settings, the ALEX trial showed alectinib extended median progression-free survival to 35 months versus 11 months for crizotinib, with a five-year OS of 63% versus 46%[2].

1.2 Cardiotoxicity of Tyrosine Kinase Inhibitors

Despite therapeutic efficacy, osimertinib and alectinib can cause clinically relevant cardiac adverse events. QT interval prolongation is a known complication of osimertinib compared to other EGFR-TKIs. In a retrospective analysis, the FDA Adverse Event Reporting System reported QT interval prolongation in 1.3% of patients, with a median onset of 23 days[16]. Clinical trials further reported corrected QT (QTc) interval prolongation in 2.4–22% of osimertinib-treated patients, with some cases progressing to ventricular arrhythmias, including ventricular fibrillation[17,18]. Although often asymptomatic, QTc interval prolongation may evolve into life-threatening arrhythmias like Torsade de Pointes, necessitating treatment discontinuation and urgent clinical intervention[19]. Preclinical models suggest that osimertinib may exert pro-arrhythmic effects by inhibiting cardiac ion channels, including hERG, Nav1.5, and L-type Ca^{2+}, thereby disrupting ventricular repolarisation[20].

Alectinib is primarily associated with sinus bradycardia. A retrospective cohort study of 93 patients showed a 51% incidence of bradycardia, with mean heart rate (HR) decreasing from 78 to 65 beats per minute (bpm)[21]. Clinical trials have reported all-grade bradycardia in 1–6% of patients, most reversible upon dose reduction or temporary discontinuation[18,21]. QTc interval prolongation during alectinib is less common, reported in 3% of patients, with grade 3–4 events reported in 2%[18].

1.3 Technical Background on Electrocardiograms

Electrocardiography is a non-invasive method for assessing cardiac electrical activity. Signal quality depends on electrode positioning, contact integrity, and filtering algorithms. Modern systems use various filters (e.g. high-pass, low-pass, and notch filters) to suppress artefacts caused by motion, muscle activity, or electrical interference. For instance, a high-pass filter with a cutoff frequency around 0.5 Hz reduces baseline drift, while a notch filter at 50 or 60 Hz suppresses powerline interference. Real-time QRS detection is enhanced by algorithms like Pan–Tompkins by improving signal clarity and reducing noise[22].

A 12-lead electrocardiogram (ECG) device, the clinical gold standard, uses ten electrodes placed on the limbs and chest to capture twelve vectors of cardiac activity, enabling detailed diagnosis of arrhythmias, ischaemia, and infarction. In contrast, single-lead ECG systems monitor cardiac activity using two electrodes to monitor a single vector. While these systems are less suited for diagnosing complex conditions that require spatial resolution, such as ST-segment elevation myocardial infarction, they can reliably detect rhythm disturbances such as bradycardia, tachycardia, and QT abnormalities[23,24].

1.4 Remote ECG Monitoring in TKI Therapy

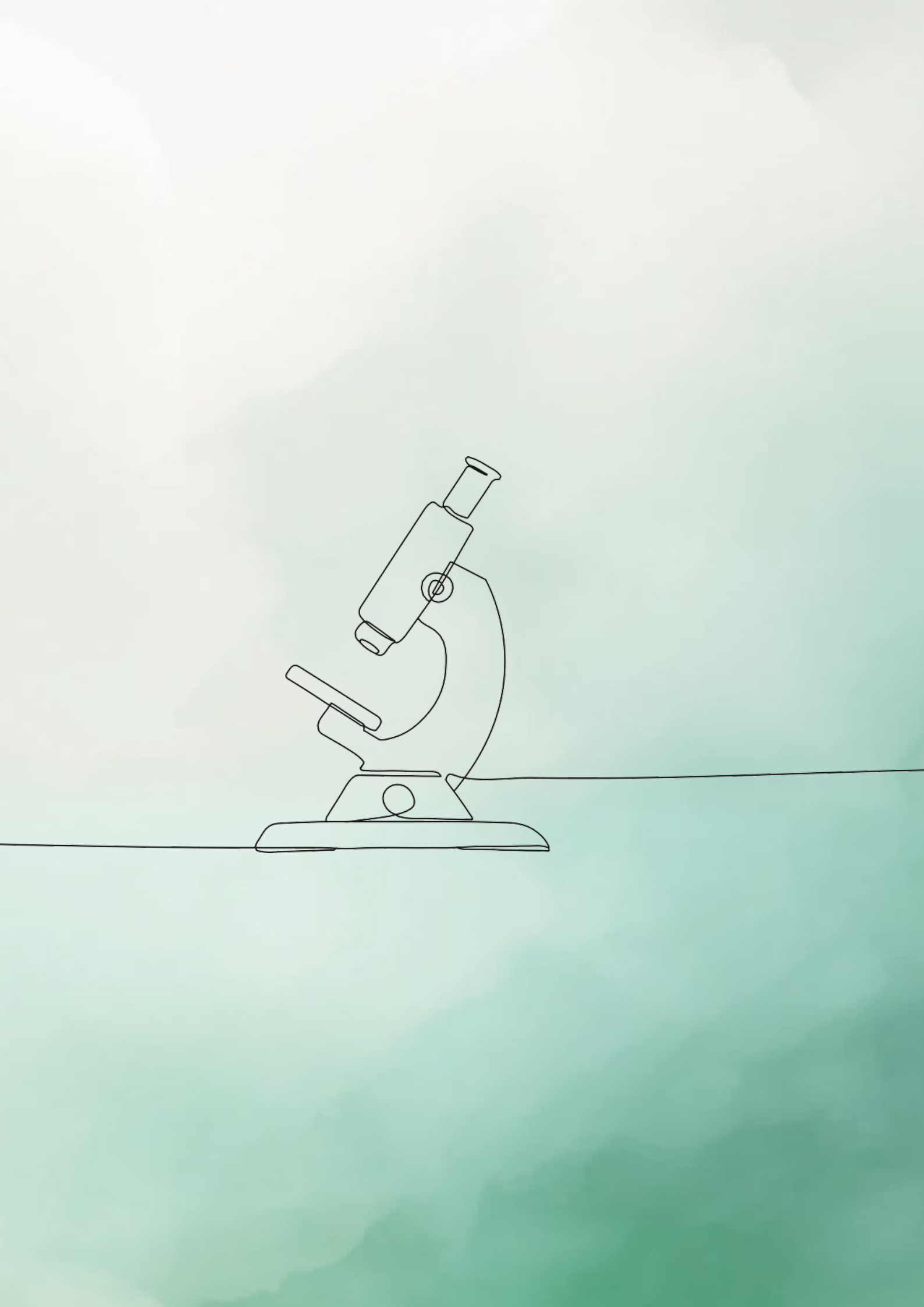
1.4a Clinical Rationale

Given the cardiotoxic risks of osimertinib and alectinib, continuous ECG monitoring is advised. However, conventional 12-lead ECGs are impractical for routine use in oncology. These recordings

are resource-intensive, time-consuming, and episodic, providing only momentary snapshots of cardiac activity. Single-lead wearable ECGs offer a feasible alternative, enabling continuous rhythm surveillance. These devices enable early arrhythmia detection, such as QT(c) interval prolongation and bradycardia, that may go unnoticed between standard hospital-based assessments. This approach can enhance patient safety, enable timely interventions, and reduce the burden on patients and healthcare providers[24]. Although osimertinib and alectinib affect cardiac electrophysiology via different mechanisms, ventricular repolarisation and the sinoatrial node, both medications can result in clinically relevant arrhythmias. The shared need for ECG-based cardiac surveillance during TKI therapy justifies their combined inclusion in this thesis. Stratified analyses will ensure drug-specific interpretation of outcomes.

1.4b ECG Monitoring Using the Corsano CardioWatch Wearable

The Corsano CardioWatch is a CE-MDR and FDA-certified medical-grade wearable designed for continuous vital sign monitoring. In addition to a single-lead ECG feature, it captures HR, heart rate variability (HRV), respiratory rate (RR), oxygen saturation (SpO_2), temperature, and physical activity[25-32]. Unlike consumer-grade wearables, the CardioWatch is classified as a medical device, ensuring secure data handling, high signal fidelity, and compatibility with electronic patient dossier (EPD). Its ECG feature complies with EN-IEC 60601-2-47:2015, the harmonised safety standard for ambulatory ECG systems[33]. While the device has been technically validated for signal acquisition and parameter output, its parameter consistency, clinical accuracy and practical usability in a real-world clinical setting have not yet been established.



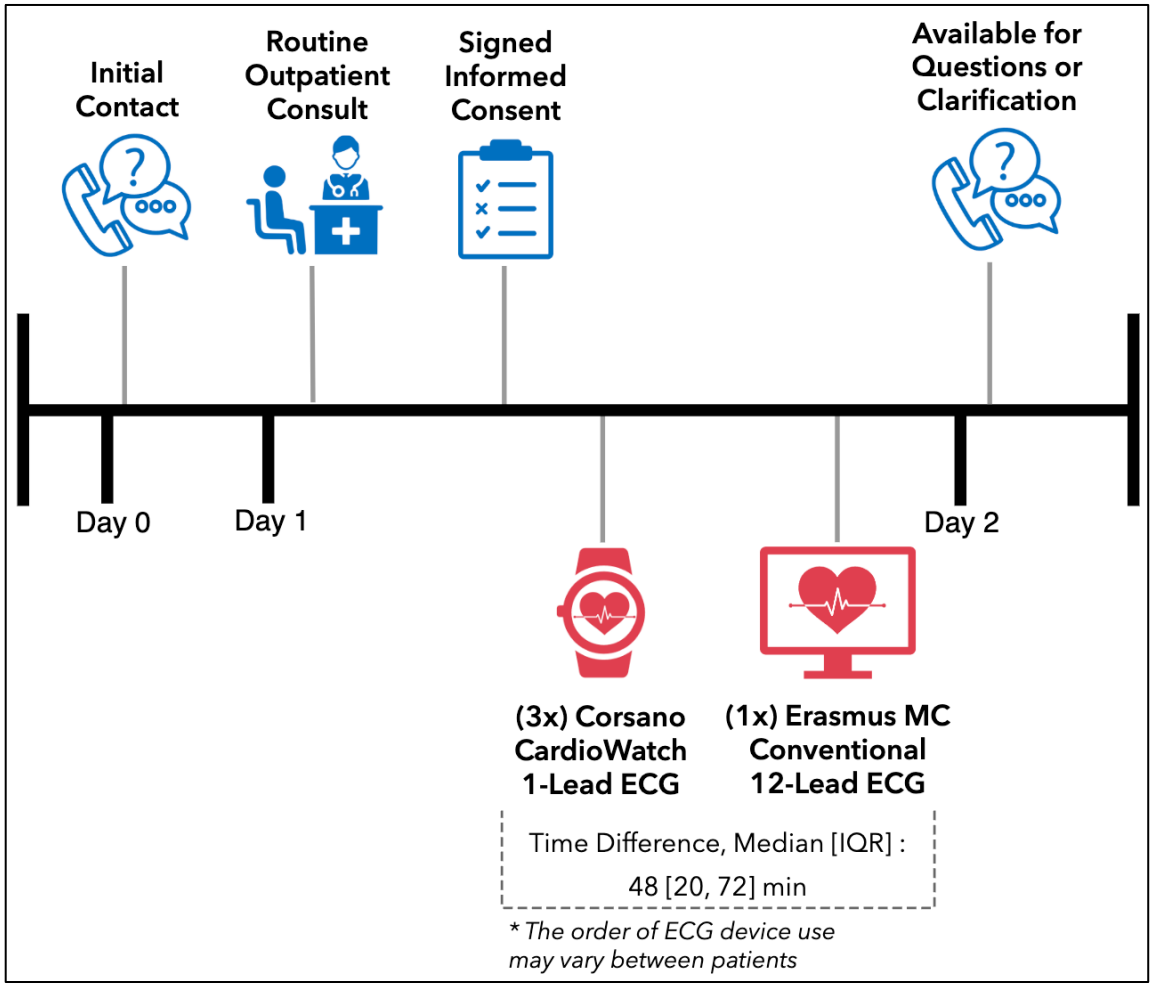
2 MATERIALS AND METHODS

2.1 Study Design

2.1a Study Procedures

This thesis included data from the prospective, non-WMO feasibility MOVIS-RESP trial (METC-2024-0524) conducted at the Department of Pulmonary Medicine, Erasmus MC, Rotterdam, The Netherlands. The inclusion period extended from 18 February to 24 March 2025. All study procedures were integrated into routine clinic care, and the additional burden to participants was minimal. Each patient underwent three consecutive single-lead ECG recordings using the Corsano CardioWatch 287-2 and one conventional 12-lead ECG using the ACTA GNOSIS IV ECG recorder (Esaote Biomedical, Florence, Italy) of the Erasmus MC. These are hereafter referred to as the 'Corsano ECG' and the 'EMC ECG', respectively. All recordings were scheduled within 90 minutes to minimise temporal (physiological) variability due to circadian or activity-related influences. Diagnostic feedback was given to patients exclusively by specialised medical doctors after examining the gold-standard EMC ECG. A detailed overview of the study protocol and ECG acquisition is provided in **Figure 1**.

Figure 1. *Overview of The Study Protocol and ECG Timepoints.*



Abbreviations: ECG, Electrocardiogram; IQR, Interquartile Range.

2.1b Patient Population

Eligible participants were adults aged 18 years or older with a histologically confirmed diagnosis of NSCLC, receiving outpatient treatment with either osimertinib (EGFR-TKI) or alectinib (ALK-TKI). Patients were required to be proficient in Dutch, capable of operating a smartphone, and able to provide written informed consent. Individuals with significant mental or cognitive impairment, inability to wear the Corsano CardioWatch (e.g. due to skin damage, amputation, or allergy), or inability to undergo blood pressure measurement via cuff (e.g. due to lymphedema or dialysis shunt) were excluded. Pregnant or breastfeeding individuals were also excluded from participation.

2.1c Ethical Considerations

The study was conducted according to the principles of the Declaration of Helsinki and the 'Gedragscode Gezondheidsonderzoek'. Written informed consent was obtained before participation. The MSc Technical Medicine (TM) student informed patients who met the inclusion criteria about the study during routine clinical visits. The TM student explained the study's objectives, procedures, risks, and benefits. Participants received an information sheet and were given sufficient time to consider their decision and ask questions before consenting. Recruitment occurred through invitations during clinical visits. Efforts were made to ensure a diverse study population.

2.1d Handling and Storage of Data

Data from vital signs, demographics, medical history, and medical information are obtained from the EPD of the EMC as part of the standard clinical routine. All data from EMC's EPD will be stored in Castor, a validated, secure data management system. Additional vital sign data will be collected using the Corsano CardioWatch specifically for this trial. Data obtained using the Corsano CardioWatch will be stored in the Castor data management system and the CardioWatch cloud, compliant with HIPAA, GDPR, FDA 21 CFR part 11, ISO 13485, and ISO 27001 standards. More details are in the CardioWatch System Security Overview[34]. Following EMC guidelines, data will be preserved for ten years after collection.

2.1e Privacy Protection

Data was handled confidentially. Each patient received an anonymous identification code (i.e., study number). A subject identification code list could trace data back to individual patients, and the Principal Investigator of the EMC safeguarded the key to this code. Handling personal data complied with the Dutch Personal Data. If third parties request to conduct translational analysis both within and outside the European Union, the Principal Investigator shall agree with these parties, ensuring that data and/or samples are managed following EU legislation.

2.2 Electrocardiography Devices

2.2a Reference Standard: Erasmus MC 12-Lead ECG

The standard reference ECG was recorded using the conventional 12-lead ACTA GNOSIS IV ECG recorder. Recordings were acquired for ten seconds under resting conditions in the supine position and performed by trained clinical personnel following institutional protocols[35,36]. The 12-lead system uses ten surface electrodes to provide a spatially comprehensive assessment of cardiac electrical activity, enabling detailed interval measurement and rhythm classification.

2.2b Investigational Device: Corsano CardioWatch Single-Lead ECG

The Corsano CardioWatch 287-2 is a CE-MDR and FDA-certified wearable medical device designed for ambulatory physiological monitoring, including single-lead ECG (**Figure 2**). The device complies with the EN-IEC 60601-2-47:2015 standard governing the safety and performance of ambulatory ECG systems[33]. Data are synchronised via the Corsano Trials smartphone application and uploaded to the Corsano Cloud Platform, compliant with HIPAA, GDPR, FDA 21 CFR part 11, ISO 13485, and ISO 27001 standards[34]. Subsequently, all data are stored in Castor, a validated and secure data management system used at EMC. A detailed technical description of the device is provided in **Supplementary File 1**.

ECG signal acquisition with the Corsano CardioWatch relies on a three-electrode configuration for user comfort and reliable signal capture. Two dry-contact electrodes are embedded on the underside of the device casing, acting as the positive and reference electrodes, while a third electrode is integrated into the metallic top frame to serve as the negative electrode. During recording, participants wear the device on one wrist and place the opposite hand on the metal housing, creating a closed-loop circuit across the upper limbs. This arrangement generates a short-duration single-lead ECG tracing, comparable to lead I in a standard 12-lead ECG.

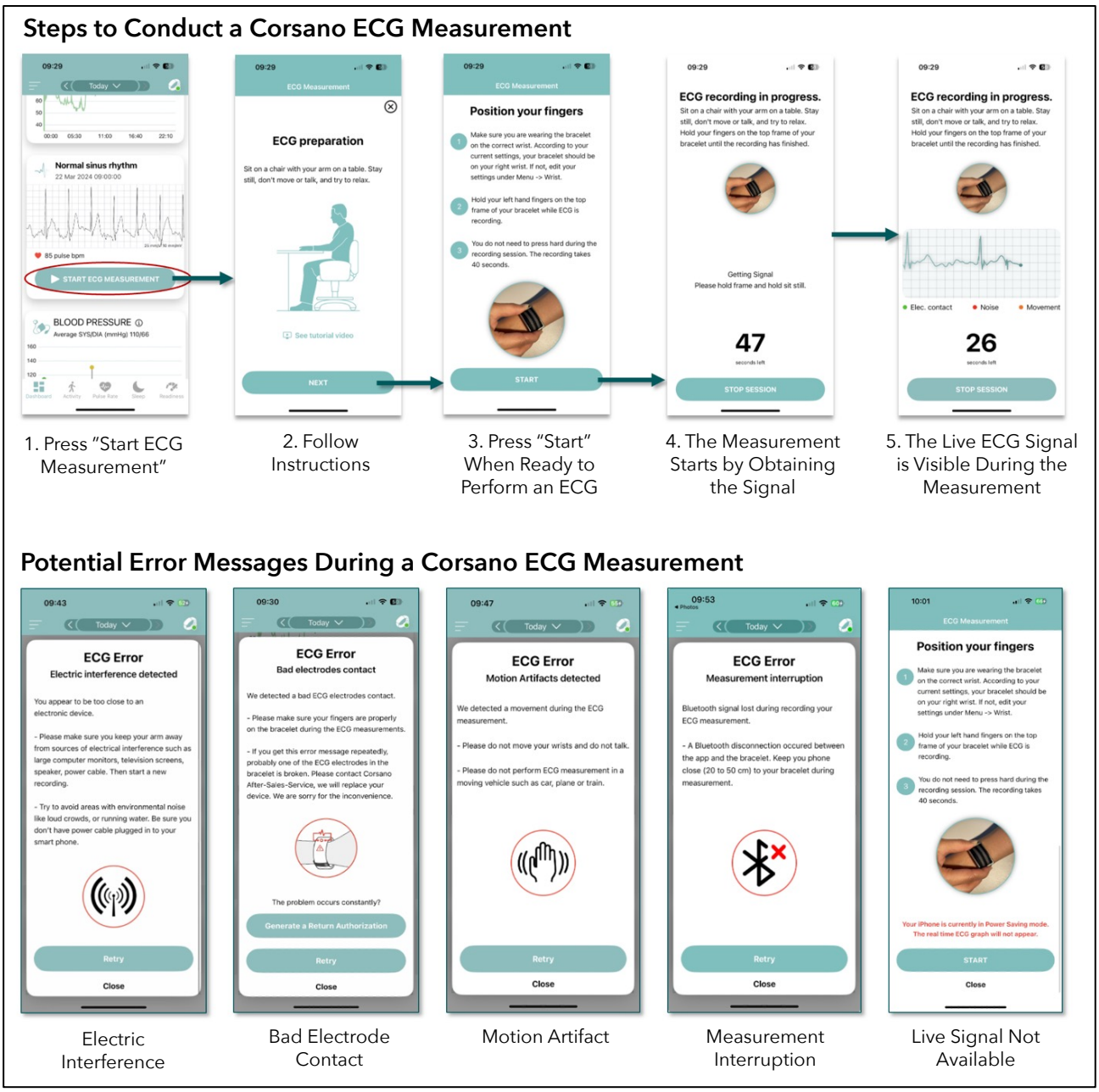
Figure 2. *Overview of The Study Protocol and ECG Acquisition.*

Abbreviations: ECG, Electrocardiogram.

Figure 3 illustrates the procedure for obtaining a Corsano ECG. Recordings were performed under controlled conditions by an MSc Technical Medicine student, who operated the Corsano mobile application to initiate and stop each ECG. Patients were not responsible for device handling or data

collection. Before each recording, the electrode area was slightly moistened to optimise skin contact. Participants were instructed to remain seated, minimise movement, refrain from speaking, and remove metallic jewellery or electronic devices from the upper limbs. Each ECG session lasted approximately one minute. During acquisition, the device occasionally displayed error messages such as 'electrical interference,' 'bad electrode contact,' 'motion artefact,' or 'live signals not available' (**Figure 3**). In such instances, recordings were repeated to ensure adequate signal quality. For each patient, three valid Corsano ECGs were collected before proceeding.

Figure 3. *The Procedure for Obtaining a Corsano ECG and the Possible Error Messages.*



Abbreviations: ECG, Electrocardiogram.

2.3 ECG Data Processing

EMC ECGs were exported in PDF format via the EPD (ChipSoft, The Netherlands). Corsano ECGs were retrieved through the Corsano Cloud Platform, downloaded in structured comma-separated values (CSV) format, and summarised PDF reports. All data were processed using R (version 4.5.0). A unified script was developed to manage the complete ECG pipeline, including importation, variable cleaning, merging, preprocessing, and signal quality control.

2.3a Signal Analysis and Parameter Extraction

EMC ECGs were analysed using the Modular ECG Analysis System (MEANS)[37]. Interval parameters were digitised into a structured dataset. Recordings with incomplete data were excluded. HR was derived from the average RR interval. The RR interval was defined as the time between two QRS complexes. The PR interval was defined as the time from the onset of the P wave to the start of the QRS complex. QRS duration was defined as the time from the beginning to the end of the QRS complex. The QT interval was defined as the time from the start of the QRS complex to the end of the T wave. The QTc Bazett was calculated as $QT / \sqrt{RR}$[38].

A proprietary algorithm of Corsano pre-processed all ECGS using standard filtering techniques, high-pass, low-pass, and notch filters, to minimise baseline drift, muscular artefacts, and powerline interference. Raw signal traces were not available. The proprietary algorithm generated automated measurements for HR, RR, PR, QRS, QT, QTc Bazett, and the signal quality index (SQI) (range 0–100)[32]. Rhythm classifications and associated confidence levels were extracted from the summary PDF reports using text-parsing routines implemented in R. Corsano's proprietary algorithms are compliant with the EN-IEC 60601-2-47:2015 medical standard for ambulatory ECGs.

For EMC ECGs, rhythm interpretation was conducted by a clinician as part of routine care. For Corsano ECGs, rhythm classification was determined based on the most frequently reported across the three recordings. All rhythm outcomes were categorised for use in descriptive and concordance analyses. A trained clinician confirmed each ECG diagnosis from both devices.

2.3b Data Cleaning and Structuring

To harmonise data from both sources, variable names were standardised using the janitor package, and date formats were unified. Duplicate or inconsistent entries were removed. Each ECG entry was tagged with a source-specific identifier for traceability. For intra-device reproducibility, all three Corsano ECG recordings per patient were retained in long format. For inter-device agreement, the mean value of the three Corsano recordings was calculated per patient. Corsano and EMC ECGs were matched if acquired within a 90-minute interval. Shared parameters (HR, PR, QRS, QT, QTc, RR) were then aligned for comparison. Clinical variables, age, sex, NSCLC subtype, TKI therapy type, and disease stage, were imported from the Castor database. Derived variables included time since diagnosis, duration of TKI therapy, and the time interval between each Corsano and EMC ECG.

2.3c Signal Quality Assessment

The SQI provided by Corsano's proprietary algorithm was used to assess eligibility for ECG recording. SQI values range from 0–100, with higher values reflecting better signal fidelity. For intra-device reproducibility analyses, all three Corsano ECGs were required to have an SQI ≥ 80. If any

recording fell below this threshold, the patient was excluded. For inter-device comparisons, only Corsano ECGs meeting the same SQI threshold were retained.

2.4 Statistical Analyses

All statistical analyses were performed in R (version 4.5.0), using *BlandAltmanLeh, caret, DescTools, flextable, forestmodel, ggpubr, gtsummary, irr, janitor, labelled, psych, readxl, rstatix, tidyverse*, and *gtsummary* packages.

2.4a Descriptive Analyses

Clinical categorical characteristics were reported as counts and percentages, while continuous characteristics were presented as medians with interquartile ranges (IQR). Based on normality assumptions, group comparisons were conducted using the chi-square test, Fisher's exact test for categorical data, and the Mann–Whitney U test or Student's t-test for continuous data.

2.4b Data Preparation and Assumption Testing

Continuous variables were evaluated for outliers with the Grubbs' test and visually inspected via boxplots. The Shapiro–Wilk test evaluated the normality of each parameter distribution, supported by quantile–quantile plots. Variables not meeting normality were analysed using non-parametric alternatives. No transformations were applied unless stated. All statistical tests were two-sided and adjusted for multiple testing as feasible, with a significance threshold of $p < 0.05$.

2.4c Intra-Device Reproducibility in Corsano ECGs

Test–retest reliability of three Corsano ECGs was evaluated using the following methods used:

- The coefficient of variation (CV) was calculated for each patient per ECG parameter to quantify variability. A CV <10% indicated an 'excellent', 10–20% 'good', and ≥20% 'poor' variation.
- Differences across the three recordings were tested using a repeated-measures analysis of variance (ANOVA) or the Friedman test based on normality of data distribution.
- Intraclass correlation coefficients (ICCs) were calculated using a two-way mixed-effects model for single measurements with absolute agreement (ICC[2,1]) to quantify the reliability of measurements across recordings. An ICC ≥0.85 indicated an 'excellent', 0.75–0.84 'good', 0.50–0.74 'moderate', and ≤0.50 'poor' agreement.

2.4d Inter-Device Agreement in ECG Parameter Values

The agreement between single-lead Corsano ECG and 12-lead EMC ECG common parameters (HR, PR interval, QRS duration, QT interval, and Bazett QTc) was evaluated using the following methods

- Bland–Altman analysis assessed measurement agreement by calculating the mean bias and 95% limits of agreement between devices. This method visualises both systematic error and random variability. Additionally, the coefficient of repeatability (CR) was calculated as 1.96 times the standard deviation of the paired differences. The CR quantifies the smallest change that indicates a significant difference between two paired repeated measurements, with smaller values showing better repeatability.
- Intraclass correlation coefficients (ICC[2,1]) quantified the absolute agreement between Corsano and EMC ECG parameters, interpreted similarly to intra-device analysis thresholds.

- Linear regression analysed the strength and direction of the association. Pearson's correlation coefficient (r) was calculated assuming linearity and normality. Spearman's correlation coefficient (ρ) was used for non-normally distributed parameters. A correlation coefficient ≥0.85 indicates 'excellent', 0.75–0.84 'good', 0.50–0.74 'moderate', and ≤0.50 'poor' agreement.

2.4e Inter-Device Concordance in ECG Diagnostic Classifications

Diagnostic concordance between Corsano and EMC ECGs was evaluated in categorical rhythm-based diagnoses. The EMC ECG served as the clinical reference standard. For each binary classification, the following diagnostic performance metrics were calculated:

- Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using standard 2×2 contingency tables.
- Accuracy: defined as the proportion of correctly classified cases across the total population.
- Cohen's kappa coefficient (κ): to assess inter-device agreement beyond chance. Values were interpreted following conventional thresholds: slight (0.01–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and almost perfect (>0.80).
- Confusion matrices: summarising true positives, true negatives, false positives, and false negatives, to visualise misclassification patterns.

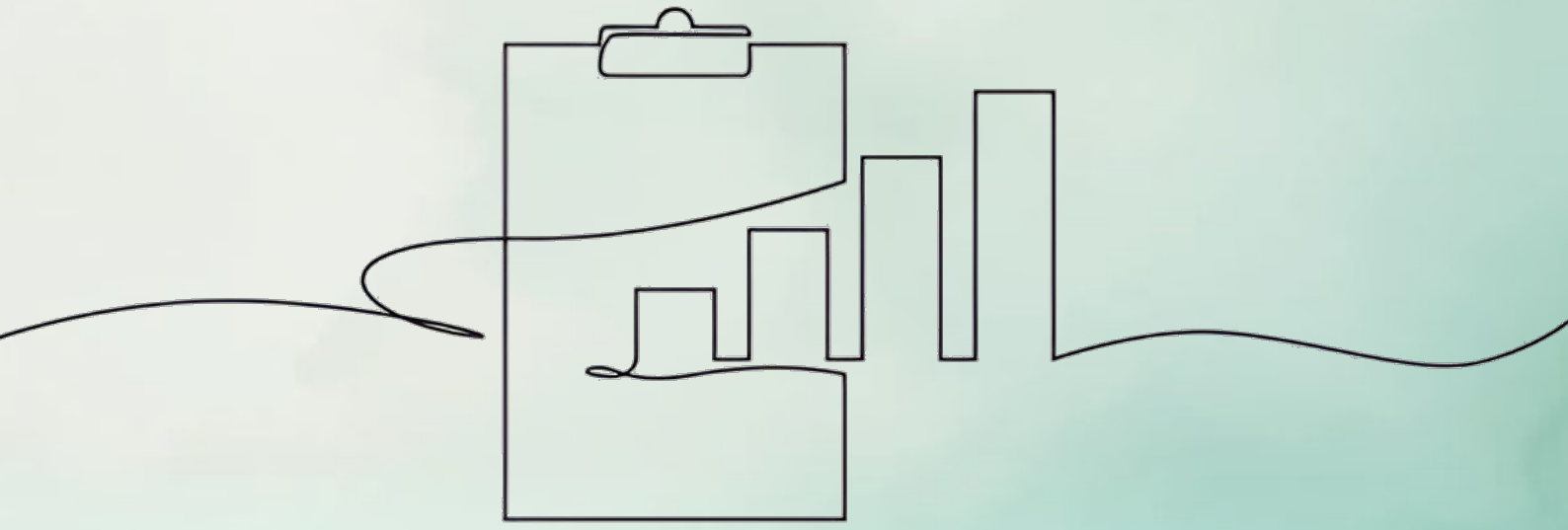
Analyses were based on per-patient classification. For the Corsano ECGs, classifications were based on the dominant rhythm across three recordings. The EMC ECG classifications were derived from automated measurements reviewed by a qualified clinical professional. Bar plots further illustrated classification performance, enabling comparison of metric distributions across categories.

2.4f Influence of Clinical Characteristics on Inter-Device ECG Discrepancy

The association between clinical variables and ECG discrepancies between Corsano and EMC ECGs was evaluated. ECG discrepancies were calculated as the absolute difference between Corsano and EMC measurements for the ECG parameters HR, RR interval, PR interval, QRS duration, QT interval, and Bazett QTc interval.

Correlations were assessed between ECG discrepancies and the continuous clinical predictors age at inclusion, body mass index (BMI), duration of TKI therapy, and time between ECG acquisitions. If normally distributed, Pearson's correlation was used; otherwise, Spearman's correlation was applied. Bootstrapped 95% confidence intervals (1,000 replicates) were generated for Spearman correlations.

Univariate linear regression models were fitted for each ECG parameter to enable assessment of the association between categorical clinical characteristics and ECG discrepancy. The predictors included the four continuous variables and three categorical characteristics: Fitzpatrick skin type, forearm hair density, and TKI type. All models used the absolute inter-device difference as the dependent variable. Predictors were appropriately coded as continuous or factor variables. Models were only retained if at least ten complete observations were available for the respective predictor. The estimated beta coefficient, 95% confidence interval, p-value, and p-values adjusted for multiple testing with the Benjamini-Hochberg correction were reported for each regression. Results were presented in tabular format and as forest plots, grouped by ECG parameter.



3 RESULTS

3.1 Study Population and Data Inclusion

A total of 71 patients with NSCLC were enrolled in the ECG substudy of the MOVIS-RESP trial, conducted at the Department of Pulmonary Medicine, Erasmus MC. The median age at inclusion was 66 years (IQR 58–74), and 72% of participants were female. The median time since diagnosis was 42 months (IQR 17–81). Most patients had adenocarcinoma (92), and 86% were diagnosed with stage IV disease (IVa, 23%; IVb, 63%). Of the total cohort, 39 patients (55%) were treated with osimertinib (EGFR-TKI) and 32 (45%) with alectinib (ALK-TKI). Among EGFR-positive cases, 40% had an Exon 19 deletion or insertion. The median duration of TKI therapy was 35 months (IQR 13–56). Baseline demographic and clinical characteristics are summarised in **Table 1**.

A subgroup analysis assessed whether baseline characteristics differed by TKI type and could influence ECG metrics (**Supplementary Table S1**). As expected, based on treatment protocols, several statistically significant differences emerged. Dosing and intake frequency differed significantly (p-adj < 0.001). Mutation status was mutually exclusive by treatment: all alectinib recipients had ALK-positive disease, while all osimertinib patients had EGFR mutations (p-adj < 0.001). Additionally, osimertinib-treated patients had a shorter time since diagnosis (35 vs. 58 months, p-adj = 0.046) and a shorter duration of TKI therapy (26 vs. 41 months, p-adj = 0.035) than those receiving alectinib.

Table 1. *Baseline demographic and clinical characteristics of the included patients.*

Variable	N = 71*
Age at inclusion [years]	66 [58, 74]
Sex	
Female	51 (72)
Male	20 (28)
BMI [kg/m²]	27 [24, 32]
Smoking status	
Current	3 (4)
Former	11 (15)
Never	57 (80)
Alcohol status	
Current	23 (32)
Former	29 (41)
Never	19 (27)
Skin type (Fitzpatrick)	
Type II	8 (11)
Type III	52 (73)
Type IV	7 (10)
Type V	4 (6)
Forearm hair density	
Dense	6 (9)
Moderate	12 (17)
Nil	15 (21)
Sparse	38 (54)
Time between EMC and Corsano ECG [min]	48 [20, 72]
Stage at diagnosis	
Ia/Ib	10 (14)
IVa	16 (23)
IVb	45 (63)
NSCLC subtype	
Adenocarcinoma	65 (92)
NOS	6 (8)
Mutation	
ALK	32 (45)
EGFR	39 (55)
Specify EGFR	
Exon 19del(ins)	28 (40)
Exon 21 p.L858R	11 (15)
Missing	32 (45)
Time since diagnosis [months]	42 (17, 81)
Name current TKI	
Alectinib	32 (45)
Osimertinib	39 (55)
Intake frequency TKI [dd]	
1	39 (55)
2	32 (45)
Dose current TKI [mg]	
40 to 80	39 (55)
300 to 600	32 (45)
Duration of TKI therapy [months]	35 [13, 56]

*Median [IQR]; n (%).

Abbreviations: ALK, Anaplastic Lymphoma Kinase; BMI, Body Mass Index; ECG, Electrocardiogram; EGFR, Epidermal Growth Factor Receptor; NOS, Not Otherwise Specified; NSCLC, Non-Small Cell Lung Cancer; TKI, Tyrosine Kinase Inhibitor.

3.1a ECG Acquisition and Signal Quality

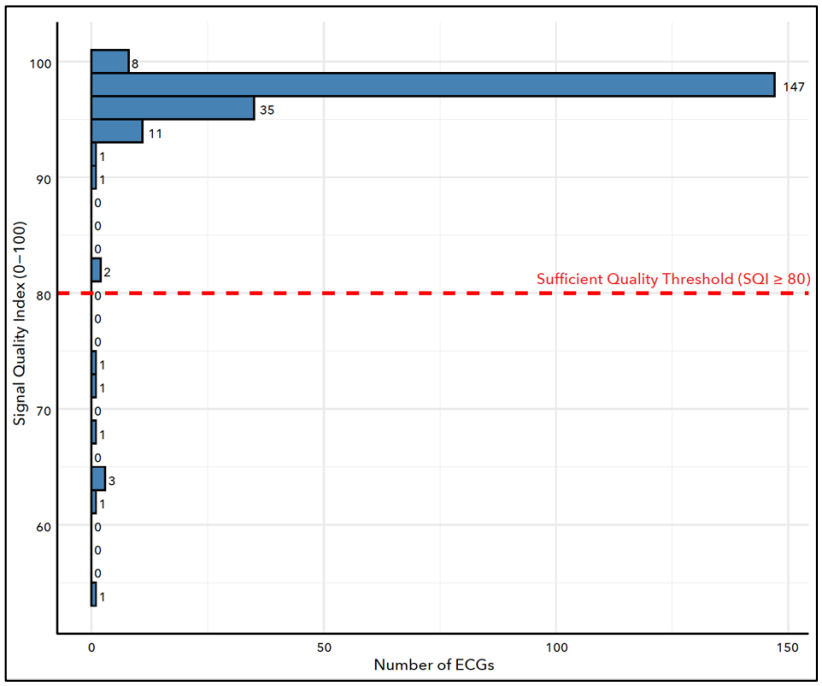
All 71 patients received a 12-lead ECG as part of routine clinical care using the institutional ECG system. All EMC ECGs were of analysable quality. In addition, each participant underwent three consecutive single-lead Corsano ECGs. In total, 213 Corsano ECGs were collected. Of these, 205 recordings (96%) met the predefined signal quality threshold (SQI ≥ 80), while eight recordings (4%) were excluded due to insufficient quality (**Figure 4**). The median time between Corsano and EMC ECG recordings was 48 minutes (IQR 20–72). A summary of Corsano ECG quality metrics is provided in **Table 2**. For the intra-device reproducibility analysis, 66 patients were included, each with three Corsano ECGs with an SQI ≥ 80. For the inter-device agreement analysis, 70 patients with at least one high-quality recording were included. Individual ECGs with SQI < 80 were excluded.

Table 2. *Summary of the Corsano ECG quality metrics.*

Total Corsano ECGs, n	Good Quality Corsano ECGs (SQI ≥ 80), n	Poor Quality Corsano ECGs (SQI < 80), n	Proportion Analysable Corsano ECGs (%)	Patients with Three Good Quality Corsano ECGs, n
213	205	8	96.2	66

Abbreviations: ECG, Electrocardiogram; SQI, Signal Quality Index.

Figure 4. *The Distribution of SQI Values across all 213 Corsano ECGs.*



Abbreviations: ECG, Electrocardiogram; SQI, Signal Quality Index.

3.2 Intra-Device Reproducibility of Corsano ECG Parameters

This section evaluates the reproducibility of specific parameters across three consecutive Corsano ECG recordings. Only patients with three Corsano ECGs with a SQI ≥ 80 were included, yielding data from 66 individuals (198 ECGs). The analysis concentrated on parameters that overlap with those measured by the EMC system (HR, QRS duration, RR interval, PR interval, QT interval, and the Bazett QTc) to support subsequent comparative evaluations. **Table 3** summarises the analytical outcomes for these primary parameters. Additional analyses of the Corsano CardioWatch parameters are visualised in **Supplementary Figures S1–S4** and outlined in **Supplementary Table S2.**

Table 3. *Summary of Intra-Device Reproducibility Analysis of the Primary Corsano ECG Parameters.*

Parameter	HR [bpm]	PR interval [ms]	QT interval [ms]	QTc interval Bazett [ms]	QRS duration [ms]	RR interval [ms]
Patients, n*	66	23	66	66	66	66
Corsano ECGs, n**	198	69	198	198	198	198
Median [IQR]	78 [70–87]	145 [129–165]	375 [355–395]	490 [434–531]	105 [98–113]	762 [688–859]
Mean CV [±SD], %	2.0 [±2.0]	7.3 [±4.8]	2.6 [±2.3]	2.9 [±2.4]	4.8 [±4.9]	2.0 [±1.9]
ICC [95% CI]	0.97 [0.96–0.98]	0.78 [0.62–0.89]	0.82 [0.75–0.88]	0.91 [0.87–0.94]	0.63 [0.5–0.74]	0.98 [0.97–0.99]
Friedman p-value***	0.48	0.78	0.92	0.32	0.53	0.78

*Patients were excluded if any ECG had SQI < 80. **Patients were additionally excluded for a specific parameter if any ECG had a value of 0. ***No adjustment for multiple testing applied due to interdependence among parameters. Normality testing is unreliable due to the small sample size per patient (3 ECGs); the Friedman test is used.

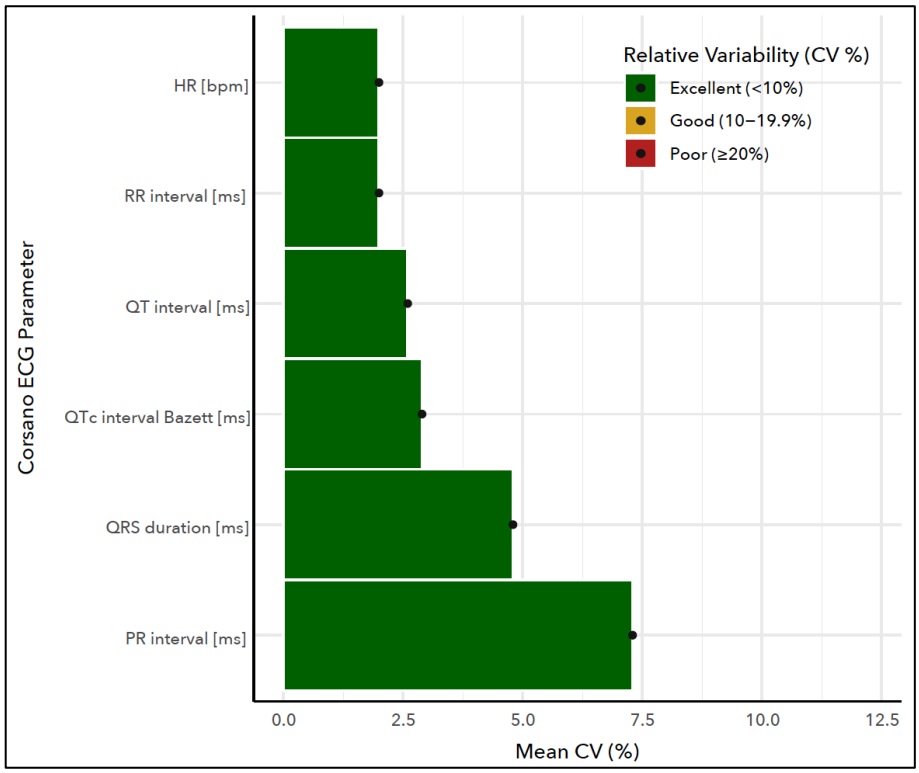
Colour legend: ICC – green (≥0.85), golden (0.75–0.84), orange (0.50–0.74), red (<0.50); CV – green (<10%).

Abbreviations: bpm, beats per minute; CI, Confidence Interval; ECG, Electrocardiogram; HR, Heart Rate; ICC, Intraclass Correlation Coefficients (ICC); SD, Standard Deviation.

3.2a Coefficient of Variation

The CV was calculated for each primary parameter to measure intra-subject variability across recordings. CVs offer insight into measurement consistency under stable clinical conditions, particularly for parameters prone to physiological variation. All six primary parameters demonstrated low relative variability and fell within the 'excellent' reproducibility range (CV <10%) (**Figure 5**). HR and RR intervals had a mean (± SD) CV of 2.0% (±2 SD), the QT interval showed a mean CV of 2.6% (±2.3 SD), and the QTc (Bazett) 2.9% (±2.4 SD). PR interval and QRS duration had slightly higher variability, with a mean CV of 7.3% (±4.8 SD) and 4.8% (±4.9 SD), respectively.

Figure 5. *Barplots Coefficient of Variation Values of the Six Primary Corsano ECG Parameters.*

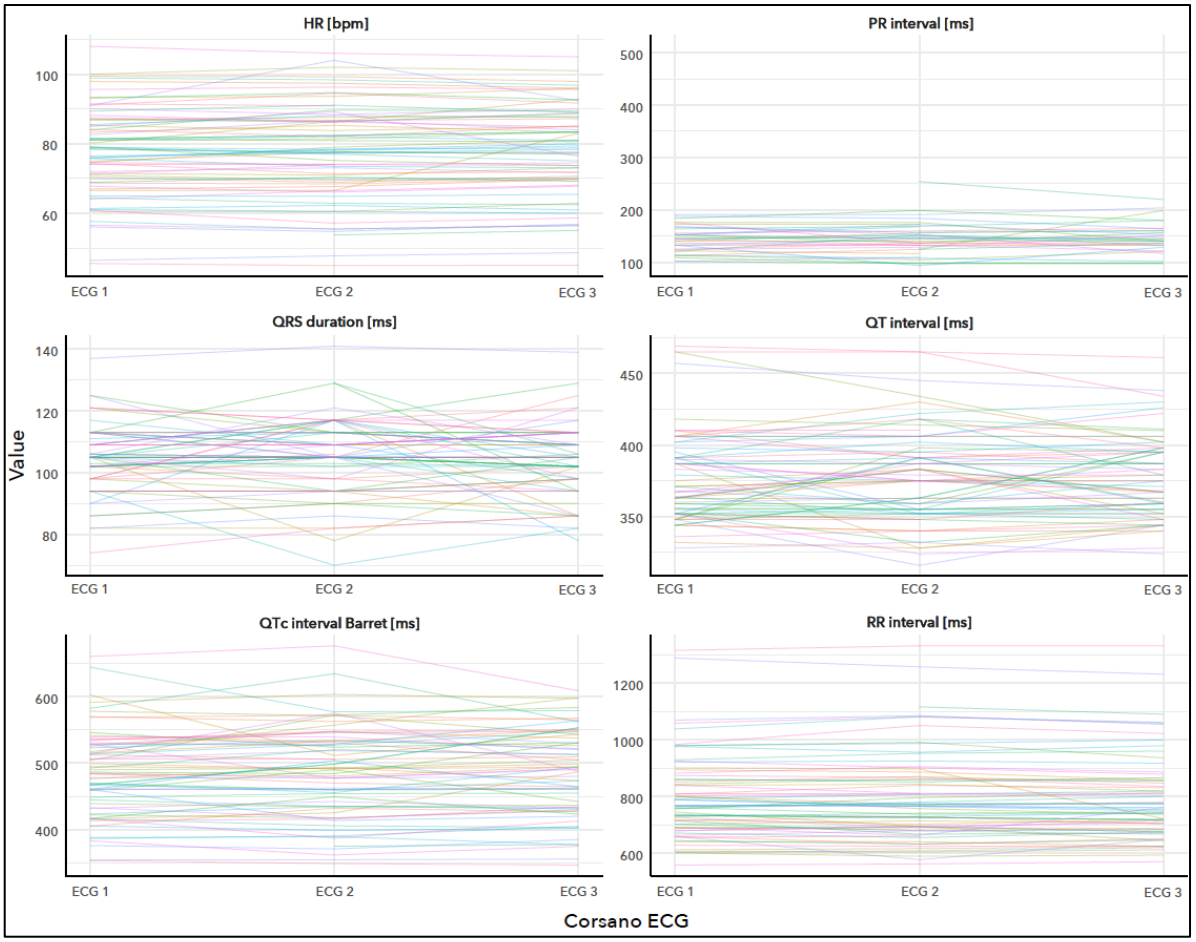


Abbreviations: bpm, beats per minute; CV, Coefficient of Variation; ECG, Electrocardiogram; HR, Heart Rate.

3.2b Repeated-Measures Statistical Testing

The Friedman test assessed each parameter for potential systematic differences across the three consecutive Corsano ECG recordings. This non-parametric alternative to repeated-measures ANOVA was selected due to the limited number of observations per subject and deviations from normality. Given the exploratory aim of the analysis and the interrelated nature of the parameters, no correction for multiple comparisons was applied. None of the six primary parameters showed statistically significant variation across recordings. Patient-level trends are illustrated in Spaghetti plots (**Figure 6**), while box plots depict parameter distributions across the ECGs (**Figure 7**). These findings suggest that parameter medians remained stable over the measurement sequence.

Figure 6. *Spaghetti Plots Visualising Patient-Level Trends Across Primary Corsano ECG Parameters.*

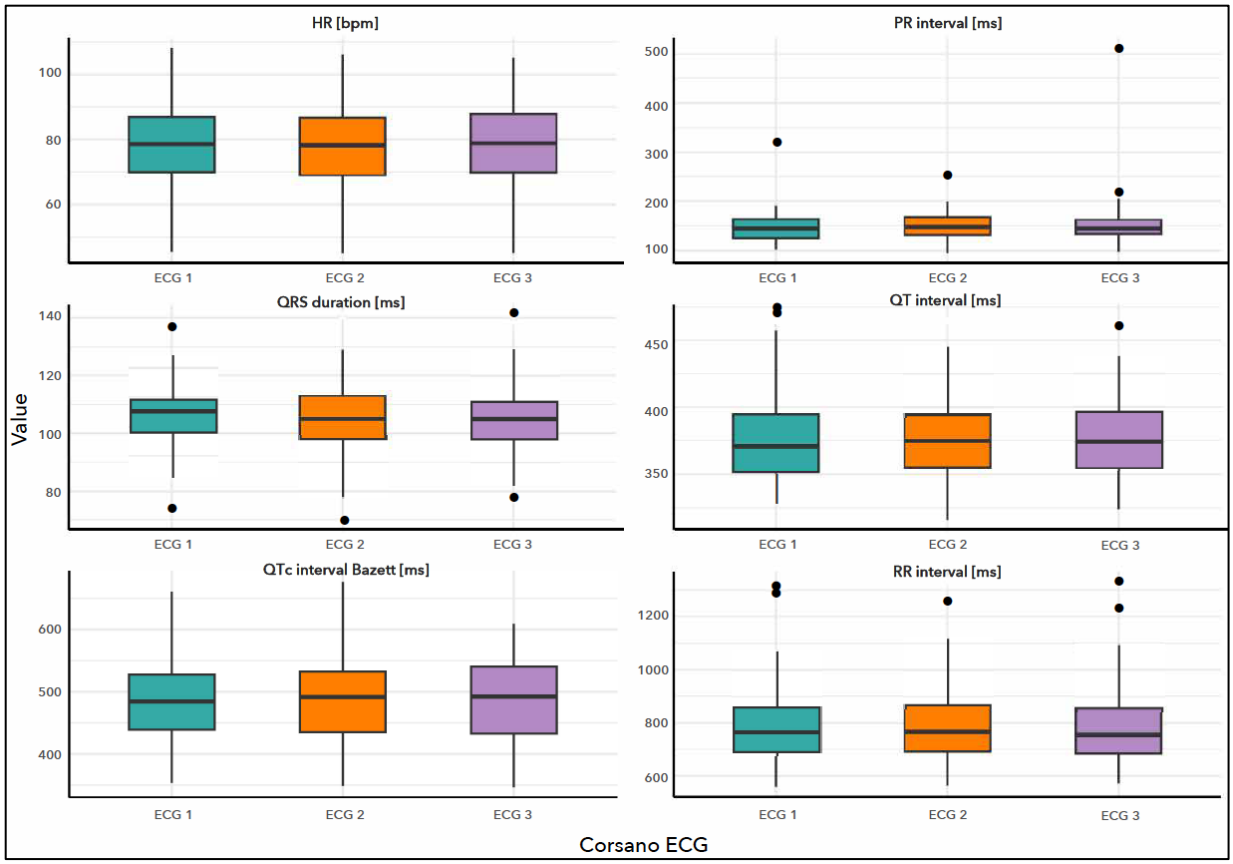


Abbreviations: bpm, beats per minute; ECG, Electrocardiogram; HR, Heart Rate.

3.2c Intraclass Correlation Coefficients

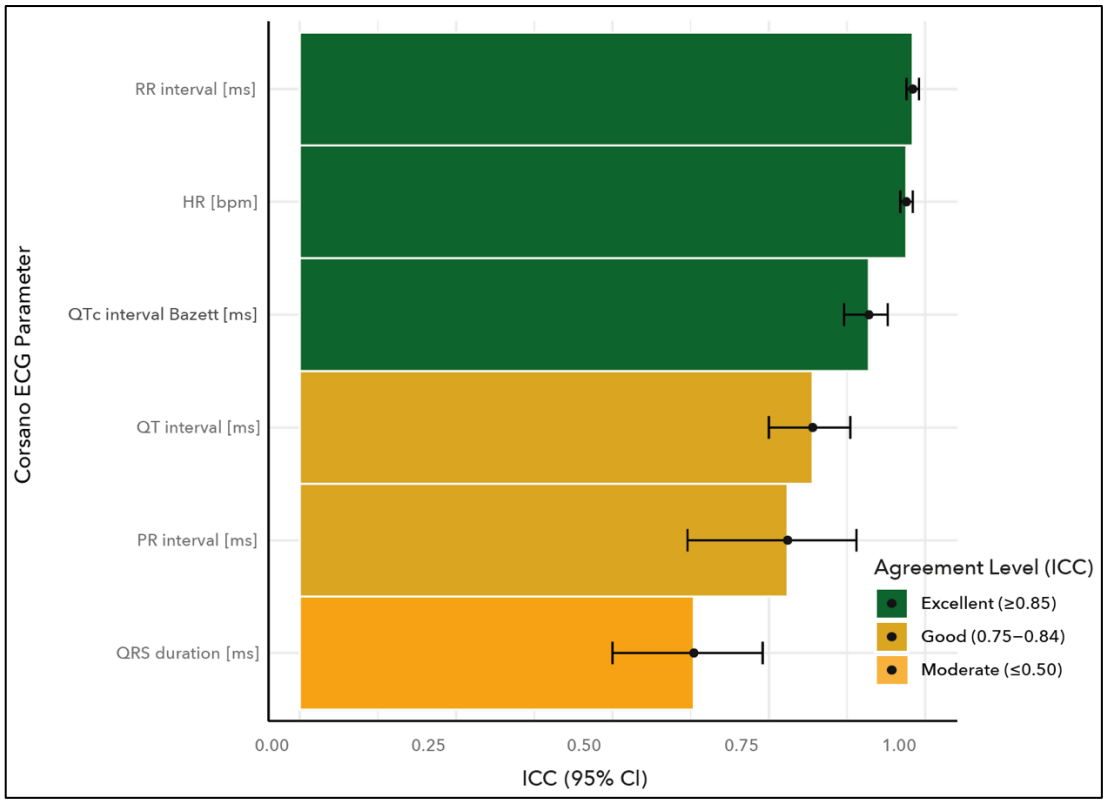
ICCs were calculated using a two-way random-effects model for single measurements (ICC[2,1]) to evaluate the absolute agreement of ECG parameter values across repeated recordings. This provides a measure of reliability that accounts for intra- and inter-subject variability. The ICCs for the six primary parameters suggest high reproducibility (**Figure 8**). HR, RR interval, and Bazett QTc interval showed 'excellent' agreement, with ICCs of 0.97 (95% CI: 0.96–0.98), 0.98 (95% CI: 0.97–0.99), and 0.91 (95% CI: 0.87–0.94), respectively. QT and PR intervals showed 'good' agreement, with ICCs of 0.82 (95% CI: 0.75–0.88) and 0.78 (95% CI: 0.62–0.89), respectively. QRS duration showed 'moderate' agreement with an ICC of 0.63 (95% CI: 0.50–0.74).

Figure 7. *Box Plots Visualising Parameter Distributions Across the Three Consecutive Corsano ECGs.*



Abbreviations: bpm, beats per minute; ECG, Electrocardiogram; HR, Heart Rate.

Figure 8. *Barplots Visualising ICC Values Between the Three Consecutive Corsano ECGs.*



Abbreviations: bpm, beats per minute; ECG, Electrocardiogram; HR, Heart Rate; ICC, Intraclass Correlation Coefficient.

3.3 Inter-Device Agreement in ECG Parameter Values

This section evaluates the level of agreement between the Corsano and EMC ECG. Six primary ECG parameters common to both systems were analysed: HR, RR interval, PR interval, QRS duration, QT interval, and Bazett QT interval. Only patients with at least one Corsano ECG recording showing a SQI ≥ 80 paired with an EMC ECG captured within a 90-minute window were included. This resulted in data from 70 patients, though the PR interval analysis was limited to 53 due to missing entries. For each case, the average Corsano ECG value was taken. The analytical outcomes for these parameters are summarised in **Table 4**.

Table 4. *Summary of Inter-Device Agreement Analysis in ECG Parameter Values.*

Parameter	HR [bpm]	PR interval [ms]	QRS duration [ms]	QT interval [ms]	QTc interval Barret [ms]	RR interval [ms]
Patients, n	70	53	70	70	70	70
Mean (EMC)	73.6	175.9	93.6	376.4	456.4	843.4
Mean (Corsano)	76.7	156.8	105.0	378.2	478.9	806.7
Mean difference (i.e., bias) [±SD]	3.1 [±6.7]	-19 [±84]	12 [±11]	2.0 [±19]	23 [±40]	-37 [±73]
Statistical test type	Paired t-test	Wilcoxon	Paired t-test	Wilcoxon	Paired t-test	Wilcoxon
p-value	2.60e-04	6.29e-05	1.65e-12	0.30	1.09e-05	2.27e-04
p-adj	3.12e-04	1.26e-04	9.90e-12	0.30	3.27e-05	3.12e-04
95% LoA	-10.1–16.3	-183.6–145.5	-10.4–33.4	-35.3–38.8	-55.4–100.6	-180.5–107.1
% within 95% LoA	94.3	92.5	94.3	95.7	94.3	95.7
CR	13.2	164.6	21.9	37.0	78.0	143.8
ICC [95% CI]	0.87 [0.79–0.92]	0.32 [0.07–0.53]	0.47 [0.25–0.65]	0.80 [0.68–0.88]	0.85 [0.76–0.91]	0.79 [0.67–0.87]
Correlation type	Pearson	Spearman	Pearson	Spearman	Pearson	Spearman
Correlation (r/ρ) [95% CI]	r = 0.88 [0.81–0.92]	ρ = 0.44 [-0.27–0.28]	r = 0.33 [0.11–0.53]	ρ = 0.80 [-0.24–0.24]	r = 0.81 [0.71–0.88]	ρ = 0.88 [-0.24–0.23]
p-value	2.19e-23	9.81e-04	4.91e-03	5.73e-17	3.63e-17	1.68e-23
Normal distribution	Yes	No	Yes	No	Yes	No
Shapiro p-value	EMC: 0.3, COR: 0.88	EMC: 1.6e-11, COR: 2.5e-11	EMC: 0.11, COR: 0.085	EMC: 0.15, COR: 0.015	EMC: 0.16, COR: 0.47	EMC: 0.037, COR: 0.00061

Colour legend: 'excellent' green (≥0.85), 'good' golden (0.75–0.84), red (<0.50).

Abbreviations: bpm, beats per minute; CI, Confidence Interval; COR, Corsano; CR, Coefficient of Repeatability; ECG, Electrocardiogram; EMC, Erasmus MC; HR, Heart Rate; ICC, Intraclass Correlation Coefficients (ICC); LoA, Limits of Agreement; p-adj, p-value adjusted for multiple testing; SD, Standard Deviation.

3.3a Bland–Altman Agreement Analysis

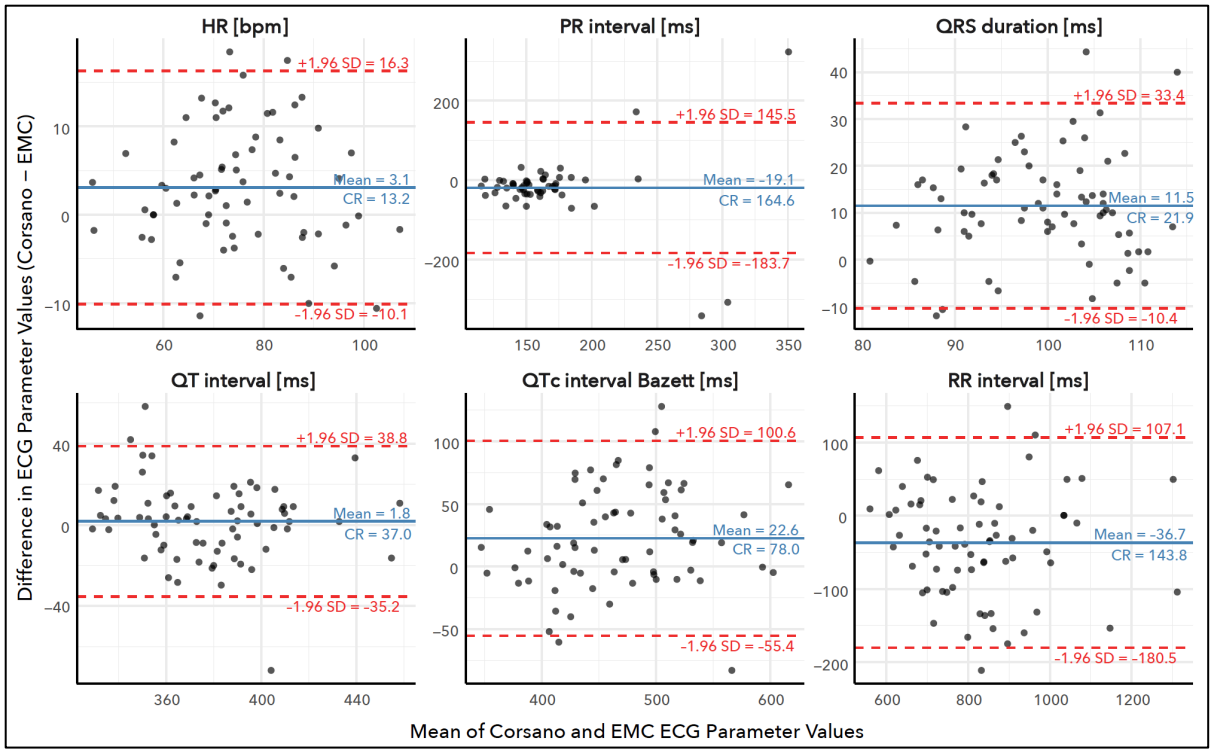
Bland–Altman analyses were conducted for each parameter to evaluate systematic measurement differences and clinical interchangeability (**Figure 9**). HR showed a bias of 3.1 bpm (Limits of Agreement (LoA): -10.1–16.3) with a CR of 13.2. The RR interval showed a bias of -36.70 ms (LoA: -180.5–107.1) with a CR of 143.8. The PR interval showed the greatest variability, with a bias of -19.1 ms (LoA: -183.8–145.51) with a CR of 164.6. QRS duration showed a bias of 11.5 ms (LoA: -10.4–33.4) with a CR of 21.9. Discrepancies for the QT and QTc intervals were minimal to moderate, with biases of 1.8 ms (LoA -35.3–38.8) and 22.6 ms (LoA -55.4– 100.6), and CRs of 37.0 and 78.0, respectively. Across all parameters, more than 92% of paired recordings fell within the 95% LoA.

3.3b Intraclass Correlation Coefficients (ICC)

To evaluate absolute agreement, ICCs using model ICC[2,1] were computed for each parameter (**Figure 10**). HR and QTc showed 'excellent' agreement with ICCs of 0.87 (95% CI: 0.79–0.92) and 0.85 (95% CI: 0.76–0.91), respectively. The QT and RR intervals showed 'good' agreement, with ICCs

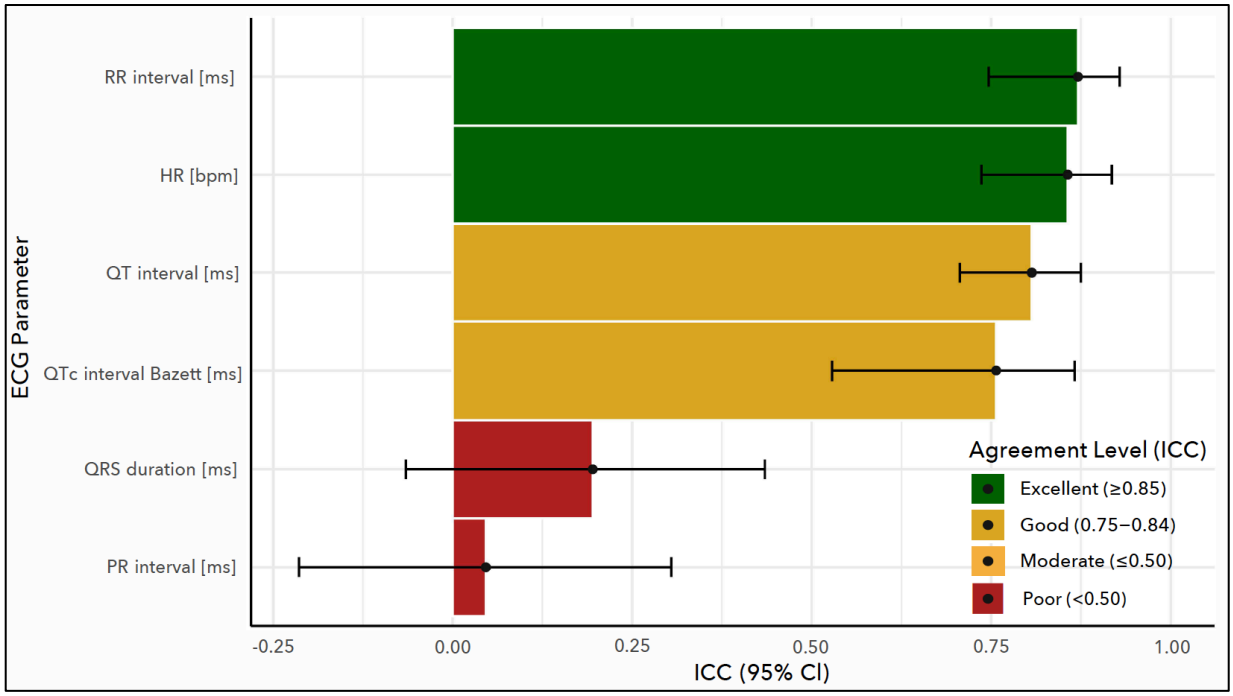
of 0.80 (95% CI: 0.68–0.88) and 0.79 (95% CI: 0.67–0.87), respectively. In contrast, QRS duration (ICC 0.47, 95% CI: 0.25–0.65) and PR interval (ICC 0.32, 95% CI: 0.07–0.53) showed 'moderate' and 'poor' agreement.

Figure 9. *Bland-Altman Plots Visualising Mean Biases, LoAs and CRs of the Corsano and EMC ECGs.*



Abbreviations: bpm, beats per minute; ECG, Electrocardiogram; HR, Heart Rate; EMC, Erasmus MC.

Figure 10. *Barplots Visualising ICC Values Between the Corsano and EMC ECGs.*

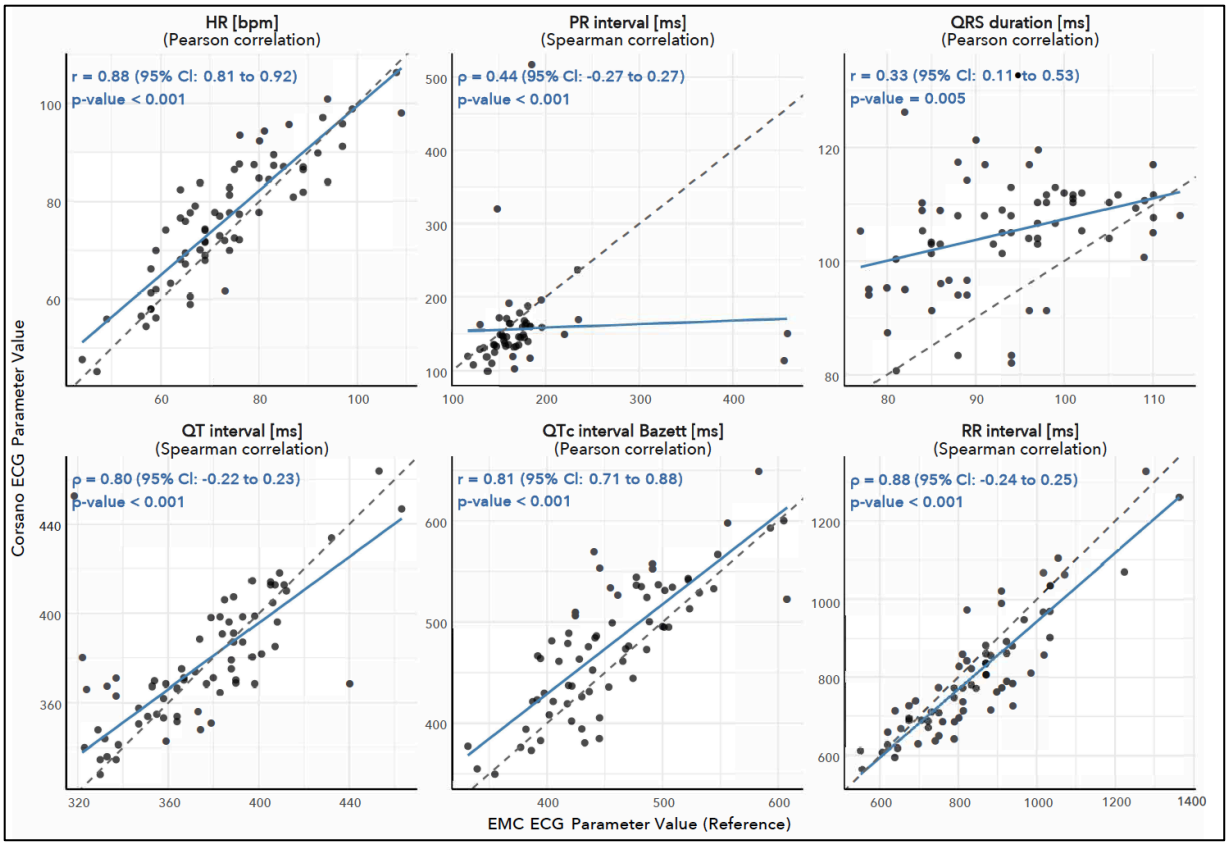


Abbreviations: bpm, beats per minute; CR, Coefficient of Repeatability. ECG, Electrocardiogram; EMC, Erasmus MC; HR, Heart Rate; ICC, Intraclass Correlation Coefficient; LoA, Limits of Agreement.

3.3c Correlation Analysis

To assess the strength of association between Corsano and EMC ECG parameters, Pearson or Spearman correlation coefficients were computed based on distributional assumptions (**Figure 11**). 'Excellent' linear correlation was observed for HR (r = 0.88, 95% CI: 0.81–0.92), RR interval (ρ = 0.88, 95% CI: -0.24–0.23), and Bazett QTc interval (r = 0.81, 95% CI: 0.71–0.88). The QT interval showed a 'good' association (ρ = 0.80, 95% CI: -0.24–0.24). In contrast, 'poor' correlations were observed for QRS duration (r = 0.33, 95% CI: 0.11–0.53) and PR interval (ρ = 0.44, 95% CI: -0.27–0.28), reflecting greater inter-device variability for these parameters. To explore individual-level variability and detect potential outliers, scatterplots were generated with fitted linear regression lines and data points coloured by patient (**Supplementary Figure 5**). Visual inspection revealed no patient-level trends.

Figure 11. *Scatterplots Linear Regressions Visualising Associations between Corsano and EMC ECGs.*



* Dashed line indicates identity (y = x); solid line indicates a linear fit.

Abbreviations: bpm, beats per minute; CI, Confidence Interval; ECG, Electrocardiogram; EMC, Erasmus MC; HR, Heart Rate; r, Pearson's correlation coefficient; ρ, Spearman's correlation coefficient.

3.4 Inter-Device Concordance in ECG Diagnostic Classifications

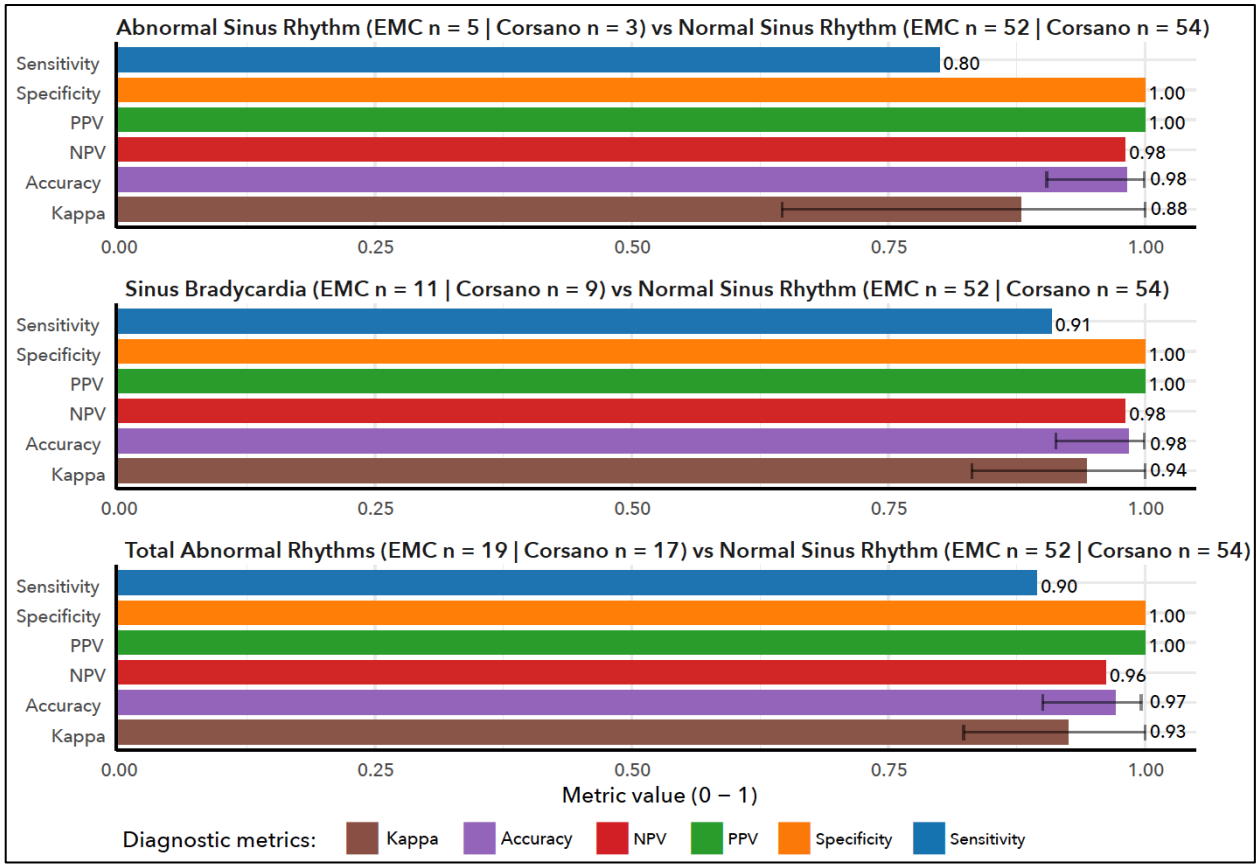
This section evaluated the level of concordance between rhythm diagnoses obtained from the Corsano and EMC ECG. The analysis addressed whether the Corsano CardioWatch could replicate clinical rhythm classification based on single-lead signal morphology. A clinical professional reviewed EMC diagnoses, while Corsano rhythm classifications were based on the dominant diagnosis across three consecutive recordings. Each abnormal rhythm diagnosis was evaluated in a binary comparison against patients with normal sinus rhythm, thereby excluding other abnormal rhythms from the comparator group. The EMC ECG was used as the reference standard.

3.4a Diagnostic Performance Metrics

Five rhythm categories were identified: normal sinus rhythm, abnormal sinus rhythm, sinus bradycardia, sinus tachycardia, and sinoatrial (SA) exit block. The total abnormal rhythms category aggregates all types of abnormal rhythms. **Supplementary Table S3** summarises the performance metrics for all rhythm diagnoses. Sinus tachycardia (EMC: n = 2; Corsano: n = 2) and SA exit block (EMC, n = 1; Corsano, n = 1) showed perfect agreement (100%) across all metrics. However, these findings should be interpreted cautiously due to the small number of positive cases.

Barplots in **Figure 12** illustrate the diagnostic metrics for total abnormal rhythms (EMC: n = 19; Corsano: n = 17), sinus bradycardia (EMC: n = 11; Corsano: n = 10), and abnormal sinus rhythm (EMC: n = 5; Corsano: n = 4). For total abnormal rhythms, the Corsano CardioWatch achieved 90% sensitivity, 100% specificity, 100% PPV, 96% NPV, and 97% accuracy (κ = 0.93). Diagnostic performance for sinus bradycardia was similarly strong, with 91% sensitivity, 100% specificity, and 98% accuracy (κ = 0.94). For abnormal sinus rhythm, sensitivity was lower at 80%, but specificity and PPV remained at 100%, with 98% for both NPV and accuracy (κ = 0.88). These results suggest strong diagnostic agreement between Corsano and EMC ECG across multiple rhythm categories.

Figure 12. *Barplots Diagnostic Agreement Between Corsano and EMC ECG in Three Arrhythmias.*



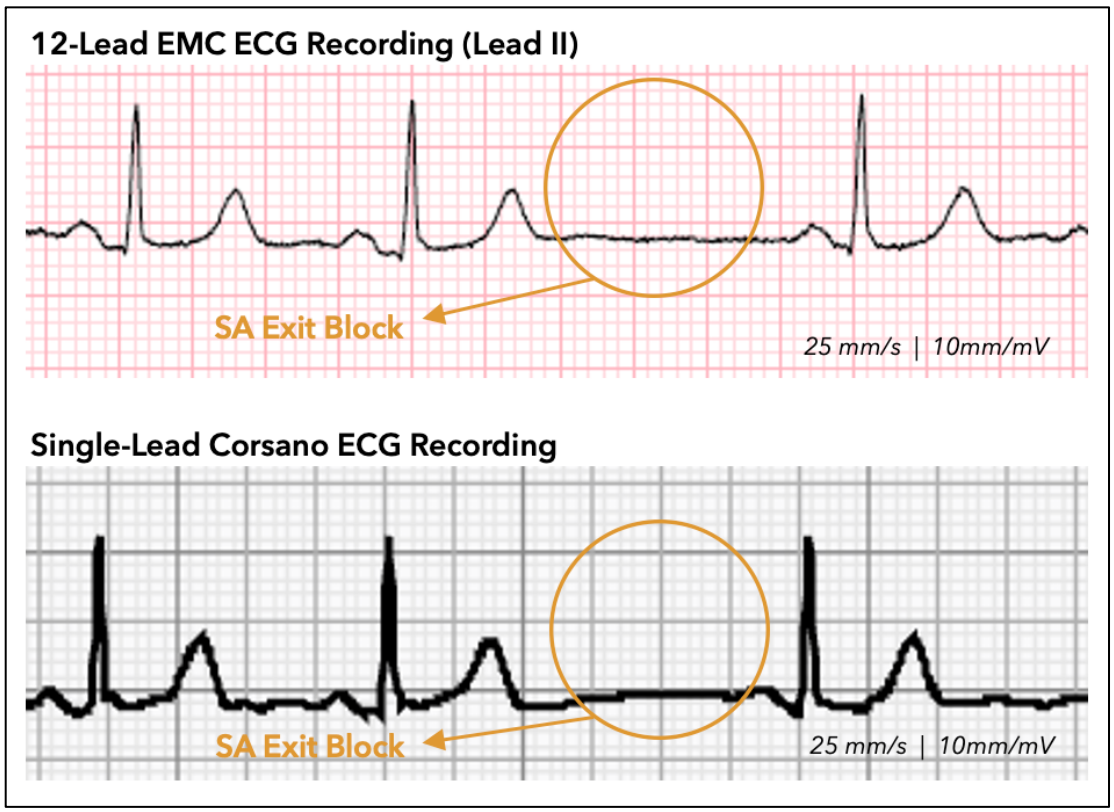
* Total Abnormal Rhythms include Sinus Bradycardia, Abnormal Sinus Rhythm, Sinus Tachycardia (n = 2), and SA Exit Block (n = 1). The latter two are not displayed due to low sample size. ** Error bars indicate 95% CI.

Abbreviations: ECG, Electrocardiogram; EMC, Erasmus MC; NPV, Negative Predictive Value; PPV, Positive Predictive Value.

3.4b Case Visualisation: SA Exit Block

To highlight the clinical relevance of rare diagnoses, an example case of SA exit block is presented in **Figure 13**, showing both the EMC ECG and the corresponding Corsano ECG. The ECG characteristics observed in both recordings were consistent with an SA exit block, supporting the Corsano CardioWatch's ability to detect infrequent but clinically meaningful arrhythmias.

Figure 13. *Case Visualisation SA Exit Block Detected by Corsano ECG and Confirmed by EMC ECG.*



Abbreviations: ECG, Electrocardiogram.

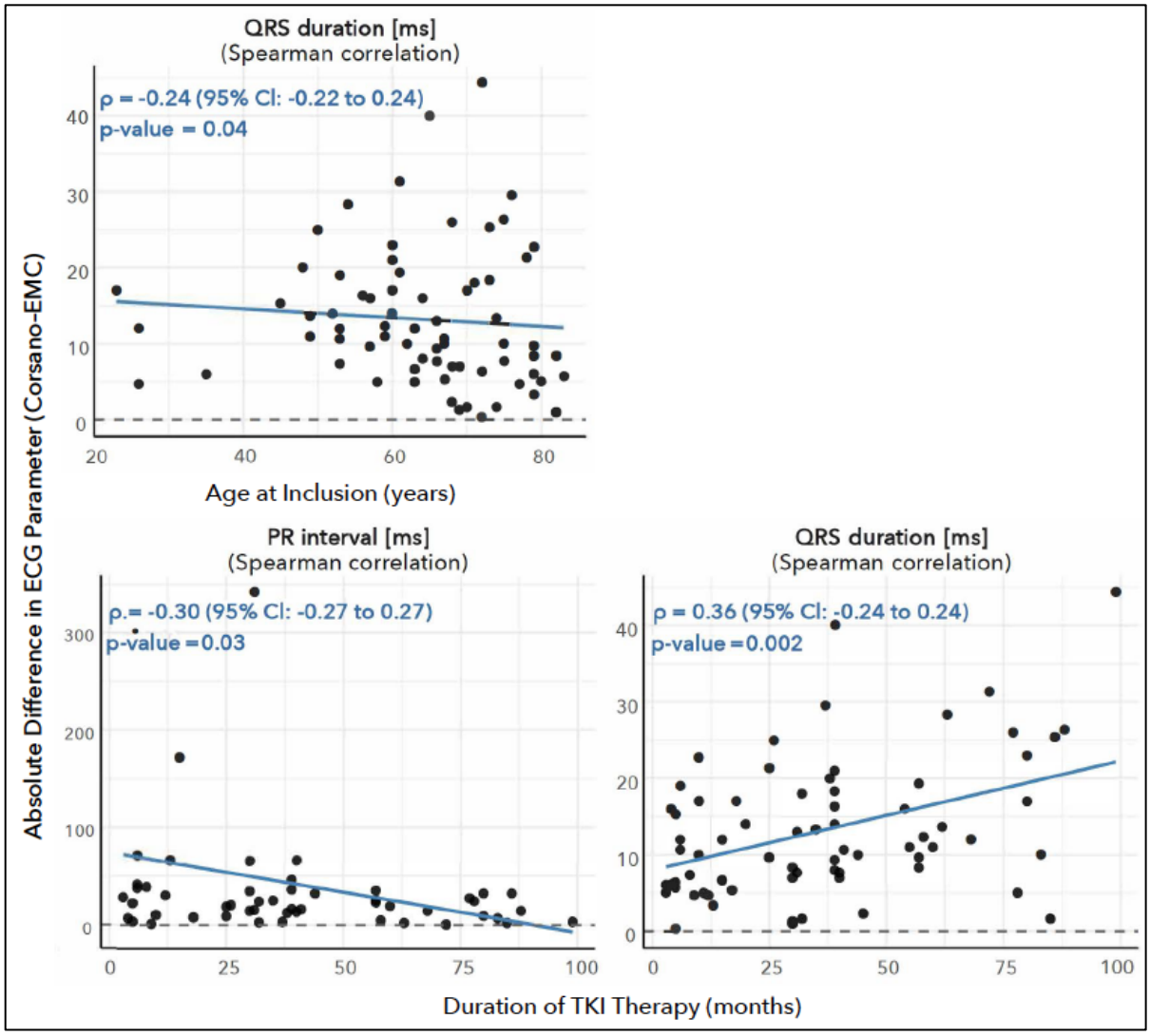
3.5 Influence Clinical Characteristics on Inter-Device Parameter Discrepancy

This section explores whether patient characteristics influenced the degree of discrepancy between Corsano and EMC ECG measurements. Discrepancies were defined as the absolute difference in ECG parameter values between Corsano and EMC. The six primary ECG parameters (HR, PR interval, QRS duration, QT interval, Bazett QTc interval, and RR interval) were included. Two complementary analyses were performed: Spearman correlation (parameters were not normally distributed) for continuous predictors and univariate linear regression for continuous and categorical variables.

3.5a Spearman Correlation for Continuous Clinical Variables

Spearman correlation coefficients were calculated to evaluate the associations between inter-device ECG parameter discrepancies and four continuous patient characteristics: age, BMI, duration of TKI therapy, and time between ECGs. Only three of 24 correlation tests were statistically significant (**Supplementary Table S4 and Supplementary Figure S6**), including the association between age and QRS duration discrepancy (ρ = –0.24; p = 0.044), TKI therapy duration and PR interval discrepancy (ρ = –0.30; p = 0.03), and TKI therapy duration and QRS duration discrepancy (ρ = 0.36; p = 0.002). However, upon visual inspection, no associations were clinically relevant (**Figure 14**).

Figure 14. *Scatterplots Linear Regression Visualising Significant Associations between ECG Parameter Discrepancies and Continuous Clinical Variables*



Abbreviations: EMC, Erasmus MC; NPV, Negative Predictive Value; PPV, Positive Predictive Value; TKI, Tyrosine Kinase Inhibitor.

3.5b Univariate Linear Regressions for Continuous and Categorical Variables

Univariate linear regression models were fitted for each ECG parameter using the four continuous predictors and three categorical variables: Fitzpatrick skin type, forearm hair density, and TKI type to explore predictors of inter-device ECG discrepancy further. No statistically significant associations were observed between age, BMI, skin type, or the time between ECGs and the discrepancy in any ECG parameter. Out of 60 tested models, only two associations remained statistically significant after adjustment for multiple comparisons (**Supplementary Table S5 and Supplementary Figure S7**). A longer duration of TKI therapy was associated with a lower PR interval discrepancy (β = –0.8 ms per month; 95% CI –1.6 to –0.1; p-adj = 0.033). Additionally, patients with no visible forearm hair showed smaller QRS duration discrepancies compared to those with any degree of hair growth (β = –9.0 ms; 95% CI –14.3 to –3.7; p-adj = 0.033). These findings suggest that subtle anatomical or treatment-related factors may influence the precision of wearable ECG measurements in select subgroups, although the overall clinical impact appears limited.

4 DISCUSSION

This thesis presents one of the first evaluations of the intra-device consistency and inter-device agreement of the single-lead ECG functionality of the Corsano CardioWatch 287-2, conducted in a clinical cohort of patients with NSCLC treated with osimertinib (EGFR-TKI) or alectinib (ALK-TKI). Due to the TKI-specific electrophysiological effects, these patients are at increased risk of ECG abnormalities, particularly sinus bradycardia and QTc prolongation[16-18,21].

Wearable ECG technology has gained traction for arrhythmia surveillance and ambulatory monitoring, with several devices now validated for clinical or consumer use[39-41]. However, most validation studies have focused on healthy volunteers or simulated testing environments, limiting generalisability to high-risk patient populations. While no peer-reviewed studies have previously examined the Corsano CardioWatch in oncology populations, recent evidence supports its diagnostic capabilities in broader cardiovascular contexts. A recent prospective study using the CardioWatch demonstrated high sensitivity (≥95%) and specificity (≥98%) for atrial fibrillation detection over 28 days when compared to 24-hour Holter monitoring. Moreover, the device strongly correlated with Holter-derived estimates of atrial fibrillation burden[42]. Importantly, this research was embedded in routine oncological care, offering insights into the performance and usability in real-world clinical settings.

Unlike many commercial wearables, the Corsano CardioWatch is both CE-MDR and FDA certified, and its ECG module adheres to the EN-IEC 60601-2-47:2015 standard for ambulatory ECG devices[33,34]. A recent systematic review identified 112 studies on wearable technology in oncology, most of which focused on user feasibility (43%) or correlational analysis (40%), while fewer evaluated technical feasibility (8%) or clinical outcomes (9%), and only 22% used medical-grade devices. Few studies assessed diagnostic accuracy or compared wearable outputs against clinical gold standards such as the 12-lead ECG[43]. This thesis addresses that gap by directly comparing ECG parameter values and rhythm classifications between Corsano and standard ECGs, while also exploring intra-device consistency and technical performance under clinical conditions.

4.1 Agreement of ECG Parameters and Diagnostic Classifications

4.1a Rationale for Statistical Approaches

This thesis employed established statistical methods to assess intra-device reproducibility and inter-device agreement of Corsano ECG measurements. Intra-device reproducibility was evaluated using the CV, ICCs, and the Friedman test. CV quantifies relative variability across repeated measures, while ICC assesses measurement reliability by accounting for intra- and inter-subject variance[44]. These metrics provide complementary insights: ICC evaluates agreement, whereas CV highlights dispersion, which may or may not reflect clinical significance[45]. The Friedman test detected systematic differences among the three Corsano ECGs, suitable for the small patient sample and non-normal distributions. Used together, CV and ICC offer a well-rounded assessment of reproducibility, as endorsed in prior ECG reliability studies[44-46].

For inter-device agreement, ICCs, Bland–Altman analysis, and linear correlation were used. ICC quantified absolute agreement between Corsano and EMC ECGs, while Bland–Altman plots

identified measurement bias and random error, reporting CRs to assess clinical interchangeability[47]. Correlation analysis (Pearson or Spearman) captured the strength of association between devices. This triad approach aligns with best practice in ECG validation studies and ensures best effort interpretation of technical and clinical agreement[44,46,47].

4.1b Intra-Device Reproducibility of Corsano ECGs

During the study period, signal quality remained consistently high, with 96% of Corsano ECGs meeting the predefined SQI threshold (SQI ≥ 80). Across the six primary ECG parameters, intra-subject variability was low, with CV remaining well below 10%, reflecting 'excellent' stability. Intraclass correlation coefficients ICCs further supported these findings, showing 'excellent' reproducibility (ICC ≥ 0.90) for HR, RR interval, and QTc, and 'good' reproducibility (ICC 0.75–0.89) for QT and PR intervals. QRS duration showed 'moderate' agreement, which aligns with existing limitations of single-lead ECGs in resolving complex waveforms like QRS[46,47]. No parameter demonstrated statistically significant differences across the three Corsano recordings, as determined by Friedman testing, indicating stable values within short acquisition intervals. Additional parameters such as heart rate variability, peak amplitudes, and entropy were also analysed and showed acceptable but higher stability. This was expected due to their physiological responsiveness to transient autonomic inputs[23,48,49]. These results suggest that, under stable clinical conditions, the Corsano CardioWatch can acquire ECG signals with stable within-patient properties, thereby justifying inter-device comparisons.

4.1c Agreement in ECG Parameter Values Between Devices

Following confirmation of intra-device reproducibility, this thesis evaluated the agreement between the ECG parameters measured by the Corsano CardioWatch and the standard 12-lead ECG system. The single-lead ECG showed 'good' to 'excellent' agreement for HR, RR interval, QT interval, and QTc interval, with ICCs and correlation coefficients above 0.75. These results align with prior studies validating wearable ECG devices[47,48,50,51]. For instance, studies using the Apple Watch and Withings ScanWatch have similarly high ICCs and narrow LoA for these parameters, particularly when manually reviewed signals[47,50].

In contrast, agreement for PR interval and QRS duration was substantially lower, with ICCs and correlation coefficients classified as 'poor' (values < 0.50). These results are consistent with known limitations of single-lead ECGs in accurately capturing parameters dependent on spatial resolution and multi-vectorial depolarisation[23,49]. These limitations are particularly evident for PR interval and QRS morphology, which are better characterised using multi-lead input. Even in simultaneous recordings studies, ICCs for PR and QRS intervals often fell below 0.70, especially under automatic measurement conditions[47]. These findings suggest that the Corsano CardioWatch offers acceptable performance for key rhythm and rate parameters but should be used cautiously for precise multi-lead measurements like PR interval and QRS duration. This aligns with prior work showing that single-lead wearables are more reliable for tracking rhythm trends than for full ECG interpretation[23,48].

4.1d Agreement in Diagnostic Classification Inter-Device

Diagnostic agreement between the Corsano and EMC ECGs was evaluated by comparing rhythm classifications across five predefined rhythm categories, with each comparison structured as a binary

classification against normal sinus rhythm. The Corsano CardioWatch achieved high diagnostic performance for the aggregated category of total abnormal rhythms, including 90% sensitivity, 100% specificity, and an overall accuracy of 97% (κ = 0.93). Sub-analyses for sinus bradycardia and abnormal sinus rhythm yielded similarly high agreement. Both devices concordantly detected two additional rhythms, sinus tachycardia (n = 2) and SA exit block (n = 1). While anecdotal, the SA exit block was detected by the Corsano CardioWatch before the EMC ECG, demonstrating the device's potential for early rhythm anomaly detection.

These findings align with studies showing that single-lead wearables, including the Corsano CardioWatch, accurately classify common arrhythmias like sinus bradycardia, tachycardia, and atrial fibrillation compared to standard ECGs, but struggle with complex ECG issues like ST-segment deviations or bundle branch blocks[23,52]. A recent study on the Apple Watch in an emergency department found strong agreement for rhythm classification against 12-lead ECGs, though accuracy decreased for non-rhythm-related abnormalities[52]. Yet, several reviews warrant caution for wearable ECGs to detect rhythm abnormalities reliant on multi-lead spatial resolution[23,53].

4.1e Influence of Clinical Characteristics on Inter-Device Discrepancy

Two analyses were performed to explore whether discrepancies between Corsano and EMC measurements were affected by patient-level factors. The clinical characteristics were selected a priori based on literature suggesting their potential to influence ECG measurements. BMI has been associated with changes in P-wave morphology, PR interval duration, and electrical axis, even within the normal range[54]. Age and affect QRS voltage and duration, and QTc interval, with differences most pronounced under 40 years of age[55]. Skin tone and forearm hair density were included due to growing concerns about wearable sensor performance in individuals with darker skin or dense hair coverage, which may impair signal acquisition[56,57].

Spearman correlations tested the association of four continuous variables (age, BMI, TKI duration, ECG interval) with discrepancies. Three out of 24 tests reached significance: age with QRS discrepancy, and TKI duration with PR and QRS discrepancies. However, all correlations were weak ($\rho < 0.37$), and visual inspection revealed no systematic trends of clinical importance. Univariate linear regression models evaluated the effects of the continuous plus three categorical variables (skin type, hair density, TKI type). In these models, two associations remained significant after multiple testing corrections: longer TKI duration with reduced PR discrepancy and absence of visible forearm hair with smaller QRS discrepancies. However, these findings are unlikely to affect clinical interpretation, given the already poor agreement for PR interval and QRS duration between Corsano and EMC ECGs.

Clinical characteristics were analysed only in relation to inter-device discrepancy. Although these characteristics were not explicitly modelled for intra-device reproducibility, signal quality was an indirect indicator: all patients had three Corsano ECGs with SQI scores ≥ 80, and exclusion rates were consistent across subgroups. Thus, stratification for intra-device reproducibility was deemed unnecessary.

4.2 Integration into Clinical Practice

4.2a Clinical Usability and Digital Integration

The Corsano CardioWatch showed usability and operational feasibility in a clinical setting, with efficient ECG acquisition and three recordings completed in under ten minutes per patient. Acquiring ECGs in a seated position, as opposed to the supine position required by 12-lead devices with more complex electrode placement, offers advantages for individuals with mobility impairments, including wheelchair users. The CardioWatch was well tolerated, and patients generally found it comfortable. Notably, wearable ECG devices are often preferred over traditional 12-lead systems due to their comfort, ease of use, and lack of adhesive electrodes—factors that promote adherence and support long-term monitoring, particularly in populations requiring frequent or continuous cardiac surveillance[23,53]. Wearable ECGs may also enhance diagnostic yield, particularly for intermittent arrhythmias, by increasing accessibility to timely rhythm recordings[53]. Moreover, existing evidence supports the role of mobile ECG technologies in AF screening, especially in low-resource settings where cases might otherwise go undetected[58].

Beyond ECG monitoring, the Corsano CardioWatch enables multi-parameter physiological assessment, including respiratory rate, SpO_2, activity tracking, and non-invasive blood pressure. Its CE-MDR and FDA certifications further reinforce its clinical readiness. A reliable digital infrastructure supports integration into healthcare workflows; in this thesis, the app and clinician dashboard were stable and user-friendly, facilitating seamless ECG collection, review, and data transfer. These observations align with findings from a recent clinical evaluation, where the CardioWatch enabled accurate continuous monitoring of vital signs and successfully interfaced with early warning systems such as NEWS2 in the intensive care unit[59].

4.2b Economic Considerations and Cost-Effectiveness

From an economic standpoint, single-lead ECG devices have shown favourable cost-effectiveness. For instance, AliveCor use in older populations reduced the need for follow-up 12-lead ECGs, achieving savings of up to £134 per patient while maintaining diagnostic accuracy[60]. Modelling also suggests that handheld ECG screening during influenza vaccination could be cost-saving, with cost-effectiveness ratios falling below the €20,000–€30,000 per QALY threshold[61]. Nevertheless, increased sensitivity in screening may lead to higher detection of subclinical or transient abnormalities, potentially resulting in overdiagnosis, false positives, and unnecessary follow-up testing—factors that may increase healthcare utilisation and cost[23,53]. Additionally, while single-lead devices are less resource-intensive, they may miss certain clinically relevant findings, making confirmatory 12-lead diagnostics necessary in some cases. Thus, although promising in cost-effectiveness, their broader economic impact hinges on appropriate clinical integration and targeted use.

4.2c Limitations of Wearable ECG Technology

Despite their clinical potential, single-lead wearable ECG devices face several practical challenges. These include the previously discussed economic considerations, where cost-effectiveness depends on appropriate clinical integration and targeted use, and the inherent limitations of single-lead

ECGs, such as reduced spatial and temporal resolution, resulting in clinical decisions in complex cases requiring a standard 12-lead ECG.

The U.S. Preventive Services Task Force advises against ECG screening in asymptomatic adults at low cardiovascular risk and highlights insufficient evidence to determine the benefit–harm ratio in those at intermediate or high risk[62]. These concerns are particularly relevant in single-lead ECGs, which may be used with lower thresholds and greater ease, potentially increasing the risk of false positives. Such false positives are especially problematic given the limited contextual information and reliance on automated interpretation, which may misclassify benign irregularities as pathological. This can result in patient anxiety, unnecessary clinical consultations, and inappropriate interventions, including unwarranted anticoagulation[53]. Frequent false or non-actionable alerts may also desensitise patients and healthcare providers, potentially resulting in ignored notifications, even when clinically important.

These challenges are further compounded by the increasing integration of artificial intelligence (AI) into ECG interpretation. While AI holds potential for enhancing diagnostic capabilities, it introduces additional challenges. There is currently no consensus on acceptable thresholds for AI accuracy[63], and clinicians remain reluctant to rely on AI-generated diagnoses due to limited transparency and unclear diagnostic criteria derived from AI models[48,64].

Furthermore, not all patient groups stand to benefit equally. For instance, in a study of 186 hospitalised geriatric patients, wearable ECG devices failed to generate traceable signals in 21% of cases, primarily due to usability difficulties[65]. Digital access and literacy further constrain utility, especially among older populations. In 2021, only 61% of adults aged 65 and older owned a smartphone, compared to 80% of younger adults[66]. This digital divide may limit engagement with smartphone-based monitoring solutions.

Finally, the surge in wearable ECG adoption has led to a proliferation of companion apps, many of which lack clinical validation and raise privacy concerns[67]. Many health apps have insufficient privacy safeguards and may transmit user data to third parties without robust encryption, compromising confidentiality[53]. In contrast, the CardioWatch meets European (MDR-CE) and U.S. (FDA 510(k)) regulatory standards for data protection and device safety[34]. Another limitation is the restricted storage capacity of some apps and devices, which prevents the retention of full-length ECG traces. This often results in the availability of only summary metrics or averaged values, limiting the ability of clinicians to review original waveforms retrospectively.

4.2d Considerations for Home-Based Implementation

Although the single-lead ECG function of the Corsano CardioWatch proved feasible in a supervised outpatient setting, transitioning to home-based use introduces additional challenges. Diagnostic accuracy depends not only on technical performance but also on consistent and correct patient use. For example, devices like the Apple Watch rely on intermittent recordings and trigger arrhythmia alerts only after several consecutive irregular readings, highlighting the importance of continuous and proper wear for detection sensitivity[68].

This user dependency underscores the need for structured onboarding, including education on device placement, troubleshooting, and minimising motion artefacts. While the Corsano platform includes instructional materials and a user-friendly interface[69], ensuring adherence and competence in unsupervised settings remains challenging. Furthermore, patients must have access to a compatible smartphone, stable Bluetooth or internet connectivity, and basic digital literacy to interact with the device and its companion app. These requirements may disproportionately impact older adults, individuals with cognitive impairments, and those from socioeconomically disadvantaged backgrounds[66],[65].

Another key consideration is the timely review and interpretation of remotely captured ECGs. Without predefined communication protocols and clinical response pathways, actionable abnormalities may be missed or result in unnecessary escalations. Furthermore, the emotional burden of self-monitoring should not be overlooked; false positives can induce anxiety, while ambiguous results may lead to overuse of healthcare services[53]. As home monitoring scales up, robust telecardiology support systems, clear triage criteria, and integration with EPD will be essential to ensure clinical safety and efficiency.

4.3 Methodological Considerations and Limitations

Several limitations should be acknowledged. First, Corsano and EMC ECGs were not recorded simultaneously, but within a median interval of 48 minutes. While this reflects a realistic clinical setting, it introduces potential physiological variation, particularly for rate- or rhythm-dependent parameters. Still, simultaneous recording was unfeasible due to technical interference and logistical constraints. Second, the research in this thesis focused on resting ECGs collected in an outpatient setting by trained clinicians, which may not reflect conditions in home use, where patients might encounter device placement or app operation challenges. Third, the performance of the CardioWatch under dynamic conditions, such as during physical activity, emotional stress, or arrhythmic episodes, remains untested. Fourth, the sample size (n = 71) was modest, limiting subgroup analyses, especially for rare rhythms like sinus tachycardia and SA exit block. Fifth, the research in this thesis was conducted at a single tertiary care centre, which may affect generalisability; broader validation across diverse institutions and populations is needed. Sixth, all Corsano ECG data were exported in pre-processed and normalised formats, and raw signals were unavailable. This constrained signal-level analysis precluded direct waveform comparisons or independent validation of signal quality. Furthermore, only automated summary statistics were extracted from the EMC ECG data, limiting the ability to perform individual lead comparisons. Lastly, some ECG parameters, such as HR and RR interval or QT and QTc interval, are mathematically linked. As a result, systematic error in one may propagate to others, potentially amplifying agreement or bias estimates.

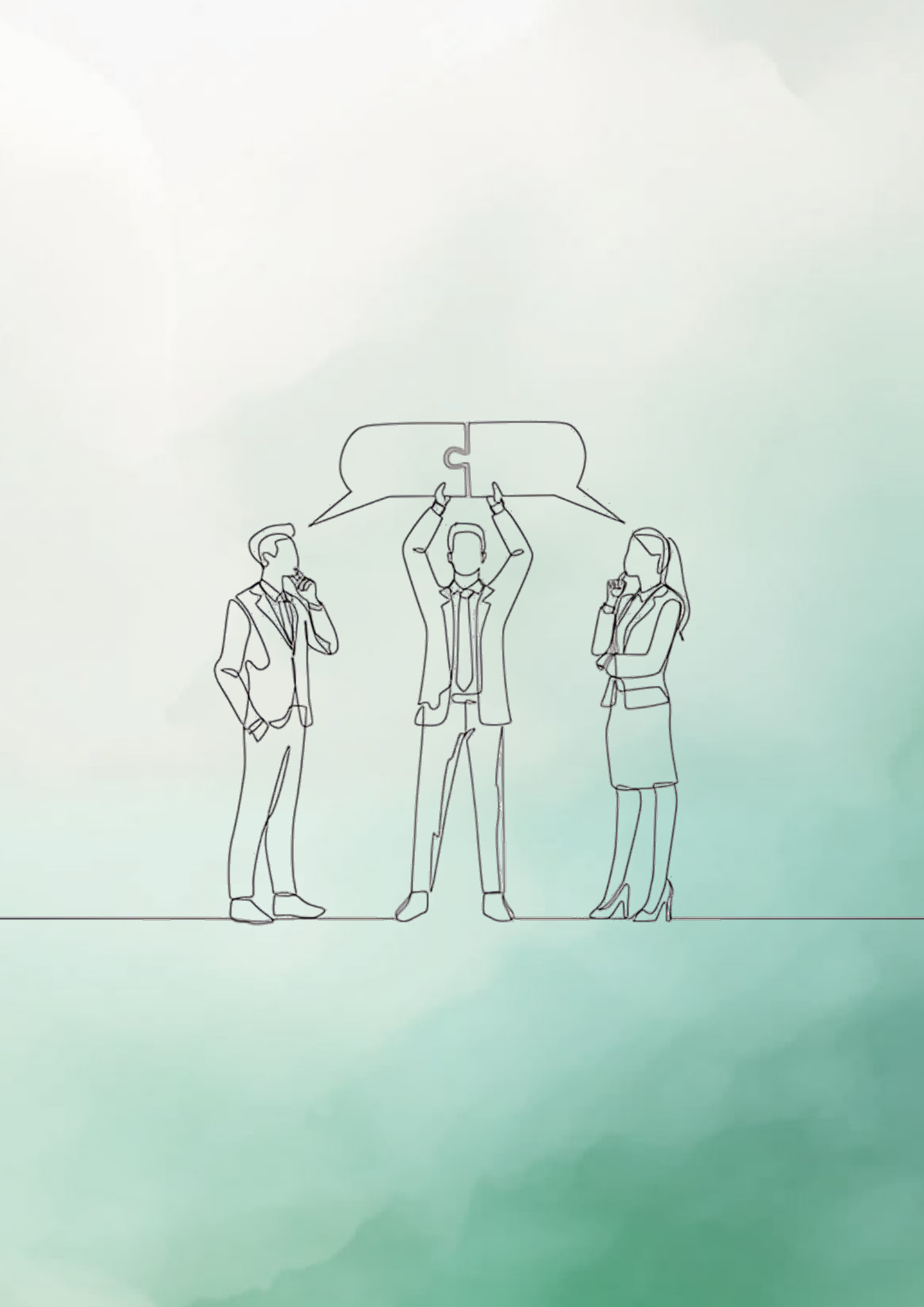
4.4 Future Perspectives

To enable the responsible and effective clinical integration of single-lead wearable ECG technologies in oncology, several research priorities must be addressed. Longitudinal studies are needed to assess device performance under unsupervised, home-based conditions, accounting for real-world variability due to physical activity, circadian fluctuations, and changes in drug levels. These

studies should also evaluate the impact of continuous ECG monitoring on clinical outcomes, treatment adaptations, early detection of cardiotoxicity, and patient quality of life, particularly in older adults and those with comorbidities, where adherence and digital literacy may be limited.

In parallel, further research should focus on developing and validating automated algorithms for rhythm classification, QT interval estimation, and artefact detection, specifically tailored to the characteristics of single-lead ECG signals. Diagnostic thresholds and correction formulas may require recalibration for wearable-derived data, and their clinical validity must be established prospectively in high-risk oncology populations.

To ensure successful adoption, implementation science frameworks should be employed to identify barriers and facilitators related to digital literacy, device accessibility, and clinician engagement. A robust telecardiology infrastructure will be essential, incorporating clinician oversight, automated triage systems, and secure integration with EPD to support scalable deployment. Continued regulatory oversight and rigorous validation of both devices and their companion applications will guarantee safety, data integrity, and clinical relevance in routine practice.



5 CONCLUSION

This thesis evaluated the single-lead ECG functionality of the Corsano CardioWatch 287-2, focusing on its clinical feasibility, parameter consistency, and parameter and diagnostic outcomes agreement with a standard 12-lead hospital ECG in patients with NSCLC receiving osimertinib or alectinib TKI therapy. The wearable was well tolerated, easy to deploy, and supported by stable digital infrastructure for reliable data transfer and high signal quality. The wearable demonstrated 'excellent' intra-device reproducibility for key ECG parameters, including HR, RR interval, and QT(c) interval. Agreement with 12-lead ECGs was 'good' to 'excellent' for HR and QTc, and 'moderate' for PR interval and QRS duration. Diagnostic concordance was high, particularly for rhythm-based classifications such as sinus bradycardia and abnormal sinus rhythm. Clinical characteristics, including age, BMI, TKI therapy duration, time between ECGs, Fitzpatrick skin type, forearm hair density, and TKI type, did not meaningfully affect inter-device agreement.

In conclusion, the Corsano CardioWatch 287-2 shows promise as a medically regulated, user-friendly tool for accurate remote ECG monitoring. It may reduce hospital burden and facilitate early identification of cardiotoxic events. Future studies should evaluate its performance in longitudinal, unsupervised home settings and assess its impact on clinical decision-making, patient safety, and long-term outcomes.

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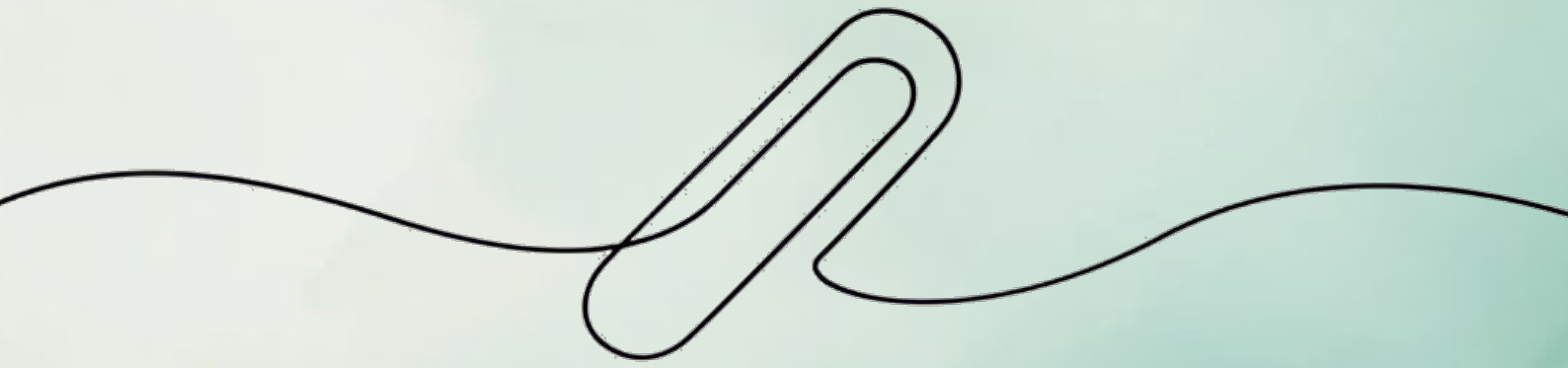


8 APPENDICES

8.1 Supplementary Tables

Supplementary Table S1. *Baseline Demographic and Clinical Characteristics of the Included Patients Stratified by TKI Treatment.*

Variable	**Alectinib**, N = 32*	**Osimertinib**, N = 39*	**p-value****	**p-adj****
Age at inclusion [years]	68 [60, 75]	65 [55, 72]	0.3	0.5
Sex			0.3	0.5
Female	25 (78)	26 (67)		
Male	7 (22)	13 (33)		
BMI [kg/m²]	30.0 [25, 33]	26.4 [23, 28]	**0.026**	0.071
Smoking status			0.2	0.5
Current	0 (0)	3 (7)		
Former	4 (13)	7 (18)		
Never	28 (88)	29 (74)		
Alcohol status			0.3	0.5
Current	13 (41)	10 (26)		
Former	13 (41)	16 (41)		
Never	6 (19)	13 (33)		
Skin type (Fitzpatrick)			0.7	0.8
Type II	2 (6)	6 (15)		
Type III	25 (78)	27 (69)		
Type IV	3 (9)	4 (10)		
Type V	2 (6)	2 (5)		
Forearm hair density			0.4	0.5
Dense	3 (9)	3 (7.7)		
Moderate	3 (9)	9 (23)		
Nil	6 (19)	9 (23)		
Sparse	20 (63)	18 (46)		
Time between ECGs [min]	46 [19, 67]	48 [27, 77]	0.4	0.5
Stage at diagnosis			0.2	0.5
Ia/Ib	7 (21)	3 (8)		
IVa	8 (25)	8 (21)		
IVb	17 (53)	28 (72)		
NSCLC subtype			0.4	0.5
Adenocarcinoma	28 (88)	37 (95)		
NOS	4 (13)	2 (5)		
Mutation			**<0.001**	**<0.001**
ALK	32 (100)	0 (0)		
EGFR	0 (0)	39 (100)		
Specify EGFR			>0.9	>0.9
Exon 19del	0 (0)	28 (72)		
Exon 21 p.L858R	0 (0)	11 (28)		
Missing	32	0		
Time since diagnosis [months]	58 [40, 84]	35 [10, 64]	**0.014**	**0.046**
Intake frequency TKI [dd]			**<0.001**	**<0.001**
1	0 (0)	39 (100)		
2	32 (100)	0 (0)		
Dose current TKI [mg]			**<0.001**	**<0.001**
40 to 80	0 (0)	39 (100)		
300 to 600	32 (100)	0 (0)		
Duration of TKI therapy [months]	41 [30, 69]	26 [10, 39]	**0.009**	**0.035**

* Median [IQR]; n (%).

** Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test.

*** False discovery rate correction for multiple testing. Bold p-values indicate statistically significant differences.

Abbreviations: ALK, Anaplastic Lymphoma Kinase; BMI, Body Mass Index; ECG, Electrocardiogram; EGFR, Epidermal Growth Factor Receptor; NOS, Not Otherwise Specified; NSCLC, Non-Small Cell Lung Cancer; TKI, Tyrosine Kinase Inhibitor.

Supplementary Table S2. *Intra-Device Reproducibility Analysis of All Corsano ECG Parameters.*

Parameter	Patients (n)*	Corsano ECGs (n)*	Median [IQR]	Mean CV [±SD] [%]	ICC [95% CI]	Friedman p-value***
HR [bpm]	66	198	78.4 [69.8–87.1]	2 [±2]	0.97 [0.96–0.98]	0.480
RMSSD [ms]	66	198	15.4 [8.1–25.9]	31.2 [±26.2]	0.76 [0.67–0.84]	0.043
SDSD [ms]	66	198	9.2 [5–18.9]	38.6 [±32.7]	0.68 [0.57–0.78]	0.087
Entropy	51	153	0.3 [0.1–0.5]	33.6 [±24.5]	0.79 [0.69–0.86]	0.025
IARS	66	198	5 [3–6]	19.5 [±18.1]	0.58 [0.45–0.7]	0.160
SDNNc [ms]	66	198	59 [53–71]	11.2 [±9.9]	0.80 [0.72–0.87]	0.540
Min HR [bpm]	66	198	72.5 [63.4–81.6]	4.3 [±5.7]	0.87 [0.82–0.92]	0.190
Max HR [bpm]	66	198	84.9 [74.2–94.2]	4.6 [±5.6]	0.85 [0.79–0.9]	0.790
RR mode [ms]	66	198	775 [675–875]	2.3 [±3.3]	0.96 [0.93–0.97]	0.550
P amp [µV]	23	69	69.5 [52–81.5]	11.3 [±6.8]	0.83 [0.69–0.92]	0.860
Q amp [µV]	15	45	-104 [-118.5–-81]	6.1 [±3.5]	0.97 [0.92–0.99]	0.250
R amp [µV]	66	198	810 [559–1130]	3.5 [±3.4]	0.99 [0.99–1]	0.520
S amp [µV]	38	114	-113 [-259–-47.5]	10.4 [±8.9]	0.98 [0.97–0.99]	0.350
J amp [µV]	62	186	-12 [-32.2–7.2]	161.3 [±317.8]	0.61 [0.48–0.72]	0.410
Median ST amp [µV]	61	183	-2 [-20.2–18.2]	130.1 [±361.4]	0.84 [0.77–0.9]	0.720
End ST amp [µV]	62	186	18 [-4–44]	125.8 [±286.3]	0.85 [0.78–0.9]	0.180
T amp [µV]	65	195	247 [174–313]	7.9 [±8.2]	0.97 [0.96–0.98]	0.058
PR interval [ms]	23	69	145 [129–164.5]	7.3 [±4.8]	0.78 [0.62–0.89]	0.780
QR interval [ms]	66	198	31 [27–47]	9 [±13.6]	0.59 [0.45–0.7]	0.330
QT interval [ms]	66	198	375 [355–395]	2.6 [±2.3]	0.82 [0.75–0.88]	0.920
QTc interval [ms]	66	198	490 [434.4–530.9]	2.9 [±2.4]	0.91 [0.87–0.94]	0.320
QTcF interval [ms]	66	198	404 [392–423]	2.5 [±2.2]	0.69 [0.58–0.79]	0.660
QRS duration [ms]	66	198	105 [98–113]	4.8 [±4.9]	0.63 [0.5–0.74]	0.530
RR interval [ms]	66	198	762 [688–859]	2 [±1.9]	0.98 [0.97–0.99]	0.780
RP interval [ms]	23	69	141 [124–160]	7.9 [±7.1]	0.64 [0.41–0.81]	0.480
P duration [ms]	23	69	98 [86–109]	9.9 [±6.5]	0.56 [0.31–0.76]	0.890
T duration [ms]	66	198	160 [148–180]	8.1 [±5.4]	0.54 [0.4–0.67]	0.400

* Patients were excluded if any ECG had SQI < 80.

** Patients were additionally excluded for a specific parameter if any ECG had a value of 0.

*** No adjustment for multiple testing applied due to interdependence among parameters. Normality testing is unreliable due to the small sample size per patient (3 ECGs).

Colour legend: ICC – darkgreen (≥0.85), golden (0.75–0.84), orange (0.50–0.74); CV – green (<10%), golden (10–19.9%), red (≥20%); Friedman p – black (p ≥ 0.05), firebrick (p < 0.05).

Abbreviations: bpm, beats per minute; CI, Confidence Interval; COR, Corsano; CR, Coefficient of Repeatability; ECG, Electrocardiogram; EMC, Erasmus MC; HR, Heart Rate; ICC, Intraclass Correlation Coefficients; IQR, Interquartile Range; LoA, Limits of Agreement; p.adj, p-value adjusted for multiple testing; SD, Standard Deviation.

Supplementary Table S3. *Classifications Performance Metrics for Inter-Device Concordance in All ECG Diagnostic*

Diagnostic Performance: Abnormal Rhythm vs Normal Sinus Rhythm

Metric	Value
Sensitivity	0.895
Specificity	1.000
PPV	1.000
NPV	0.962
Accuracy	0.971
Cohen's Kappa	0.925

Confusion Matrix: Abnormal Rhythm vs Normal Sinus Rhythm

EMC (Reference)	Corsano: Normal Sinus Rhythm	Corsano: Abnormal Rhythm
Normal Sinus Rhythm	51	0
Abnormal Rhythm	2	17

*Abnormal Rhythm, defined as predictor, is compared to Normal Sinus Rhythm, defined as reference.

Diagnostic Performance: Sinus Bradycardia vs Normal Sinus Rhythm

Metric	Value
Sensitivity	0.909
Specificity	1.000
PPV	1.000
NPV	0.981
Accuracy	0.984
Cohen's Kappa	0.943

Confusion Matrix: Sinus Bradycardia vs Normal Sinus Rhythm

EMC (Reference)	Corsano: Normal Sinus Rhythm	Corsano: Sinus Bradycardia
Normal Sinus Rhythm	51	0
Sinus Bradycardia	1	10

*Sinus Bradycardia, defined as predictor, is compared to Normal Sinus Rhythm, defined as reference.

Diagnostic Performance: Sinus Tachycardia vs Normal Sinus Rhythm

Metric	Value
Sensitivity	1
Specificity	1
PPV	1
NPV	1
Accuracy	1
Cohen's Kappa	1

Confusion Matrix: Sinus Tachycardia vs Normal Sinus Rhythm

EMC (Reference)	Corsano: Normal Sinus Rhythm	Corsano: Sinus Tachycardia
Normal Sinus Rhythm	51	0
Sinus Tachycardia	0	2

*Sinus Tachycardia, defined as predictor, is compared to Normal Sinus Rhythm , defined as reference.

Diagnostic Performance: Abnormal Sinus Rhythm vs Normal Sinus Rhythm

Metric	Value
Sensitivity	0.800
Specificity	1.000
PPV	1.000
NPV	0.981
Accuracy	0.982
Cohen's Kappa	0.879

Confusion Matrix: Abnormal Sinus Rhythm vs Normal Sinus Rhythm

EMC (Reference)	Corsano: Normal Sinus Rhythm	Corsano: Abnormal Sinus Rhythm
Normal Sinus Rhythm	51	0
Abnormal Sinus Rhythm	1	4

*Abnormal Sinus Rhythm, defined as predictor, is compared to Normal Sinus Rhythm, defined as reference.

Diagnostic Performance: SA Exit Block vs Normal Sinus Rhythm

Metric	Value
Sensitivity	1
Specificity	1
PPV	1
NPV	1
Accuracy	1
Cohen's Kappa	1

Table Confusion Matrix: SA Exit Block vs Normal Sinus Rhythm

EMC (Reference)	Corsano: Normal Sinus Rhythm	Corsano: SA Exit Block
Normal Sinus Rhythm	51	0
SA Exit Block	0	1

*SA Exit Block, defined as predictor, is compared to Normal Sinus Rhythm , defined as reference.

Supplementary Table S4. *Spearman Correlations: Influence of Continuous Clinical Characteristics on Inter-Device ECG Discrepancy.*

ECG Parameter	Predictor	Method	Correlation [95% CI]	p-value
HR [bpm]	Age at Inclusion (years)[1]	Spearman[2]	ρ = -0.19 [-0.22 to 0.25]	0.119
RR interval [ms]	Age at Inclusion (years)	Spearman	ρ = -0.15 [-0.22 to 0.23]	0.223
PR interval [ms]	Age at Inclusion (years)	Spearman	ρ = -0.06 [-0.26 to 0.26]	0.673
QRS duration [ms]	Age at Inclusion (years)	Spearman	ρ = -0.24 [-0.23 to 0.24]	0.044
QT interval [ms]	Age at Inclusion (years)	Spearman	ρ = 0.09 [-0.25 to 0.23]	0.444
QTc interval [ms]	Age at Inclusion (years)	Spearman	ρ = -0.23 [-0.24 to 0.23]	0.057
HR [bpm]	BMI (kg/m²)	Spearman	ρ = -0.12 [-0.22 to 0.22]	0.335
RR interval [ms]	BMI (kg/m²)	Spearman	ρ = -0.09 [-0.23 to 0.23]	0.443
PR interval [ms]	BMI (kg/m²)	Spearman	ρ = 0.15 [-0.29 to 0.28]	0.280
QRS duration [ms]	BMI (kg/m²)	Spearman	ρ = -0.09 [-0.25 to 0.23]	0.465
QT interval [ms]	BMI (kg/m²)	Spearman	ρ = -0.05 [-0.24 to 0.23]	0.709
QTc interval [ms]	BMI (kg/m²)	Spearman	ρ = -0.04 [-0.24 to 0.23]	0.766
HR [bpm]	Duration of TKI Therapy (months)	Spearman	ρ = -0.03 [-0.22 to 0.23]	0.817
RR interval [ms]	Duration of TKI Therapy (months)	Spearman	ρ = 0.01 [-0.24 to 0.26]	0.936
PR interval [ms]	Duration of TKI Therapy (months)	Spearman	ρ = -0.30 [-0.29 to 0.27]	0.028
QRS duration [ms]	Duration of TKI Therapy (months)	Spearman	ρ = 0.36 [-0.23 to 0.25]	0.002
QT interval [ms]	Duration of TKI Therapy (months)	Spearman	ρ = -0.05 [-0.23 to 0.23]	0.706
QTc interval [ms]	Duration of TKI Therapy (months)	Spearman	ρ = -0.05 [-0.24 to 0.23]	0.688
HR [bpm]	Time difference EMC and Corsano ECG (min)	Spearman	ρ = 0.04 [-0.20 to 0.24]	0.749
RR interval [ms]	Time difference EMC and Corsano ECG (min)	Spearman	ρ = 0.03 [-0.24 to 0.24]	0.779
PR interval [ms]	Time difference EMC and Corsano ECG (min)	Spearman	ρ = 0.17 [-0.26 to 0.26]	0.233
QRS duration [ms]	Time difference EMC and Corsano ECG (min)	Spearman	ρ = -0.05 [-0.23 to 0.23]	0.682
QT interval [ms]	Time difference EMC and Corsano ECG (min)	Spearman	ρ = 0.05 [-0.23 to 0.23]	0.670
QTc interval [ms]	Time difference EMC and Corsano ECG (min)	Spearman	ρ = 0.01 [-0.24 to 0.23]	0.903

* Only predictors with continues values are included in this analysis.

** ECG disconcordance is defined as absolute difference between Corsano and EMC ECG parameter value.

*** Green values indicate statistically significant differences.

Abbreviations: BMI, Body Mass Index; bpm, beats per minute; CI, Confidence Interval; CR, Coefficient of Repeatability; ECG, Electrocardiogram; HR, Heart Rate.

Supplementary Table S5. *Univariate Linear Regressions: Influence of Continuous and Categorical Clinical Characteristics on Inter-Device ECG Discrepancy.*

ECG Parameter	Predictor	Beta	95% CI	p-value	p-adj (FDR)
HR [bpm]	Age at Inclusion (years)	-0.06	[-0.15 to 0.02]	0.128	0.567
RR interval [ms]	Age at Inclusion (years)	-0.69	[-1.61 to 0.23]	0.138	0.567
PR interval [ms]	Age at Inclusion (years)	1.13	[-0.53 to 2.79]	0.179	0.622
QRS duration [ms]	Age at Inclusion (years)	-0.06	[-0.22 to 0.11]	0.496	0.868
QT interval [ms]	Age at Inclusion (years)	0.12	[-0.12 to 0.36]	0.334	0.868
QTc Bazett [ms]	Age at Inclusion (years)	-0.34	[-0.87 to 0.19]	0.202	0.667
HR [bpm]	BMI (kg/m²)	-0.01	[-0.12 to 0.10]	0.794	0.958
RR interval [ms]	BMI (kg/m²)	-0.08	[-1.30 to 1.13]	0.894	0.966
PR interval [ms]	BMI (kg/m²)	-1.56	[-5.80 to 2.68]	0.463	0.868
QRS duration [ms]	BMI (kg/m²)	-0.04	[-0.26 to 0.17]	0.696	0.958
QT interval [ms]	BMI (kg/m²)	-0.10	[-0.41 to 0.21]	0.524	0.887
QTc Bazett [ms]	BMI (kg/m²)	0.02	[-0.68 to 0.72]	0.954	0.981
HR [bpm]	Name of Current TKI: Alectinib	-2.35	[-4.48 to -0.22]	0.031	0.409
RR interval [ms]	Name of Current TKI: Alectinib	-11.00	[-35.26 to 13.25]	0.369	0.868
PR interval [ms]	Name of Current TKI: Alectinib	-37.17	[-78.13 to 3.80]	0.074	0.567
QRS duration [ms]	Name of Current TKI: Alectinib	-1.60	[-5.95 to 2.76]	0.467	0.868
QT interval [ms]	Name of Current TKI: Alectinib	-2.25	[-8.53 to 4.02]	0.476	0.868
QTc Bazett [ms]	Name of Current TKI: Alectinib	-16.32	[-29.71 to -2.93]	0.018	0.396
HR [bpm]	Duration of TKI Therapy (months)	0.00	[-0.05 to 0.04]	0.891	0.966
RR interval [ms]	Duration of TKI Therapy (months)	0.07	[-0.40 to 0.54]	0.782	0.958
PR interval [ms]	Duration of TKI Therapy (months)	-0.82	[-1.55 to -0.09]	0.028	0.409
QRS duration [ms]	Duration of TKI Therapy (months)	0.14	[0.07 to 0.22]	<0.001	0.033
QT interval [ms]	Duration of TKI Therapy (months)	-0.05	[-0.17 to 0.07]	0.416	0.868
QTc Bazett [ms]	Duration of TKI Therapy (months)	-0.05	[-0.32 to 0.22]	0.720	0.958
HR [bpm]	Time Between ECGs (min)	0.00	[-0.01 to 0.01]	0.684	0.958
RR interval [ms]	Time Between ECGs (min)	-0.02	[-0.11 to 0.07]	0.709	0.958
PR interval [ms]	Time Between ECGs (min)	-0.01	[-0.15 to 0.13]	0.876	0.966
QRS duration [ms]	Time Between ECGs (min)	0.00	[-0.01 to 0.02]	0.876	0.966
QT interval [ms]	Time Between ECGs (min)	0.00	[-0.02 to 0.02]	0.907	0.966
QTc Bazett [ms]	Time Between ECGs (min)	-0.02	[-0.08 to 0.03]	0.354	0.868
HR [bpm]	Fitzpatrick Skin Type: Type II	2.53	[-0.90 to 5.96]	0.146	0.567
HR [bpm]	Fitzpatrick Skin Type: Type IV	2.91	[-0.73 to 6.55]	0.115	0.567
HR [bpm]	Fitzpatrick Skin Type: Type V	0.81	[-3.87 to 5.50]	0.730	0.958
RR interval [ms]	Fitzpatrick Skin Type: Type II	18.74	[-19.49 to 56.97]	0.331	0.868
RR interval [ms]	Fitzpatrick Skin Type: Type IV	31.57	[-8.95 to 72.09]	0.125	0.567
RR interval [ms]	Fitzpatrick Skin Type: Type V	17.74	[-34.46 to 69.94]	0.500	0.868
PR interval [ms]	Fitzpatrick Skin Type: Type II	-14.27	[-75.61 to 47.07]	0.642	0.958
PR interval [ms]	Fitzpatrick Skin Type: Type IV	-25.85	[-91.33 to 39.63]	0.431	0.868
PR interval [ms]	Fitzpatrick Skin Type: Type V	67.12	[-11.15 to 145.39]	0.091	0.567
QRS duration [ms]	Fitzpatrick Skin Type: Type II	-4.79	[-11.68 to 2.11]	0.171	0.622
QRS duration [ms]	Fitzpatrick Skin Type: Type IV	1.20	[-6.11 to 8.51]	0.744	0.958
QRS duration [ms]	Fitzpatrick Skin Type: Type V	-1.04	[-10.46 to 8.38]	0.827	0.958
QT interval [ms]	Fitzpatrick Skin Type: Type II	1.62	[-8.47 to 11.71]	0.750	0.958
QT interval [ms]	Fitzpatrick Skin Type: Type IV	-1.22	[-11.91 to 9.47]	0.820	0.958
QT interval [ms]	Fitzpatrick Skin Type: Type V	2.33	[-11.45 to 16.10]	0.737	0.958
QTc Bazett [ms]	Fitzpatrick Skin Type: Type II	17.25	[-4.72 to 39.22]	0.122	0.567
QTc Bazett [ms]	Fitzpatrick Skin Type: Type IV	6.81	[-16.47 to 30.10]	0.561	0.903
QTc Bazett [ms]	Fitzpatrick Skin Type: Type V	4.75	[-25.25 to 34.75]	0.753	0.958
HR [bpm]	Forearm Hair Density: Nil	-1.02	[-3.89 to 1.86]	0.483	0.868
HR [bpm]	Forearm Hair Density: Moderate	1.18	[-1.87 to 4.23]	0.443	0.868
HR [bpm]	Forearm Hair Density: Dense	-0.04	[-4.09 to 4.00]	0.984	0.984

ECG Parameter	Predictor	Beta	95% CI	p-value	p-adj (FDR)
RR interval [ms]	Forearm Hair Density: Nil	-9.72	[-41.76 to 22.33]	0.547	0.903
RR interval [ms]	Forearm Hair Density: Moderate	3.99	[-29.95 to 37.93]	0.815	0.958
RR interval [ms]	Forearm Hair Density: Dense	5.55	[-39.48 to 50.57]	0.806	0.958
PR interval [ms]	Forearm Hair Density: Moderate	27.13	[-28.27 to 82.53]	0.330	0.868
PR interval [ms]	Forearm Hair Density: Nil	42.72	[-12.69 to 98.12]	0.128	0.567
PR interval [ms]	Forearm Hair Density: Dense	-1.55	[-74.56 to 71.46]	0.966	0.981
QRS duration [ms]	Forearm Hair Density: Nil	-8.98	[-14.27 to -3.69]	0.001	0.033
QRS duration [ms]	Forearm Hair Density: Moderate	-5.02	[-10.62 to 0.58]	0.078	0.567
QRS duration [ms]	Forearm Hair Density: Dense	-2.66	[-10.09 to 4.77]	0.478	0.868
QT interval [ms]	Forearm Hair Density: Nil	-3.37	[-11.36 to 4.62]	0.403	0.868
QT interval [ms]	Forearm Hair Density: Moderate	6.53	[-1.93 to 14.99]	0.128	0.567
QT interval [ms]	Forearm Hair Density: Dense	-6.05	[-17.28 to 5.17]	0.286	0.868
QTc Bazett [ms]	Forearm Hair Density: Nil	-13.35	[-31.37 to 4.67]	0.144	0.567
QTc Bazett [ms]	Forearm Hair Density: Moderate	0.78	[-18.31 to 19.86]	0.935	0.980
QTc Bazett [ms]	Forearm Hair Density: Dense	-11.94	[-37.26 to 13.38]	0.350	0.868

* Predictors with continues values and categorial groups are included in this analysis.

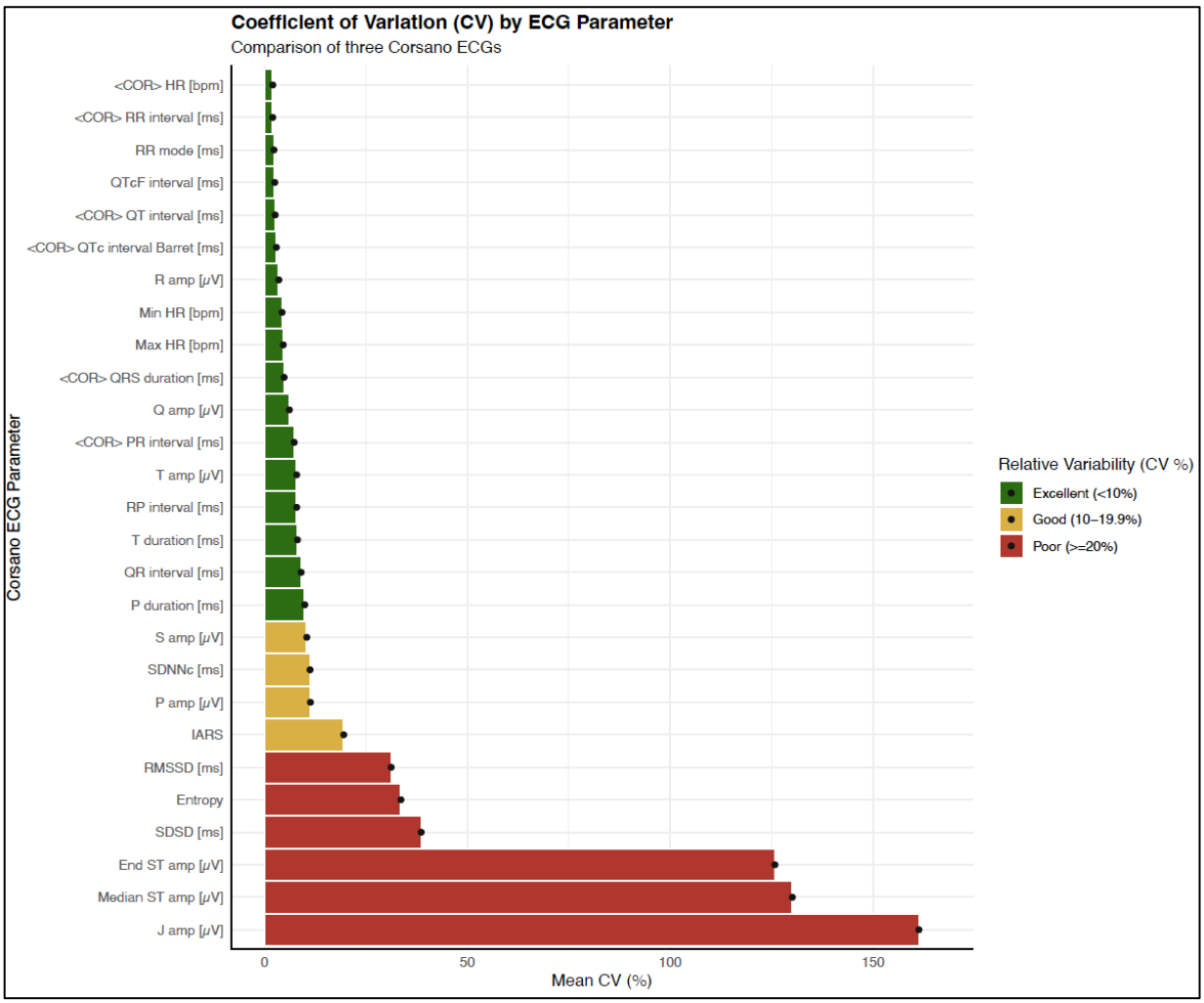
** ECG disconcordance is defined as absolute difference between Corsano and EMC ECG parameter value.

*** Green values indicate statistically significant differences.

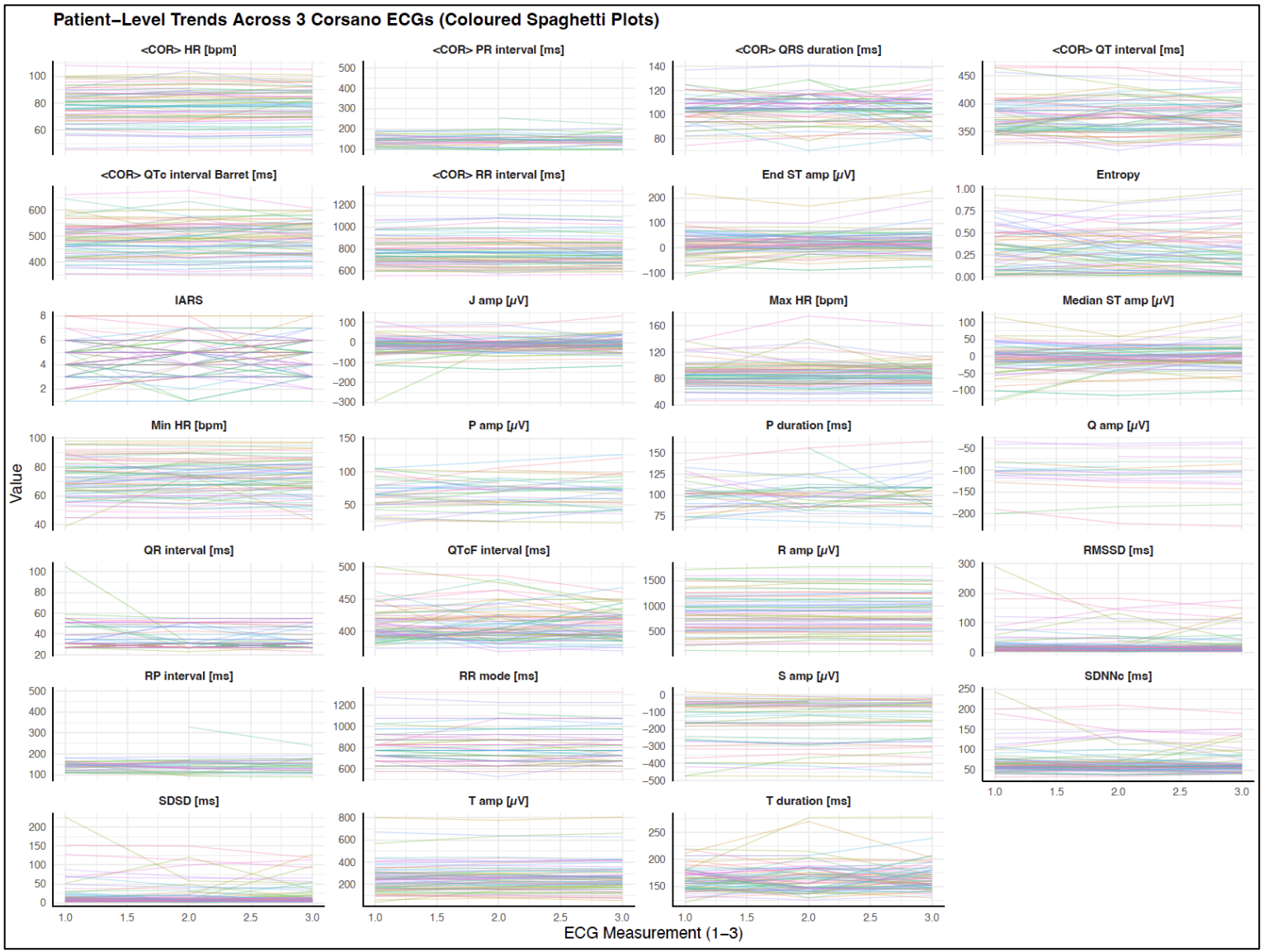
Abbreviations: BMI, Body Mass Index; bpm, beats per minute; CI, Confidence Interval; CR, Coefficient of Repeatability; ECG, Electrocardiogram; HR, Heart Rate.

8.2 Supplementary Figures

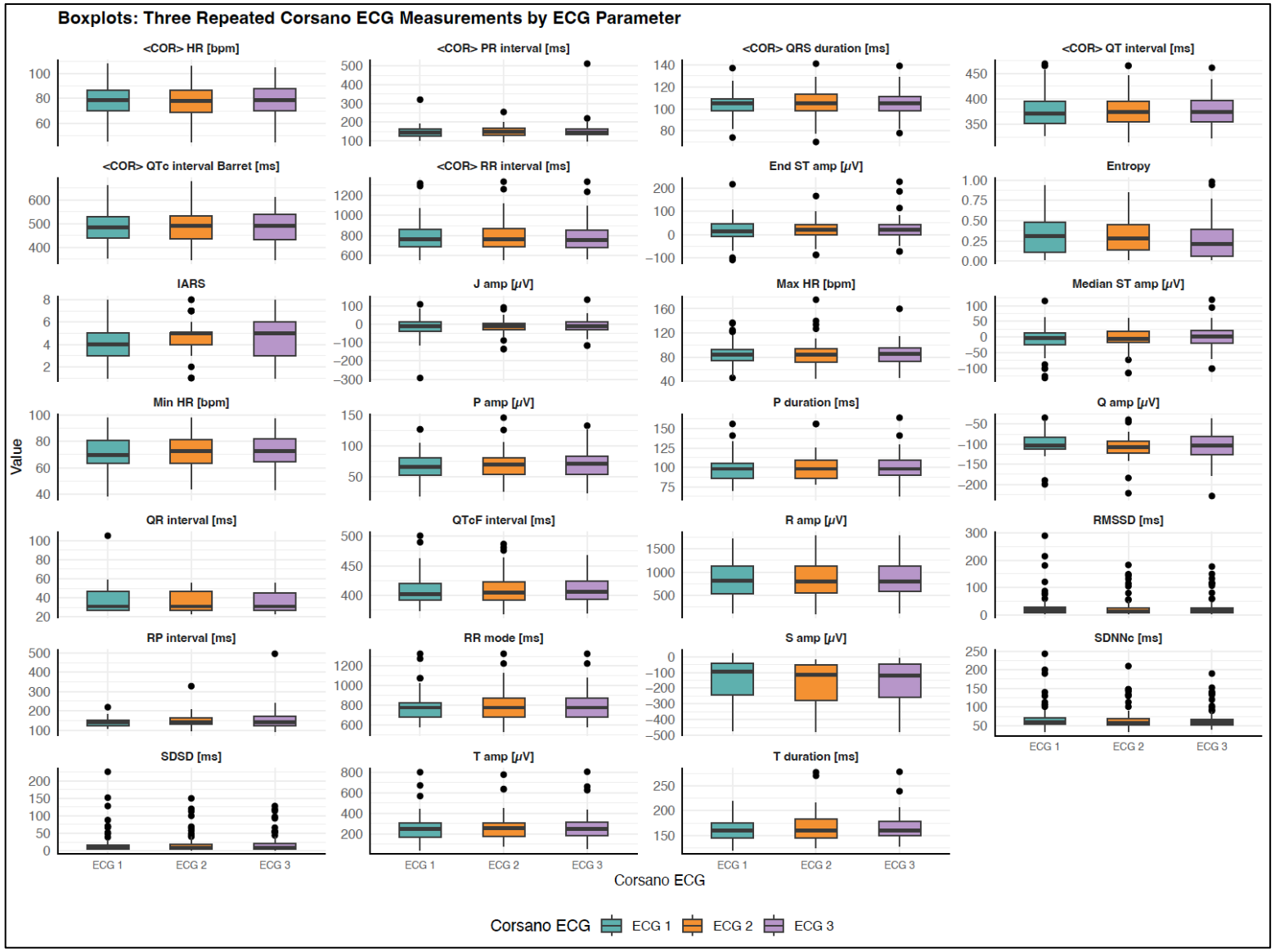
Supplementary Figure S1. *Barplots of the Coefficient of Variation Values of All Corsano ECG Parameters.*



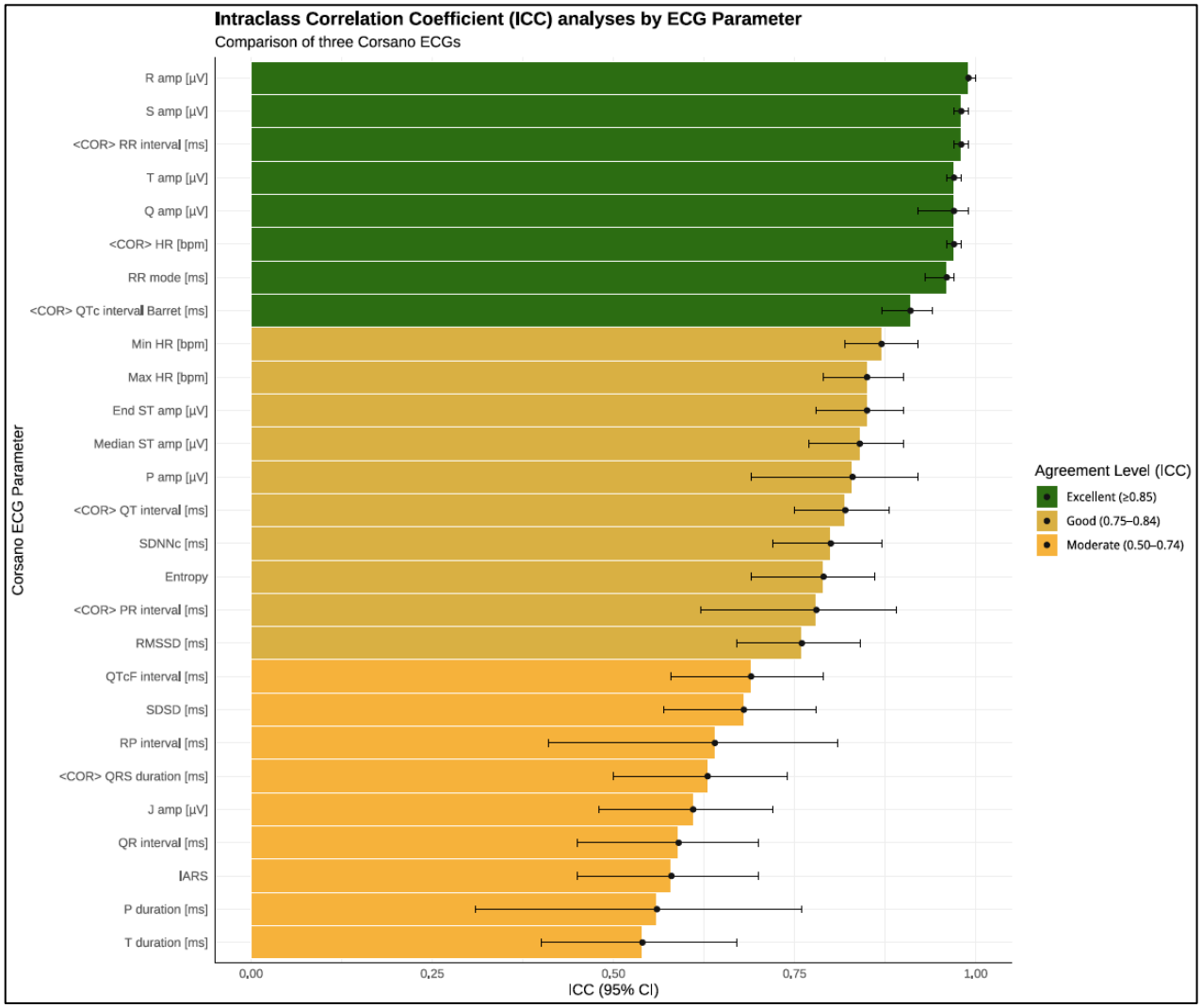
Supplementary Figure S2. *Spaghetti Plots Visualising Patient-Level Trends Across All Corsano ECG Parameters.*



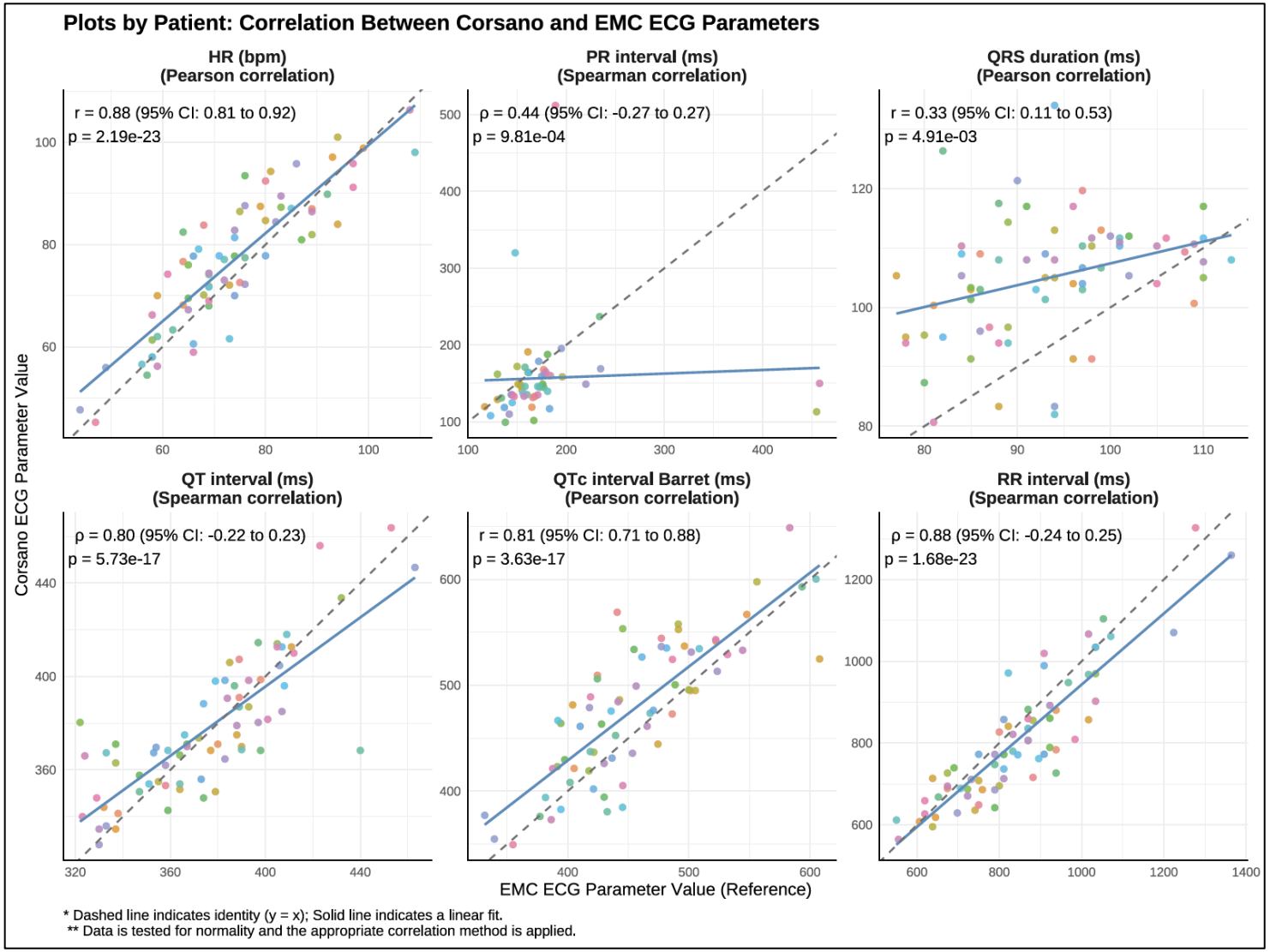
Supplementary Figure S3. *Box Plots Visualising Parameter Distributions Across All Corsano ECG Parameters.*



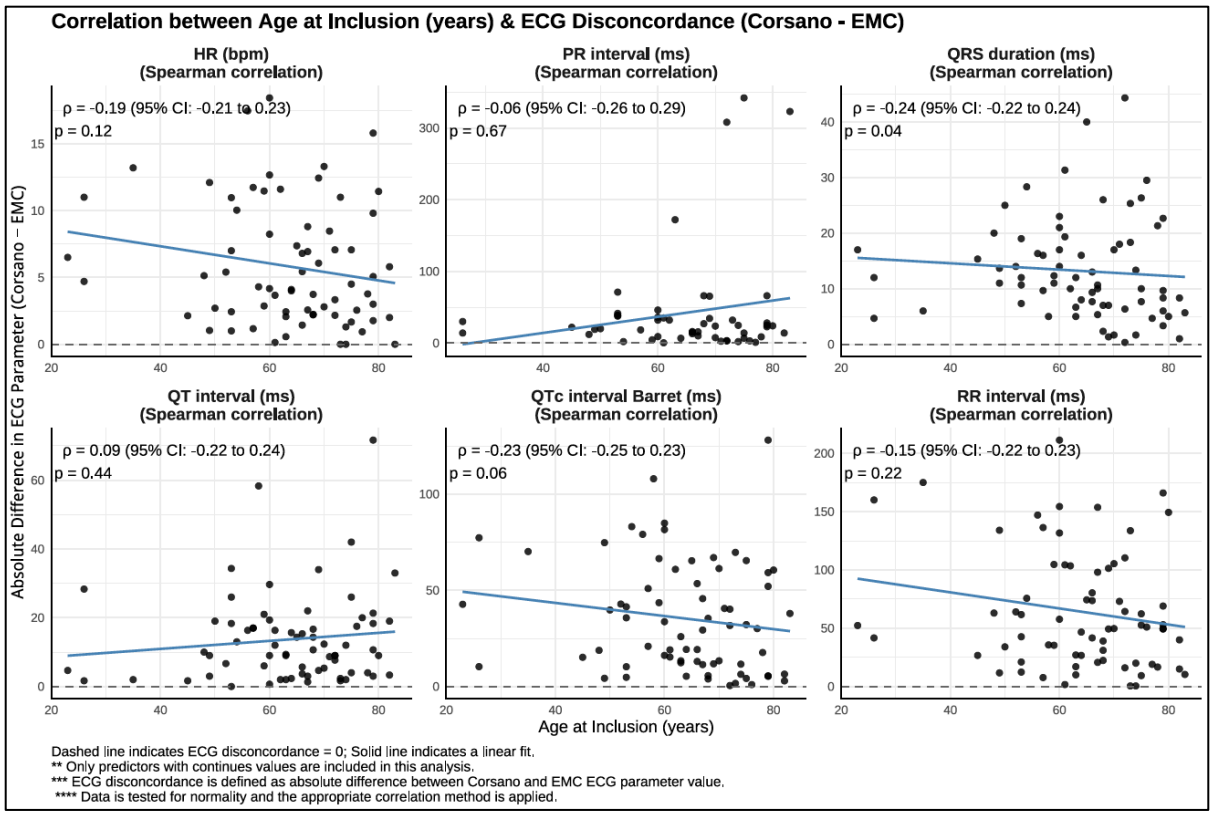
Supplementary Figure S4. *Barplots of the Intraclass Correlation Coefficients of All Corsano ECG Parameters.*

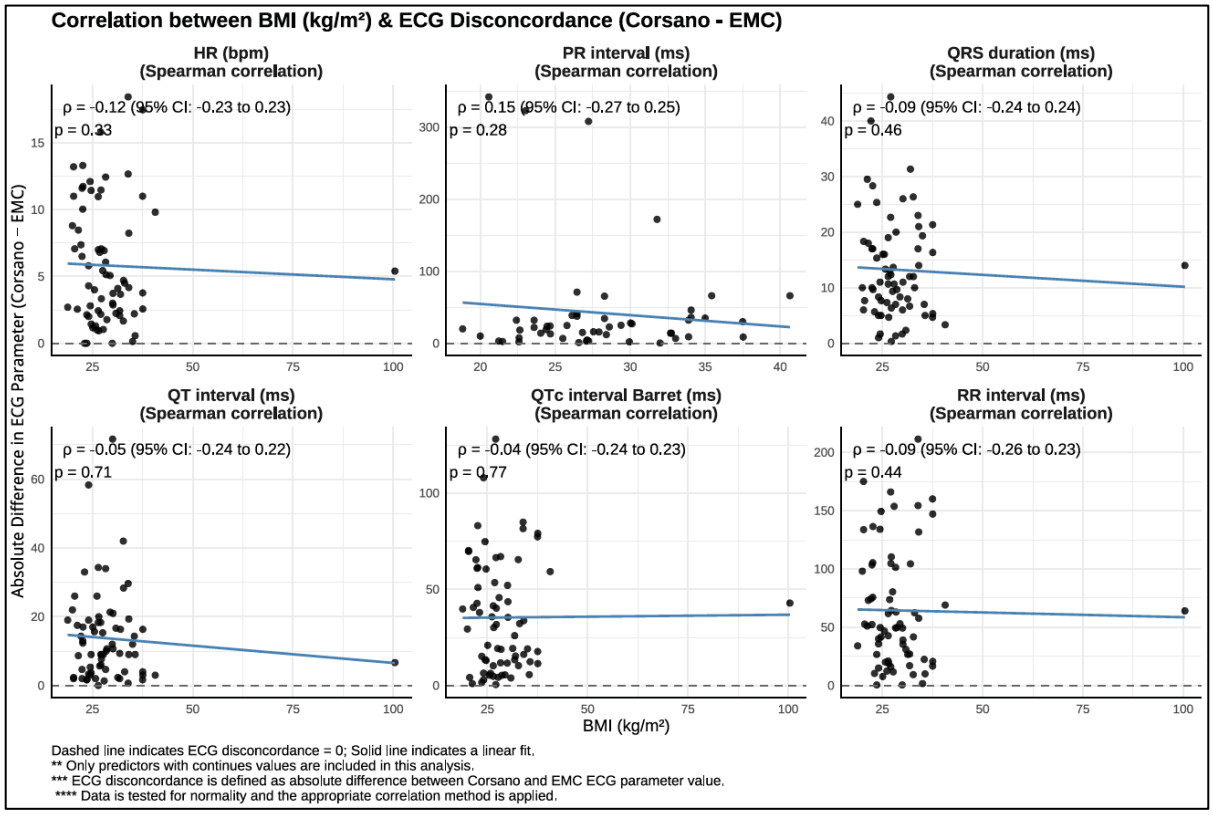


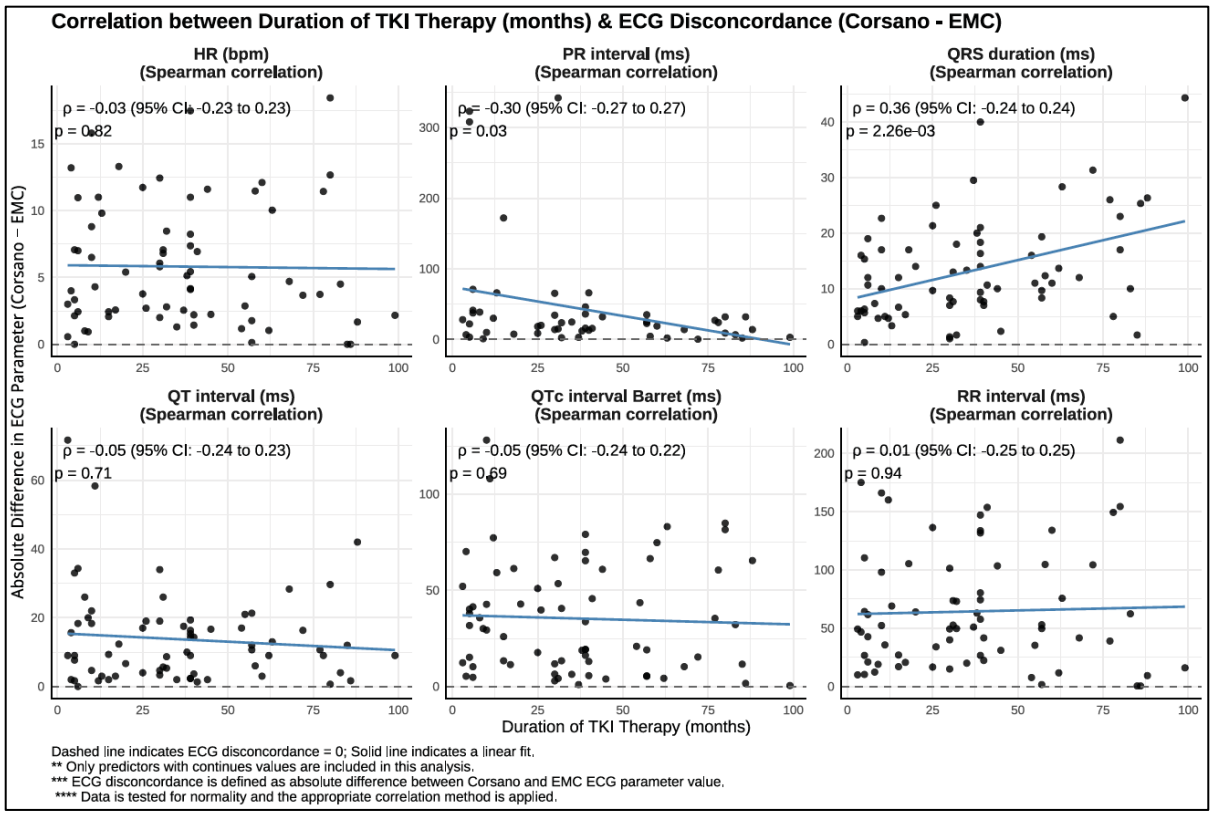
Supplementary Figure S5. *Scatterplots with Linear Regression Overlays Visualising Associations between Corsano and EMC ECG Parameters, Coloured per Patient.*

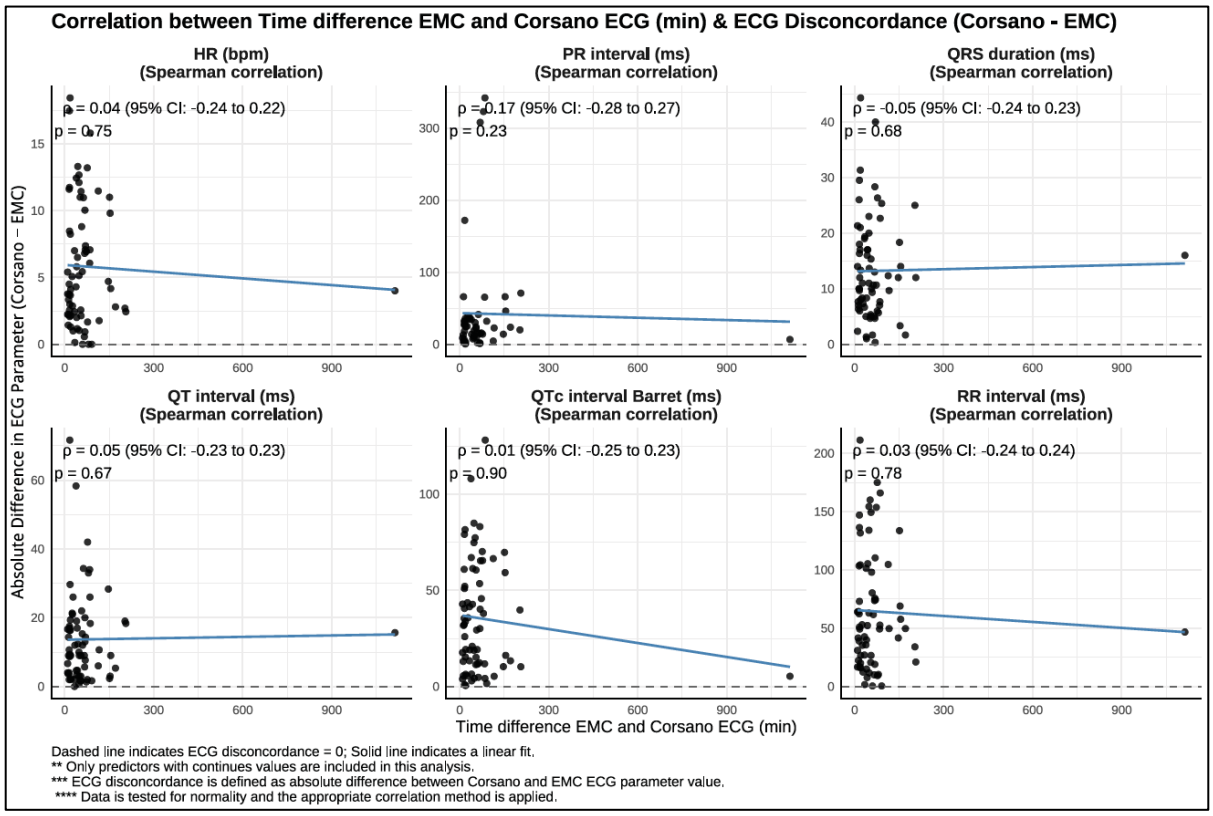


Supplementary Figure S6. *Scatterplots with Linear Regression Overlays Visualising Associations between ECG Parameter Discrepancies and Continuous Clinical Variables.*





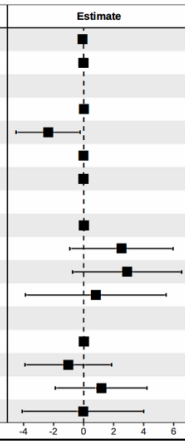

Correlation between Duration of TKI Therapy (months) & ECG Disconcordance (Corsano - EMC)
HR (bpm) (Spearman correlation)
ρ = -0.03 (95% CI: -0.23 to 0.23)
p = 0.82
PR interval (ms) (Spearman correlation)
ρ = -0.30 (95% CI: -0.27 to 0.27)
p = 0.03
QRS duration (ms) (Spearman correlation)
ρ = 0.36 (95% CI: -0.24 to 0.24)
p = 2.26e-03
QT interval (ms) (Spearman correlation)
ρ = -0.05 (95% CI: -0.24 to 0.23)
p = 0.71
QTc interval Barret (ms) (Spearman correlation)
ρ = -0.05 (95% CI: -0.24 to 0.22)
p = 0.69
RR interval (ms) (Spearman correlation)
ρ = 0.01 (95% CI: -0.25 to 0.25)
p = 0.94
Absolute Difference in ECG Parameter (Corsano – EMC)
Duration of TKI Therapy (months)
Dashed line indicates ECG disconcordance = 0; Solid line indicates a linear fit.
** Only predictors with continues values are included in this analysis.
*** ECG disconcordance is defined as absolute difference between Corsano and EMC ECG parameter value.
**** Data is tested for normality and the appropriate correlation method is applied.


Correlation between Time difference EMC and Corsano ECG (min) & ECG Disconcordance (Corsano - EMC)
HR (bpm) (Spearman correlation)
ρ = 0.04 (95% CI: -0.24 to 0.22)
p = 0.75
PR interval (ms) (Spearman correlation)
ρ = -0.17 (95% CI: -0.28 to 0.27)
p = 0.23
QRS duration (ms) (Spearman correlation)
ρ = -0.05 (95% CI: -0.24 to 0.23)
p = 0.68
QT interval (ms) (Spearman correlation)
ρ = 0.05 (95% CI: -0.23 to 0.23)
p = 0.67
QTc interval Barret (ms) (Spearman correlation)
ρ = 0.01 (95% CI: -0.25 to 0.23)
p = 0.90
RR interval (ms) (Spearman correlation)
ρ = 0.03 (95% CI: -0.24 to 0.24)
p = 0.78
Absolute Difference in ECG Parameter (Corsano – EMC)
Time difference EMC and Corsano ECG (min)
Dashed line indicates ECG disconcordance = 0; Solid line indicates a linear fit.
** Only predictors with continues values are included in this analysis.
*** ECG disconcordance is defined as absolute difference between Corsano and EMC ECG parameter value.
**** Data is tested for normality and the appropriate correlation method is applied.

Supplementary Figure S7. *Forestplots with Univariate Linear Regression Results Visualising Significant Associations between ECG Parameter Discrepancies and Continuous and Categorial Clinical Variables.*

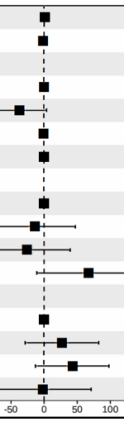
Univariate Linear Models: HR [bpm]

Variable	N	Estimate	p
Age at Inclusion (years)	70	-0.06 (-0.15, 0.02)	0.13
BMI (kg/m²)	70	-0.01 (-0.12, 0.10)	0.79
Name of Current TKI			
Name of Current TKI: Osimertinib	39	Reference	
Name of Current TKI: Alectinib	31	-2.35 (-4.48, -0.22)	0.03
Duration of TKI Therapy (months)	70	-0.00 (-0.05, 0.04)	0.89
Time Between ECGs (min)	70	-0.00 (-0.01, 0.01)	0.68
Fitzpatrick Skin Type			
Fitzpatrick Skin Type: Type III	51	Reference	
Fitzpatrick Skin Type: Type II	8	2.53 (-0.90, 5.96)	0.15
Fitzpatrick Skin Type: Type IV	7	2.91 (-0.73, 6.55)	0.12
Fitzpatrick Skin Type: Type V	4	0.81 (-3.87, 5.50)	0.73
Forearm Hair Density			
Forearm Hair Density: Sparse	38	Reference	
Forearm Hair Density: Nil	14	-1.02 (-3.89, 1.86)	0.48
Forearm Hair Density: Moderate	12	1.18 (-1.87, 4.23)	0.44
Forearm Hair Density: Dense	6	-0.04 (-4.09, 4.00)	0.98



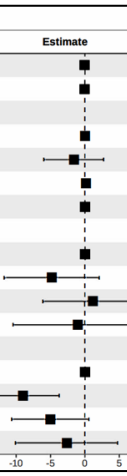
Univariate Linear Models: PR interval [ms]

Variable	N	Estimate	p
Age at Inclusion (years)	53	1.13 (-0.53, 2.79)	0.18
BMI (kg/m²)	53	-1.56 (-5.80, 2.68)	0.46
Name of Current TKI			
Name of Current TKI: Osimertinib	31	Reference	
Name of Current TKI: Alectinib	22	-37.17 (-78.13, 3.80)	0.07
Duration of TKI Therapy (months)	53	-0.82 (-1.55, -0.09)	0.03
Time Between ECGs (min)	53	-0.01 (-0.15, 0.13)	0.88
Fitzpatrick Skin Type			
Fitzpatrick Skin Type: Type III	36	Reference	
Fitzpatrick Skin Type: Type II	7	-14.27 (-75.61, 47.07)	0.64
Fitzpatrick Skin Type: Type IV	6	-25.85 (-91.33, 39.63)	0.43
Fitzpatrick Skin Type: Type V	4	67.12 (-11.15, 145.39)	0.09
Forearm Hair Density			
Forearm Hair Density: Sparse	28	Reference	
Forearm Hair Density: Moderate	10	27.13 (-28.27, 82.53)	0.33
Forearm Hair Density: Nil	10	42.72 (-12.69, 98.12)	0.13
Forearm Hair Density: Dense	5	-1.55 (-74.56, 71.46)	0.97



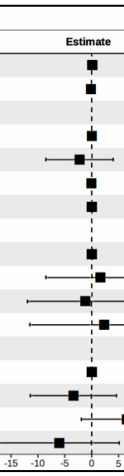
Univariate Linear Models: QRS duration [ms]

Variable	N	Estimate	p
Age at Inclusion (years)	70	-0.06 (-0.22, 0.11)	0.496
BMI (kg/m²)	70	-0.04 (-0.26, 0.17)	0.696
Name of Current TKI			
Name of Current TKI: Osimertinib	39	Reference	
Name of Current TKI: Alectinib	31	-1.60 (-5.95, 2.76)	0.467
Duration of TKI Therapy (months)	70	0.14 (0.07, 0.22)	<0.001
Time Between ECGs (min)	70	0.00 (-0.01, 0.02)	0.876
Fitzpatrick Skin Type			
Fitzpatrick Skin Type: Type III	51	Reference	
Fitzpatrick Skin Type: Type II	8	-4.79 (-11.68, 2.11)	0.171
Fitzpatrick Skin Type: Type IV	7	1.20 (-6.11, 8.51)	0.744
Fitzpatrick Skin Type: Type V	4	-1.04 (-10.46, 8.38)	0.827
Forearm Hair Density			
Forearm Hair Density: Sparse	38	Reference	
Forearm Hair Density: Nil	14	-8.98 (-14.27, -3.69)	0.001
Forearm Hair Density: Moderate	12	-5.02 (-10.62, 0.58)	0.078
Forearm Hair Density: Dense	6	-2.66 (-10.09, 4.77)	0.478



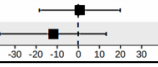
Univariate Linear Models: QT interval [ms]

Variable	N	Estimate	p
Age at Inclusion (years)	70	0.12 (-0.12, 0.36)	0.3
BMI (kg/m²)	70	-0.10 (-0.41, 0.21)	0.5
Name of Current TKI			
Name of Current TKI: Osimertinib	39	Reference	
Name of Current TKI: Alectinib	31	-2.25 (-8.53, 4.02)	0.5
Duration of TKI Therapy (months)	70	-0.05 (-0.17, 0.07)	0.4
Time Between ECGs (min)	70	0.00 (-0.02, 0.02)	0.9
Fitzpatrick Skin Type			
Fitzpatrick Skin Type: Type III	51	Reference	
Fitzpatrick Skin Type: Type II	8	1.62 (-8.47, 11.71)	0.7
Fitzpatrick Skin Type: Type IV	7	-1.22 (-11.91, 9.47)	0.8
Fitzpatrick Skin Type: Type V	4	2.33 (-11.45, 16.10)	0.7
Forearm Hair Density			
Forearm Hair Density: Sparse	38	Reference	
Forearm Hair Density: Nil	14	-3.37 (-11.36, 4.62)	0.4
Forearm Hair Density: Moderate	12	6.53 (-1.93, 14.99)	0.1
Forearm Hair Density: Dense	6	-6.05 (-17.28, 5.17)	0.3



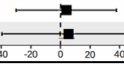
Univariate Linear Models: QTc interval Barret [ms]

Variable	N	Estimate	p
Age at Inclusion (years)	70	-0.34 (-0.87, 0.19)	0.20
BMI (kg/m²)	70	0.02 (-0.68, 0.72)	0.95
Name of Current TKI			
Name of Current TKI: Osimertinib	39	Reference	
Name of Current TKI: Alectinib	31	-16.32 (-29.71, -2.93)	0.02
Duration of TKI Therapy (months)	70	-0.05 (-0.32, 0.22)	0.72
Time Between ECGs (min)	70	-0.02 (-0.08, 0.03)	0.35
Fitzpatrick Skin Type			
Fitzpatrick Skin Type: Type III	51	Reference	
Fitzpatrick Skin Type: Type II	8	17.25 (-4.72, 39.22)	0.12
Fitzpatrick Skin Type: Type IV	7	6.81 (-16.47, 30.10)	0.56
Fitzpatrick Skin Type: Type V	4	4.75 (-25.25, 34.75)	0.75
Forearm Hair Density			
Forearm Hair Density: Sparse	38	Reference	
Forearm Hair Density: Nil	14	-13.35 (-31.37, 4.67)	0.14
Forearm Hair Density: Moderate	12	0.78 (-18.31, 19.86)	0.94
Forearm Hair Density: Dense	6	-11.94 (-37.26, 13.38)	0.35



Univariate Linear Models: RR interval [ms]

Variable	N	Estimate	p
Age at Inclusion (years)	70	-0.69 (-1.61, 0.23)	0.1
BMI (kg/m²)	70	-0.08 (-1.30, 1.13)	0.9
Name of Current TKI			
Name of Current TKI: Osimertinib	39	Reference	
Name of Current TKI: Alectinib	31	-11.00 (-35.26, 13.25)	0.4
Duration of TKI Therapy (months)	70	0.07 (-0.40, 0.54)	0.8
Time Between ECGs (min)	70	-0.02 (-0.11, 0.07)	0.7
Fitzpatrick Skin Type			
Fitzpatrick Skin Type: Type III	51	Reference	
Fitzpatrick Skin Type: Type II	8	18.74 (-19.49, 56.97)	0.3
Fitzpatrick Skin Type: Type IV	7	31.57 (-8.95, 72.09)	0.1
Fitzpatrick Skin Type: Type V	4	17.74 (-34.46, 69.94)	0.5
Forearm Hair Density			
Forearm Hair Density: Sparse	38	Reference	
Forearm Hair Density: Nil	14	-9.72 (-41.76, 22.33)	0.5
Forearm Hair Density: Moderate	12	3.99 (-29.95, 37.93)	0.8
Forearm Hair Density: Dense	6	5.55 (-39.48, 50.57)	0.8



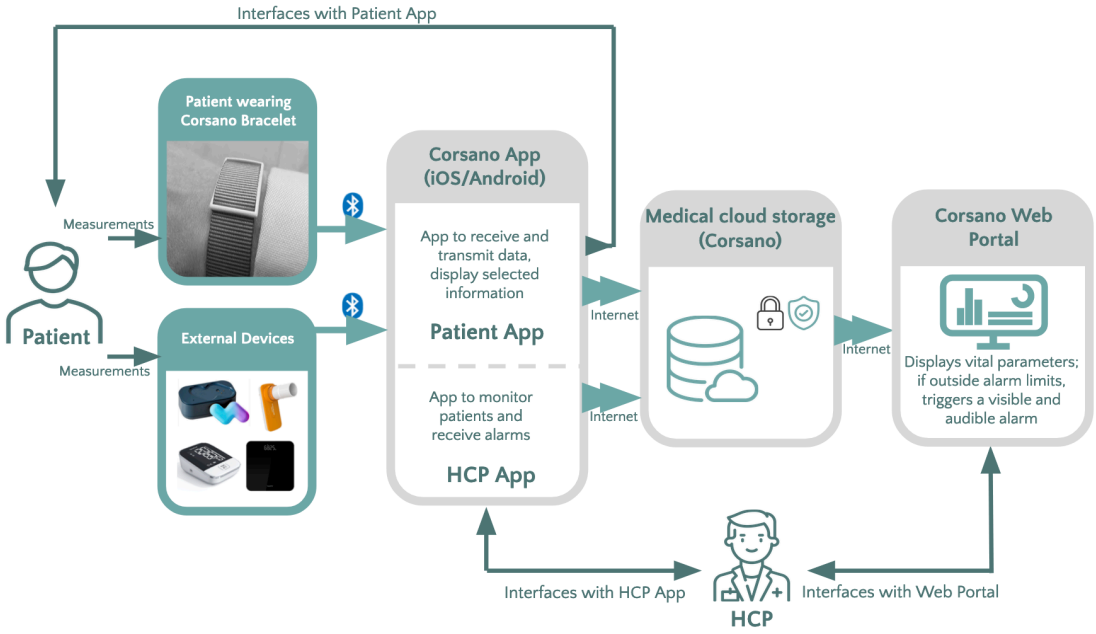
8.3 Supplementary Files

Supplementary File S1. *Technical Description Corsano CardioWatch 287-2.*

8.3a Device Overview

The Corsano CardioWatch 287-2 is a wireless, CE-MDR and FDA-certified medical device for continuous physiological monitoring in home and clinical settings. This study primarily uses the device for its single-lead electrocardiography (ECG) functionality. Additional physiological parameters measured by the device include heart rate (HR), heart rate variability (HRV), respiratory rate (RR), oxygen saturation (SpO_2), cuffless non-invasive blood pressure (NIBP), core body temperature (CBT), sleep, and physical activity. While these functions support broader clinical integration, this investigation focuses on the ECG output for cardiac surveillance during tyrosine kinase inhibitor (TKI) therapy.

Figure 1. *Illustration of the Corsano continuous monitoring platform.*



8.3b Device Configuration and ECG Functionality

The CardioWatch ECG functionality uses a single-lead configuration with three dry-contact electrodes—two on the back and one in the metallic frame. To record, wear it on one wrist while the opposite hand touches the metal frame, forming an electrical circuit across the upper limbs, corresponding to a lead I-equivalent recording. The device samples and records ECG waveforms for short intervals to derive parameters such as heart rate, PR interval, QRS duration, QT interval, and corrected QT interval (QTc). The CardioWatch complies with EN-IEC 60601-2-47:2015, a harmonised standard for safety and performance.

8.3c System Components and Data Transmission

Internally, the CardioWatch features the CardioWatch Module 287-2 by Manufacture Modules Technologies (MMT), which includes core electronics for data acquisition and storage, and uses Bluetooth Low Energy for wireless transmission. It has local memory to buffer data during

connectivity loss. Physiological data are transmitted to the Corsano Trials app, available on Android and iOS, which relays this data to the secure CardioWatch cloud for remote storage and review. The app does not provide real-time interpretation or diagnostic feedback, reducing patient distress from false positives.

The Corsano cloud platform complies with HIPAA, GDPR, FDA part 11, ISO standards, ensuring secure handling of sensitive health data. Personal identifiers are not stored; each device has a unique serial number linked to participants by healthcare professionals. Access to data visualisation tools is restricted to authorised personnel via secure login. Further specifications and protocols are available in the *<CardioWatch 287-2 System Security Overview>*.

8.3d Supplementary Monitoring Capabilities

Although not the focus of this thesis, the CardioWatch supports continuous monitoring of additional physiological parameters. The PPG sensor, on the underside of the device, employs green, red, and infrared LEDs with photodiodes to measure HR and SpO_2. RR and HRV can be estimated from ECG and PPG signals. A three-axial accelerometer captures movement across spatial planes, aiding in detecting activity levels, posture, and sleep patterns. Additionally, a heat flux sensor estimates CBT by modelling the thermal gradient between the core and the skin surface. These features are integrated into the device casing, which contacts the skin via a medical-grade strap compliant with CE-MDR requirements. A detailed overview of the device components is available in the *<CardioWatch 287-2 Specifications Sheet>* provides a detailed overview of the device components.

8.3e Regulatory Status and Validation Studies

The Corsano CardioWatch is fully certified for use in measuring ECG, HR, HRV, RR, SpO_2, and physical activity. FDA clearance is currently pending for CBT, NIBP, and sleep tracking. Regulatory certification and performance validation are supported by multiple ongoing or completed clinical studies, including the MULTI-VITAL study (NL80236.000.22), the RECAMO trial (NL83281.000.22, NCT05899959), the ACW2 trial (NCT05542732), and the HIIT-OXI-NIBP-POS trial (NL85330.058.23).

8.3f Safety Considerations and Risk Management

A risk assessment conducted in accordance with ISO 14971:2019 concludes that all foreseeable risks have been appropriately minimised through a combination of design features, procedural safeguards, and software architecture. Residual risks are considered acceptable considering the anticipated clinical benefits. Identified risks include user anxiety caused by artefactual signal interpretations, although the absence of on-device diagnostic outputs mitigates this issue. Another theoretical risk is data misattribution across users, which has not been observed in practice due to robust internal safeguards. Overall, the benefit-to-risk ratio is deemed to be highly favourable for the intended clinical application. A full risk overview is available in the *<CardioWatch 287-2 Safety Data Sheet>*.