QTinno:
Automated ECG Analysis Solution for Drug Safety Studies

Key Features of QTinno Engine:

Use of Vector Magnitude Virtual Lead

- Produces single "virtual" ECG lead with full electrical information
- Uses all 12 leads and all complexes in an ECG
- Improves signal-to-noise ratio over standard 12-lead ECG

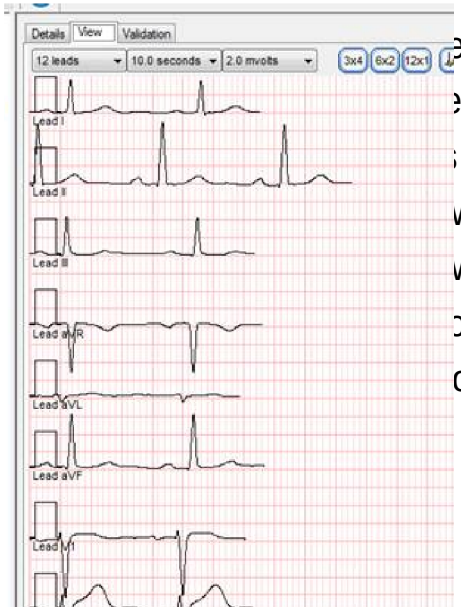
Iterative curve fitting algorithms optimize fiducial point accuracy

- Least-square fit of 3rd-order polynomial to VM data
- Multiple iterations done to optimize fitting
- Approach is noise-resistant and baseline-independent

Confidence Factor (CF) flags problematic ECGs for human review, based on:

- ECG signal quality, including excessive noise, missing leads, etc
- Measurement quality, including goodness of fit, heart rate variability, etc
- Currently, CF score <70 flags an ECG for possible overread – typically 2-4% of early-phase study

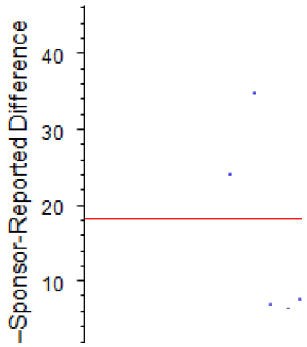
CSRC Blinded TQT Study - Characteristics



Bland-Altman Comparison of Sponsor Data and QTinno for Changes from Baseline

	Mean Diff	Std Dev
dQT	0.44 ms	8.3 ms
dQTcF	0.35 ms	9.4 ms
dRR	0.70 ms	27.9 ms
dPR	0.02 ms	5.7 ms
dQRS	0.31 ms	6.5 ms

Bland-Altman Plot for dQTcF



QTinno Measurement Variability Significantly Lower Than Sponsor-Submitted Data

Comparison of Within-Subject Average Standard Deviation (SD) for QTcF

Null Hypothesis: *Average QTinno SD = Average Sponsor-Reported SD*

Results:

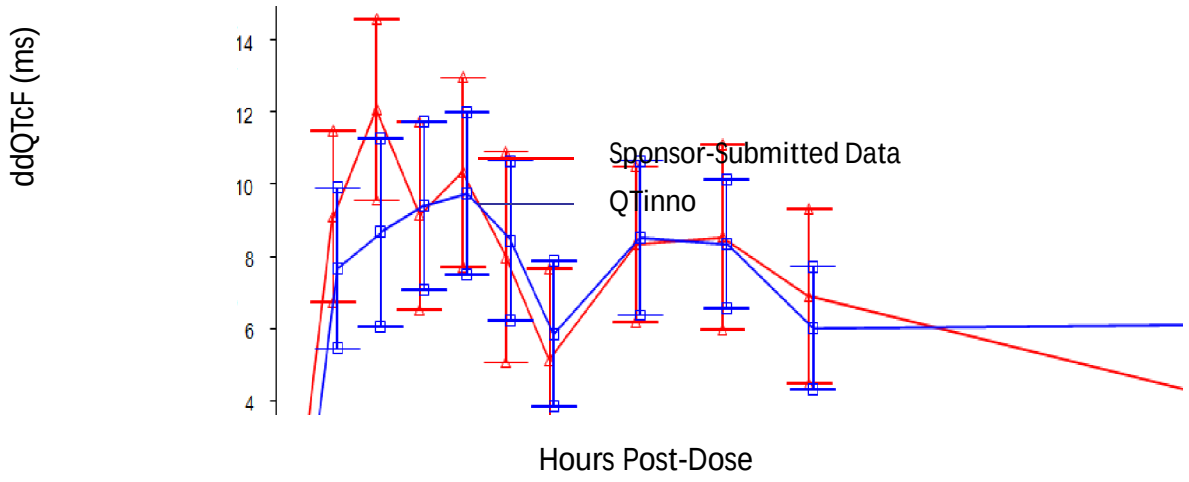
	Mean SD	Lower CL	Upper CL	t value	p value
Sponsor	7.16 ms	6.91 ms	7.43 ms	---	---
QTinno	5.43 ms	5.19 ms	5.67 ms	---	---
Difference	*1.74 ms*	*1.53 ms*	*1.95 ms*	*16.06*	*p<0.0001*

Conclusions:

Null Hypothesis rejected

QTinno variability is highly significantly lower than Sponsor-reported data

Assay Sensitivity – ddQTcF by Hour



	Sponsor	QTinno
Mean ddQTcF	7.3 ms	7.0 ms
Peak ddQTcF	12.1 ms	9.8 ms
Time of Peak	2 hrs	4 hrs
Ave 90% CI	5.2 ms	4.4 ms

Mixed Model Covariance Estimates Combined and by Treatment Group

Treatment Group	Method	Between-Subject Standard Deviation (ms)	Within-Subject Standard Deviation (ms)
All	Sponsor-Reported	12.94	7.25
	QTinno	12.07	6.07
Moxifloxacin	Sponsor-Reported	12.75	7.81
	QTinno	11.54	6.40
Placebo	Sponsor-Reported	13.06	6.66
	QTinno	12.60	5.73

Theoretical Statistical Power Calculations

Sample Size	Method	Average Peak Moxi Effect (ms)	Time of Peak Moxi Effect (hrs)	Between-Subject Std Dev (ms)	Power
10	Sponsor-Reported	15.49	4.65	12.81	0.418
10	QTinno	14.52	4.87	11.88	0.419
20	Sponsor-Reported	14.33	3.74	12.90	0.585
20	QTinno	13.54	4.15	11.98	0.594
30	Sponsor-Reported	13.86	3.41	12.91	0.701
30	QTinno	13.12	3.86	12.01	0.713
40	Sponsor-Reported	13.62	3.25	12.93	0.787
40	QTinno	12.92	3.77	12.04	0.800
50	Sponsor-Reported	13.46	3.15	12.92	0.867
50	QTinno	12.78	3.75	12.05	0.867

In parallel-group study, power is most affected by between-subject SD, which was about 7% lower for QTinno than Sponsor-reported

Theoretical power was almost identical at all sample sizes – possibly because the peak moxi effect reported by QTinno was about 5% lower than Sponsor-reported

Backup

Summary and Conclusions

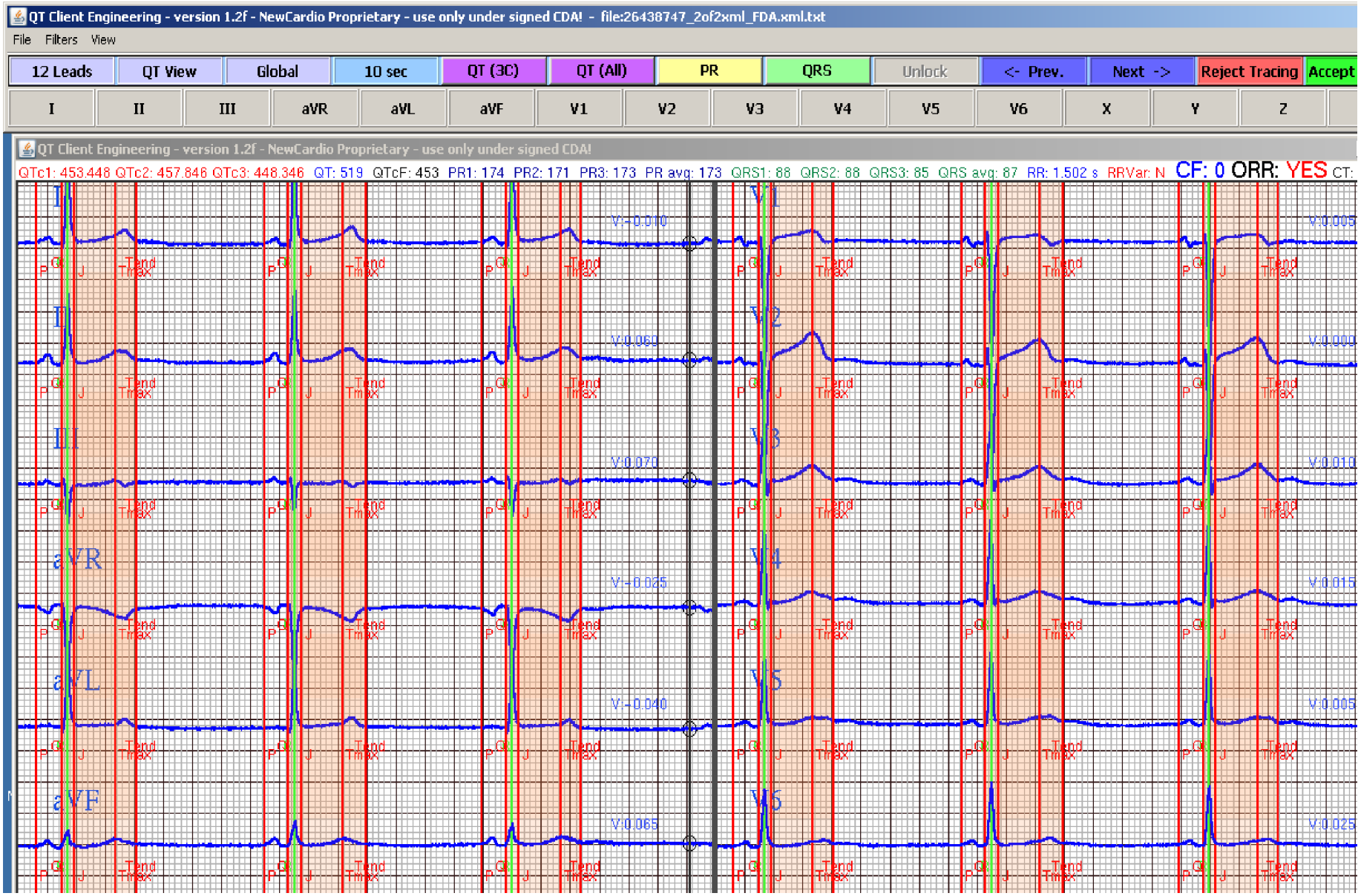
Sponsor-reported and QTinno raw measurements, and single and double delta measurements, were closely comparable

Both measurement methods reported valid hourly ddQTcF curves and demonstrated assay sensitivity at multiple time points

QTinno measurement variability was lower than Sponsor-reported data

- Average within-subject SDs across all triplicates/subjects/timepoints 24% lower for QTinno ($p<0.001$)
- In hourly ddQTcF curves, 90% CIs for QTinno were narrower than Sponsor-reported at all time points (average 17% narrower for raw measurements, 9% narrower for mixed model data)
- Between- and within-subject standard deviations by mixed model lower for QTinno (7% and 16%, respectively)

In bootstrap simulations, theoretical power was nearly identical at all sample sizes


QT Client Engineering - version 1.2f - NewCardio Proprietary - use only under signed CDA! - file:26438747_2of2xml_FDA.xml.txt
File Filters View
12 Leads
QT View
Global
10 sec
QT (3C)
QT (All)
PR
QRS
Unlock
<- Prev.
Next ->
Reject Tracing
Accept
I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
X
Y
Z
QT Client Engineering - version 1.2f - NewCardio Proprietary - use only under signed CDA!
QTc1: 453.448 QTc2: 457.846 QTc3: 448.346 QT: 519 QTcF: 453 PR1: 174 PR2: 171 PR3: 173 PR avg: 173 QRS1: 88 QRS2: 88 QRS3: 85 QRS avg: 87 RR: 1.502 s RRVar: N CF: 0 ORR: YES CT:

Slide 10

Vector Magnitude (VM) Lead Improves Signal-to-Noise Ratio