

# ECG-BASED BLOOD POTASSIUM ESTIMATES

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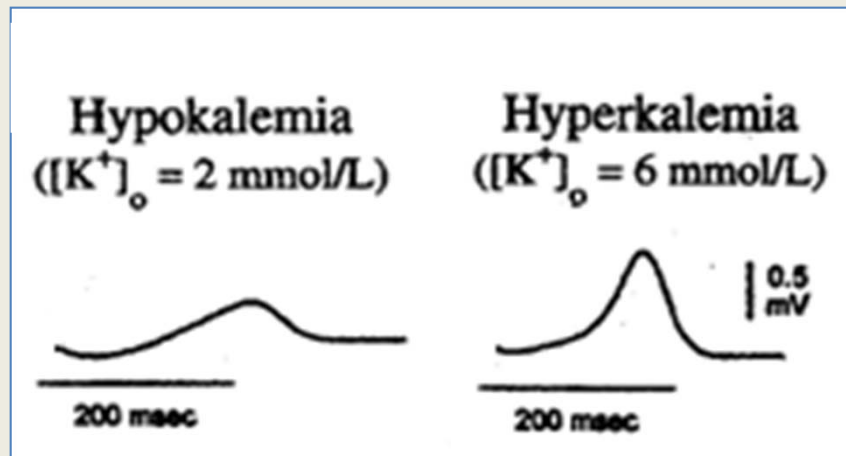
2<sup>nd</sup> Conference on Cardiac Arrest & Sudden Death - Cardiovascular Therapy  
Copenhagen, Denmark - June 16-18, 2011



- Both hypo- and hyperkalemia can be important arrhythmogenic factors  
➔ it would be important to monitor blood potassium concentration [K<sup>+</sup>] in critical patients
- Maintenance of normal potassium homeostasis is an important limiting factor in the therapy of cardiovascular diseases: a drug therapy may simultaneously improve clinical outcomes and enhance the risk of potassium-related adverse events: *an appropriate balance of benefit and risk depends on monitoring of serum potassium*
- A *noninvasive* monitoring of serum potassium would be of great importance and useful especially in patients already undergoing specific monitoring



- ECG effects of potassium are well known since many years, the earliest electrocardiographic manifestation of hyperkalemia being the appearance of narrow-based, peaked T waves



Gima and Rudy, Circ Res 2002

- Nevertheless, qualitative evaluation of ECG changes to diagnose potassium level resulted in poor sensitivity and specificity whereas, in spite of preliminary positive observations, quantitative measurement of the height of T waves did not correlate with K, even if normalized to QRS

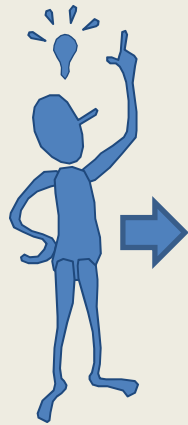
# AIMS

- To develop a method to automatically estimate blood potassium concentration  $[K^+]$  from ECG analysis
- To validate it on dialysis patients undergoing rapid  $[K^+]$  variations
- To give a mechanistical interpretation of the link between  $[K^+]$  and ECG by testing the estimator on LQT2 patients, where such link is likely to be disrupted.

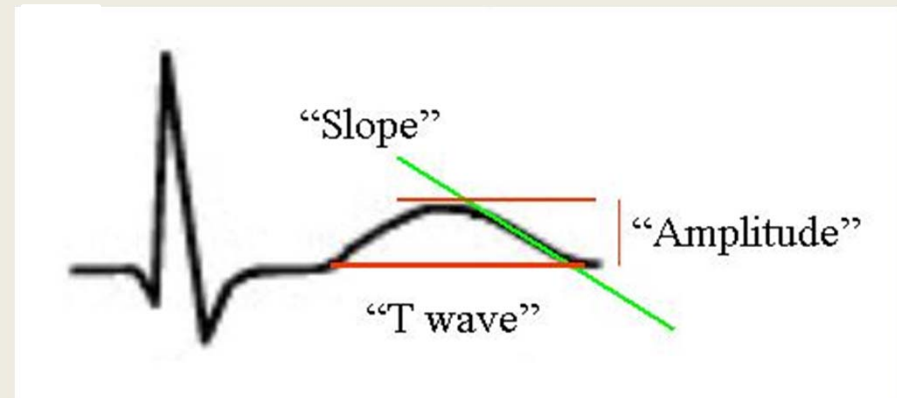


# METHODS: ALGORITHM TO COMPUTE SERUM POTASSIUM CONCENTRATION FROM ECG

We looked for a way to describe an amplitude-invariant measurement of the sharpness of T-wave



the ratio of the T wave slope to amplitude ( $T_{S/A}$ ) [1/s]



We assumed there is a direct relationship between  $T_{S/A}$  and serum potassium concentration

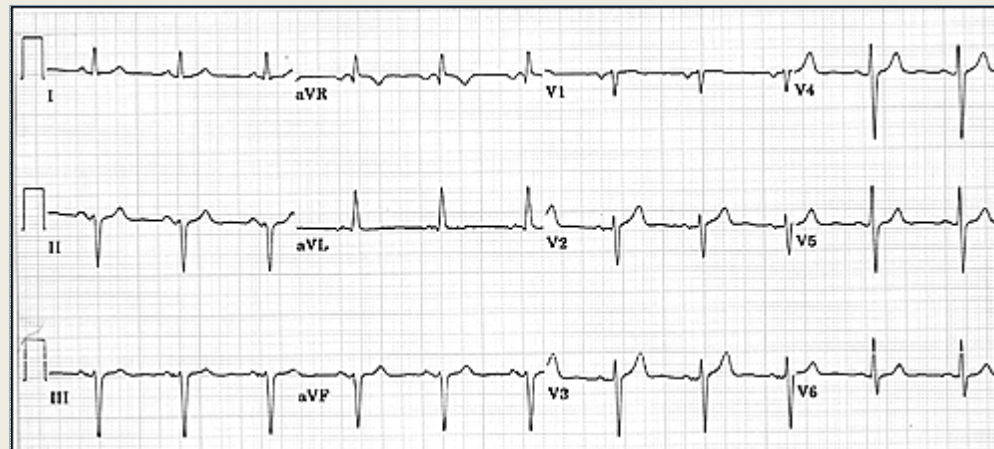


# METHODS: ALGORITHM TO COMPUTE SERUM POTASSIUM CONCENTRATION FROM ECG

12-leads ECG data were preprocessed and exported (SuperECG, Mortara Instrument Inc.).

The most significant two eigenleads were used to calculate the slope and amplitude of the T-wave for each beat.

A 2-minute window median value of the  $T_{S/A}$  was used for the  $[K^+]$  estimation



# METHODS: CLINICAL VALIDATION

## Hemodialysis therapy as unique “experimental model”

- Patients are treated 3 times a week
- Each session is about 4 hour long
- Patients are stationary and undergo significant changes in blood composition and hemodynamic parameters:

	Pre-dialysis	End-dialysis
K (mM)	5.36 ± 0.81	3.43 ± 0.51
Na (mM)	137 ± 4	141 ± 5
Ca (mM)	1.06 ± 0.11	1.26 ± 0.24
HR (bpm)	66 ± 13	75 ± 18
WL (kg)	---	2.28 ± 0.61



**Severi et al. Nephrol Dial Transpl 2008**



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# METHODS: CLINICAL VALIDATION

Holter ECG recordings in

**39** (learning set) + **12** (testing set) dialysis sessions

3 per patient, 3 weeks, the same day of the week

**13+4** patients

Reference values for  $[K^+]$  were obtained at:

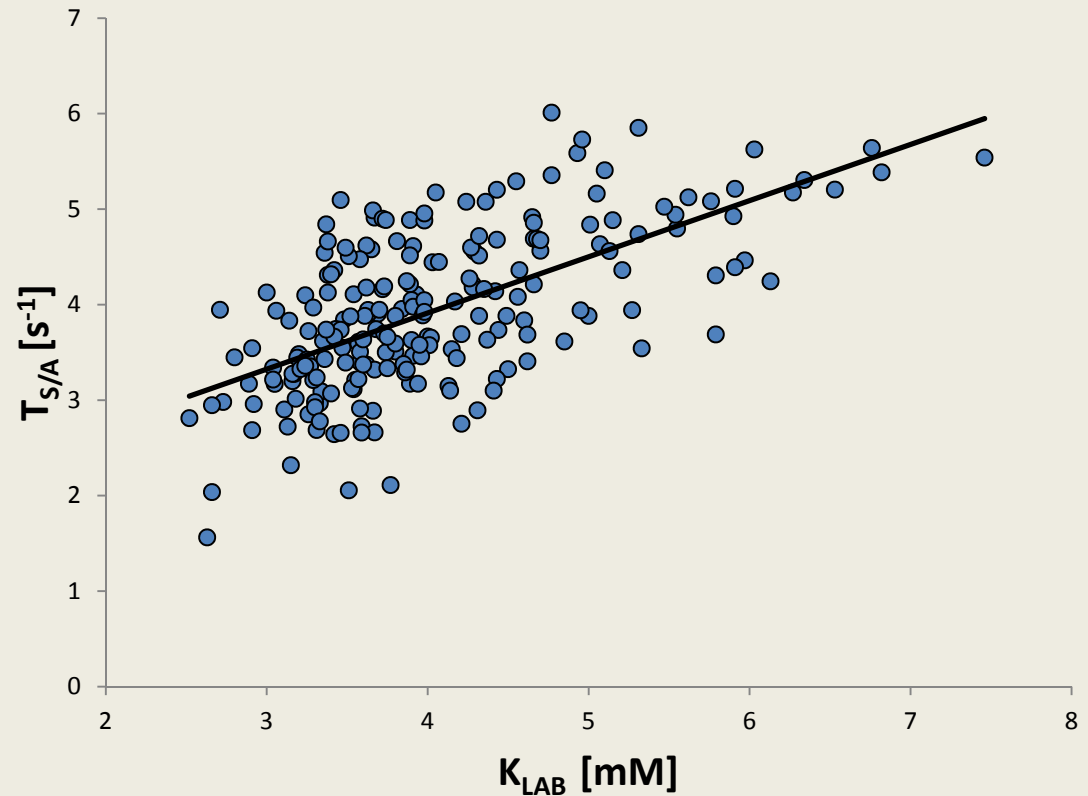
0, 30, 60, 120, 180, 240 min from the start of dialysis  
by blood samples (RapidLab 855, Bayer).



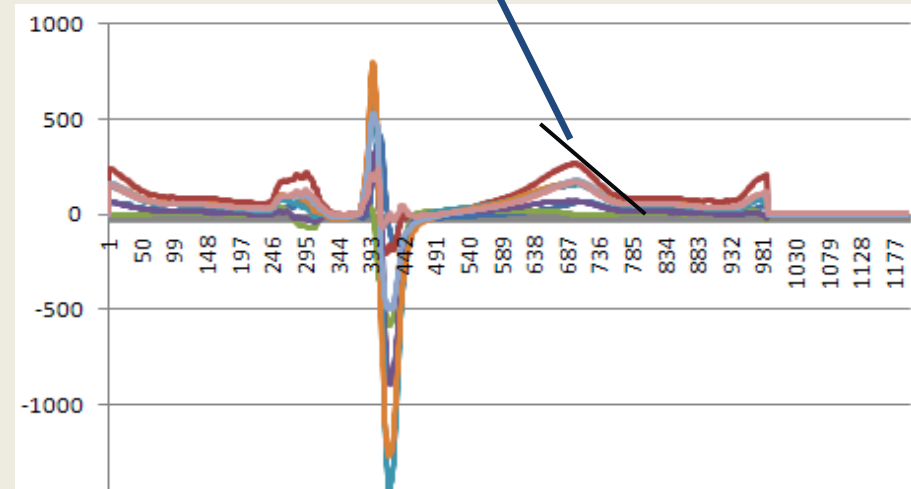
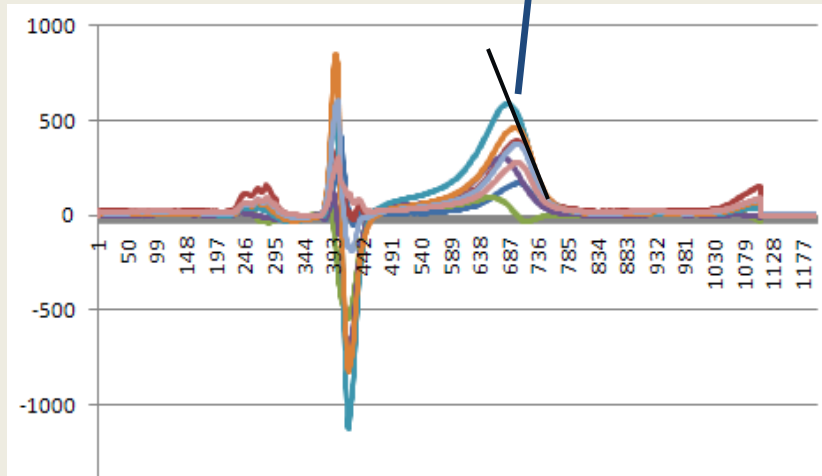
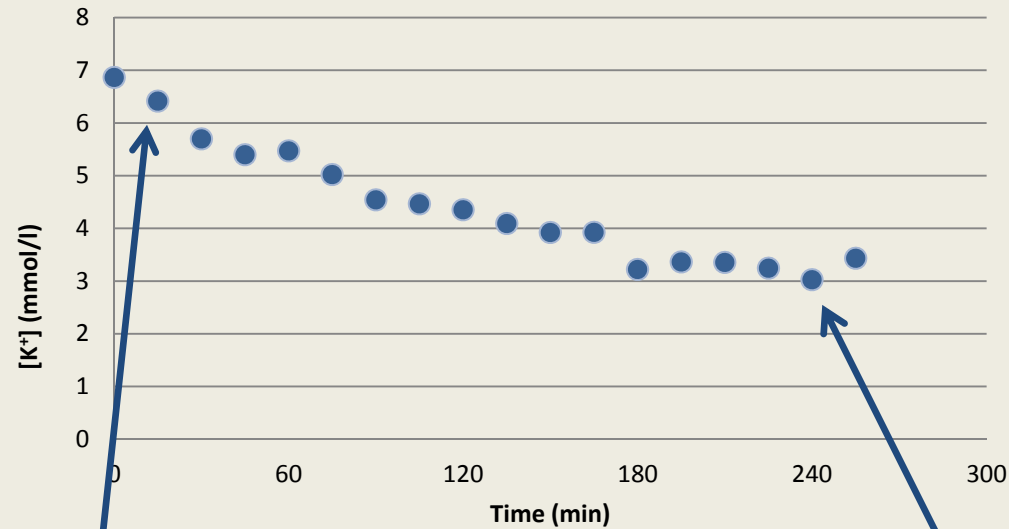
## RESULTS: OVERALL CORRELATION

A significant correlation ( $r=0.63$ ,  $p<0.0001$ ) was found between  $T_{S/A}$  and  $[K^+]$

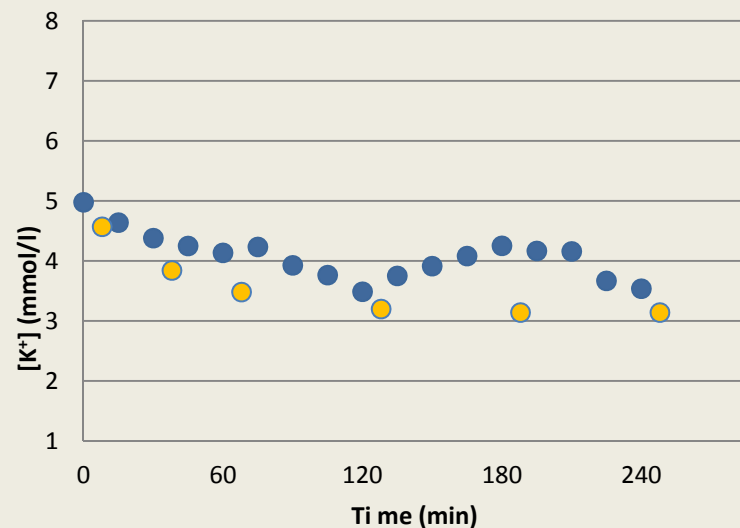
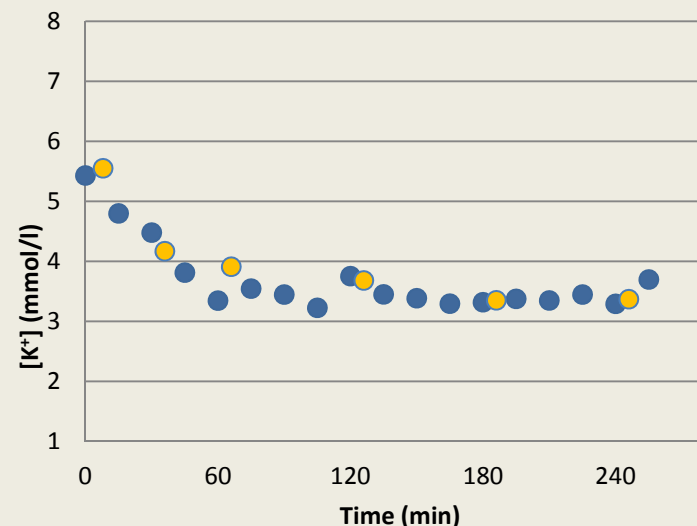
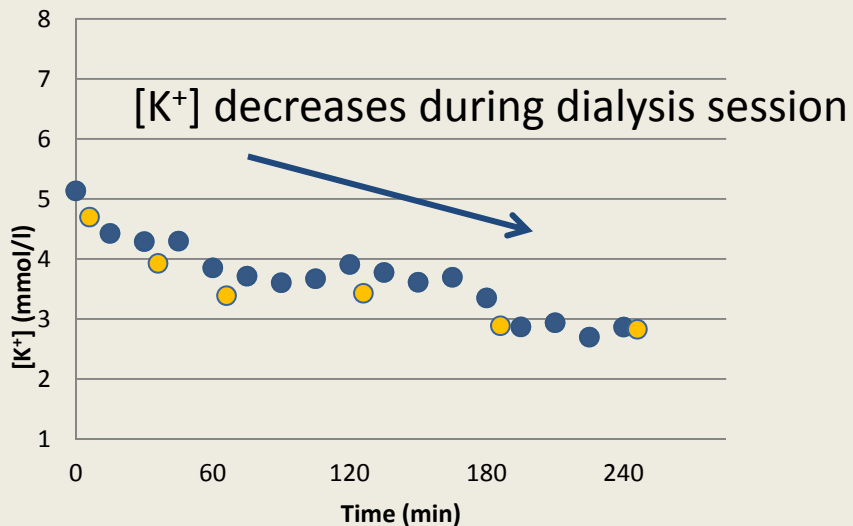
$$K_{ECG} = 1.34 * T_{S/A} + 1.38$$



# RESULTS: ECGs UNDERLYING SINGLE ESTIMATES



# RESULTS: SINGLE SESSION ESTIMATES

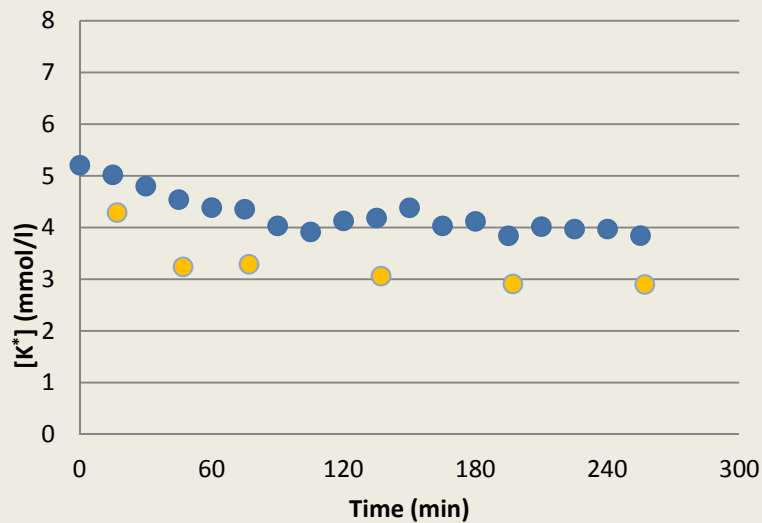
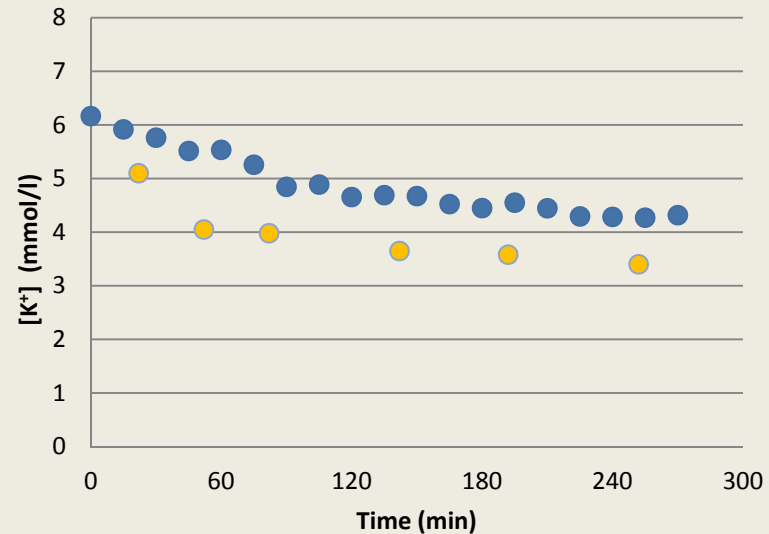
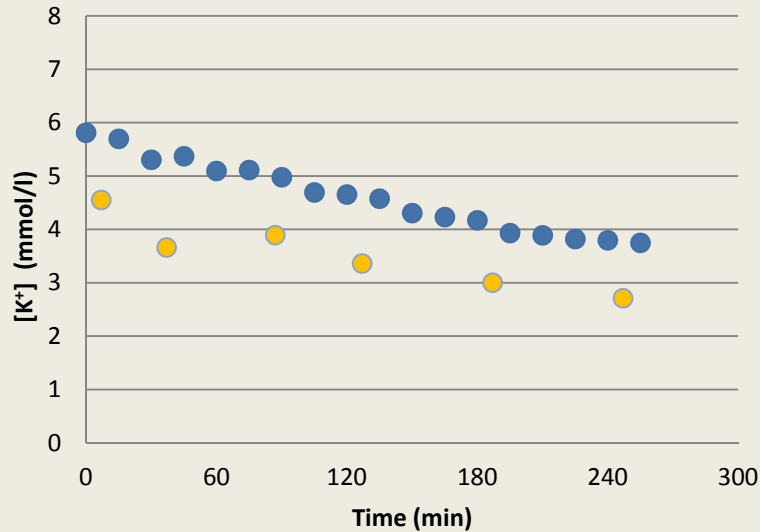


- ECG-based [K<sup>+</sup>] estimates
- Reference [K<sup>+</sup>]

The agreement was good  
(absolute error:  $0.49 \pm 0.16$  mmol/l)  
for most of the sessions (30/39).



# RESULTS ON $[K^+]$ : SINGLE SESSION ESTIMATES



- ECG-based  $[K^+]$  estimates
- Reference  $[K^+]$

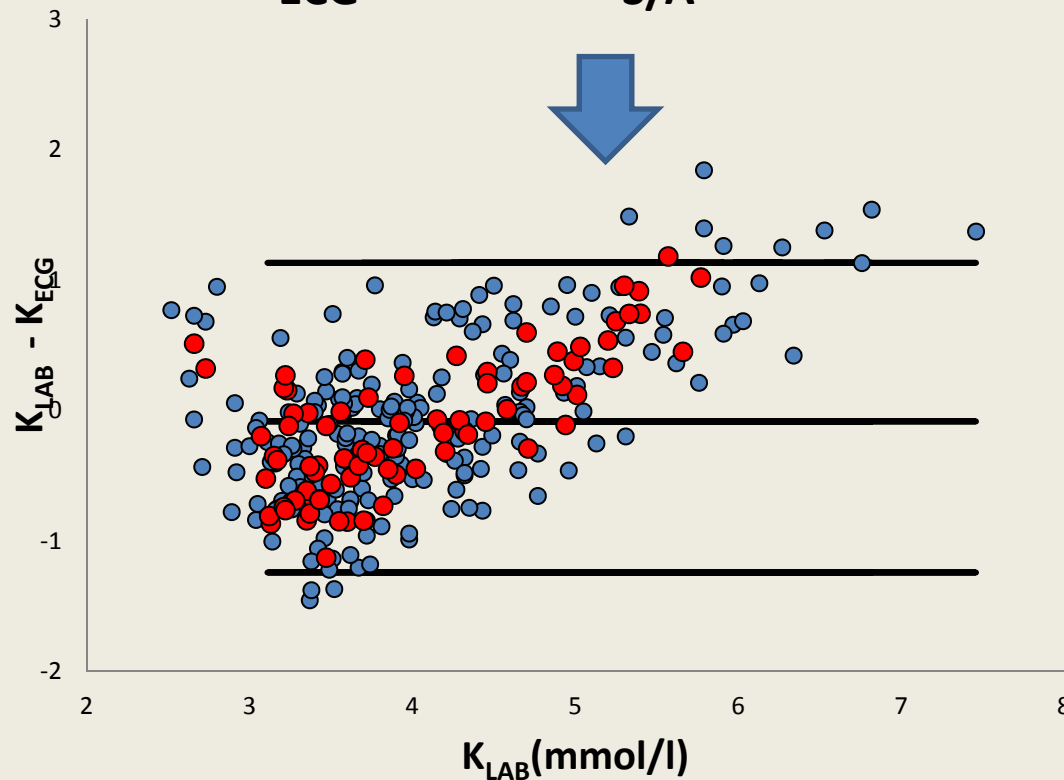
In some sessions (9/39)  
we found the presence of a  
systematic error (bias)



## RESULTS: PATIENT-SPECIFIC CALIBRATION

$K_{LAB}$  (first and last) measurements from first session were used to correct the bias for each patient in successive sessions

$$K_{ECG} = 1.44 * T_{S/A} + \text{patient-bias}$$



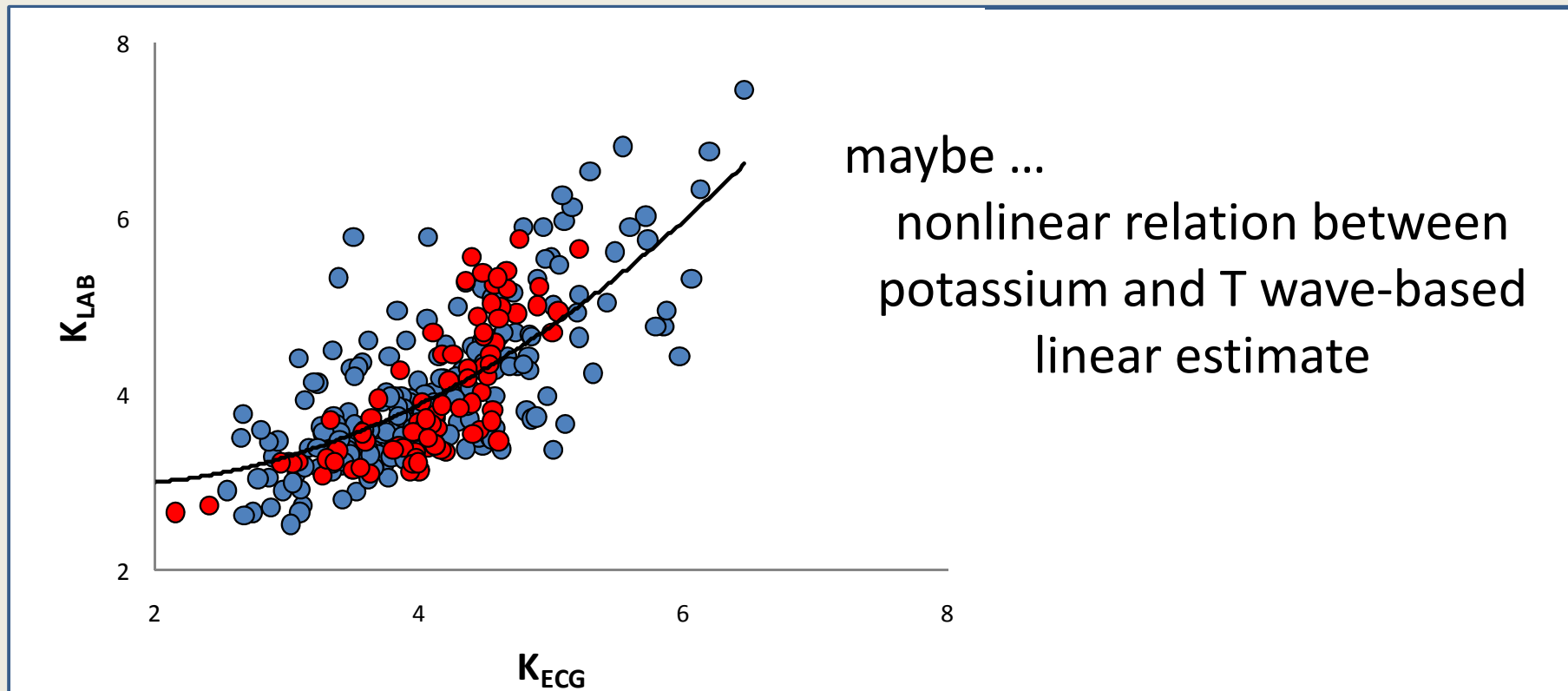
Error (mM):  
mean = 0.09  
sd = 0.59

Absolute error (mM):  
mean = 0.48  
sd = 0.35



# RESULTS: NONLINEAR ESTIMATOR

An interesting observation:



Optimal quadratic estimator:  
Absolute error =  **$0.46 \pm 0.37$**  mM

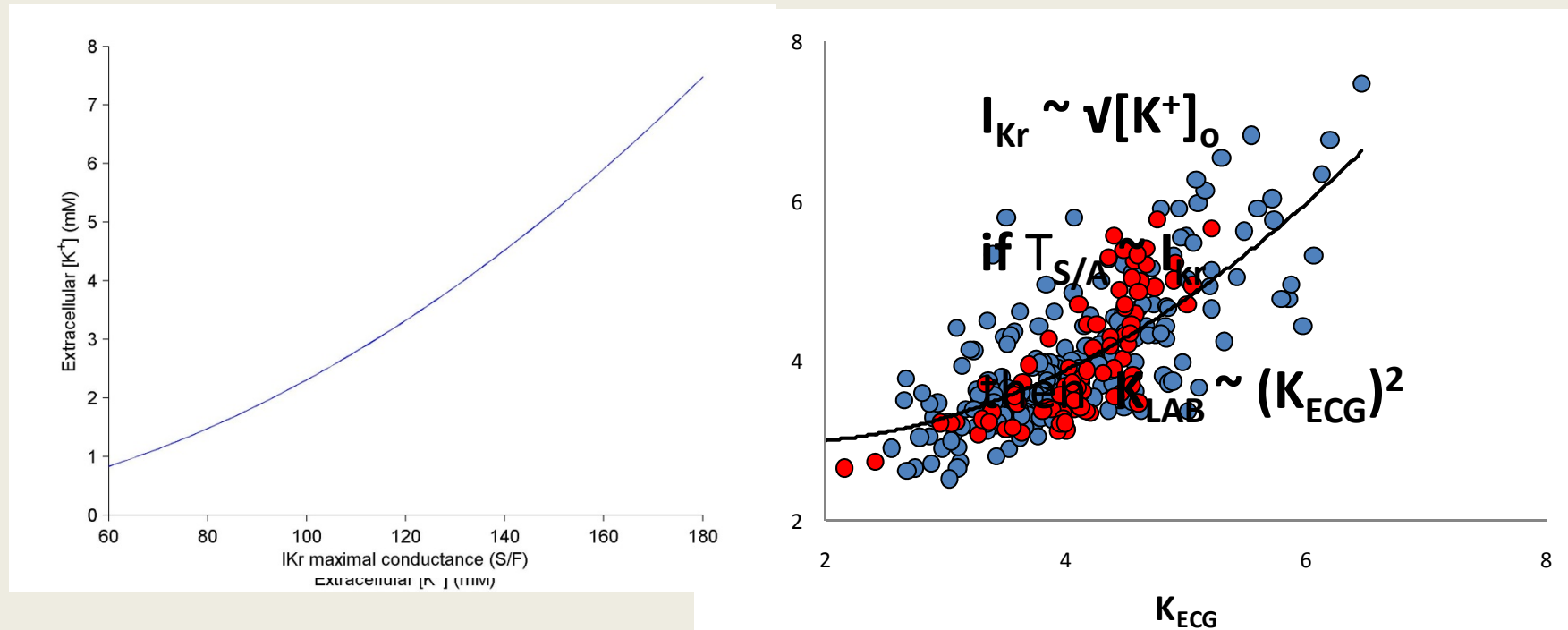


# RESULTS: RELATION WITH POTASSIUM CURRENTS

Potassium currents have a fundamental role in repolarization

Increased outward potassium currents occur in the presence of increased extracellular  $[K^+]$ ;

The maximal conductance of  $I_{Kr}$  and  $I_{K1}$  depends nonlinearly on extracellular  $K^+$



## RESULTS: LQT2 PATIENTS

LQT2 →  $I_{Kr}$  loss of function → for normal  $[K^+]$  the current is lower than normal, that is it is equal to that present in normal subjects in hypokalemia

→ In these patients our methods should underestimate  $[K^+]$

Patient #	Age	$K_{LAB}$	$K_{estimate}$
3119	22	4.60	2.33
3146	34	4.50	2.89
3147	7	4.80	3.66
3128	53	3.90	2.88
3523	42	4.40	4.60
3665	32	4.20	2.69
3688	35	4.70	3.32

$P < 0.01$

mean  
std dev

4.44  
0.31

3.20  
0.75



## CONCLUSIONS

- We have presented a method to estimate blood potassium concentration  $[K^+]$  from the ECG
- Results on dialysis patients are promising
- Results on LQT2 patients support our interpretation of a key role of outward potassium current at the cellular level
- Following a comprehensive validation, this method could be effectively applied to monitor patients at risk for hyper- and hypo-kalemia which are among the main risk factors for cardiac arrhythmias as well as being indicators for worsening of heart or kidney conditions.





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**Thank you** for your attention