

# Use of finger prick sampling to monitor immunosuppressant drug levels in transplant patients

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# Cyclosporin Publication: Ther Drug Monit, 24, (2002) 757-767

*Therapeutic Drug Monitoring*  
24:757-767 © 2002 Lippincott Williams & Wilkins, Inc., Philadelphia

## Simultaneous and Rapid Analysis of Cyclosporin A and Creatinine in Finger Prick Blood Samples Using Liquid Chromatography Tandem Mass Spectrometry and Its Application in C2 Monitoring

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**Summary:** A simple and rapid liquid chromatography tandem mass spectrometry (LC-MS/MS) method for the simultaneous analysis of cyclosporin A (CsA) and creatinine using capillary blood has been developed. Venous and capillary blood samples were taken predose and at C<sub>2</sub> from 65 heart and lung transplant recipients (65 × 4



# Tacrolimus Publication: Ann Clin Biochem (2002), 39, 487- 492.

*Original Article*

## Evaluation of a rapid micro-scale assay for tacrolimus by liquid chromatography-tandem mass spectrometry

BG Keevil<sup>1</sup>, SJ McCann<sup>1</sup>, DP Cooper<sup>2</sup> and MR Morris<sup>2</sup>



### Abstract

#### Addresses

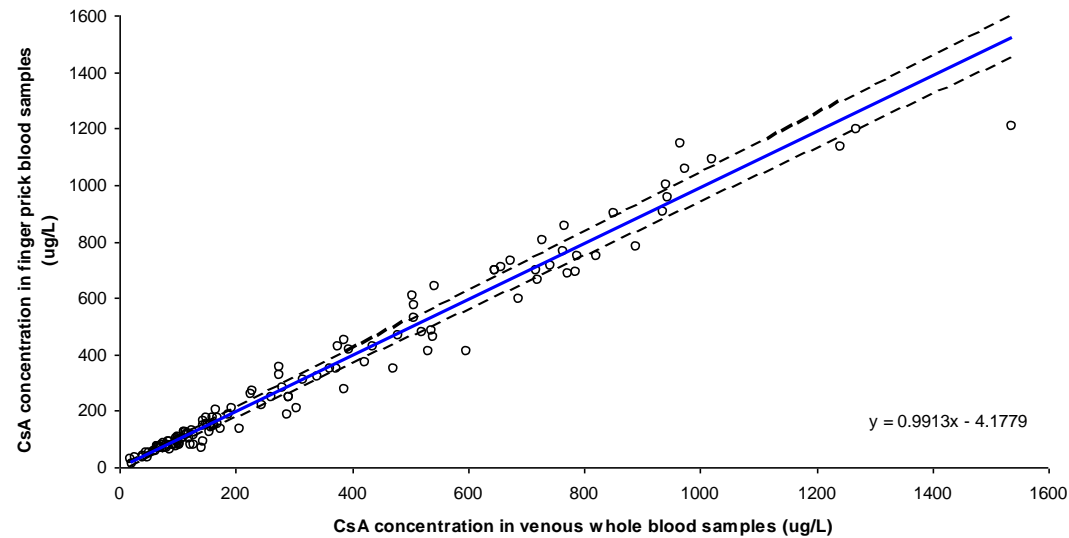
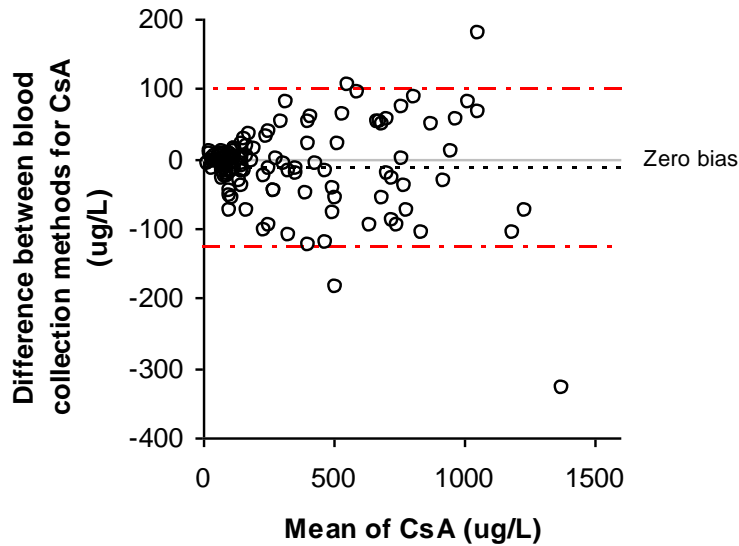
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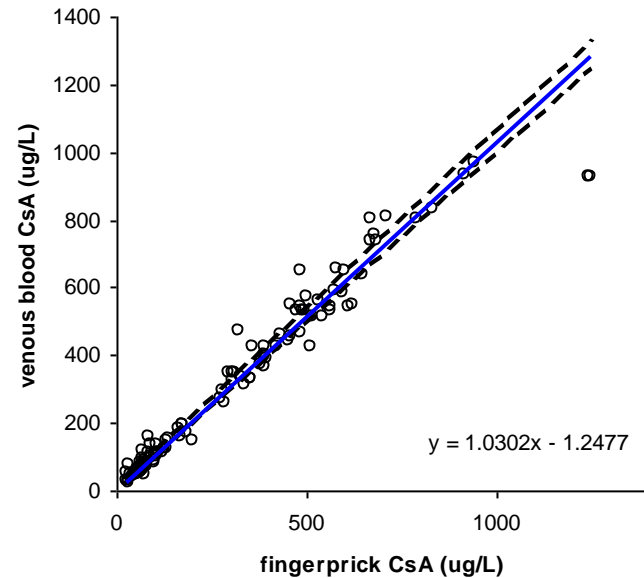
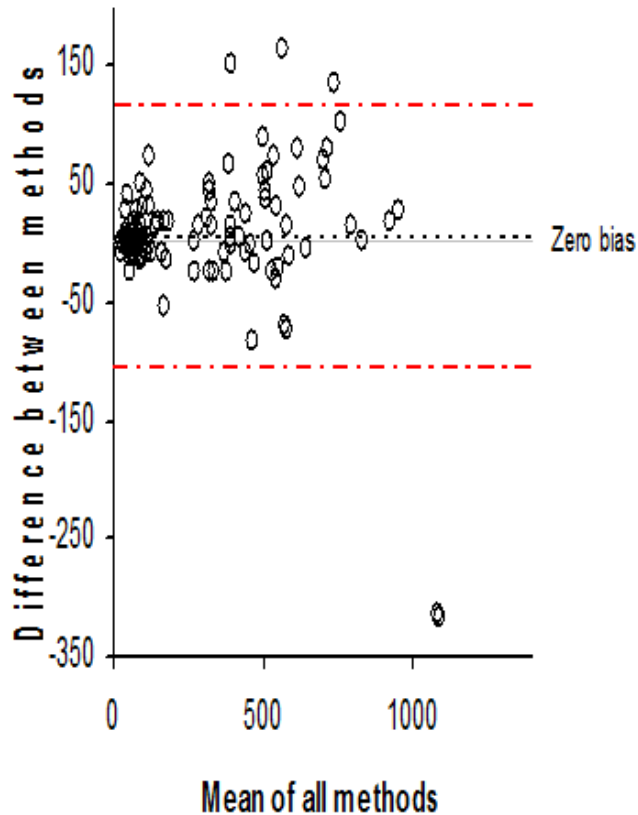
**Background** The immunosuppressive drug tacrolimus has complex and unpredictable pharmacokinetics, therefore regular monitoring is required in patients receiving tacrolimus therapy. We have developed a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for measuring tacrolimus concentrations in whole blood and have compared it with a microparticle enzyme immunoassay.

**Methods** For the LC-MS/MS assay, samples were prepared in a 96-deep well microtitre plate by adding 10  $\mu$ L of blood to 40  $\mu$ L of 0.1 mol/L zinc sulphate solution. Proteins were precipitated by adding 100  $\mu$ L acetonitrile containing ascomycin internal standard. After vigorous mixing and centrifugation, 20  $\mu$ L of the supernatant

# Venous and fingerprick taken at C0 and C2 65 patients n=130 paired samples adult heart and lung



Venous and fingerprick taken at C0 and C2 60 patients n=120 paired samples paediatric renal



# Adult home monitoring

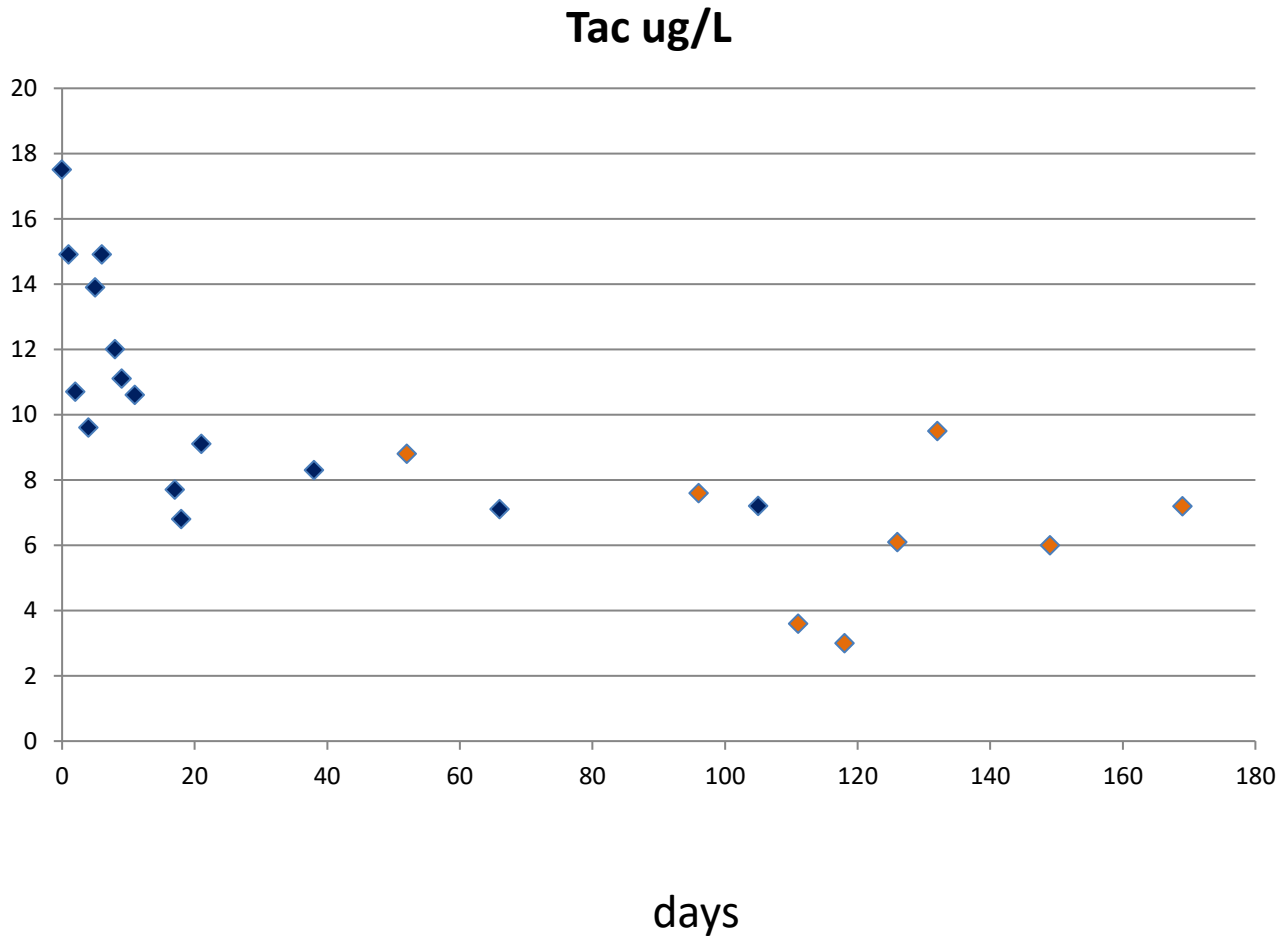
- 52 stable heart Tx patients
- 225 samples
- 14 (6%) unsuitable – clotting 10, insuff 4
- Discomfort not a problem
- Mean postal time 1 day, max 5 days.

# **Monitoring of cyclosporine levels in transplant recipients using self-administered fingerprick sampling.**

- Dose adjustment on fp result in 20 % of patients
- 10-15 % reduction in clinic visits

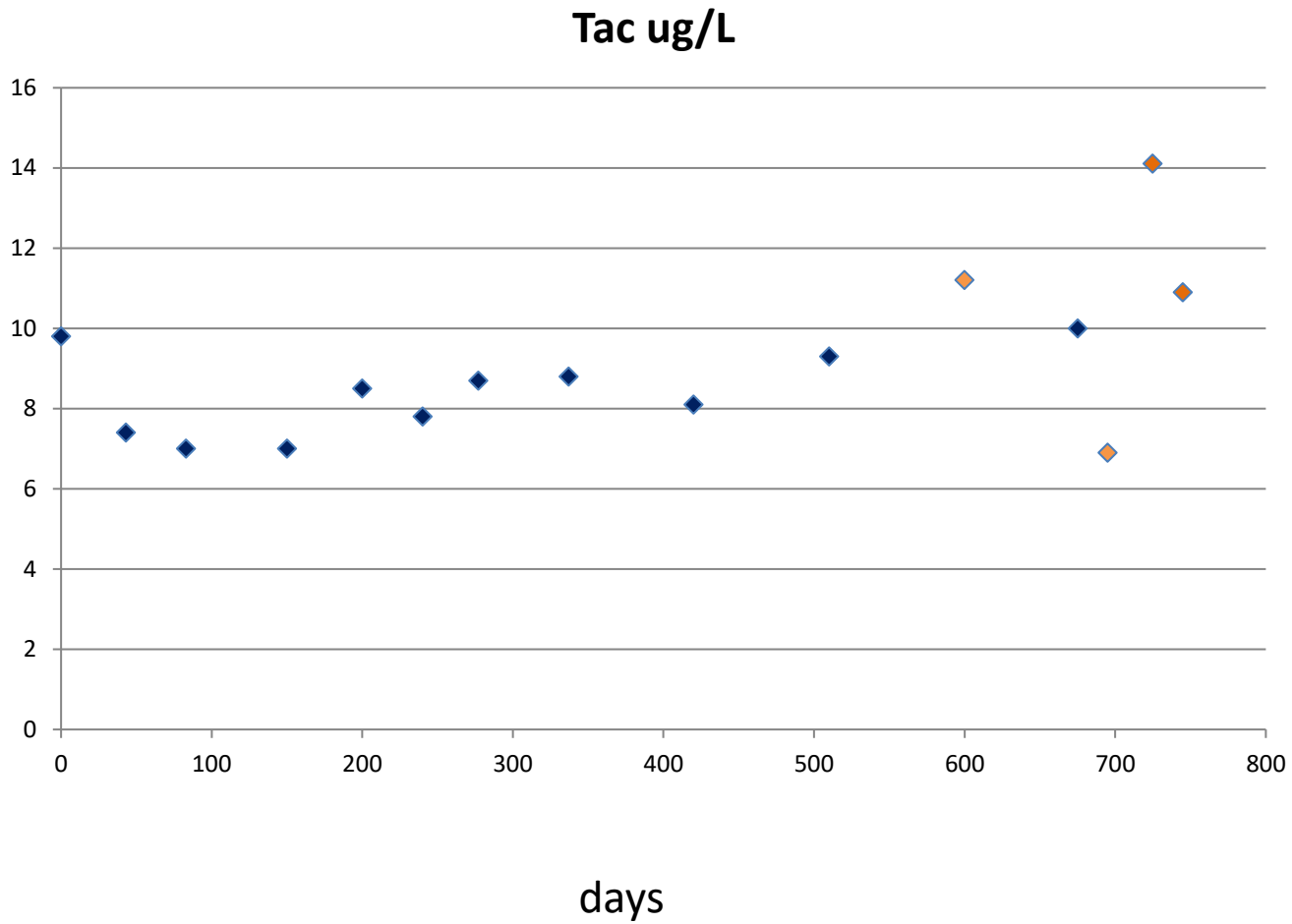
**Yonan N, Martyszuk R, Machaal A, Baynes A, Kevil BG  
Clin Transplant. 2006;20:221-5**

# Heart and lung 2018

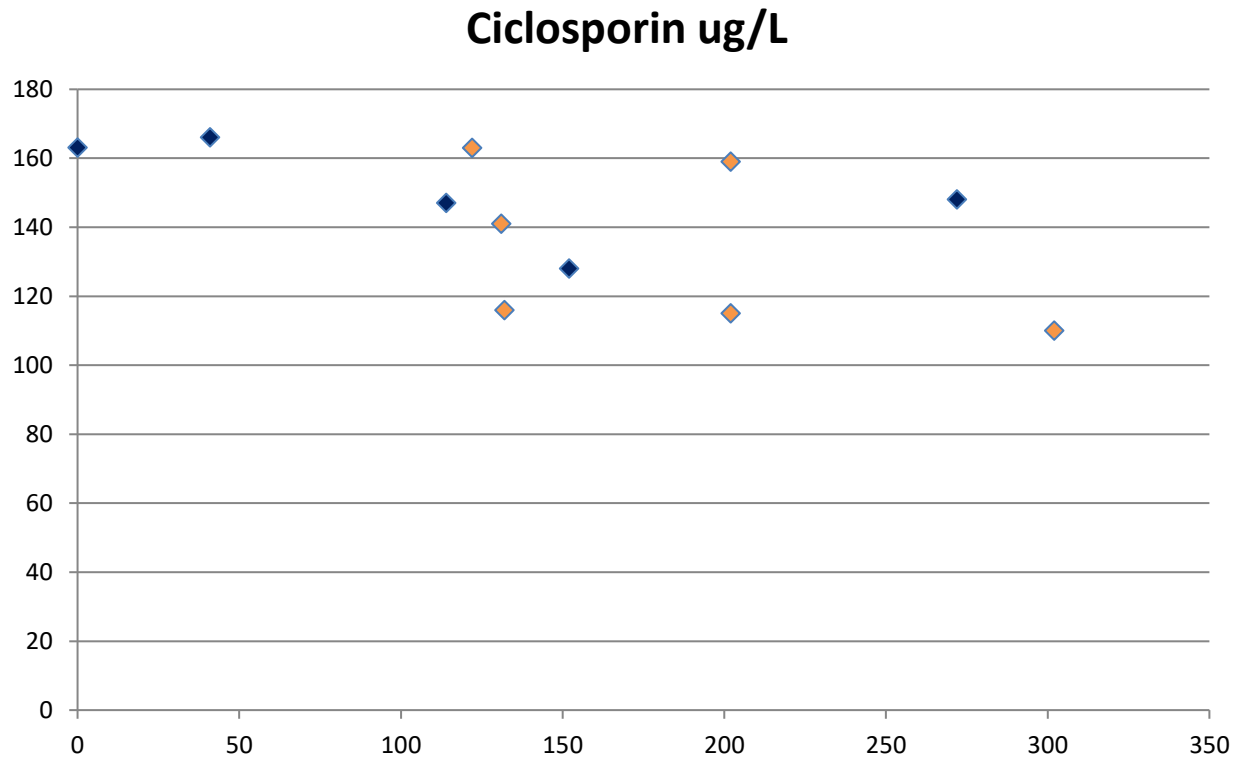




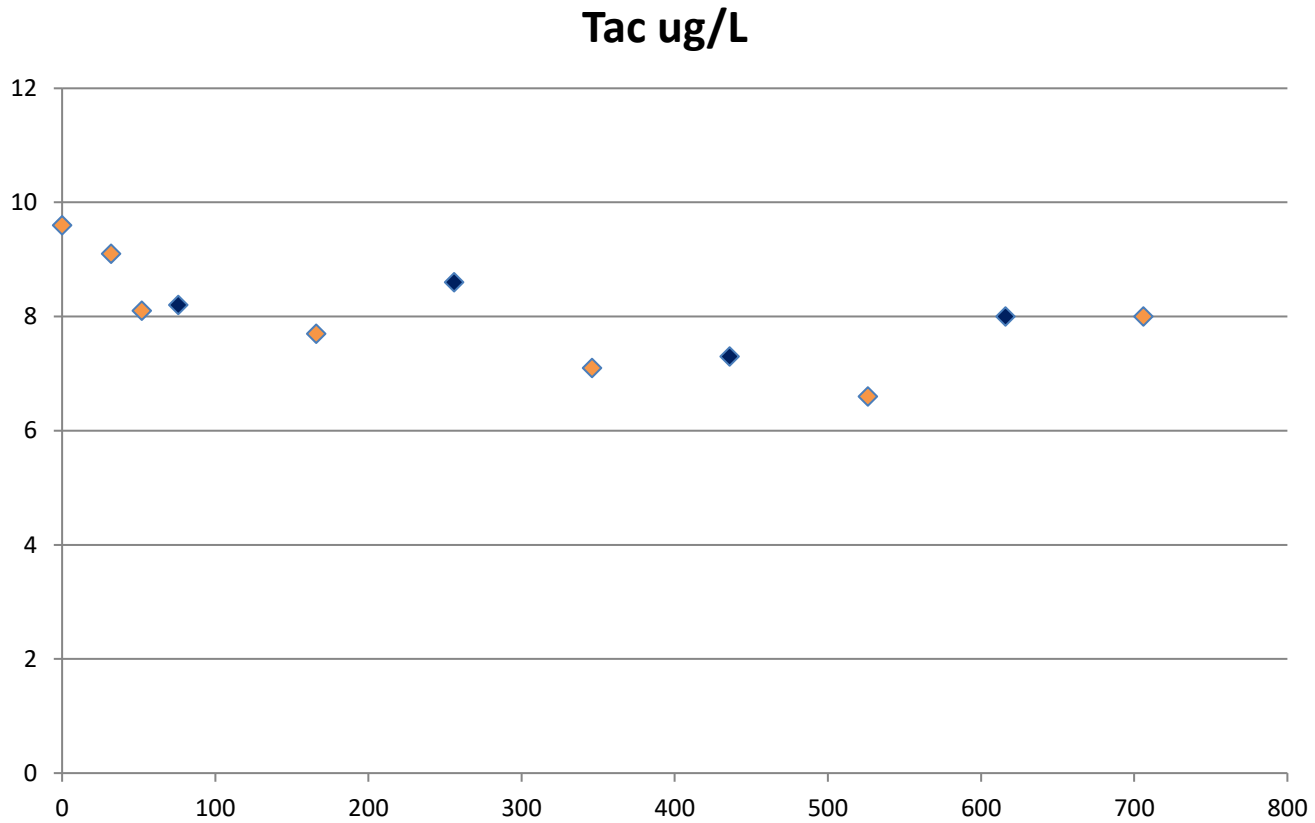
# Single lung 2016



# Heart Tx 2014

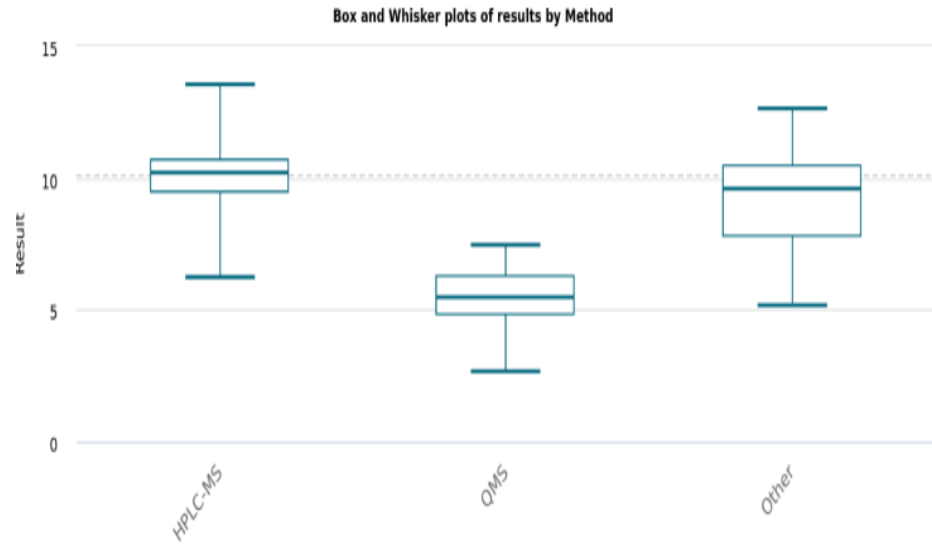
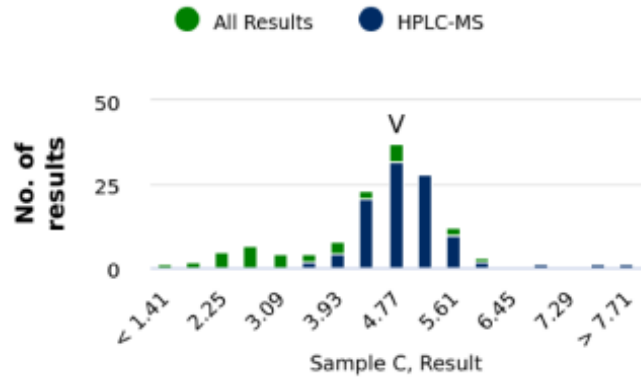
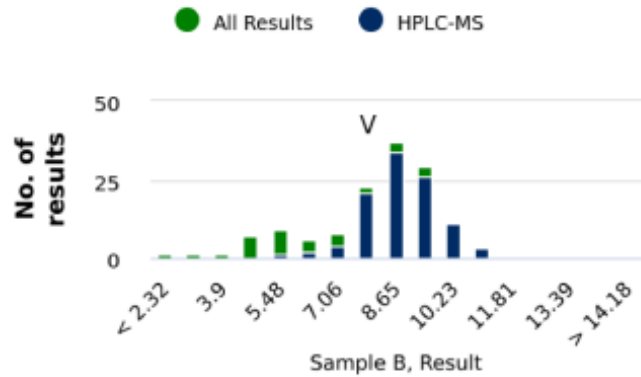
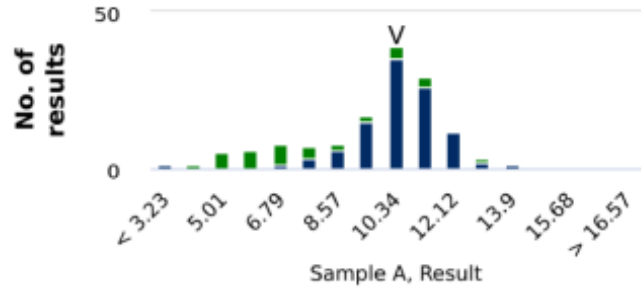


# Heart Tx 2012



Can we send samples to other labs?

# Everolimus



# Sirolimus

Spec.	Pool	Pool description / Treatments / Additions				
163A	SI246	Manipulated human whole blood				
163B	SI248	Manipulated human whole blood				
163C	SI250	Manipulated human whole blood				

	All methods	Mass Spectrometry	In-house [600]	Your A score is	Your B score is	Your C score is
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		-4.6	↔
					7.3	↔
				The A limit is		
				The B limit is +/-	20.0	
				The C limit is	20.0	

Specimen : 163A	n	Mean	SD	CV(%)	Your result
All methods [ALTM]	8	0.19	0.24	124.5	<3
Mass Spectrometry	5	0.15	0.10	65.6	Target value ( )
In-house [600]	5	0.15	0.10	65.6	Standard Uncertainty
non-numeric results	35				Your specimen: %bias Accuracy Index
					Weighed-in value
					Method mean
					In-house [600]

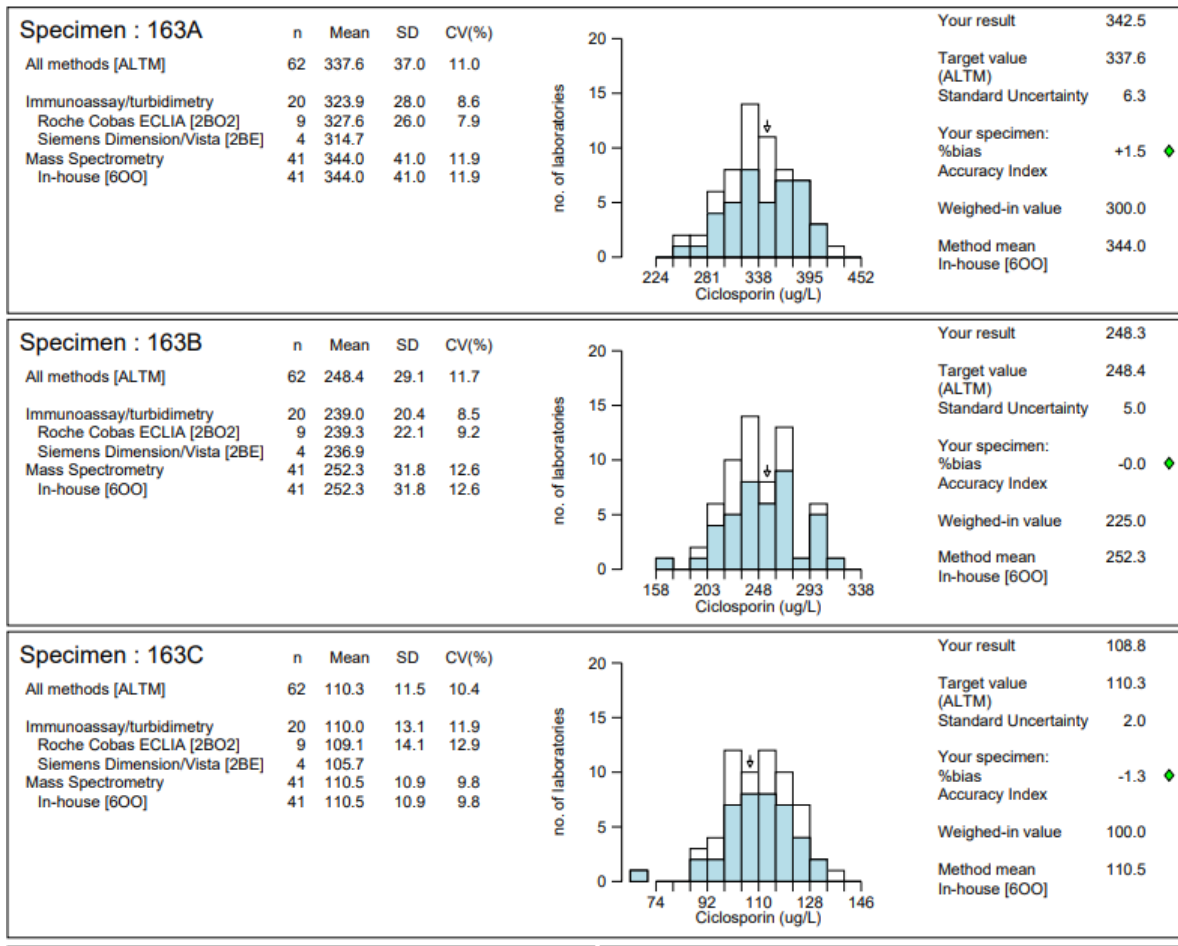
  

Specimen : 163B	n	Mean	SD	CV(%)	Your result
All methods [ALTM]	44	8.69	0.97	11.2	8.55
Immunoassay/turbidimetry	6	9.77	1.89	19.4	Target value
Roche Cobas ECLIA [2BO2]	4	10.57			(ALTM)
Mass Spectrometry	37	8.51	0.85	10.0	Standard Uncertainty
In-house [600]	37	8.51	0.85	10.0	Your specimen: %bias Accuracy Index
					Weighed-in value
					Method mean
					In-house [600]

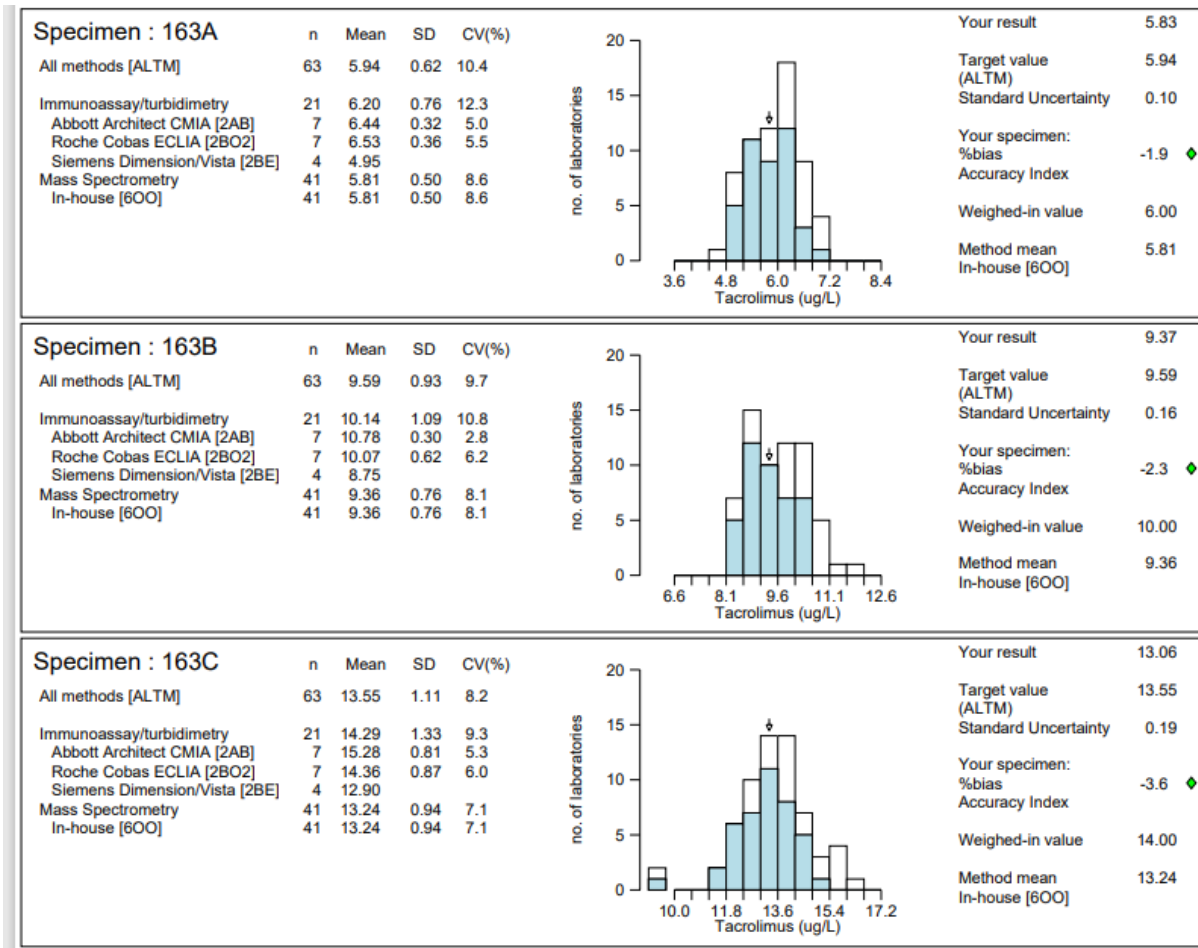
  

Specimen : 163C	n	Mean	SD	CV(%)	Your result
All methods [ALTM]	44	14.58	1.61	11.0	15.2
Immunoassay/turbidimetry	6	16.71	2.34	14.0	Target value
Roche Cobas ECLIA [2BO2]	4	16.85			(ALTM)
Mass Spectrometry	37	14.26	1.44	10.1	Standard Uncertainty
In-house [600]	37	14.26	1.44	10.1	Your specimen: %bias Accuracy Index
					Weighed-in value
					Method mean
					In-house [600]

# Ciclosporin



# Tacrolimus

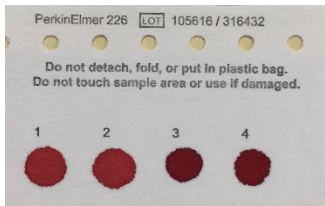




# Which drugs by fingerprick ?

## Dried blood

- Ciclosporin
- Tacrolimus



Lab cost £32

Cost includes creatinine

## Wet blood

Lab cost £18  
Tube £0.2  
lancet £0.1  
postage £13.75

Total cost £32

Mitra



Mitra £16.10

- Ciclosporin
- Tacrolimus
- Everolimus
- Sirolimus



Capitainer




Capitainer £8


# Postage (UN3373)


Safebox™ leaflet (April 2022)


royalmail.com/sites/royalmail.com/files/2022-04/Safebox-leaflet-April-2022.pdf


## Safebox™ step by step


- 

1  
Place the sample(s) in a leak proof primary receptacle.  
**Sample quantity cannot exceed 50ml per consignment**
- 

2  
Wrap sample(s) in absorbent sheet and place into the grip seal bag and close.
- 

3  
Place the filled grip seal bag into the PathoSeal bag.
- 

4  
Close the PathoSeal bag following the instructions printed on the bag.
- 

5  
Place the completed PathoSeal bag and paperwork into the Safebox.
- 

6  
CHECK all contents are included as required before closing.

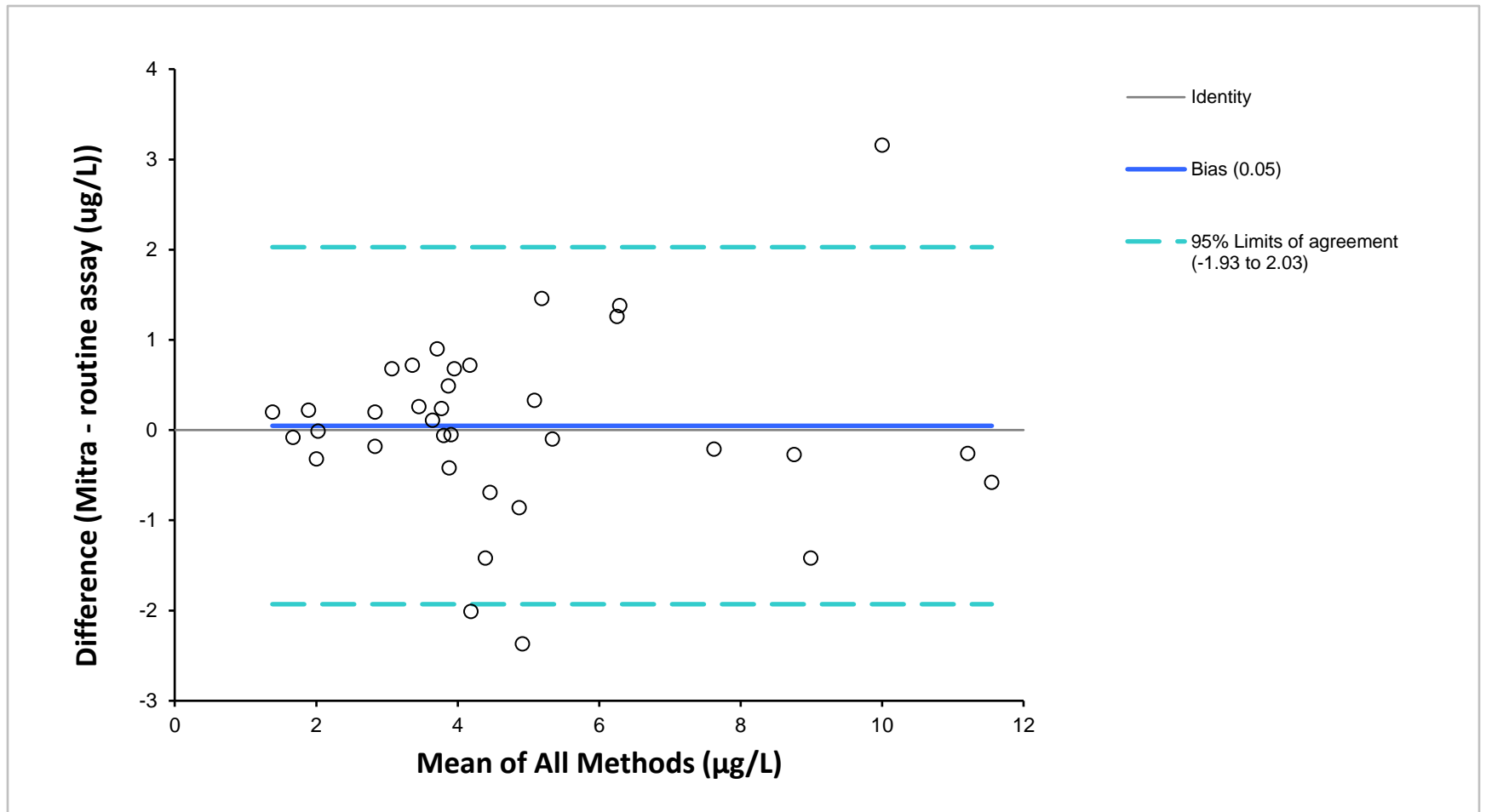
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06/09/2022

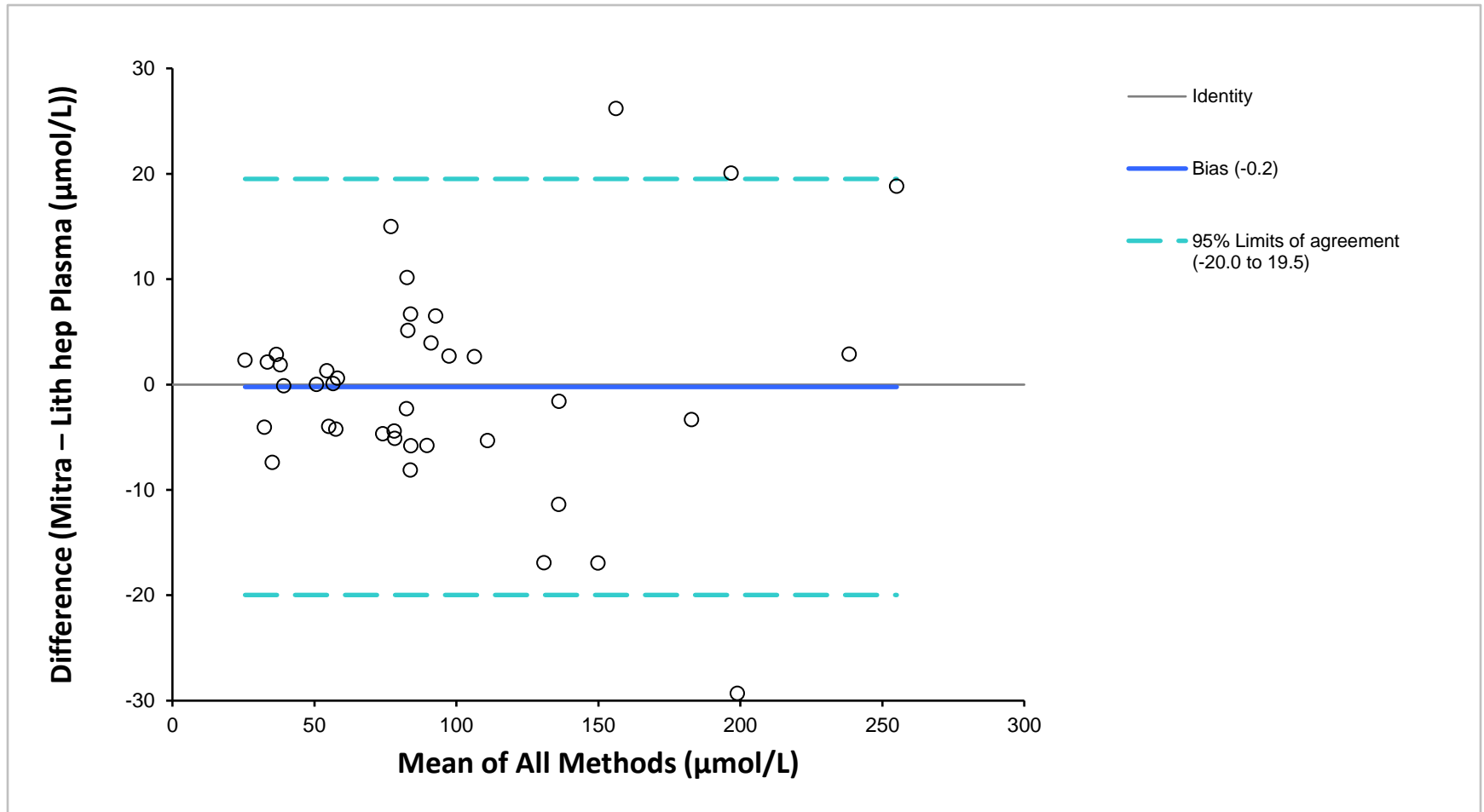
# Patient Samples

- Small pilot study with 33 paediatric renal transplant patients on FK506 therapy
- 4 x finger prick Mitra<sup>®</sup> samples collected alongside venous EDTA whole blood & lithium heparin plasma
- Wide range of haematocrit values (11% - 46%)
- Samples posted and analysed at Wythenshawe biochemistry

# FK506 (n=35)



# Creatinine (n=39)



# Seven day stability

- Mitra<sup>®</sup> tips analysed then left on the bench at ambient temperature in a sealed specimen bag
- Re-analysed after 1 week
- Creatinine = -0.2  $\mu\text{mol/L}$  (-0.2%)
- FK506 = -0.32  $\mu\text{g/L}$  (-5.8%)
- Within acceptable limits; able to post

# Nottingham Paediatric Nephrology.

## Patient response survey

- 83% said test was 'very easy' and remainder 'easy'
- 83% definitely preferred over venous sampling
- 60% said they could perform independently; training required
- Comments were positive;
  - 'It's easier and quicker than coming to the hospital all the time'
  - 'It doesn't hurt and it's quicker'

# Do we need special equipment?

- Need LC-MS/MS to handle 10uL of sample.
- Most major H/L transplant centres use LC-MS/MS
- Extra lab cost from handling tips and including creatinine in the method.



# Is it Scalable to all centres?

- Potentially yes.
- Some patients may not be happy doing it.
- More work for the laboratory.
- IT problems especially between centres.

# Acknowledgements

- Transplant team at Wythenshawe
- David Marshall
- James Rudge (Neoteryx)
- Dr Jon Jin Kim and his team at Nottingham Children's Hospital