



**Join us for the
2023 NephroCAGE Symposium
Aug 2, 2023 @ 6.00am PDT / 9.00am EDT / 3.00pm CEST**

**Marcel G. Naik
Physician
Charité**



NEPHRO CAGE

German-Canadian consortium on AI for improved kidney transplantation outcome
3rd International NephroCAGE Symposium, Aug 2, 2023



THE UNIVERSITY OF BRITISH COLUMBIA



Supported by:
Federal Ministry for Economic Affairs and Climate Action
on the basis of a decision by the German Bundestag

NephroCAGE clinical demonstrator Bringing latest AI to the medical doctors

Dr. Marcel G. Naik
Physician
Charité



NEPHROCAGE

German-Canadian consortium on AI for improved kidney transplantation outcome
3rd International NephroCAGE Symposium, Aug 2, 2023



on the basis of a decision by the German Bundestag

Agenda

- Clinical importance in transplantation
- Epitope data flow
- Data integration into the electronic health record
- Bringing latest AI to the medical doctors
- Outlook

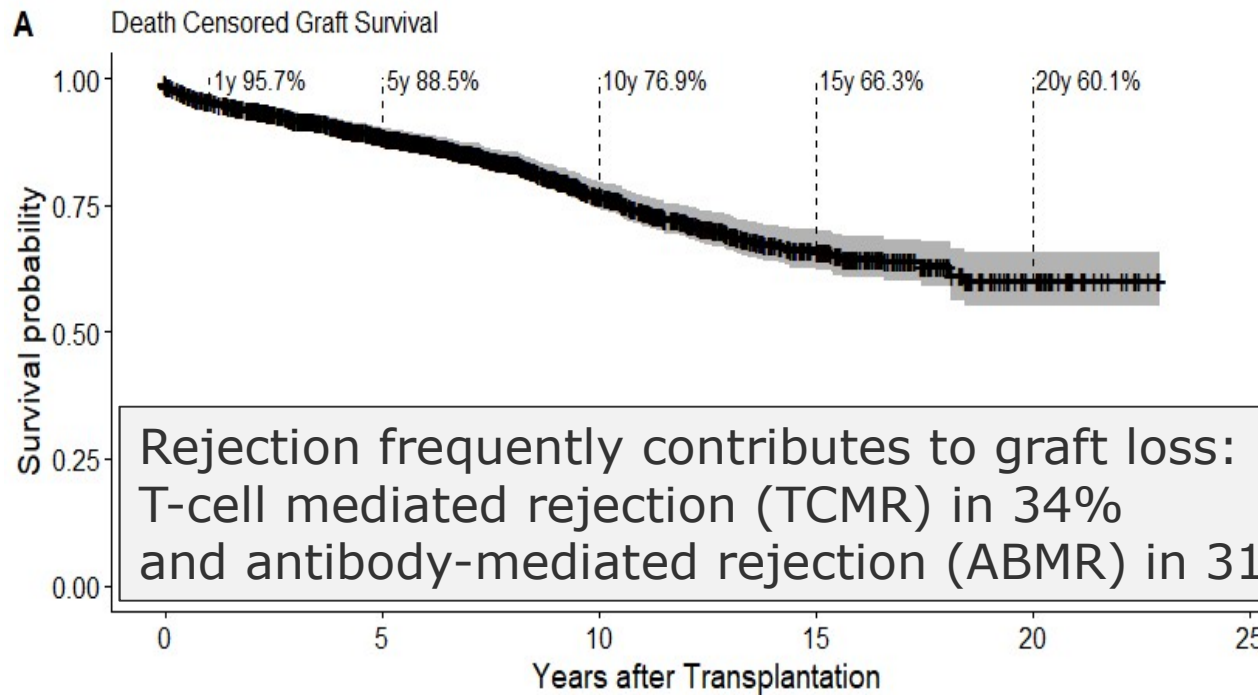
**3rd Int'l NephroCAGE
Symposium, Aug 2,
2023**

Marcel G. Naik
Physician
Charité

Chart 3



Clinical importance: graft loss over time



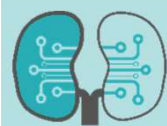
Rejection frequently contributes to graft loss:
T-cell mediated rejection (TCMR) in 34%
and antibody-mediated rejection (ABMR) in 31%

Exploring the complexity of Death-censored kidney allograft failure
Mayrdorfer, Liefeldt, Wu et al. JASN 32, 2021
<https://doi.org/10.1681/ASN.2020081215>

3rd Int'l NephroCAGE Symposium, Aug 2, 2023

Marcel G. Naik
Physician
Charité

4

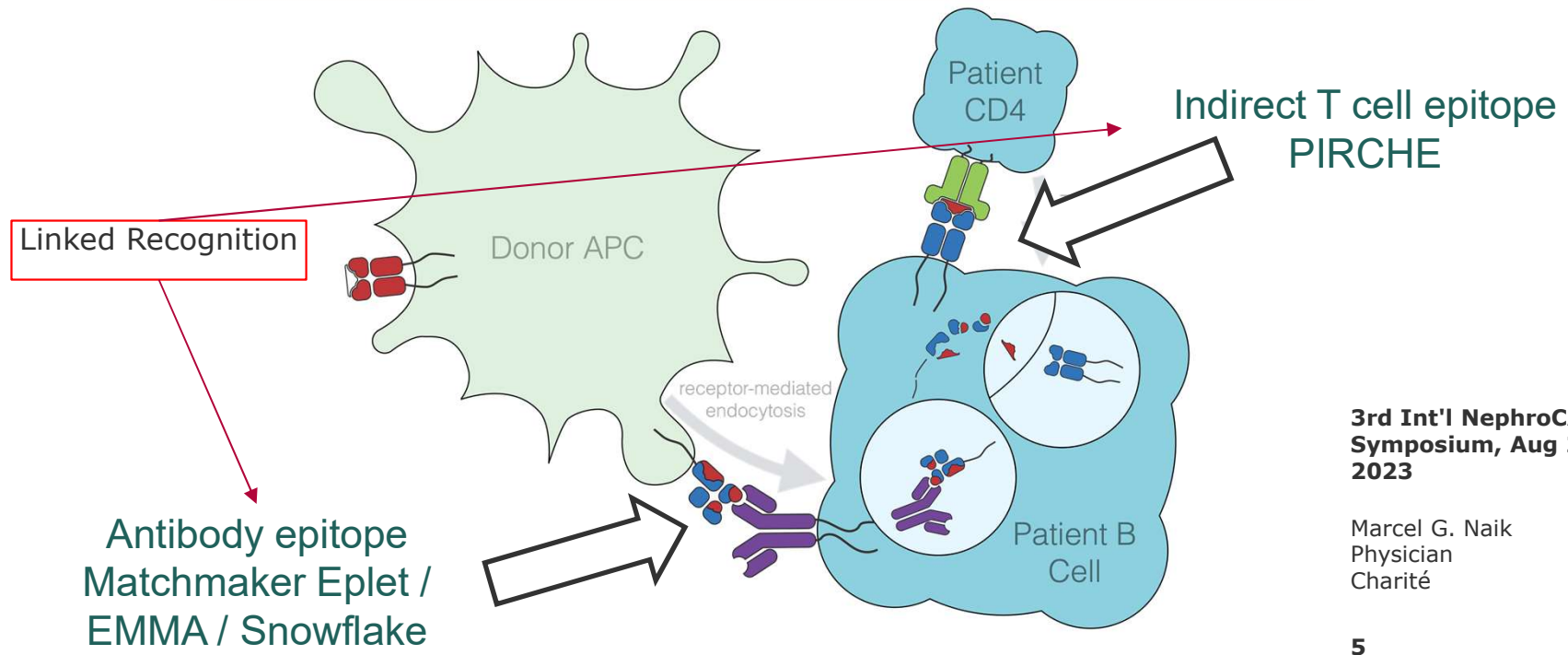


NEPHRO CAGE

German-Canadian consortium on AI for improved kidney transplantation outcome
3rd International NephroCAGE Symposium, Aug 2, 2023



Immunological background HLA Epitop Matching

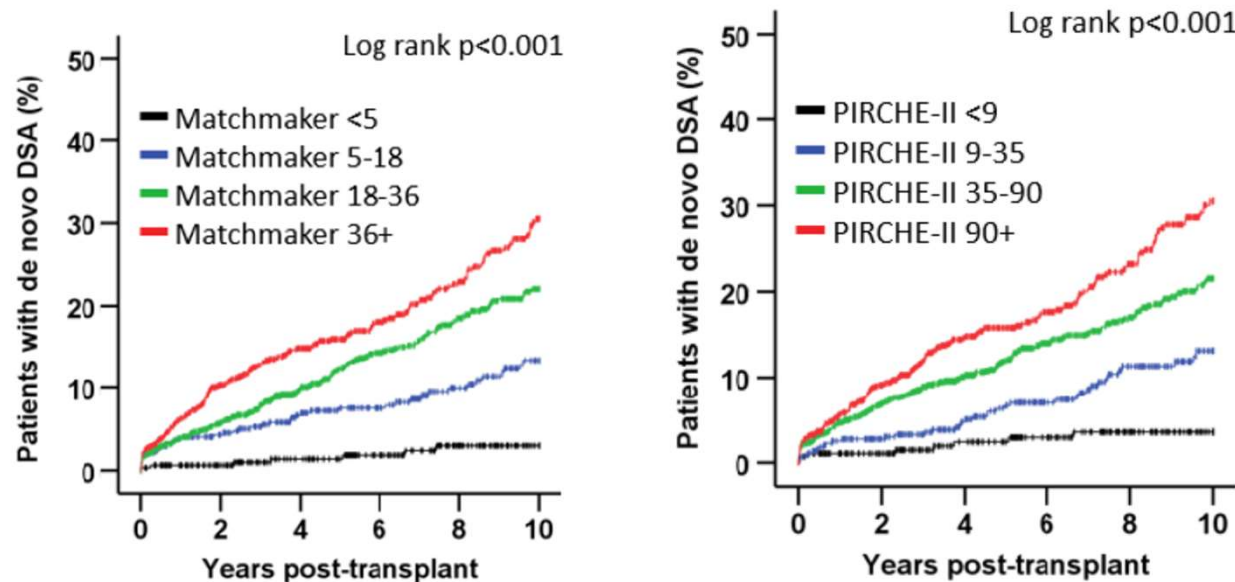


3rd Int'l NephroCAGE Symposium, Aug 2, 2023

Marcel G. Naik
Physician
Charité

5

Epitope match is associated with development of donor specific antibodies and rejection



Donor-Recipient Matching Based on Predicted Indirectly Recognizable HLA Epitopes Independently Predicts the Incidence of De Novo Donor-Specific HLA Antibodies Following Renal Transplantation

Lachmann, Niemann, Reinke et al., AJT 2017; 17: 3076-3086 doi: 10.1111/ajt.14393

3rd Int'l NephroCAGE Symposium, Aug 2, 2023

Marcel G. Naik
Physician
Charité

6

Way to Demonstrator

Development of a clinical demonstrator application to present the CPM, that had been developed using a federated learning approach	WP7
Task 1: Implementation of web interface.	Finished
Task 2: Hosting of Web service.	Started
Task 3: Concept for integration of demonstrator in TBase with an interface to the HLA-lab.	Finished
Task 4 Data integration epitope matching service.	Finished
Task 5 concept for visualization.	Finished
Task 6 validation concept.	Open

3rd Int'l NephroCAGE Symposium, Aug 2, 2023

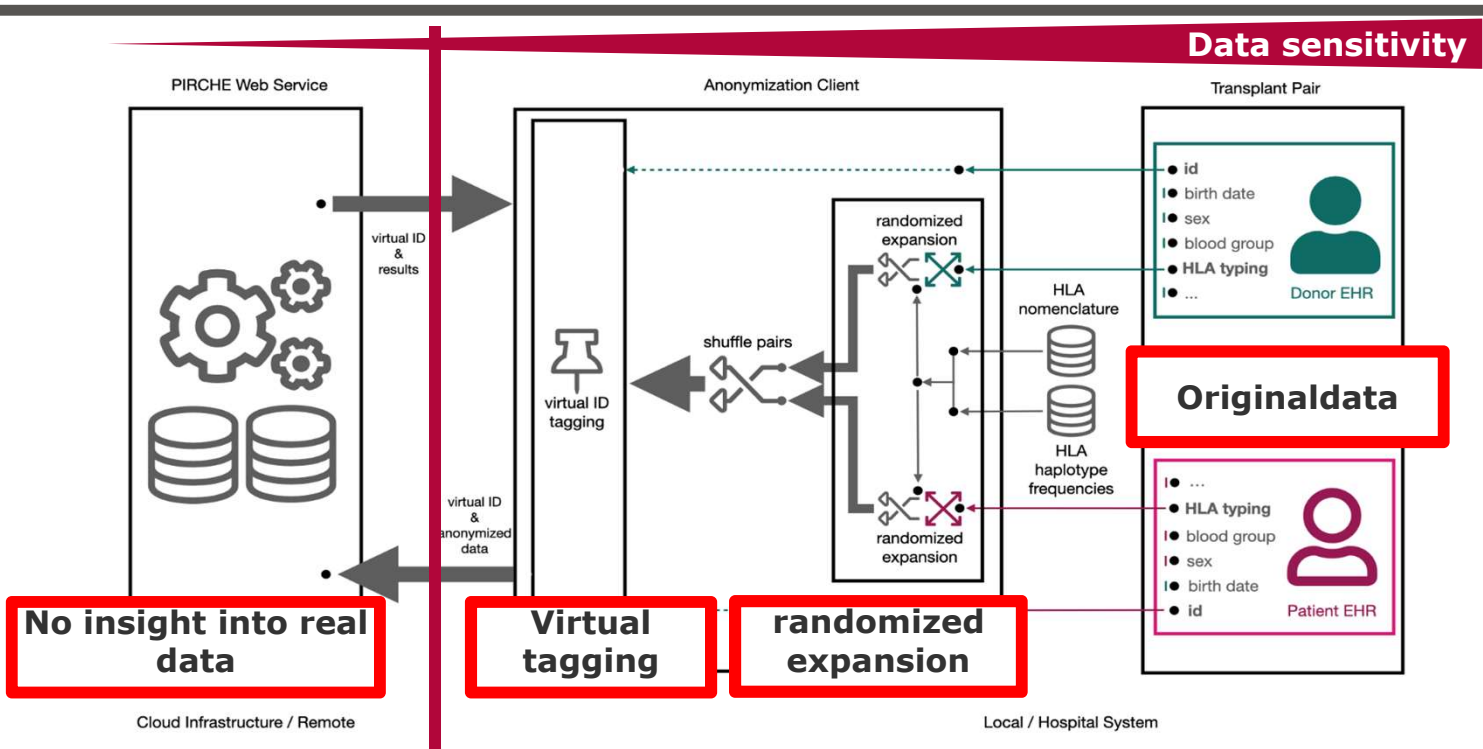
Marcel G. Naik
Physician
Charité

7

6. Deployment of the developed CPM in hospital sites



Anonymized data flow for epitope matching



3rd Int'l NephroCAGE Symposium, Aug 2, 2023

Marcel G. Naik
Physician
Charité



▼ HLA-Typisierung

Patient/Donor	Abnahmedatum	
278069	08.09.2012	A1 A2 B8 B12 B44 Cw5 Cw7 DR1 DR4 DQ1 DQ5 DQ3 DQ8
180912	28.03.2006	A10 A26 A19 A31 B22 B55 Cw3 Cw3 Cw10 Cw9 DR2 DR16 DR5 DR11 DQ1 DQ5 DQ3 DQ7
299240	12.02.2012	A2 B12 B44 B15 B62 Cw3 Cw10 Cw16 DR4 DR7 DQ2 DQ3 DQ8
76312	13.06.1994	A2 B12 B44 B15 B62 Bw4 Bw6 Cw3 Cw10 Cw5 DR4 DR7 DR53 DQ3 DQ3 DQ7 DQ9
235590	04.08.2011	A1 A9 A24 B7 Cw3 Cw10 Cw7 DR2 DR15 DR7 DQ1 DQ6 DQ3 DQ9
233695	16.03.2006	A1 A2 B8 B15 B62 Cw3 Cw9 Cw7 DR3 DR17 DR5 DR11 DQ2 DQ3 DQ7
154383	12.12.2001	A1 A2 B8 B12 B45 Cw6 Cw7 DR3 DR17 DR4 DQ2 DQ3 DQ8
148884	08.03.2009	A2 A28 A68 B12 B44 B15 B62 Cw1 Cw5 DR4 DR6 DR13 DQ1 DQ6 DQ3 DQ8
106576	19.10.1996	A9 A24 A28 A68 B8 B14 B65 Bw6 Cw7 Cw8 DR3 DR17 DR6 DR13 DR52 DQ2 DQ3 DQ7
248572	26.05.2007	A1 A9 A24 B7 Cw3 Cw10 Cw7 DR2 DR15 DR7 DQ1 DQ6 DQ3 DQ9
113035	15.08.2005	A1 A2 B8 B15 B62 Cw3 Cw9 Cw7 DR3 DR17 DR5 DR11 DQ2 DQ3 DQ7
414371	26.02.2014	A19 A30 A28 A69 B35 B41 Cw7 Cw17 DR3 DR17 DR10 DQ1 DQ5 DQ2
142141	03.01.2000	A2 B12 B44 B15 B62 Bw4 Bw6 Cw3 Cw10 Cw5 DR4 DR53 DQ3 DQ3 DQ7 DQ9

- > HLA-Antikörper
- > Crossmatches





> HLA-Typisierung

▼ HLA-Antikörper

Tabelle erweitern für mehr Informationen: AN

Abnahmedatum	Befundtext
08.09.2012	Aktuell keine spezifischen HLA Kl. I IgG-Ak im Serum nachgewiesen. Bestätigung der aus Vorbefunden bekannten und starken HLA Kl. II IgG AK, die auf Grund der DR4-DQ7-DQA3 Assoziation als potentiell donorspezifisch zu betrachten sind.
12.02.2012	Kein Nachweis Komplement-bindender und zytotoxischer HLA IgG Antikörper. Die bekannten HLA Kl. II IgG Antikörper sind weiterhin stark nachweisbar.
28.03.2006	Keine Änderungen im Ak-Profil (qualitativer Antikörperrnachweis-Test) im Vergleich zur letzten Spezifizierung aus 12/2021. Potent. Donorspezif. HLA Kl.II IgG Ak gegen das Spenderantigen DQA3 sowie keine spez. Kl.I AK bekannt. Kein Anzeichen einer Änderung in der HLA-Reaktivität und folglich aktuell nicht erneut spezifiziert.

> Crossmatches



- Stammdaten
- Fest.Med.Daten
- Fragebögen
- Ärzte
- Diagnose
- Prozeduren
- Verlauf
- Labor
- Medikation
- Untersuchun...
- Krankenhaus
- Transplantati...
- Bewegungss...
- Lupus
- TMZ-Kurve
- TMZ-Dashbo...
- HLA

> HLA-Typisierung

> HLA-Antikörper

∨ Crossmatches

Tabelle erweitern für mehr Informationen: AN ○

Abnahmedatum	Name	Befundtext	mit DTT	ohne DTT	T-Zellen mit DTT	T-Zellen ohne DTT	B-Zellen mit DTT	B-Zellen ohne DTT
08.09.2012	Max Schmidt	Es liegen keine wiederholte Inkompatibilitäten zur 1. TX vor.	neg	neg	neg	neg	neg	neg
12.02.2012	Hertha Giese	Es wurden bislang fragliche HLA Kl. I und starke HLA Kl. II IgG HLA IgG Ak nachgewiesen (s. Ak-Vorbefunde). Es gibt keine donorspezifischen HLA Kl. II IgG Ak.	neg	pos	neg	neg	neg	neg
28.03.2006	Benjamin Rüttig	LCT-Kreuztest gegen isolierte T- und B-Lymphozyten des o.g. Spenders mit dem Patientenserum vom 17.08.2022 war negativ (1. Crossmatch). Der Mismatchgrad zwischen Spender und Empfänger beträgt: HLA-A/B/C/DR/DQ/DP: 1/2/2/2/1/1	neg	neg	neg	pos	neg	neg

Training for doctors

- Establishment of a risk prediction model to support clinicians
 - Death-Censored Graft Loss
 - Rejection
 - Infection
 - Prediction for next 90 days
- Questions
 - How good can it get?
 - How good can clinicians master that task?
 - Can a CPM be used to support clinicians?

Roland Roller et al.

Evaluation of a clinical decision support system for detection of patients at risk after kidney transplantation.
Front Public Health. 2022 Oct 25;10:979448. doi: 10.3389/fpubh.2022.979448. eCollection 2022

**3rd Int'l NephroCAGE
Symposium, Aug 2,
2023**

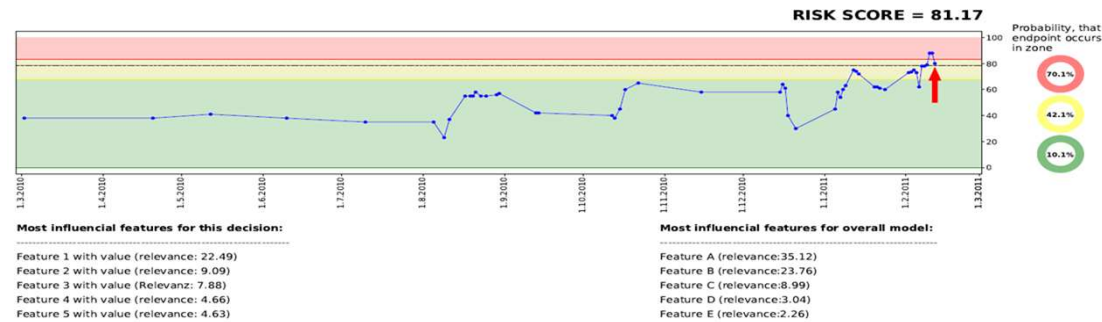
Marcel G. Naik
Physician
Charité

12

Study design

AI versus Medical Doctor (MD) versus AI+MD

- 120 Data points displayed in TBase (all data disaccessible)
- 8 doctors (4 juniors, 4 seniors)
- Two rounds:
 - Round 1: MD without AI support
 - Round 2: MD with AI support



Roland Roller et al.

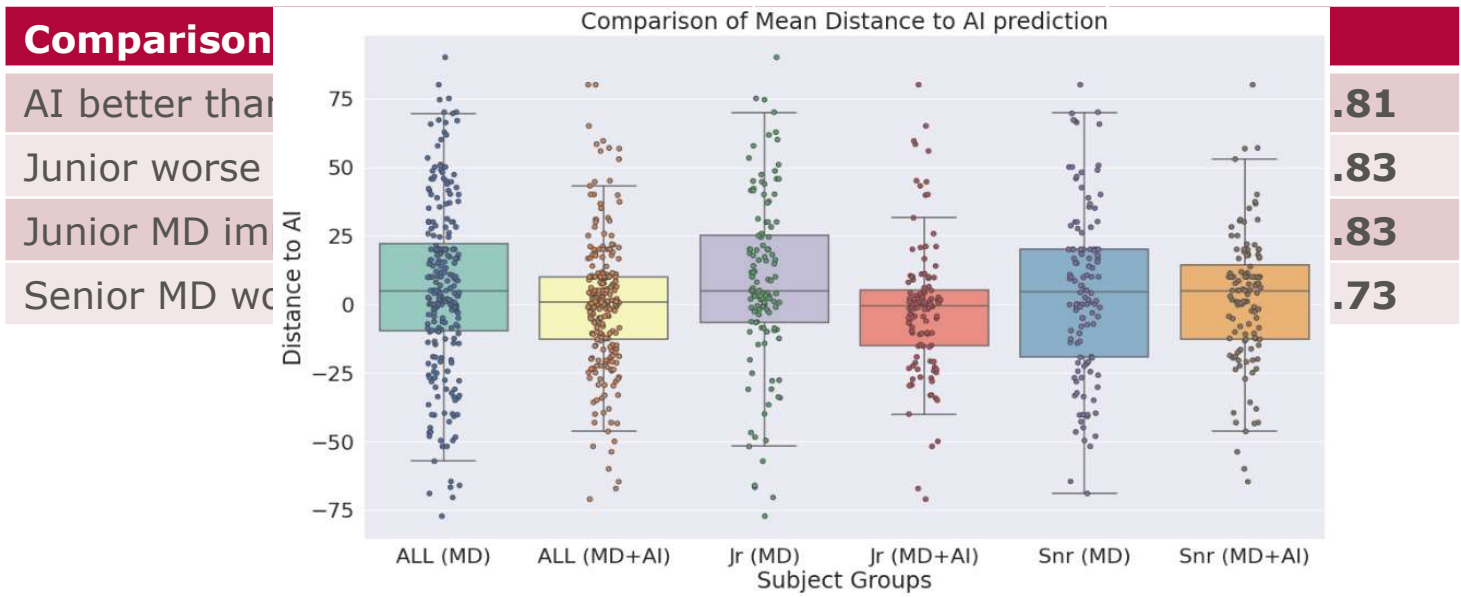
Evaluation of a clinical decision support system for detection of patients at risk after kidney transplantation. Front Public Health. 2022 Oct 25;10:979448. doi: 10.3389/fpubh.2022.979448. eCollection 2022

3rd Int'l NephroCAGE Symposium, Aug 2, 2023

Marcel G. Naik
Physician
Charité

13

Results



Roland Roller et al.

Evaluation of a clinical decision support system for detection of patients at risk after kidney transplantation.

Front Public Health. 2022 Oct 25;10:979448. doi: 10.3389/fpubh.2022.979448. eCollection 2022

3rd Int'l NephroCAGE Symposium, Aug 2, 2023

Marcel G. Naik
Physician
Charité

14

Outlook

- Better HLA data display and data flow locally
- Novel comprehensive web-based kidney graft loss risk calculator
- First transcontinental federated learning approach in transplant medicine
- Improved risk assessment including HLA epitopes
 - may pave the road for better outcomes
 - basis for personalized immunosuppression
 - doctors and patient education
 - starting point for interventional studies

**3rd Int'l NephroCAGE
Symposium, Aug 2,
2023**

Marcel G. Naik
Physician
Charité

15



Thank you



marcel.naik@charite.de

+4930 450 614 604

16