



Functional imaging and cost-effectiveness for subtyping Primary Aldosteronism

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Outline

- Unilateral PA vs Bilateral PA
- CT, AVS, PET-CT
- Hybrid Hormones
- Sodium MRI

Primary Aldosteronism (PA) is curable

ANNALS OF
INTERNAL MEDICINE

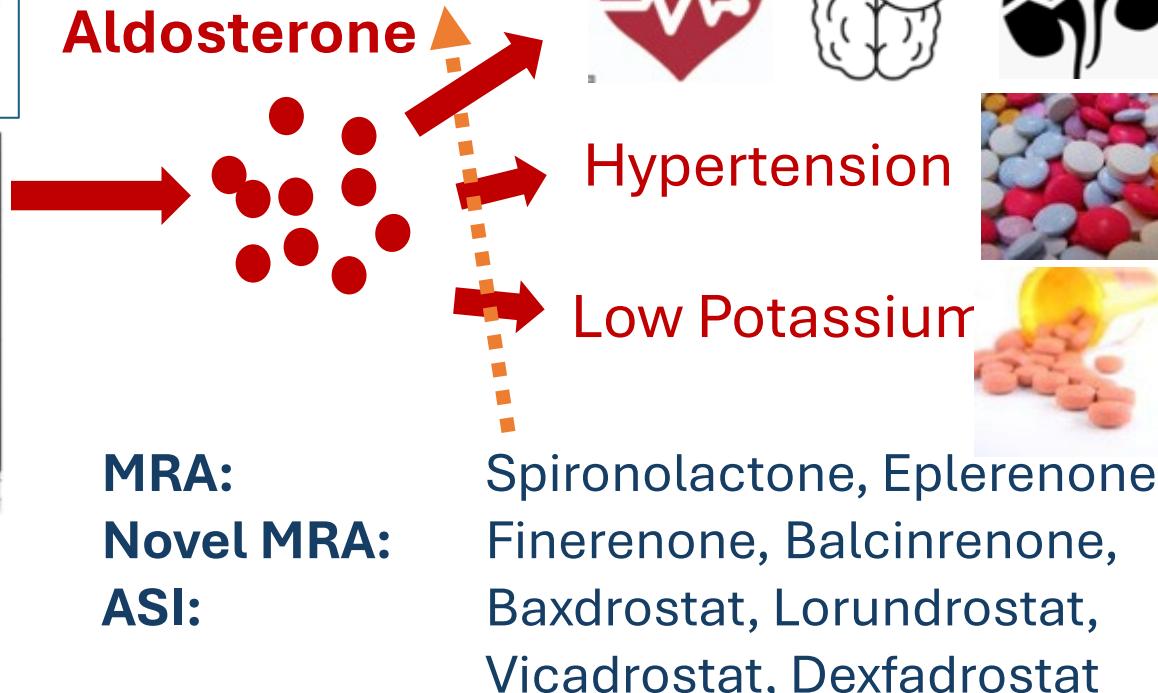
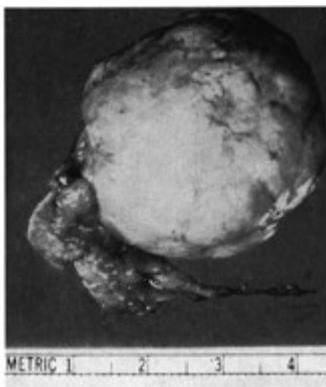
VOLUME 44

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NUMBER 1

PRIMARY ALDOSTERONISM, A NEW CLINICAL ENTITY *†

By JEROME W. CONN, M.D., F.A.C.P., and LAWRENCE H. LOUSS, Sc.D.,
Ann Arbor, Michigan

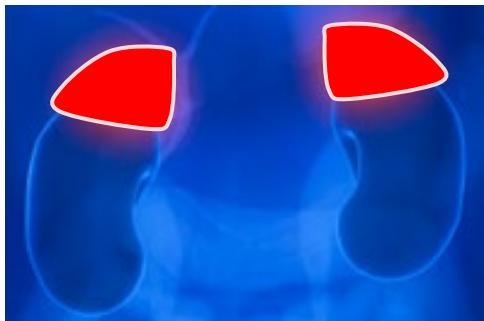


Mineralocorticoid Receptor Antagonists, MRA
Aldosterone Synthase Inhibitors, ASI

PA is Either Bilateral or Unilateral

Bilateral

Idiopathic Adrenal
Hyperplasia (BAH/IAH)



MRA
(Mineralocorticoid-
receptor antagonists)

Unilateral

Aldosterone-producing
Adenoma (APA)



Unilateral
Adrenalectomy

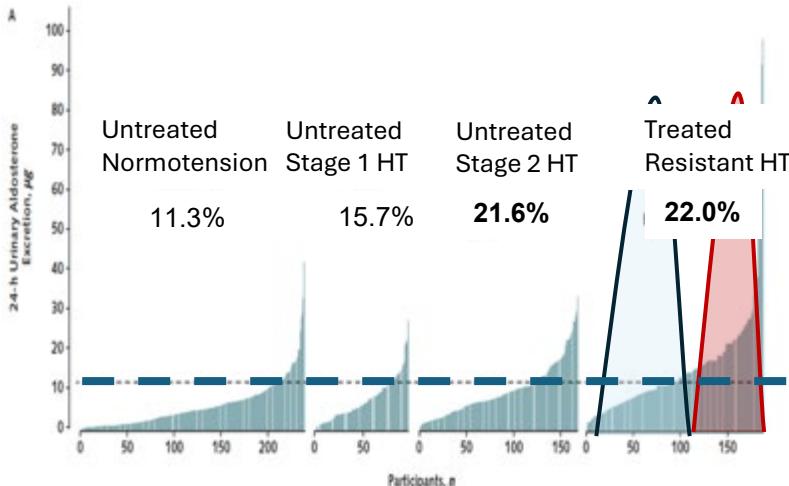
Like Hypertension, PA is a spectrum

Medscape Internal Medicine

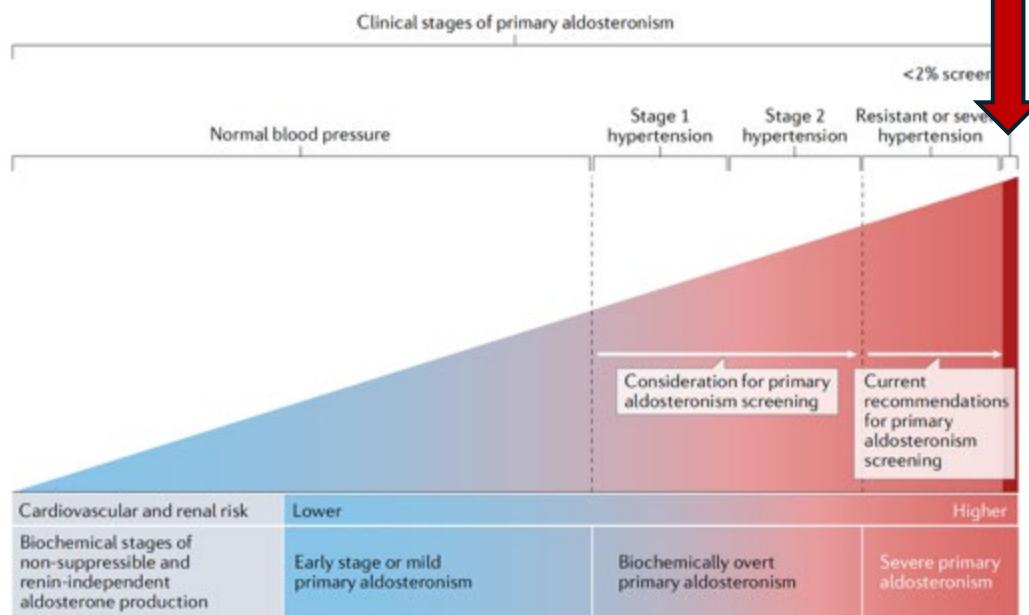
Mitchel L. Zoler
May 28, 2020

'Game Changer': Aldosterone-Driven Hypertension More Common Than Thought

Figure 2. Distribution of renin-independent aldosterone production, by blood pressure category.



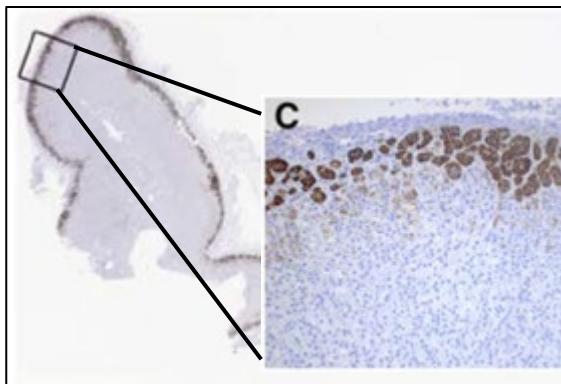
Brown et al. The Unrecognized Prevalence of Primary Aldosteronism Annal of Int Med 2020



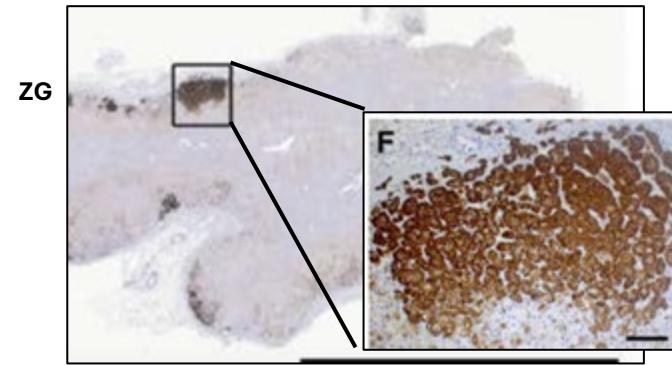
Turcu AF, Yang J, Vaidya A. Primary aldosteronism - a multidimensional syndrome. Nat Rev Endocrinol. 2022 Nov;18(11):665-682.

Aldosterone explains age-related hypertension

Typical 16yr

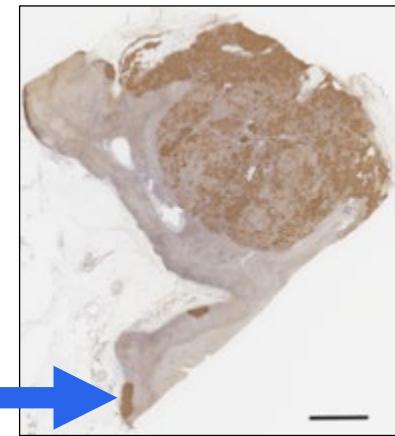


Typical 52yr



APCCs (Aldosterone-producing cell clusters)
→ same mutations as APAs
→ **CACNA1D, ATP1A1, ATP2B3, KCNJ5**

Pri Aldo (Conn's)



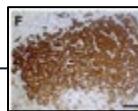
APA (Aldosterone-producing adenoma)
95% somatic mutations
KCNJ5, CACNA1D, ATP1A1, ATP2B3

HISTALDO Classification

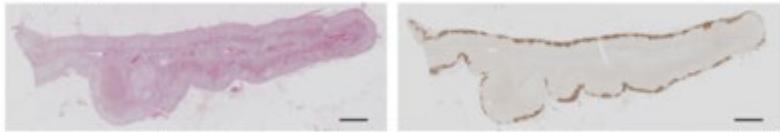
“Non-Classical”



Diffuse Hyperplasia



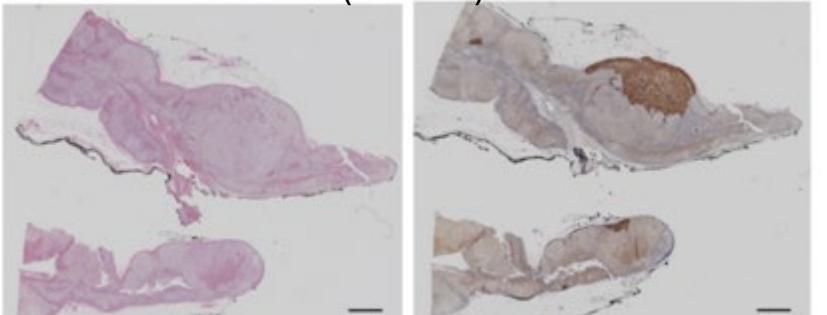
Adrenal #4



Aldosterone-producing micronodules (APM)

Adrenal #21

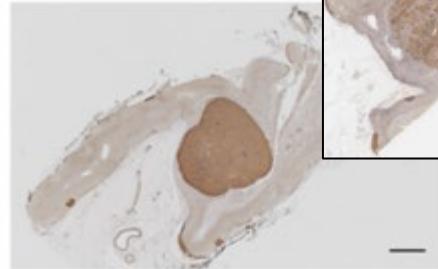
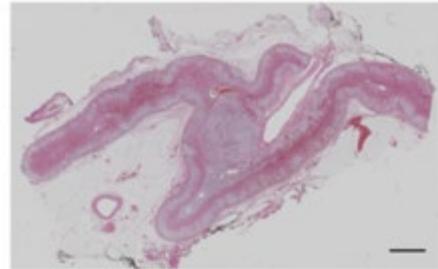
(APCCs)



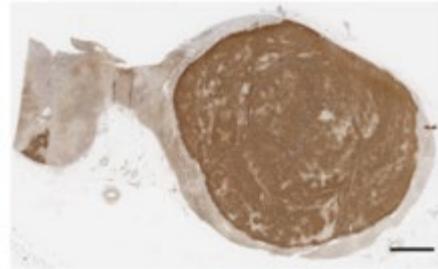
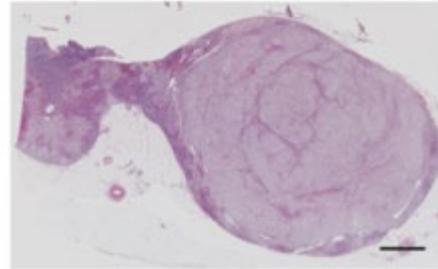
“Classical”



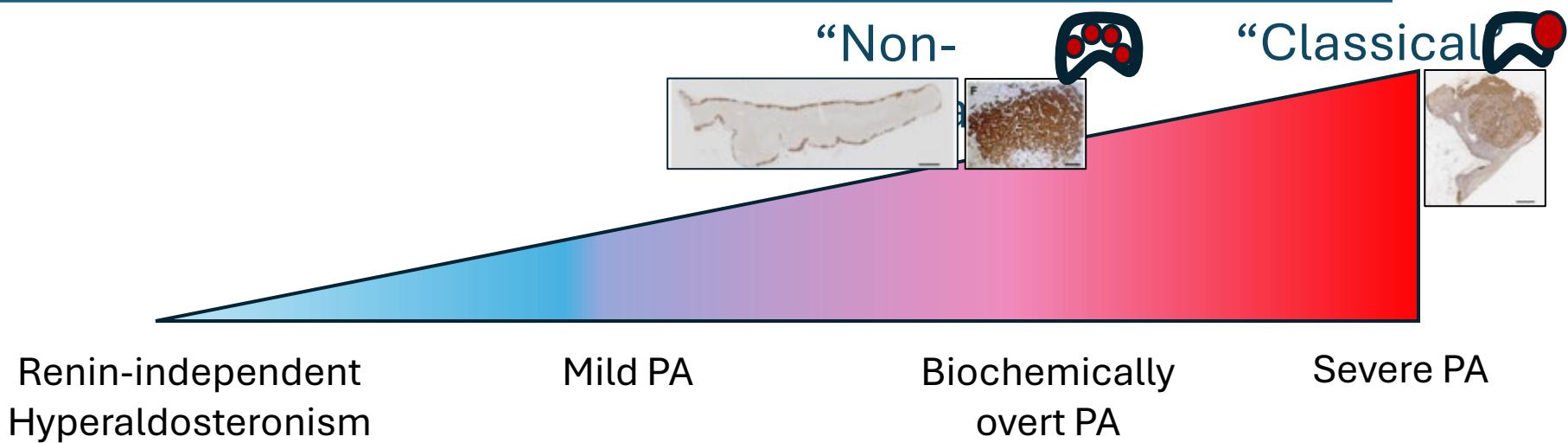
Adrenal #2



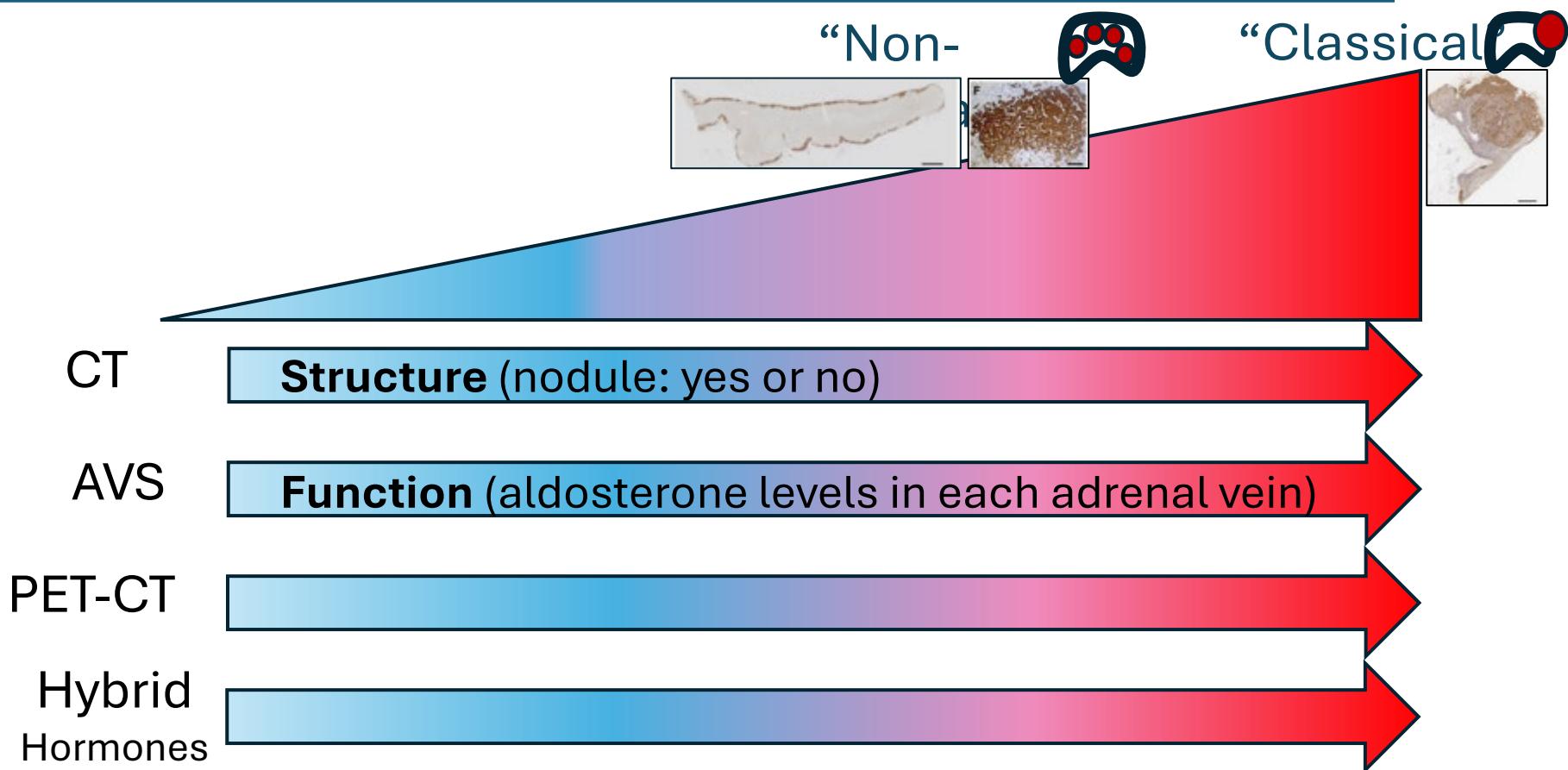
Adrenal #3



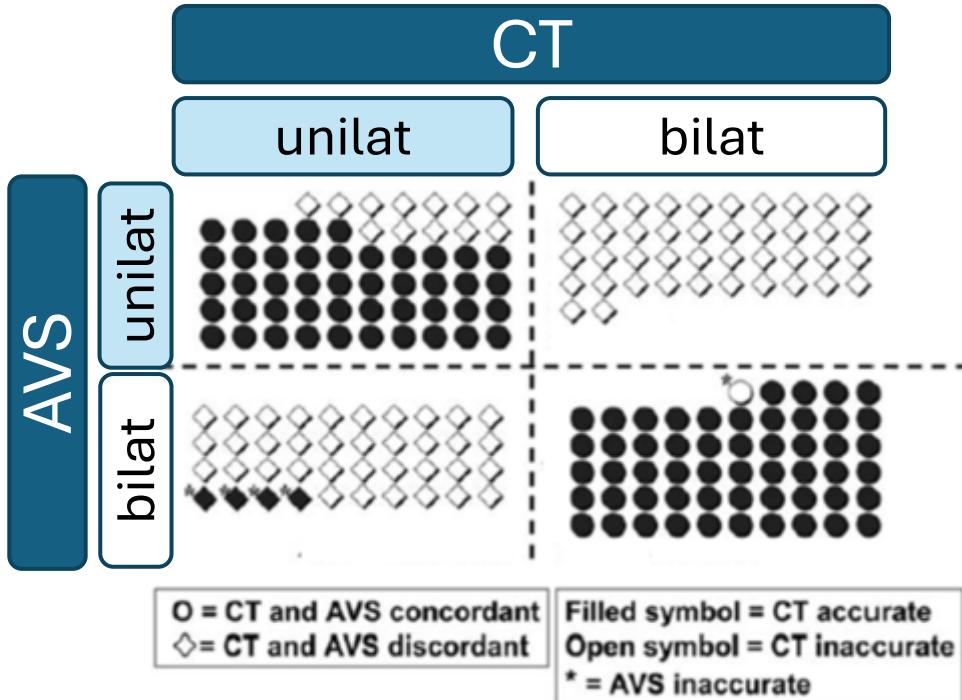
Dichotomy vs Spectrum of PA



Dichotomy vs Spectrum of PA

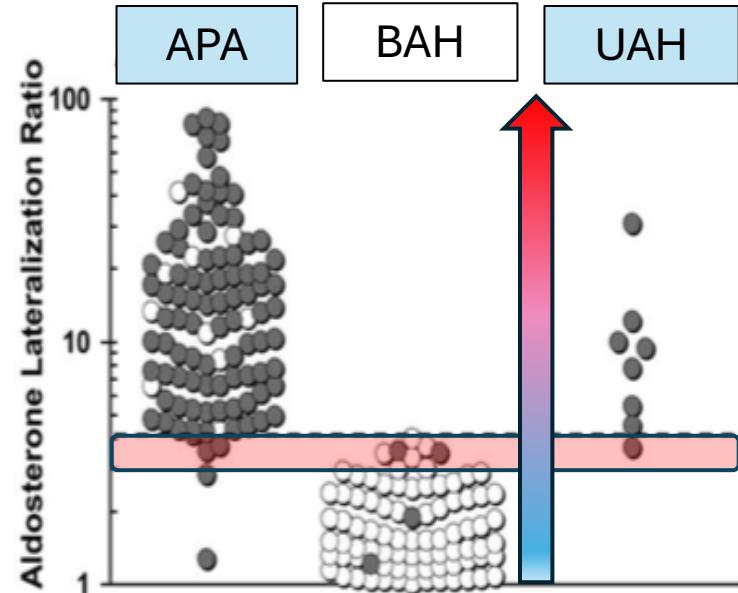


Subtyping: CT vs AVS



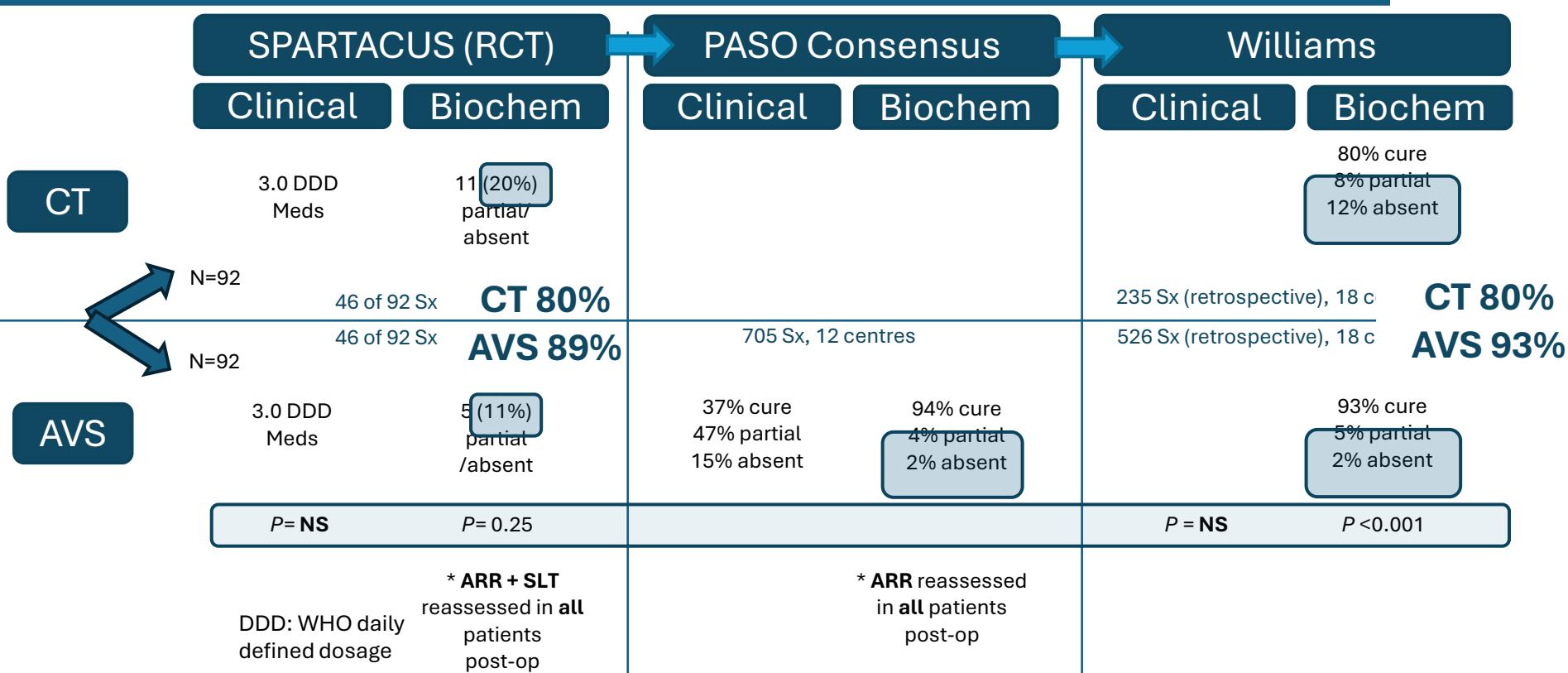
CT correctly identified unilateral or bilateral PA
in **only 53%**

CT 53% vs AVS 100%

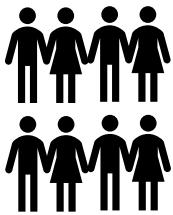


Young. Surgery 2004;136:1227-35

Subtyping: CT vs AVS



AVS in Asymmetrical Bilateral PA

 → 

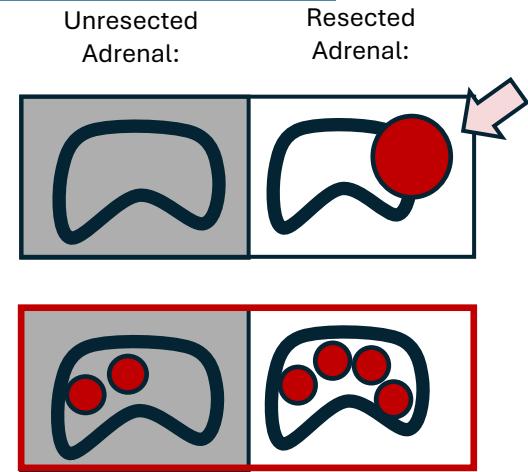
262 patients with PA
(3 centers)
Underwent Adx
AVS Lat Ratio ≥ 4

42 (16%) absent
biochemical cure

+ 21 cases
(+4 centers)


73% adrenals
Multiple CYP11B2+ areas


63% adrenals
CACNA1D mutations



Michigan (USA)
Tohoku (Japan)
Monash (Australia)

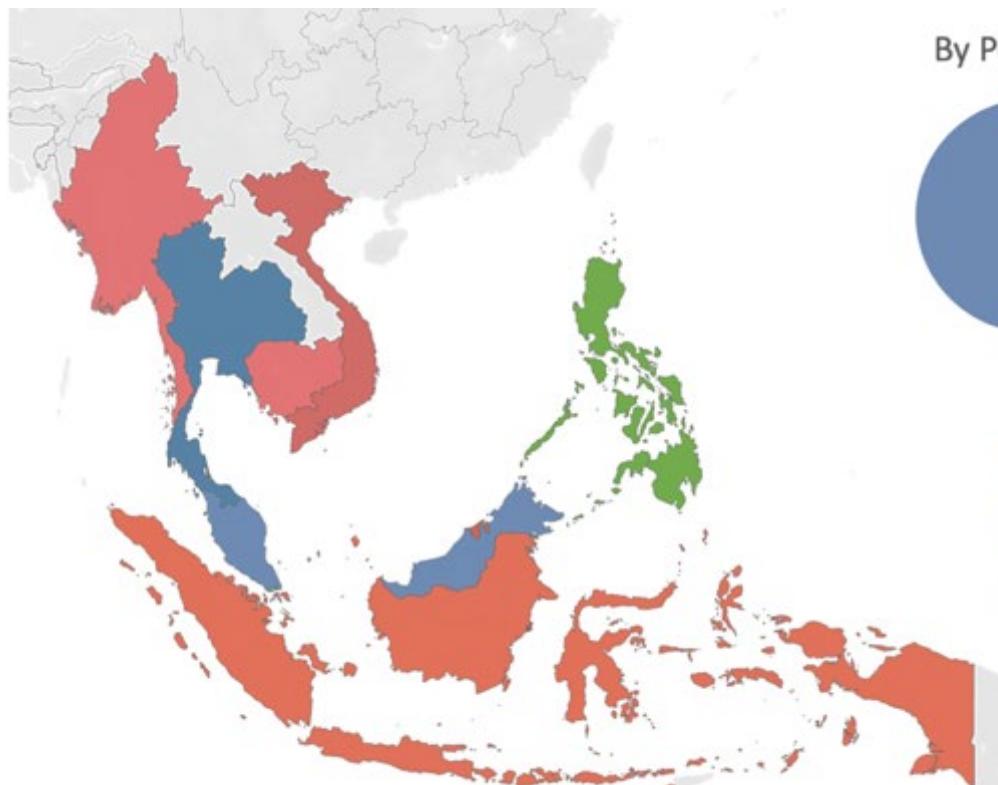
Munich (Germany)
Pennsylvania (USA)
Brigham (USA)
Montréal (Canada)

Higher risk of absent cure:

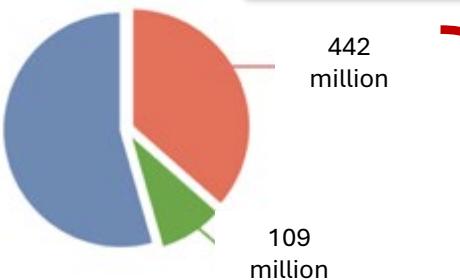
- Black > White
- LI ≥ 4 at baseline, <4 post-ACTH
- **AVS \neq CT**

Turcu AF, Tezuka Y, Lim JS, Salman Z, Sehgal K, Liu H, Larose S, Parksook WW, Williams TA, Cohen DL, Wachtel H, Zhang J, Dorwal P, Satoh F, Yang J, Lacroix A, Reincke M, Giordano TJ, Udager AM, Vaidya A, Rainey WE. Multifocal, Asymmetric Bilateral Primary Aldosteronism Cannot be Excluded by Strong Adrenal Vein Sampling Lateralization: An International Retrospective Cohort Study. Hypertension. 2024 Mar;81(3):604-613.

Lack of AVS service in ASEAN



By Population



■ Routinely performed

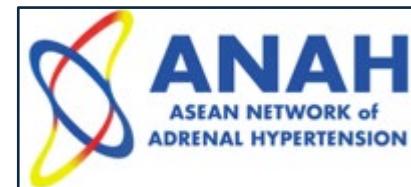
■ Limited

■ Not performed (due to inability to afford, lack of availability of facilities, or assays)

Health Care Challenges in the Management of Primary Aldosteronism in Southeast Asia

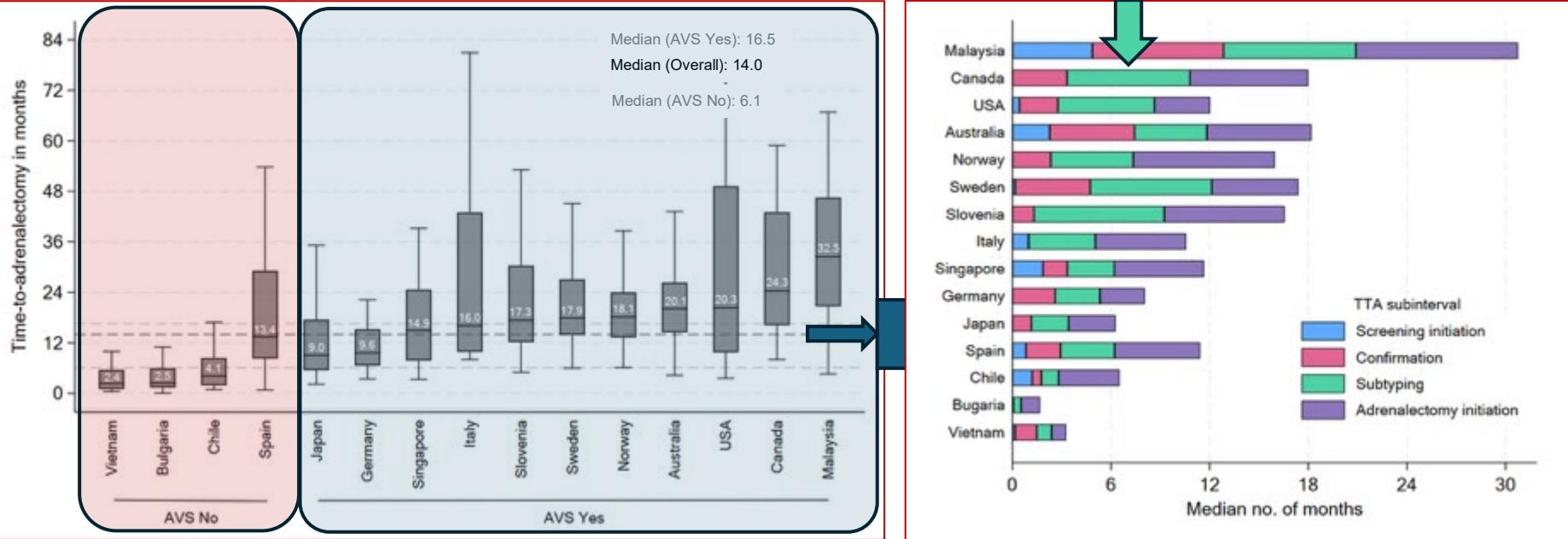
Norlela Sukor,^{1,2} Sarat Sunthornyothisin,² Thang V. Tran,⁴ Tri Juli Tarigan,⁵ Leilani B. Mercado-Asis,⁶ Satha Sum,⁷ Moe Wint Aung,⁸ Alice M. L. Yong,⁹ Tania Tedjo,¹⁰ Michael Villa,¹¹ Nang Ei Khang,¹² Elena Aisha Azizan,^{1,2} Waye Hann Kang,¹³ Vivien Lim,¹⁴ Ada E. D. Teo,¹⁵ Meifen Zhang,¹⁶ Hieu Tran,⁴ and Troy H. Puar^{16,17}

0.55 Billion individuals have no access to AVS



Time to Adrenalectomy

Charmaine Ter



	No AVS (n=193)	AVS (n=472)	P-value
Total Time to Adrenalectomy	6.1 months	16.5 months	<0.001
Biochemical (complete)	66.4%	86.8%	<0.001
Clinical (complete + partial)	76.2%	71.4%	0.356

ENDO 2024 Abstract SAT-721
 C Ter, XH Koh, M Araujo-Castro, E Gkaniatsa,
 M Reincke, TV Tran, H Tran, M Stowasser, MA Grytaas,
 A Turcu, J Matrozova, N Sukor, T Kocjan, R Baudrand,
 M Tsuiki, M Murakami, J Yang, T Katabami, M Naruse,
 M St-Jean, F Ceccato, T Puar

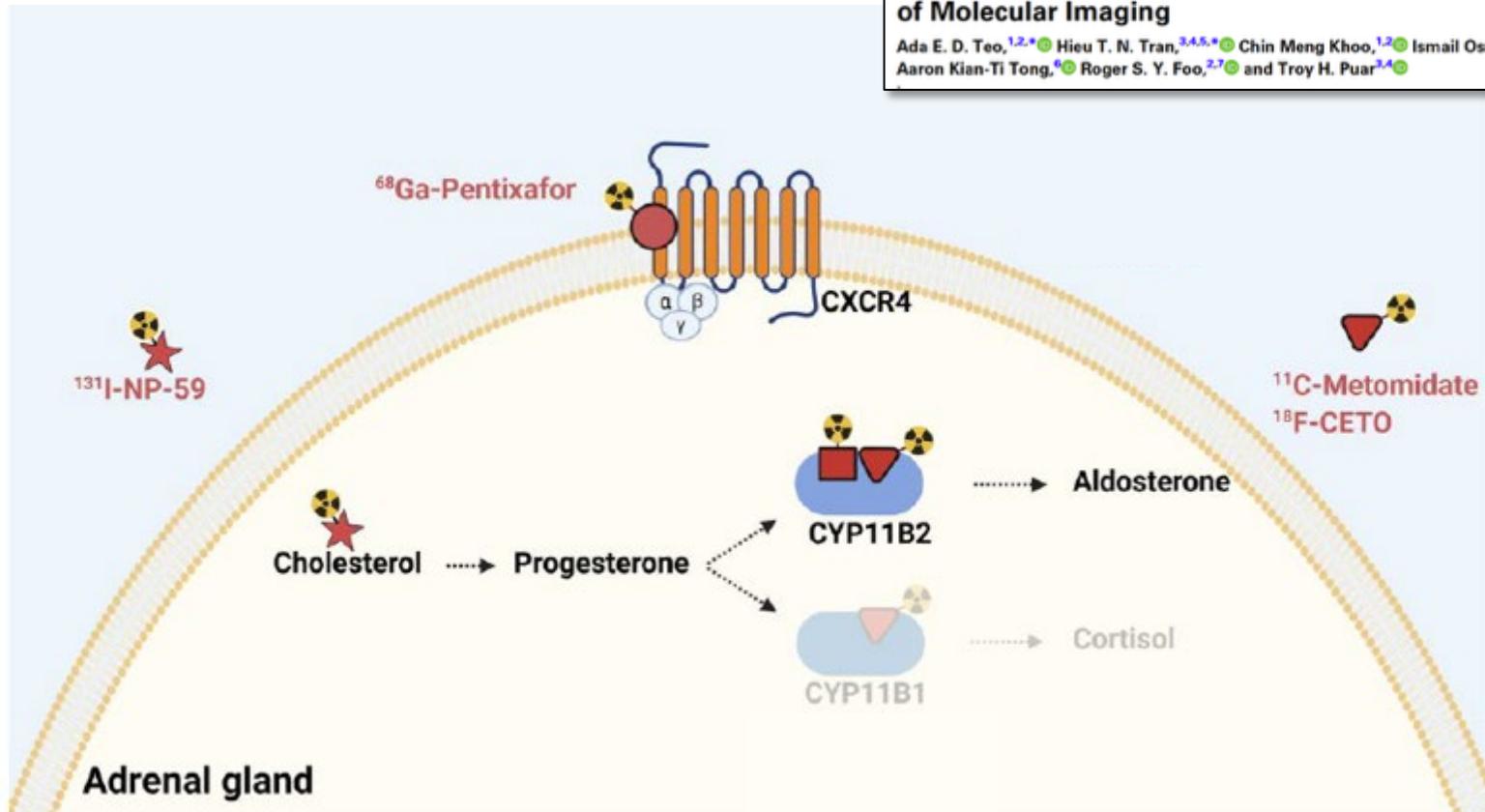
Localization with PET-CT

The Journal of Clinical Endocrinology & Metabolism, 2025, 00, 1–10
https://doi.org/10.1210/jcem/dga096
Advance access publication 21 July 2025
Approach to the Patient



Approach to the Patient With Primary Aldosteronism: Role of Molecular Imaging

Ada E. D. Teo,^{1,2,*} Hieu T. N. Tran,^{3,4,5,*} Chin Meng Khoo,^{1,2} Ismail Osman,³ Aaron Kian-Ti Tong,⁶ Roger S. Y. Foo,^{2,7} and Troy H. Puar^{3,4}



Localization with PET-CT

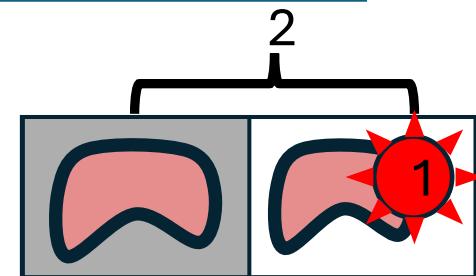
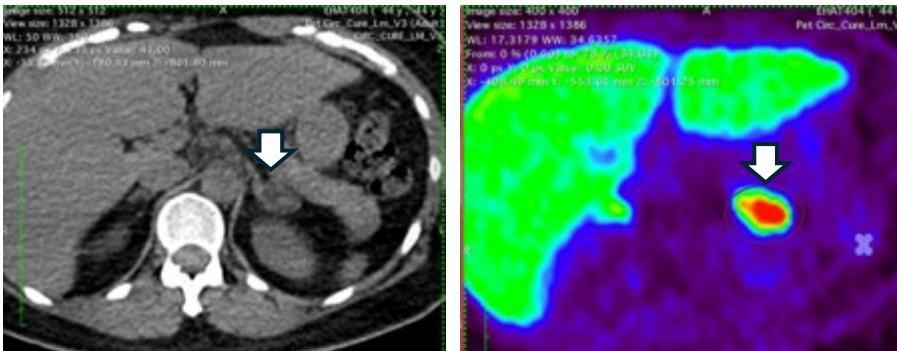


11C-Metomidate (dexa pre-Rx)

18F-CETO (dexa pre-Rx)

18F-AldoView

68Ga-Pentixafor

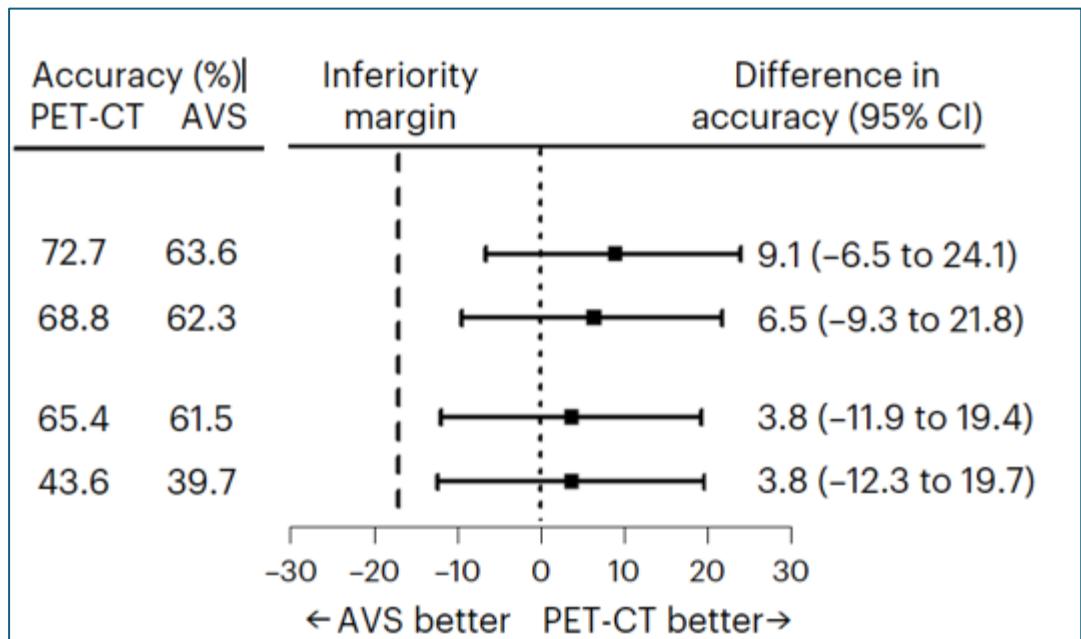
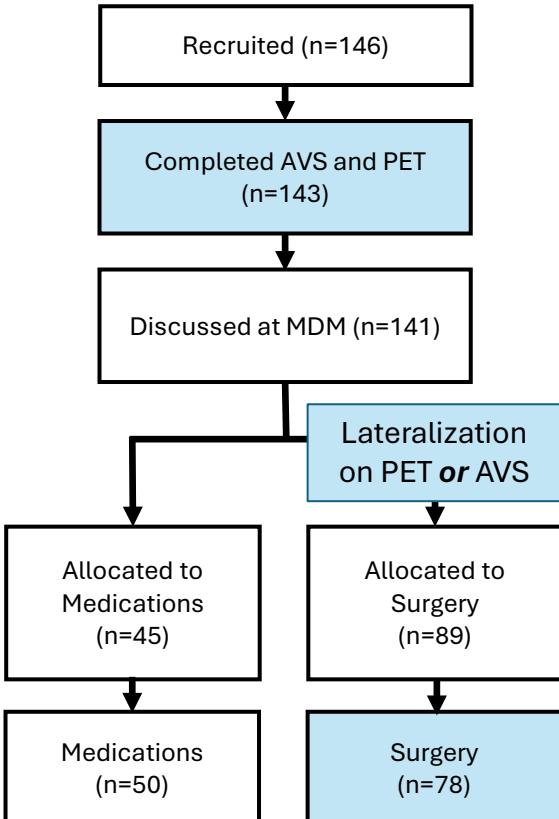


PET Criteria

- 1. Structure:** Uptake (SUV_{max}) over nodule, *and*
- 2. Function:** Ratio $> 1.25X$ compared to contralateral

11C-Metomidate PET-CT (MATCH)

Article
[¹¹C]metomidate PET-CT versus adrenal vein sampling for diagnosing surgically curable primary aldosteronism: a prospective, within-patient trial



11C-Metomidate PET-CT **non-inferior** to AVS

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FIG. 2.

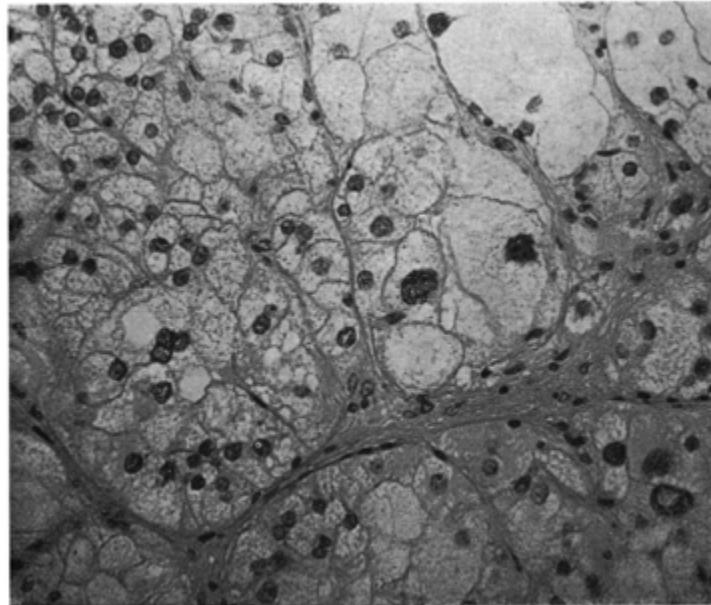


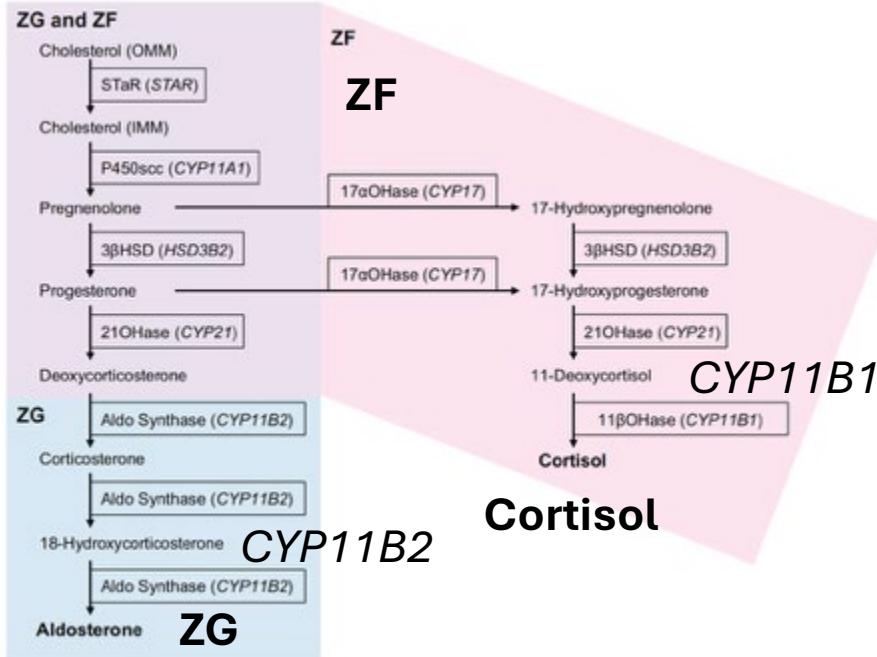
FIG. 4.

Zona-fasciculata (ZF)
Usually produce **cortisol**
not aldosterone

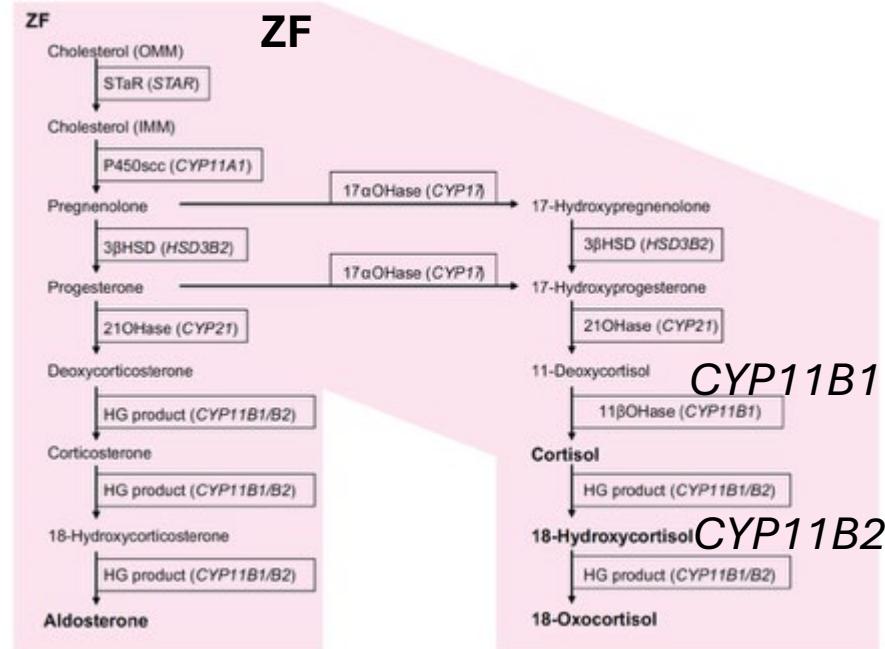
KCNJ5
somatic mutations

KCNJ5 APA produce 'Hybrid' Hormones: CYP11B2+CYP11B1

Normal Adrenal



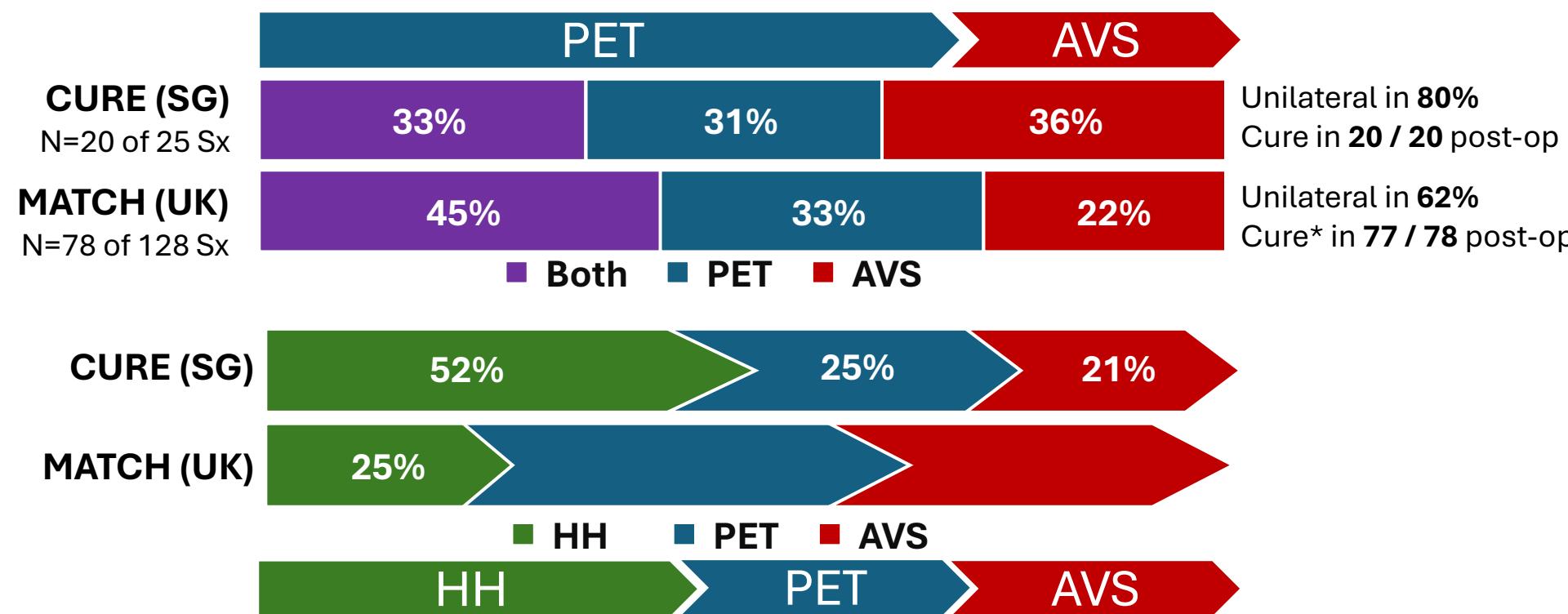
KCNJ5 APA



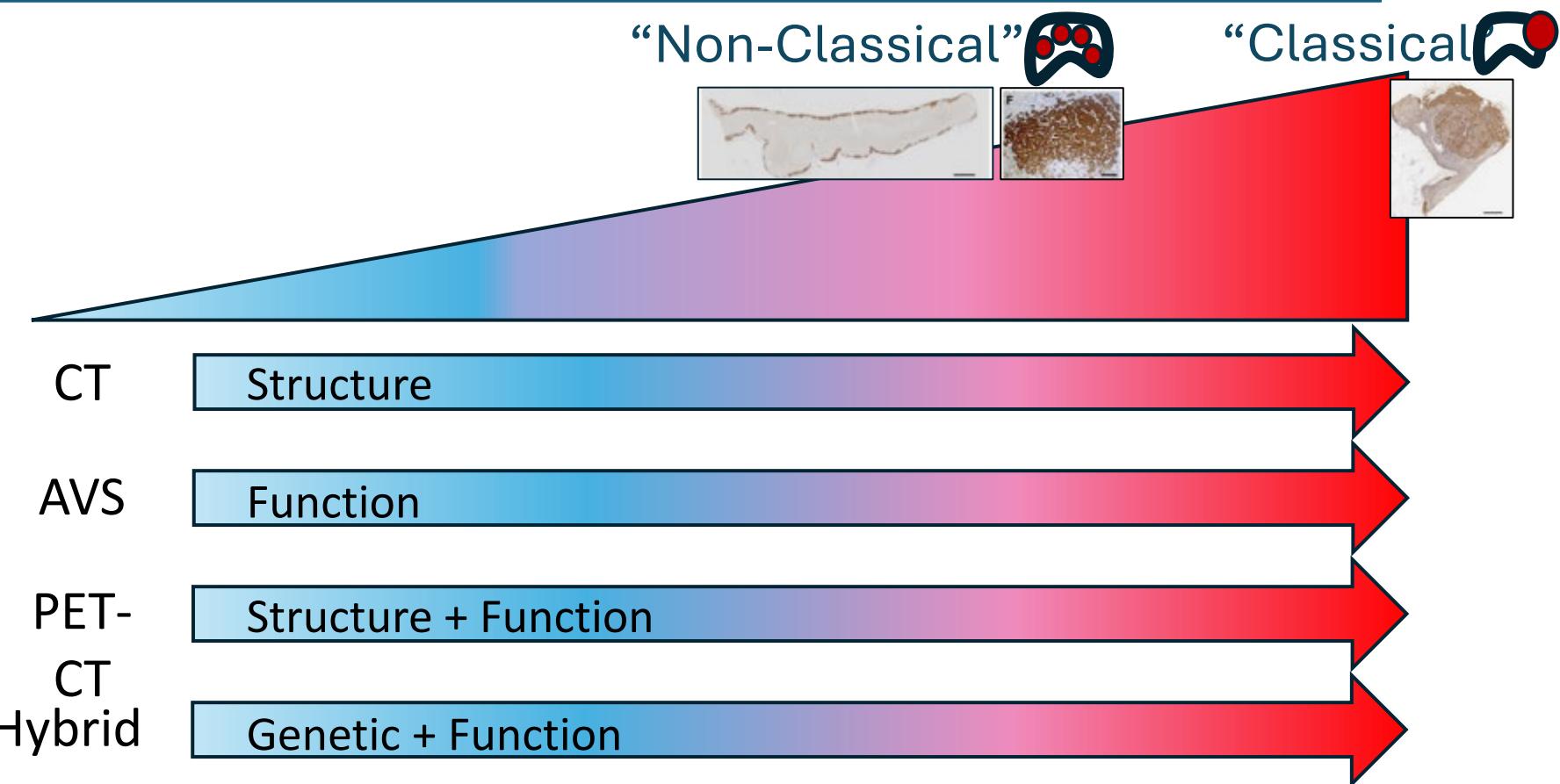
Aldosterone

18-OH cortisol
18-oxocortisol

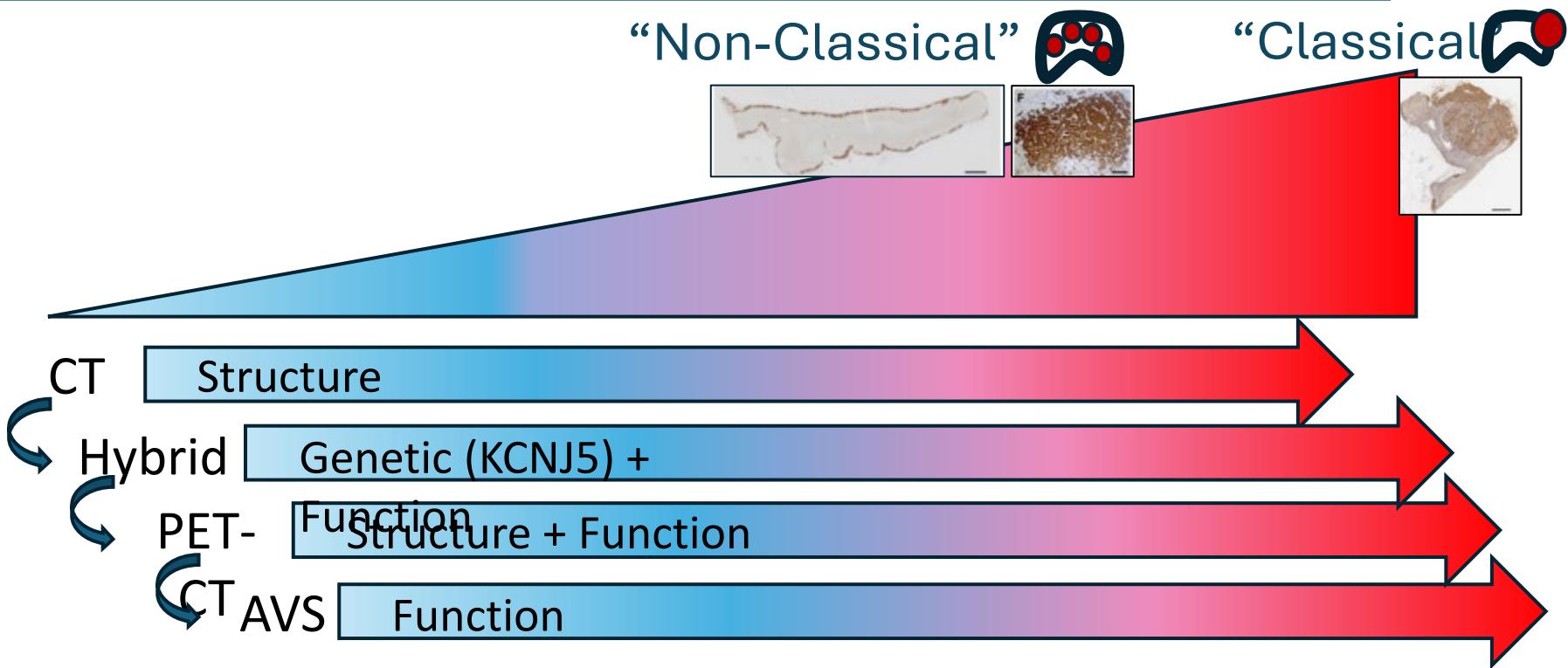
11C-Metomidate PET-CT vs AVS vs Hybrid Hormones

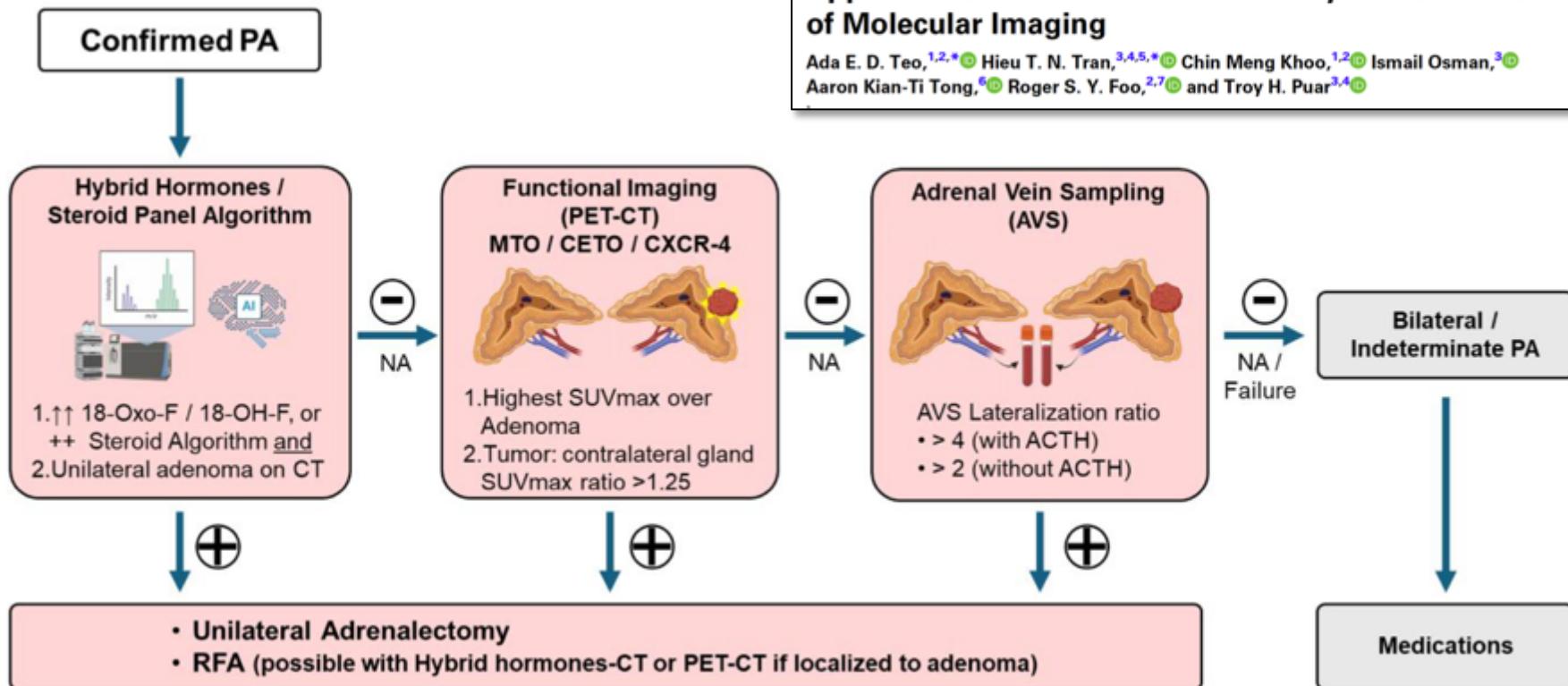


Dichotomy vs Spectrum of PA



Dichotomy vs Spectrum of PA



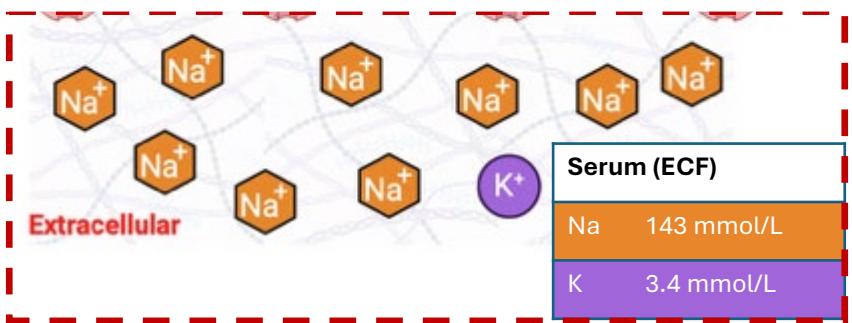


Hyperaldosteronism and Na retention



Norihiko
Morisawa

Jens
Titze



+ DOCA + NaCl 1%

	Water %	Nitrogen %	Potassium mEq./kilo	Sodium mEq./kilo	Phosphorus mEq./kilo
Dry ashing Left lumbar	72.3	3.0	K ↓	Na ↑	
Right lumbar	72.1	3.0	58 66	43 47	
Wet ashing Left lumbar		2.8	61	54	70
Right lumbar		3.1	54	53	62
Farago et al. 1951 Human lumbar			106	21	
Baldwin et al. 1952 Human muscle			95		60
Shohl 1949 Human muscle			93	31	71
Hastings 1952 Rat muscle	76.0	3.5	107	28	80

* Expressed in terms of wet weight.

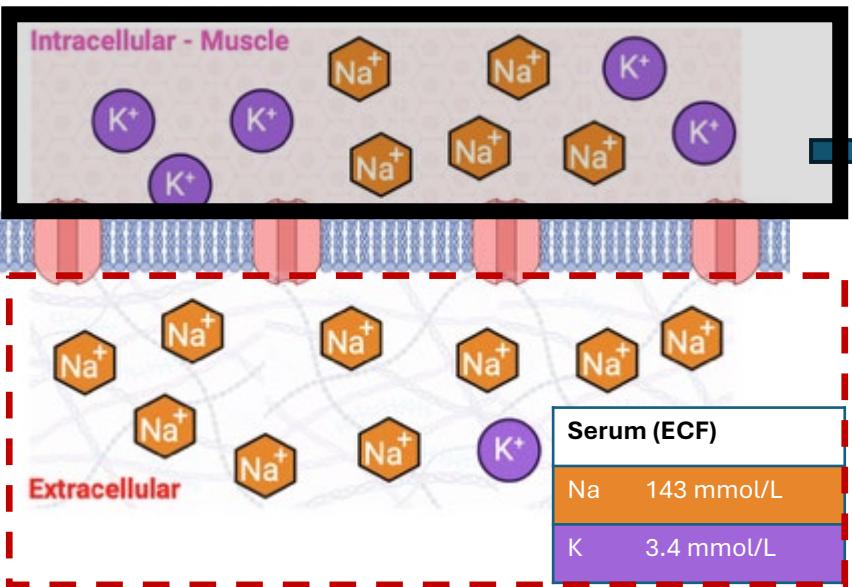
CONN JW, LOUIS LH. Primary aldosteronism, a new clinical entity. Ann Intern Med. 1956

Hyperaldosteronism and Na retention

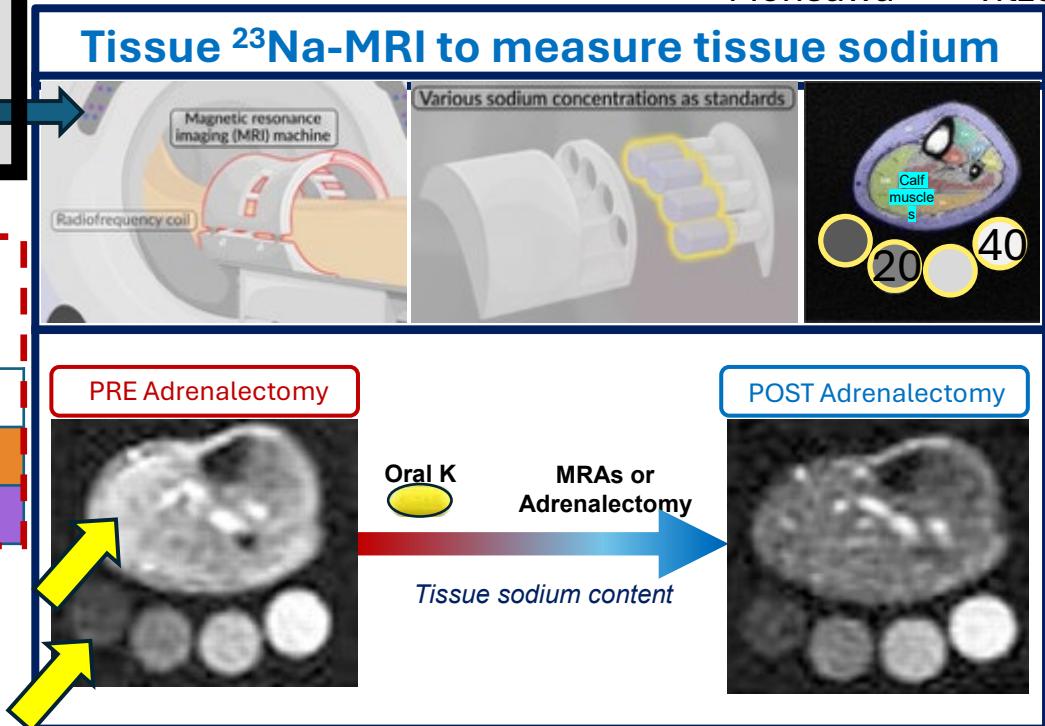


Norihiko
Morisawa

Jens
Titze



+ DOCA + NaCl 1%



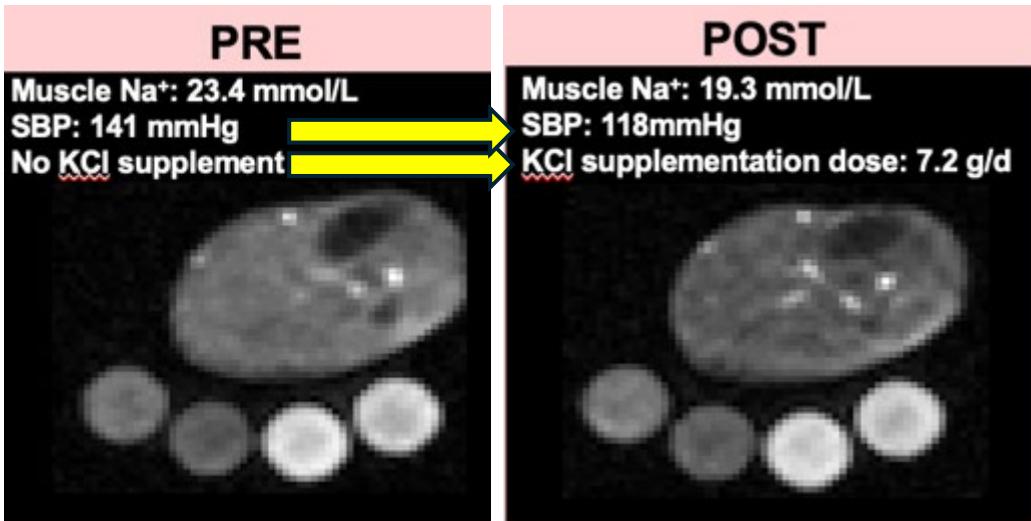
Hyperaldosteronism and Tissue Na



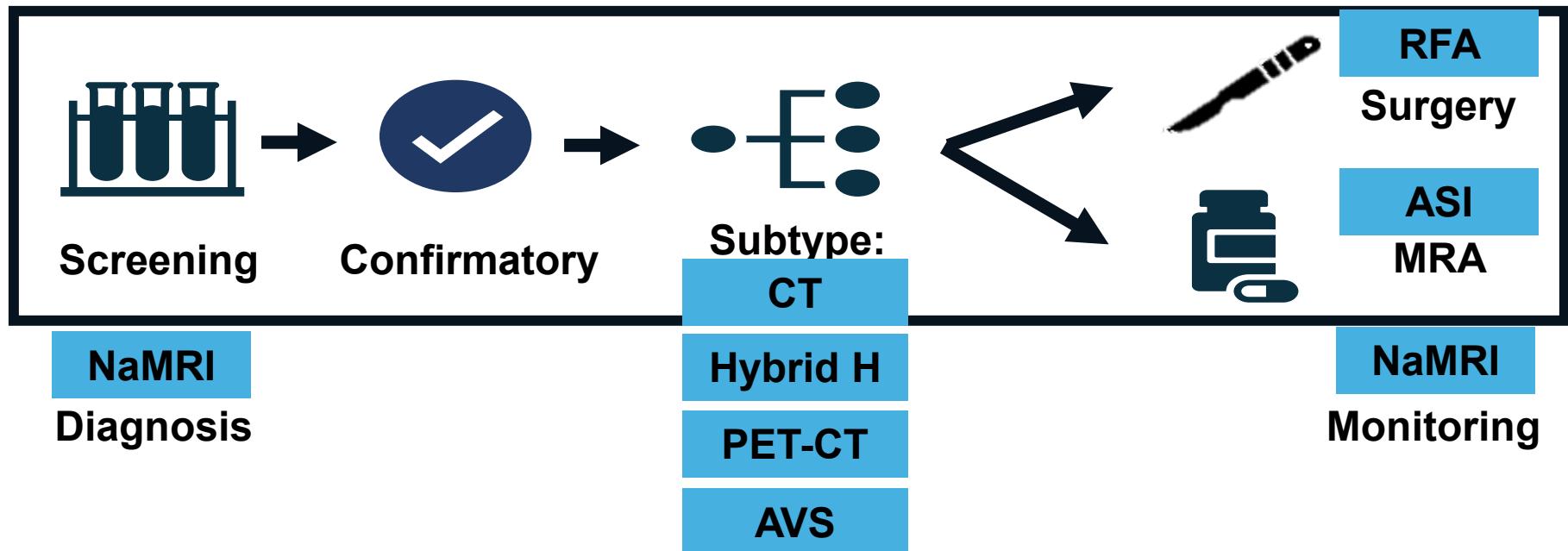
Hieu Tran Jens Titze

Diagnosis

Monitoring



Conclusion



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Calvin Chin

Loh Lih Ming, Kek Peng Chin
Swee Du Soon, Aaron Tong
Dawn Lim

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Daphne Lee, Dinesh



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Guo Liang, Patricia,
Yiling
Prof Morris Brown

Prof Mark Gurnell
Dr Heok Cheow

Thang Tran
Hieu Tran

Jaap Deinum
Ad Hermus
Kei Takase
Kei Omata



Students, Residents, Fellows

Yvonne Chan; Tan Yen Kheng, Tan Min On; Sarah Tan, Van Nguyen; Gaytri Gupta, Tang Fengjie; Sherry Seah, Charmaine Ter; **Hieu Tran, Ismail Osman**

We welcome residents & fellows!



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