



## Functional imaging and cost-effectiveness for subtyping Primary Aldosteronism

### Asst Prof Troy Puar

Head, Dept of Endocrinology & Adrenal Hypertension Centre  
President, ASEAN Network of Adrenal Hypertension (ANAH)  
Vice-President, Chapter of Endocrinologists, FAMS  
Secretary, Endocrine & Metabolic Society of Singapore (EMSS)



Changi  
General Hospital  
SingHealth

**CGH Adrenal Hypertension Centre**  
[Troy\\_puar@cgh.com.sg](mailto:Troy_puar@cgh.com.sg)

# Outline

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

# Primary Aldosteronism (PA) is curable

## ANNALS OF INTERNAL MEDICINE

VOLUME 44

JANUARY, 1956

NUMBER 1

### PRIMARY ALDOSTERONISM, A NEW CLINICAL ENTITY\*†

By JEROME W. CONN, M.D., F.A.C.P., and LAWRENCE H. LOUIS, ScD.,  
*Ann Arbor, Michigan*

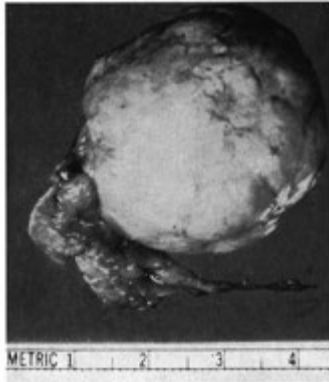
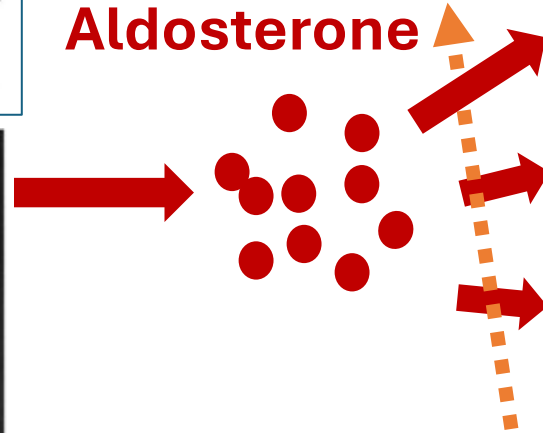


FIG. 2.

**Aldosterone**



**Hypertension**

**Low Potassium**



**MRA:**

**Novel MRA:**

**ASI:**

Spironolactone, Eplerenone

Finerenone, Balcinrenone,

Baxdrostat, Lorundrostat,

Vicadrostat, Dexfadrostat

Mineralocorticoid Receptor Antagonists, MRA  
Aldosterone Synthase Inhibitors, ASI

# PA is **Either** Bilateral or Unilateral

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## Bilateral

Idiopathic Adrenal  
Hyperplasia (BAH/IAH)



MRA  
(Mineralocorticoid-  
receptor antagonists)

## Unilateral

Aldosterone-producing  
Adenoma (APA)



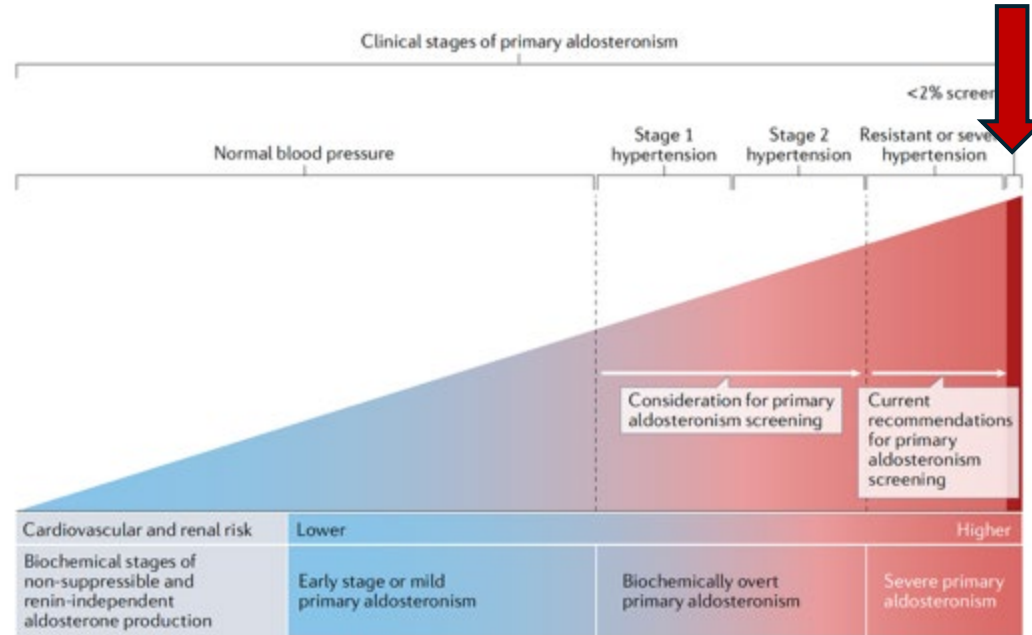
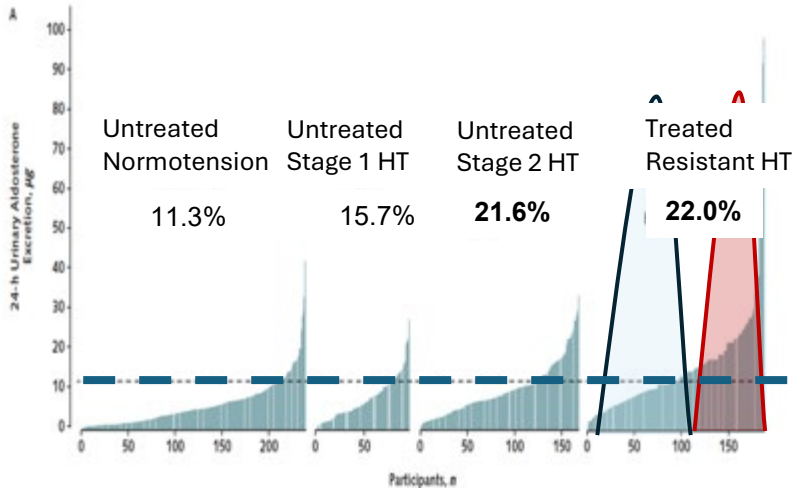
Unilateral  
Adrenalectomy

# Like Hypertension, *PA is a spectrum*

## Medscape Internal Medicine 'Game Changer': Aldosterone-Driven Hypertension More Common Than Thought

Mitchel L. Zoler  
May 28, 2020

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

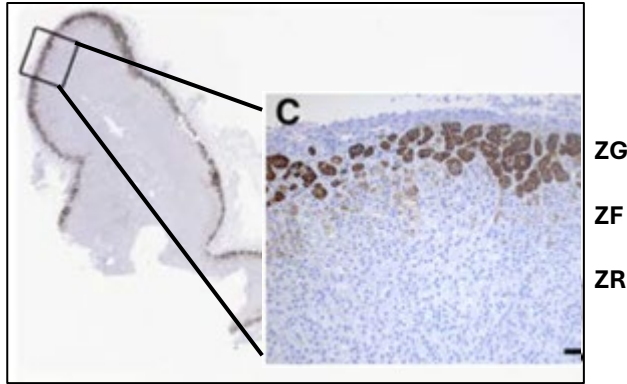


Brown et al. The Unrecognized Prevalence of Primary Aldosteronism Annals of Internal Medicine 2020

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

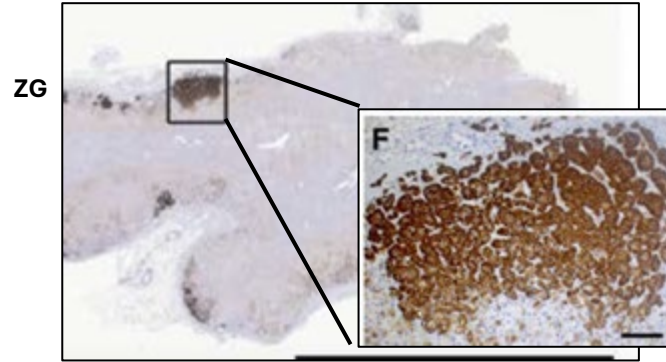
Typical 16yr



Normal ZG

Environment?  
Salt?

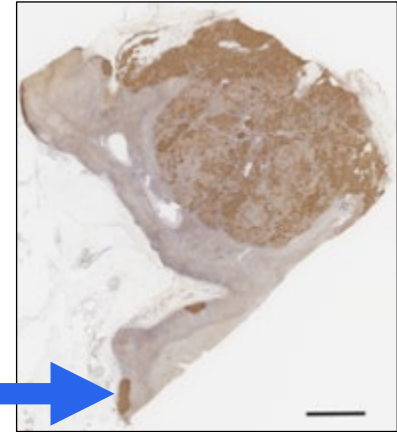
Typical 52yr



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*



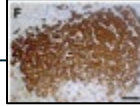
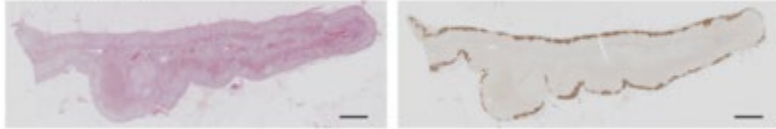
# HISTALDO Classification

## “Non-Classical”



### Diffuse Hyperplasia

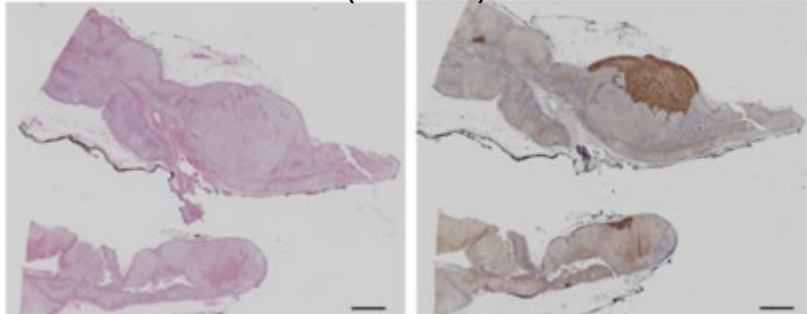
Adrenal #4



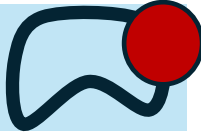
### Aldosterone-producing micronodules (APM)

Adrenal #21

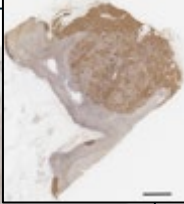
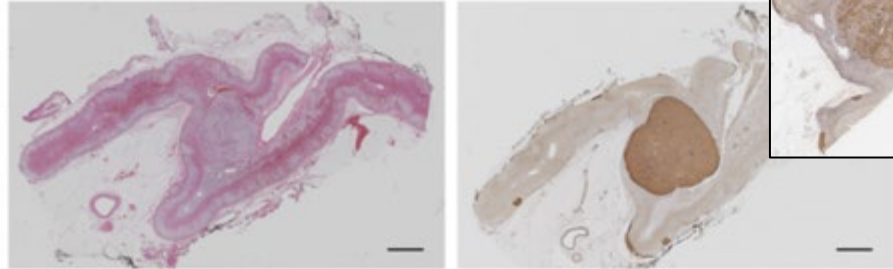
(APCCs)



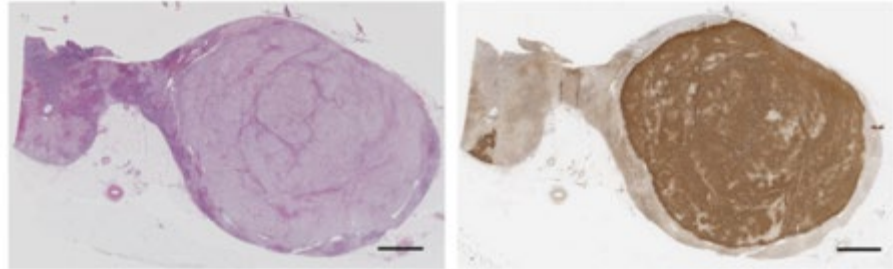
## “Classical”



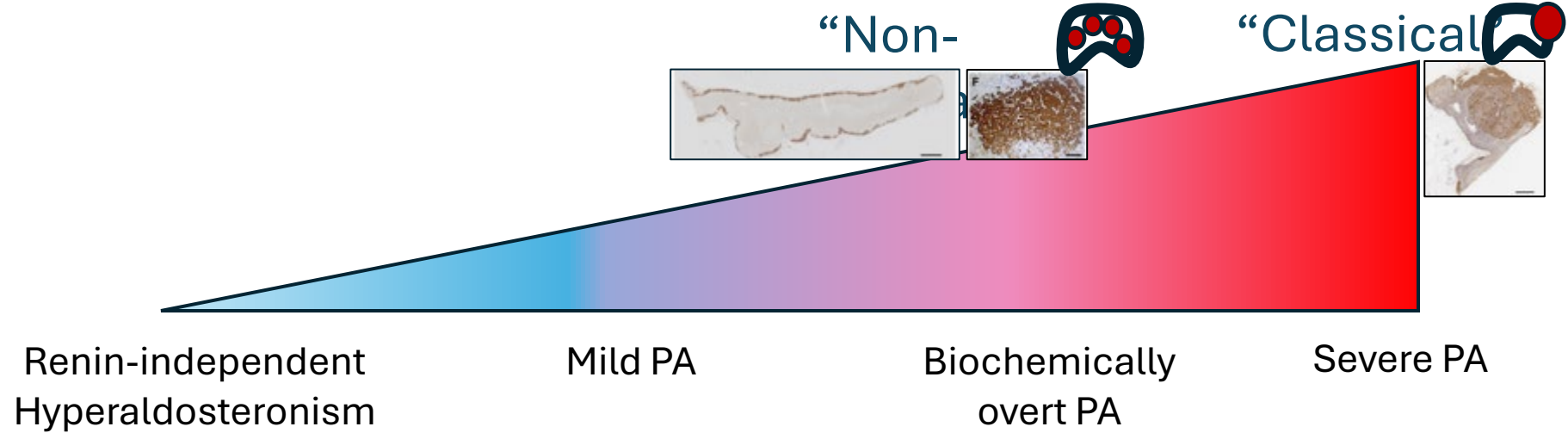
Adrenal #2



Adrenal #3

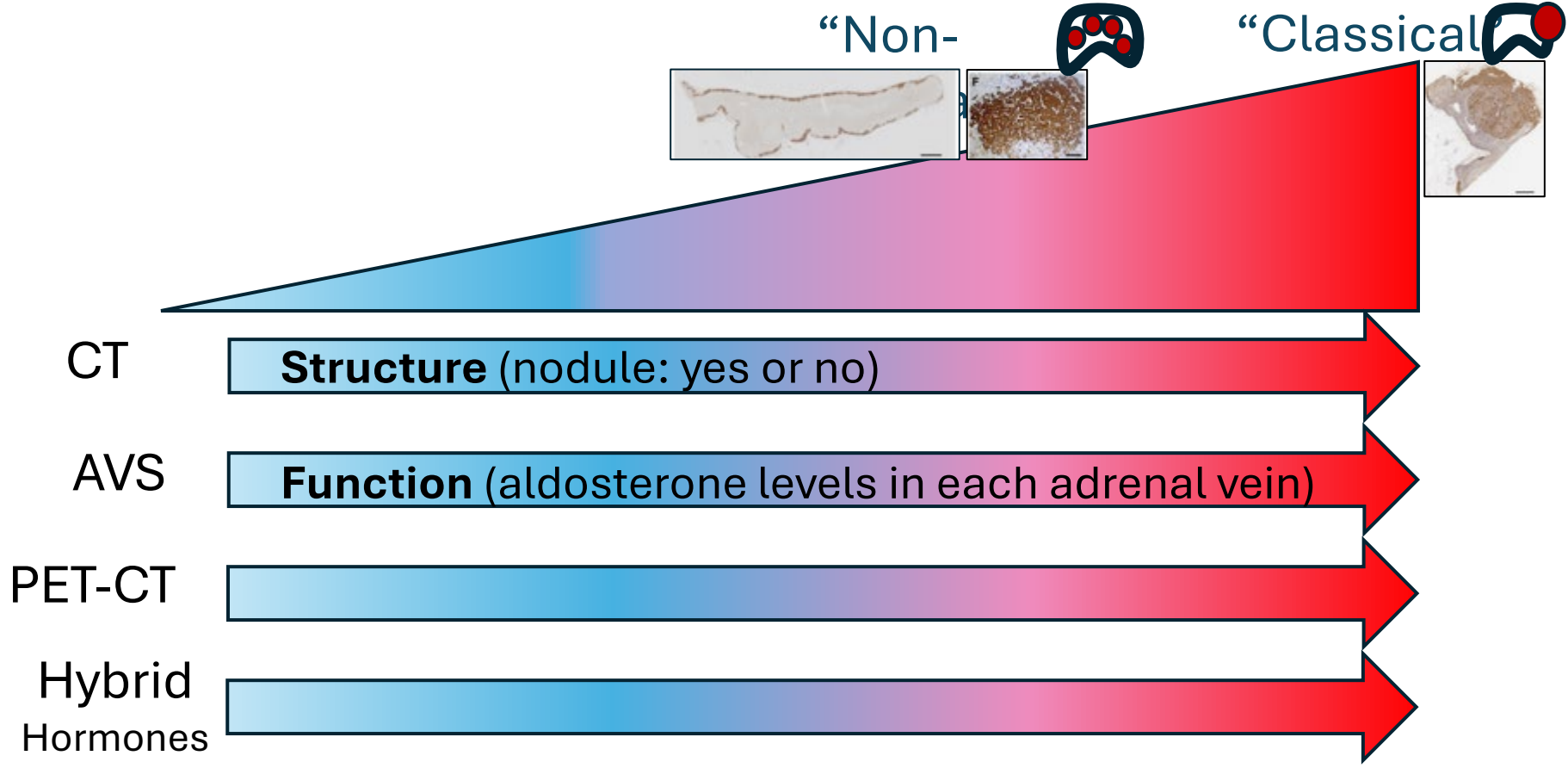


# Dichotomy vs Spectrum of PA

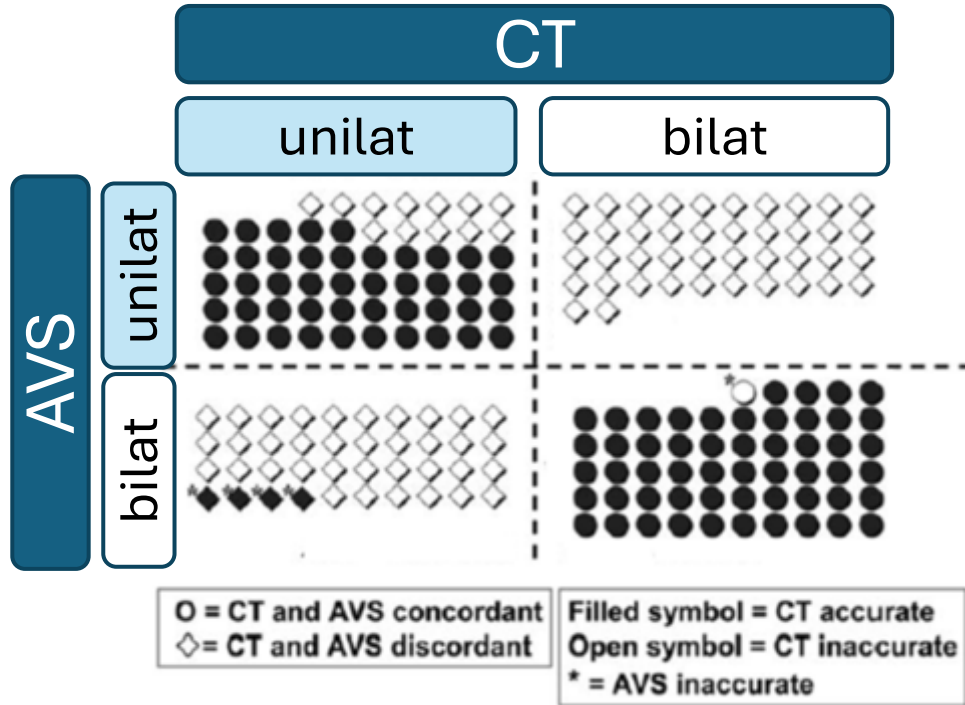




# Dichotomy vs Spectrum of PA

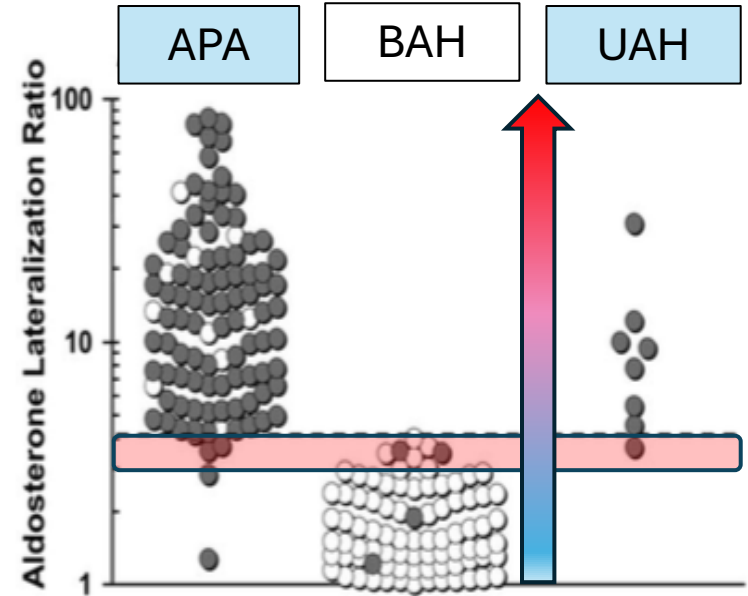


# Subtyping: CT vs AVS



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

**CT 53% vs AVS 100%**

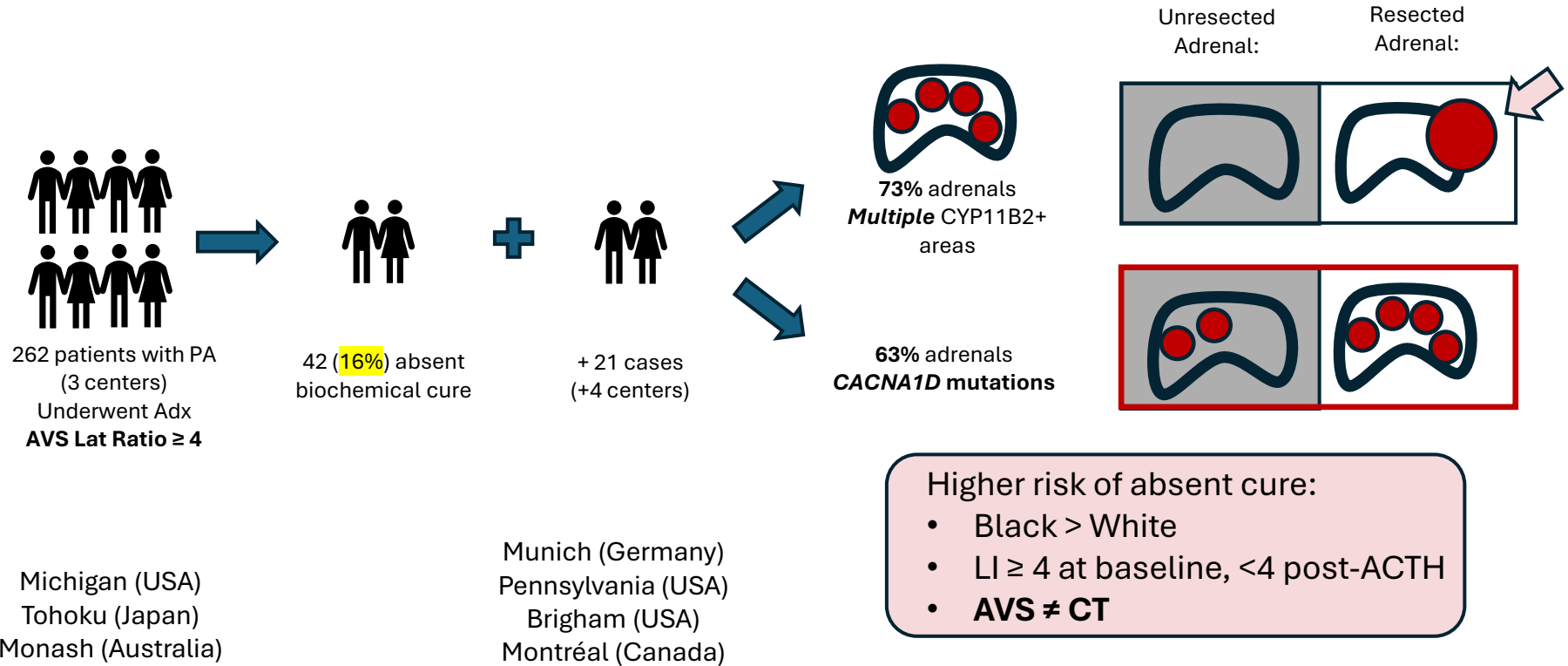


Young. Surgery 2004;136:1227-35

# Subtyping: CT vs AVS

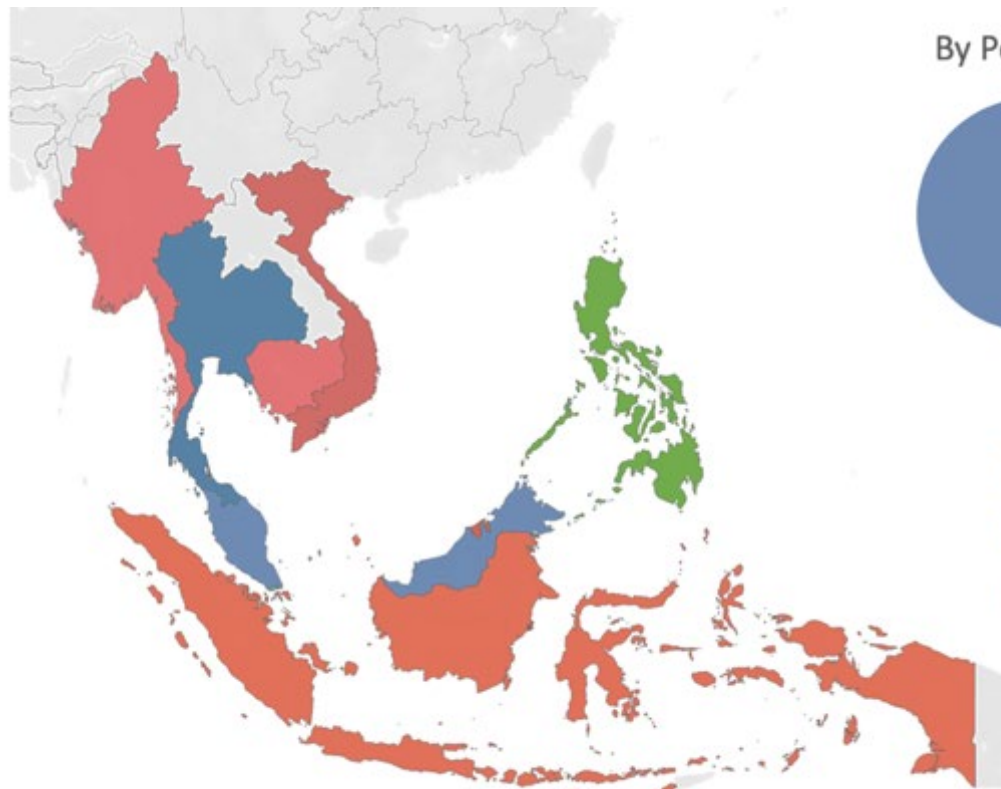
	SPARTACUS (RCT)		PASO Consensus		Williams	
	Clinical	Biochem	Clinical	Biochem	Clinical	Biochem
CT	3.0 DDD Meds	11 (20%) partial/ absent				80% cure 8% partial 12% absent
	N=92	46 of 92 Sx	705 Sx, 12 centres		235 Sx (retrospective), 18 c	
		<b>CT 80%</b>				<b>CT 80%</b>
AVS	3.0 DDD Meds	5 (11%) partial /absent	37% cure 47% partial 15% absent	94% cure 4% partial 2% absent	526 Sx (retrospective), 18 c	93% cure 5% partial 2% absent
	N=92	46 of 92 Sx				<b>AVS 93%</b>
		<b>AVS 89%</b>				
	<i>P= NS</i>	<i>P= 0.25</i>			<i>P= NS</i>	<i>P &lt;0.001</i>
	DDD: WHO daily defined dosage	* <b>ARR + SLT</b> reassessed in <b>all</b> patients post-op	* <b>ARR</b> reassessed in <b>all</b> patients post-op			

# AVS in Asymmetrical Bilateral PA



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



442 million

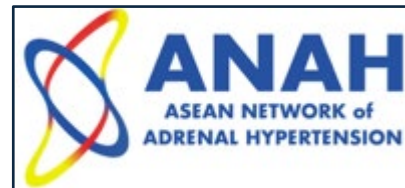
109 million

0.55 Billion individuals have no access to AVS

■ Routinely performed

■ Limited

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

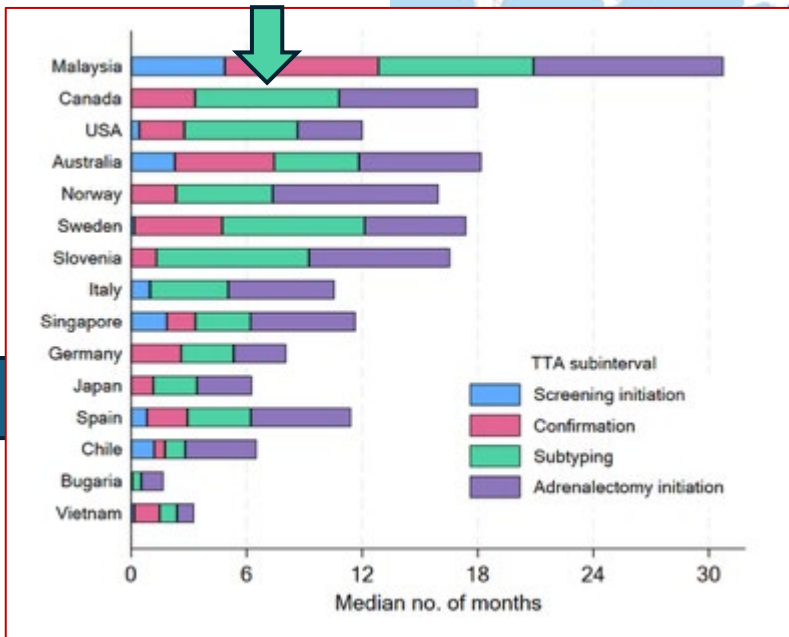
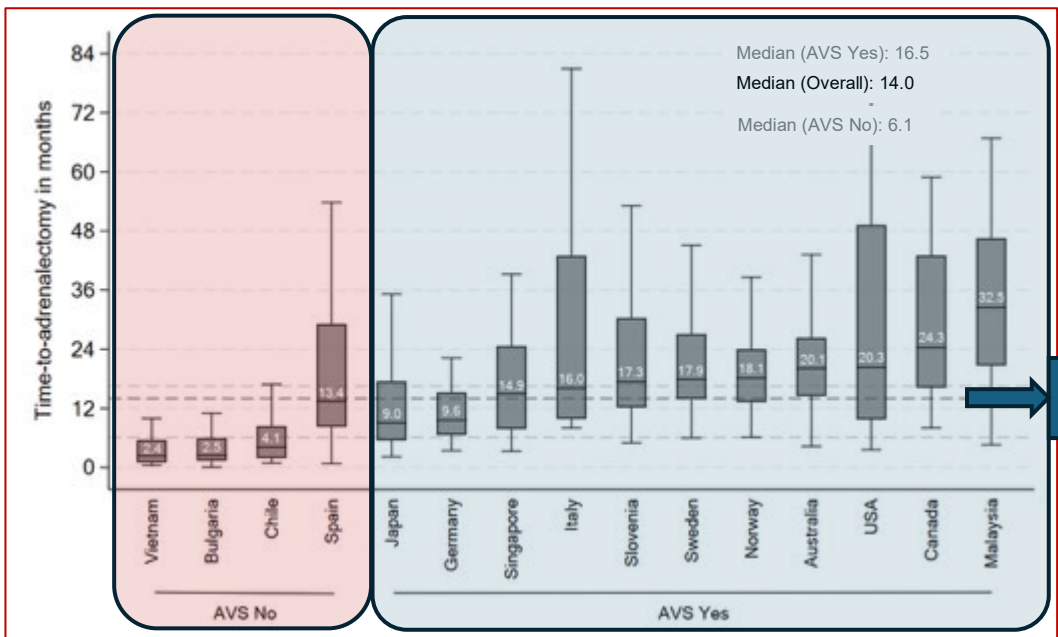


## Health Care Challenges in the Management of Primary Aldosteronism in Southeast Asia

Norlela Sukor,<sup>1,2</sup> Sarat Sunthornyothin,<sup>3</sup> Thang V. Tran,<sup>4</sup> Tri Juli Tarigan,<sup>5</sup> Leilani B. Mercado-Asis,<sup>6</sup> Satha Sum,<sup>7</sup> Moe Wint Aung,<sup>8</sup> Alice M. L. Yong,<sup>9</sup> Tania Tedjo,<sup>10</sup> Michael Villa,<sup>11</sup> Nang Ei Ei Khaing,<sup>12</sup> Elena Aisha Azizan,<sup>1,2</sup> Waye Hann Kang,<sup>12</sup> Vivien Lim,<sup>14</sup> Ada E. D. Teo,<sup>15</sup> Meifen Zhang,<sup>16</sup> Hieu Tran,<sup>4</sup> and Troy H. Puar<sup>16,17</sup>

# 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

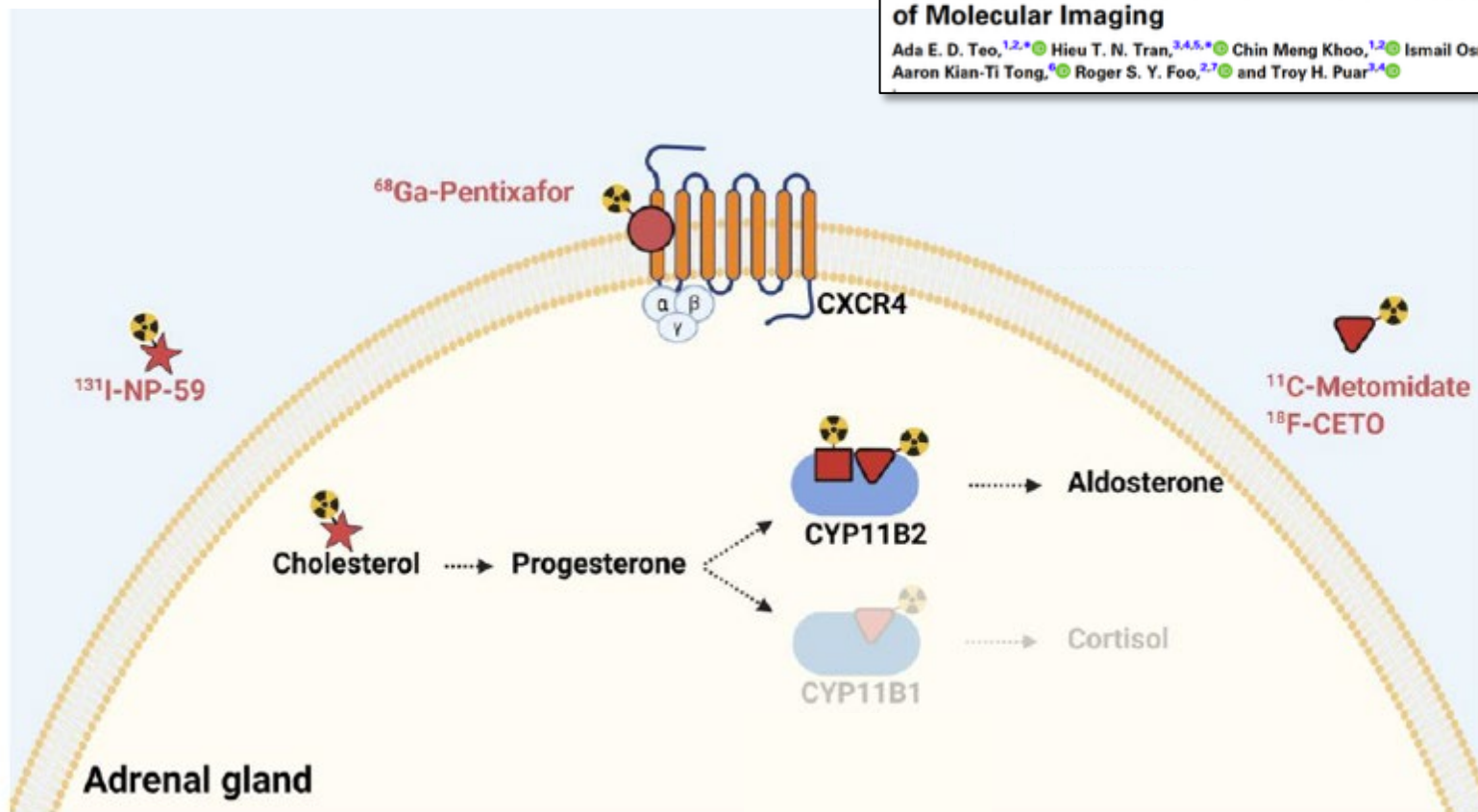
ENDO 2024 Abstract SAT-721

C Ter, XH Koh, M Araujo-Castro, E Gkaniatsa, M Reincke, TV Tran, H Tran, M Stowasser, MA Grytaas, A Turcu, J Matrozoza, 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

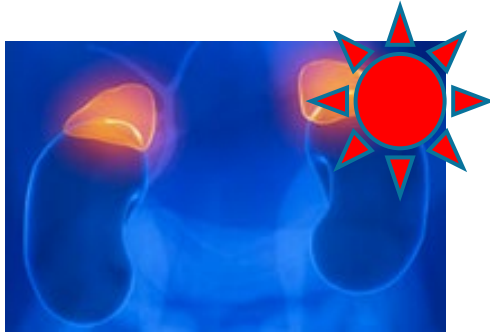
## Approach to the Patient With Primary Aldosteronism: Role of Molecular Imaging

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





# Localization with PET-CT

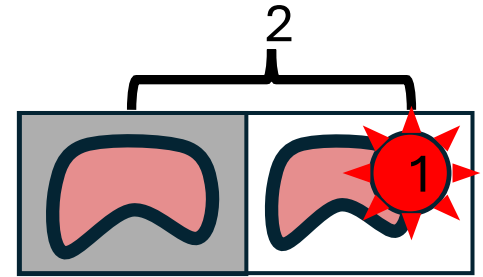


**11C**-Metomidate (dexamethasone pre-Rx)

**18F**-CETO (dexamethasone pre-Rx)

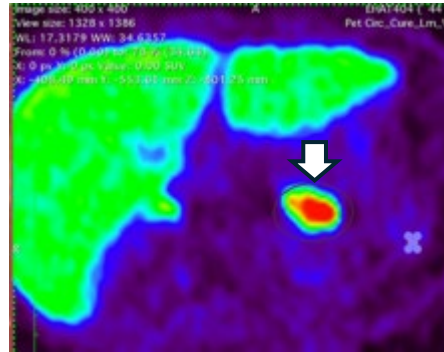
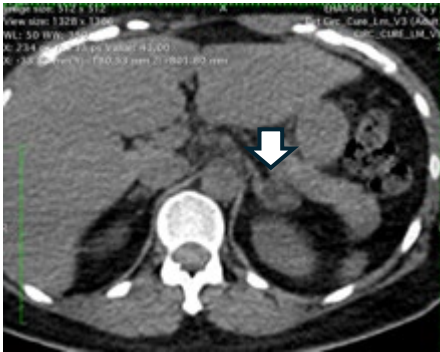
**18F**-AldoView

**68Ga**-Pentixafor



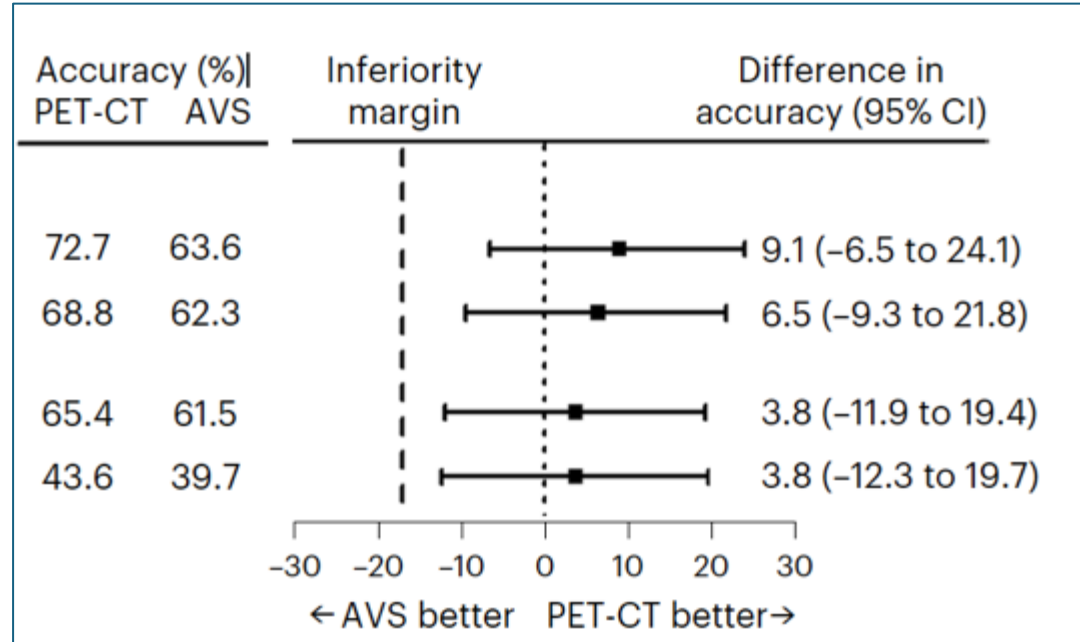
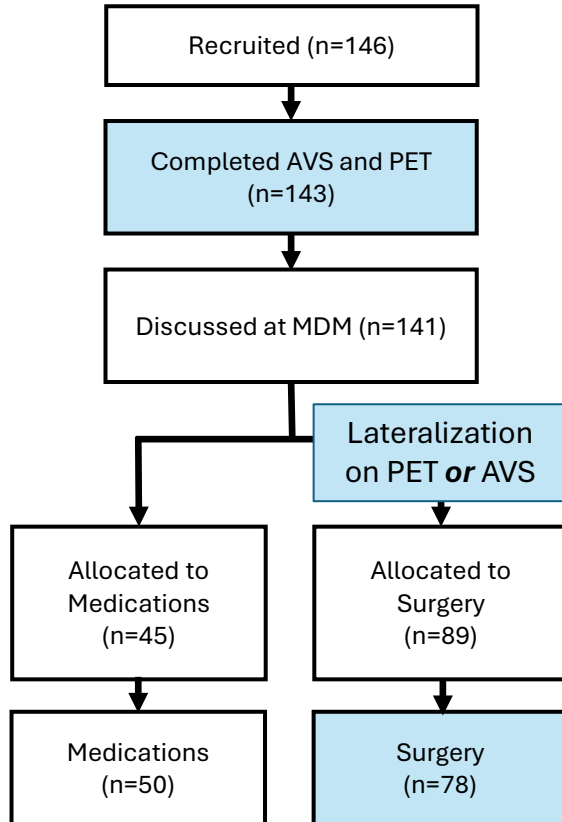
## PET Criteria

- 1. Structure:** Uptake (SUVmax) over nodule, and
- 2. Function:** Ratio > 1.25X compared to contralateral



# 11C-Metomidate PET-CT (MATCH)

**[<sup>11</sup>C]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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VOLUME 44 JANUARY, 1956 NUMBER 1

## PRIMARY ALDOSTERONISM, A NEW CLINICAL ENTITY\*†

By JEROME W. CONN, M.D., F.A.C.P., and LAWRENCE H. LOUIS, ScD.,  
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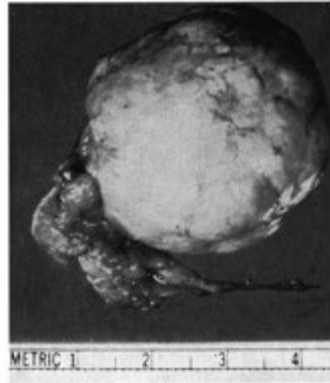


FIG. 2.

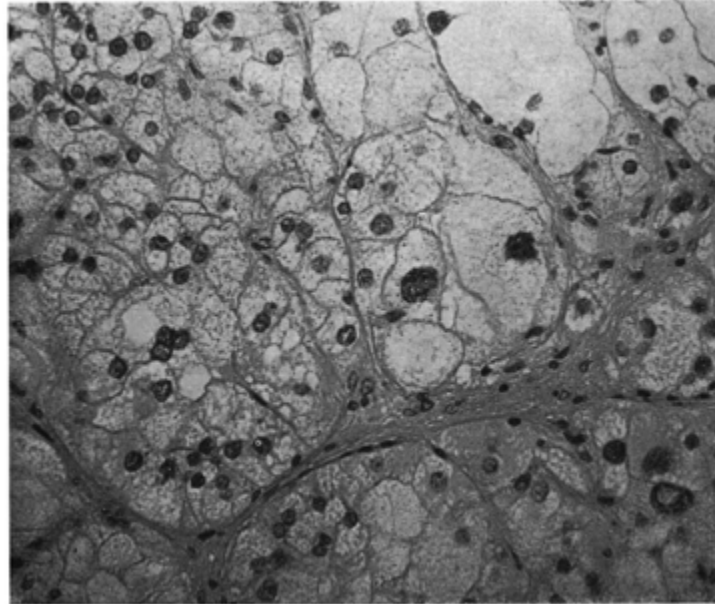


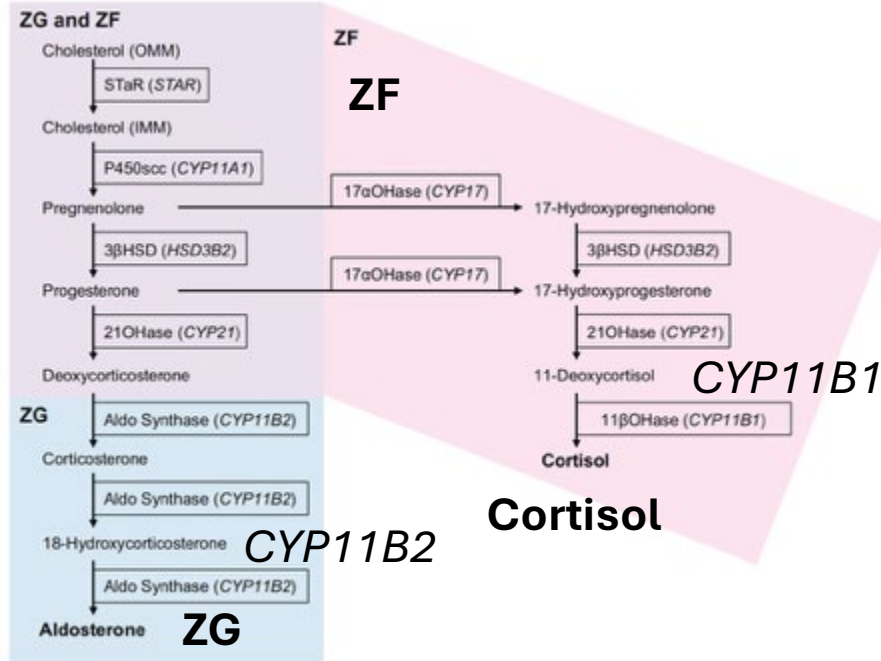
FIG. 4.

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

**KCNJ5**  
**somatic mutations**

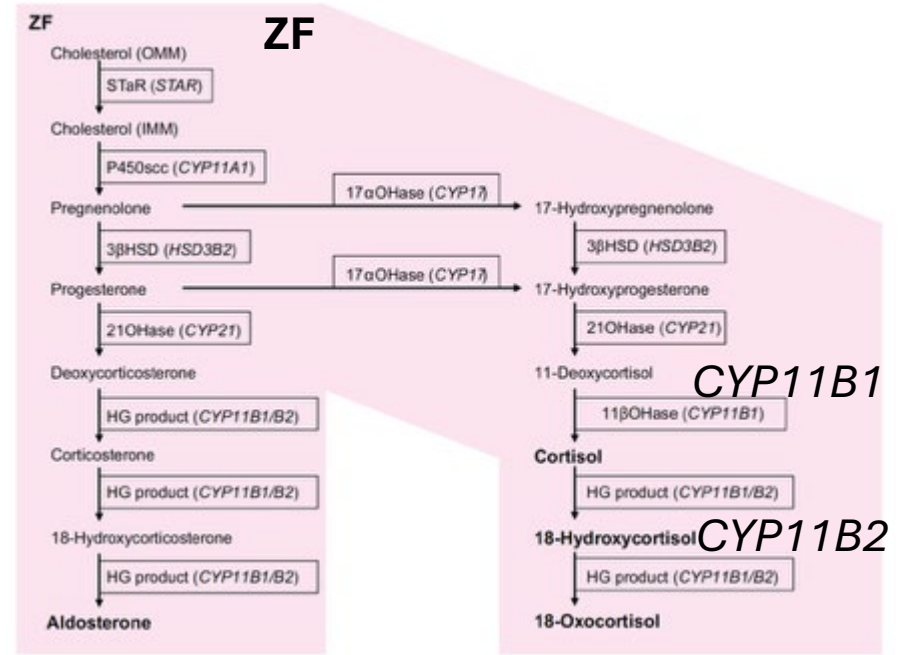
# KCNJ5 APA produce 'Hybrid' Hormones: *CYP11B2*+*CYP11B1*

## Normal Adrenal



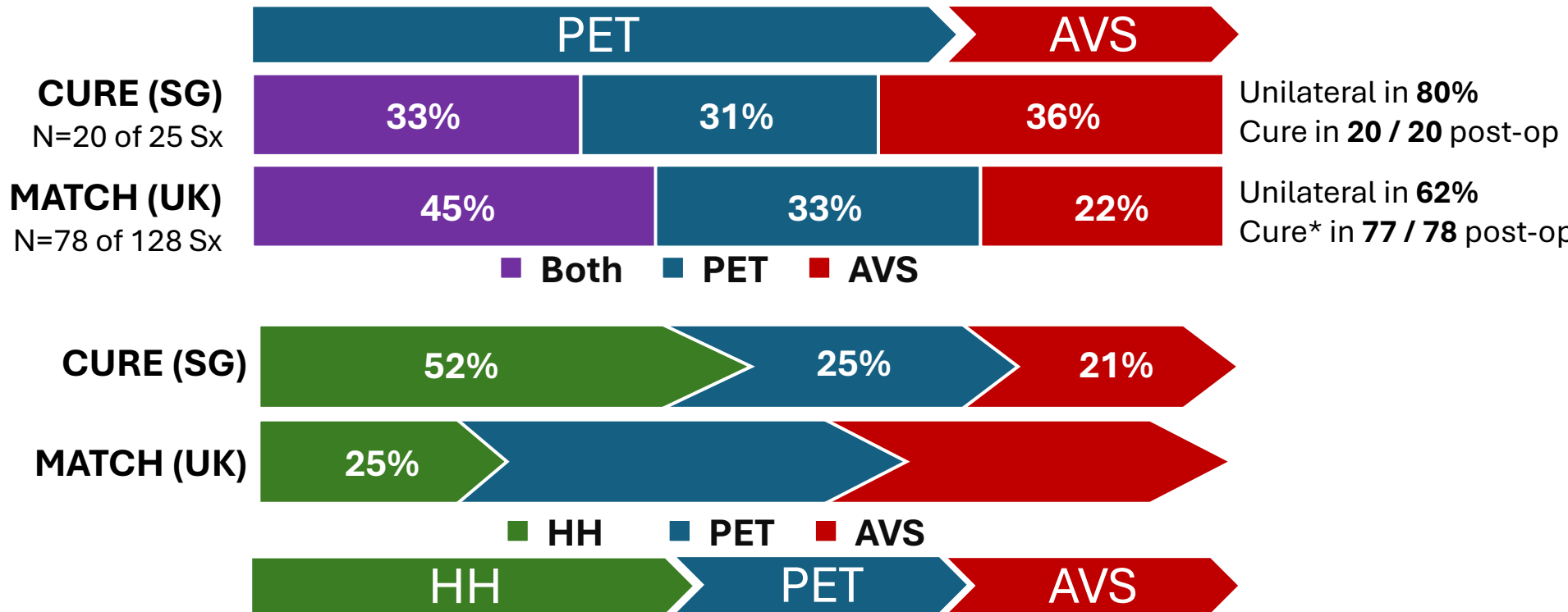
Aldosterone

## KCNJ5 APA



18-OH cortisol  
18-oxo cortisol

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



Wu X, et al. [<sup>11</sup>C]metomidate PET-CT vs AVS for diagnosing surgically curable PA: a prospective, within-patient trial. Nat Med. 2023

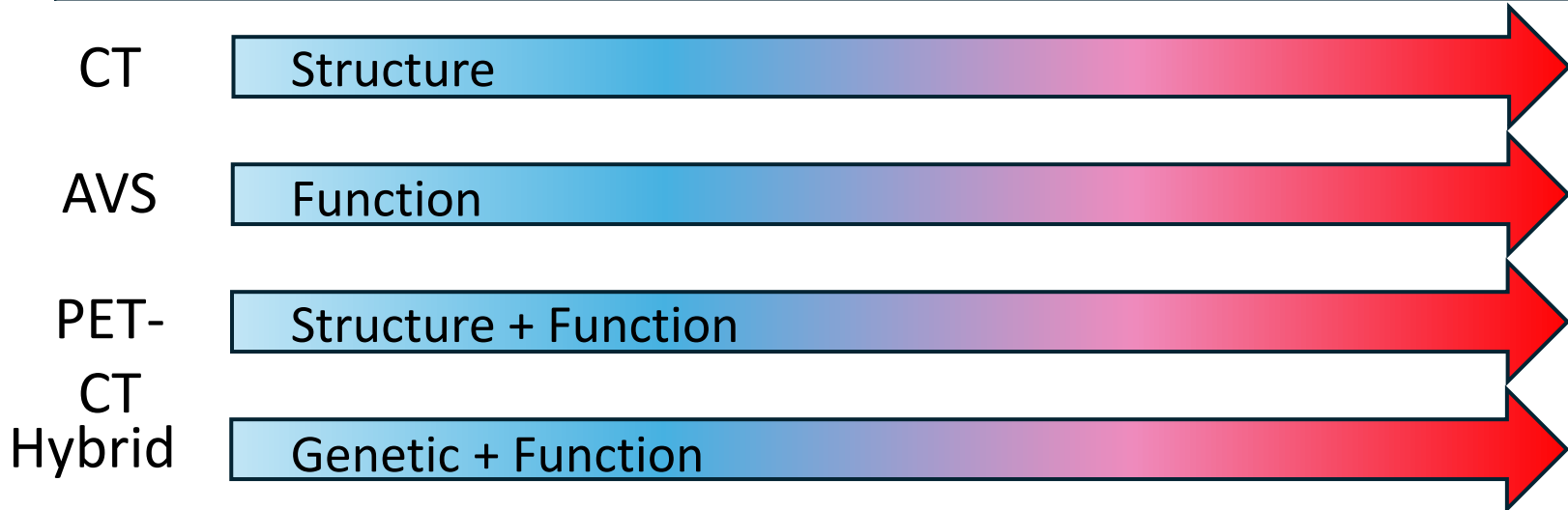
Puar TH, et al. for PA CURE investigators. 11C-Metomidate PET-CT vs AVS to subtype PA: a prospective clinical trial. J Hyperten 2022

# Dichotomy vs Spectrum of PA

“Non-Classical”



“Classical”

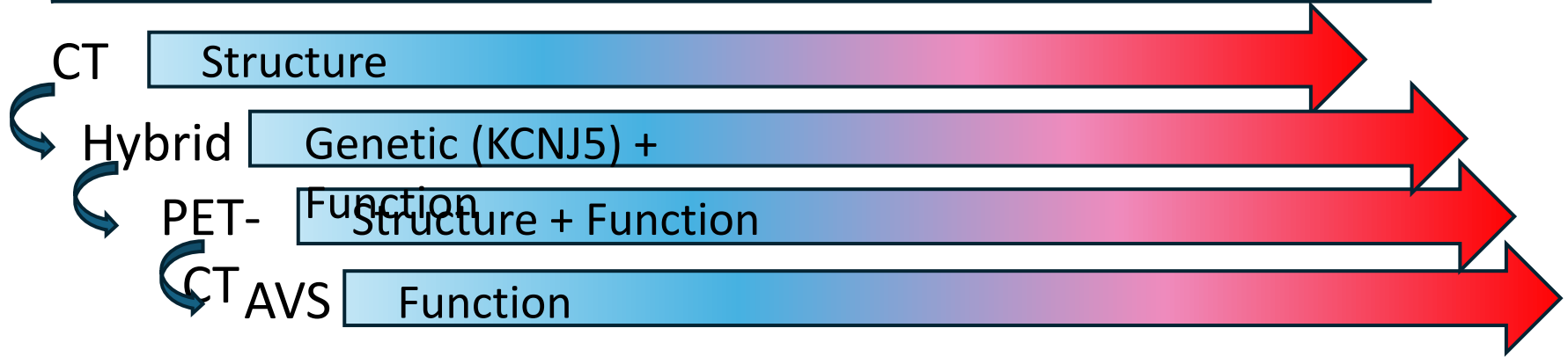
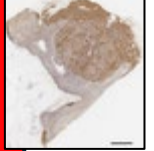


# Dichotomy vs Spectrum of PA

“Non-Classical”



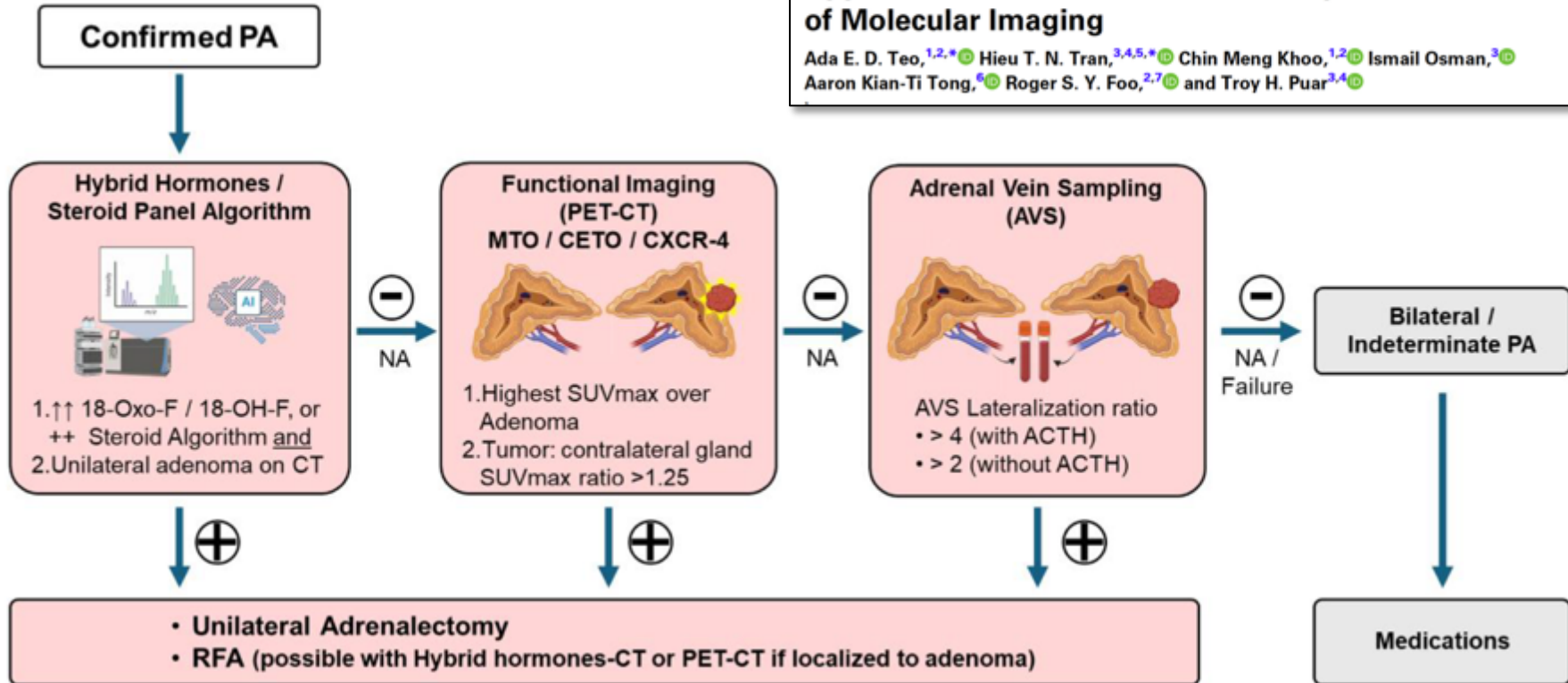
“Classical”





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

Ada E. D. Teo,<sup>1,2,\*</sup> Hieu T. N. Tran,<sup>3,4,5,\*</sup> Chin Meng Khoo,<sup>1,2</sup> Ismail Osman,<sup>3</sup>  
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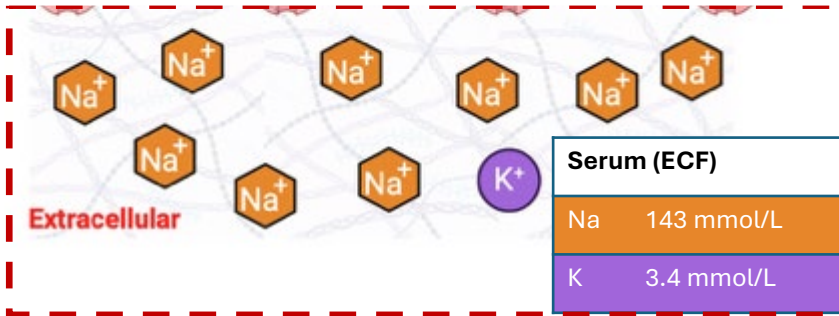
# Hyperaldosteronism and Na retention



Norihiko  
Morisawa



Jens  
Titze



+ DOCA + NaCl 1%

**TABLE 3**  
**Chemical Composition\* of Muscle Obtained at Operation (M. W.)**

	Water %	Nitrogen %	Potassium mEq./kilo	Sodium mEq./kilo	Phosphorus mEq./kilo
Dry ashing			<b>K</b>	<b>Na</b>	
Left lumbar	72.3	3.0	58	43	
Right lumbar	72.1	3.0	↓ 66	↑ 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

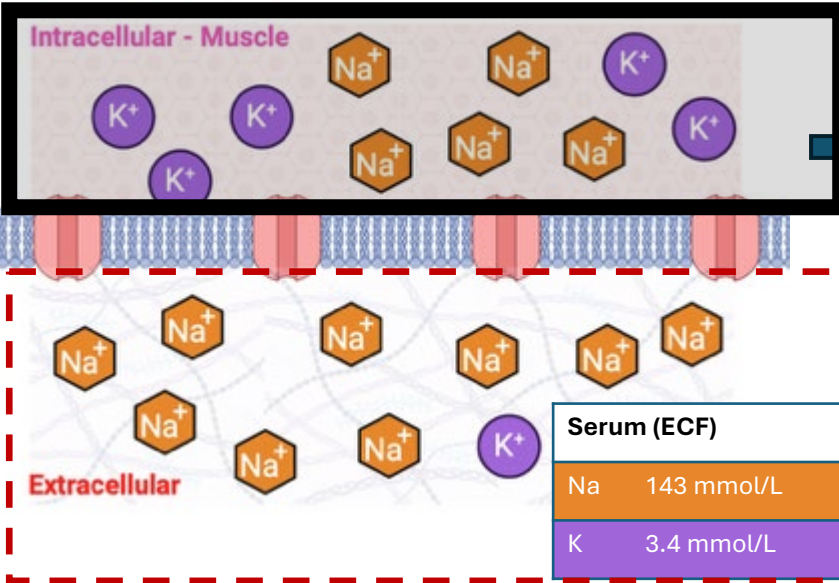
# Hyperaldosteronism and Na retention



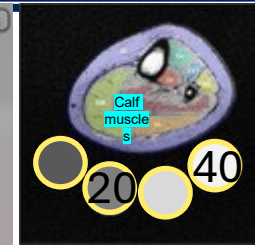
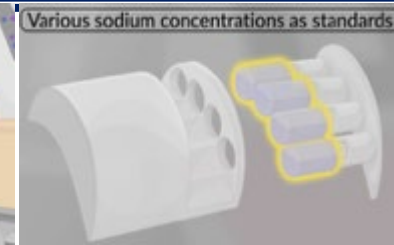
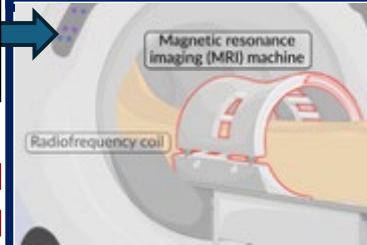
Norihiko  
Morisawa



Jens  
Titze



## Tissue $^{23}\text{Na}$ -MRI to measure tissue sodium



PRE Adrenalectomy



Oral K

MRAs or  
Adrenalectomy

Tissue sodium content

POST Adrenalectomy



+ DOCA + NaCl 1%

# Hyperaldosteronism and Tissue Na

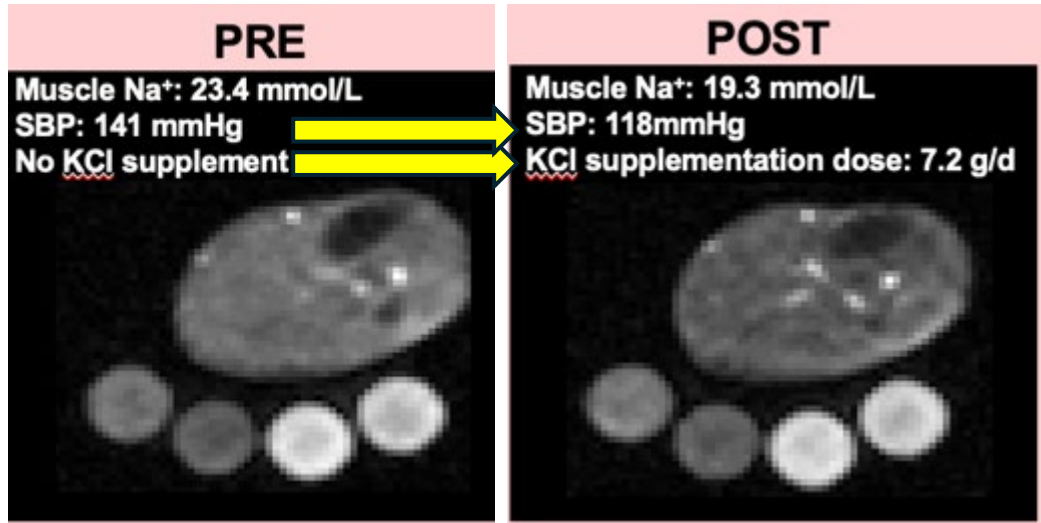


Hieu Tran Jens Titze

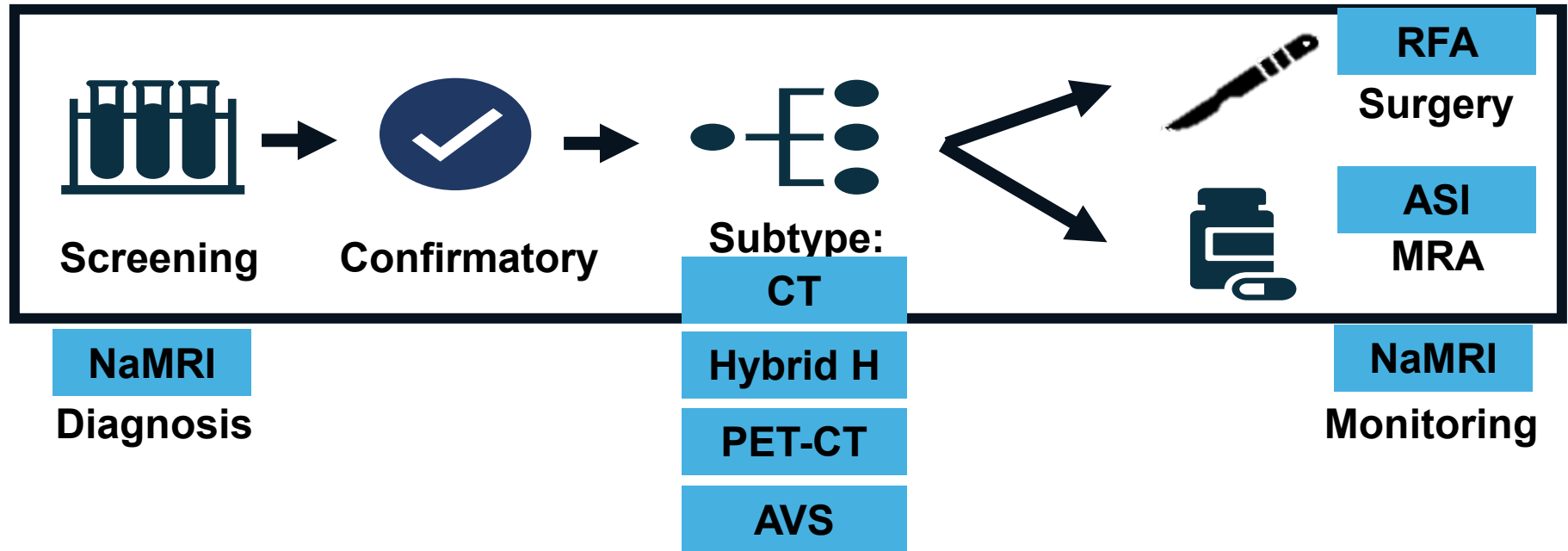


Diagnosis

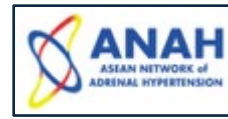
Monitoring



# Conclusion



# Acknowledgements



**Roger Foo**  
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Rajeev Parameswaran  
**Ada Teo**



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Joan Khoo, Wong Kang Min  
Andrew Wong  
Aw Tar Choon, **Prasanna**



Khong Pek-Lan  
David Green



Matthew Chuah  
Brenda Chiang



**Jens Titze**, Norihiko Morisawa  
Adriana Marton, Ehsan Saffari



Yee Szemen  
Kurumbian Chandran



Calvin Chin



Shi Luming, Julie,  
Guo Liang, Patricia,  
Yiling  
Prof Morris Brown



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



Prof Mark Gurnell  
Dr Heok Cheow



Joanne Ngeow  
John Chambers



Alvin Tan, Daniel Chew,  
Rinkoo Dalan, Liew Huiling



**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!***



Changi General Hospital  
SingHealth



**CGH Adrenal Hypertension Centre**  
[troy\\_puar@cgh.com.sg](mailto:troy_puar@cgh.com.sg)