Na^+ storage in dialysis patients

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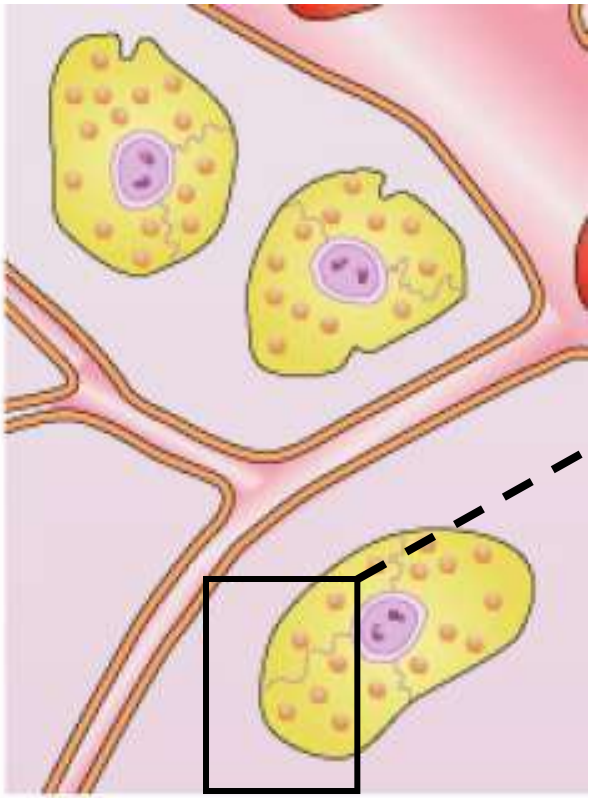
Na^+ and the „internal environment“

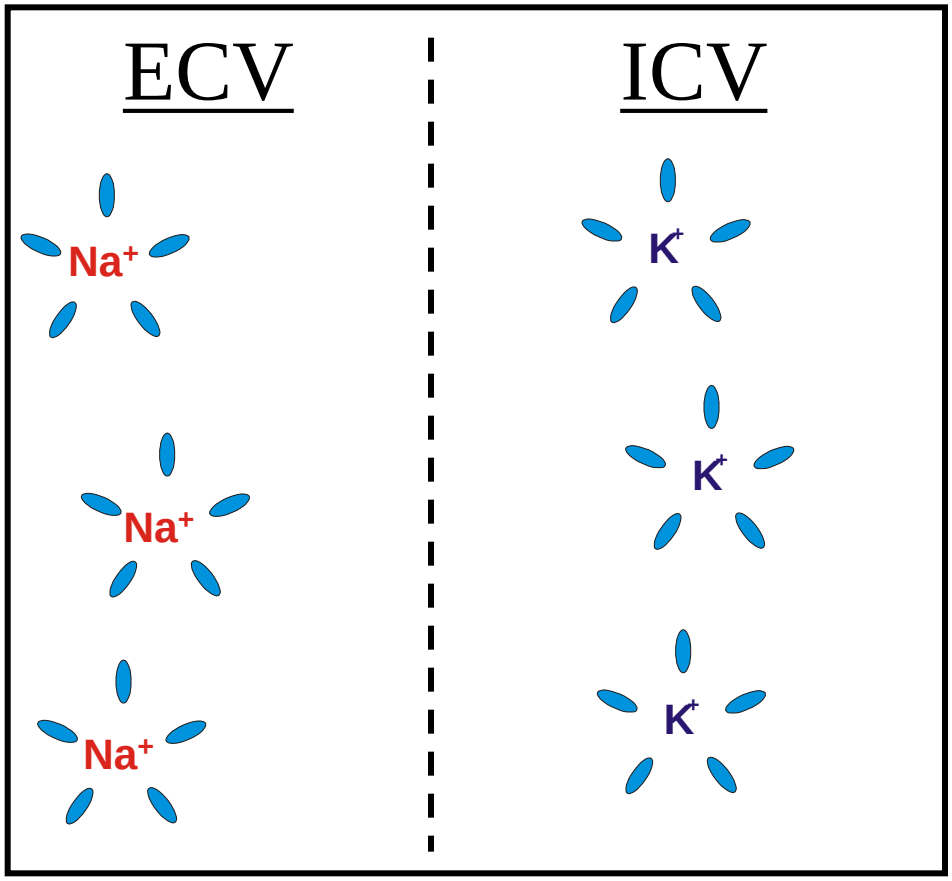
« La fixité du milieu intérieur est la condition d'une vie libre et indépendante. »

Claude Bernard
1813-1878

".... the blood constitutes an actual organic environment, an intermediary between the external environment (in which the complete individual lives) and the living molecules, which cannot safely be brought into contact with their external environment ..."

Na^+, K^+, and water and the internal environment



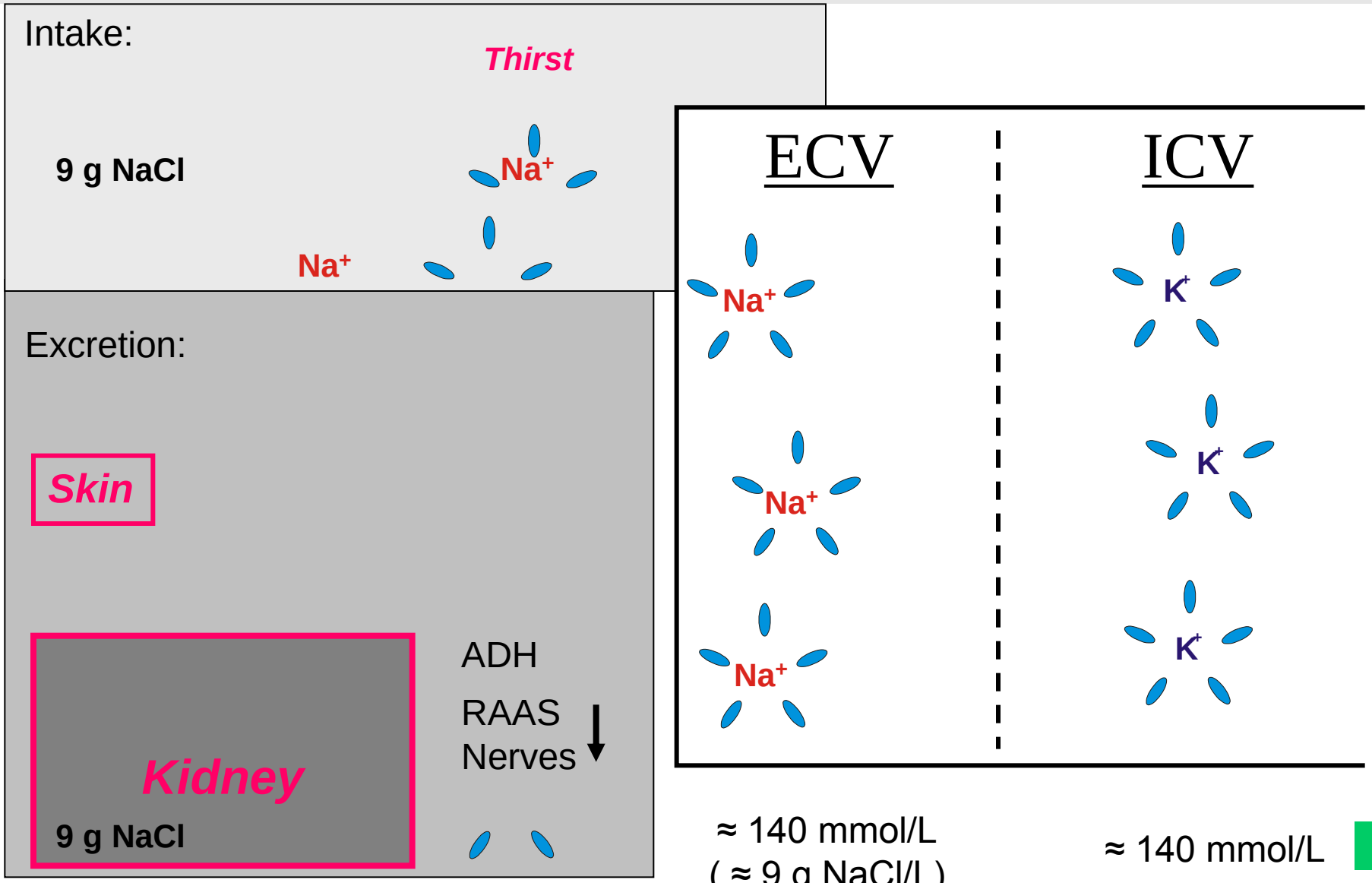


Iso-Osmolality:

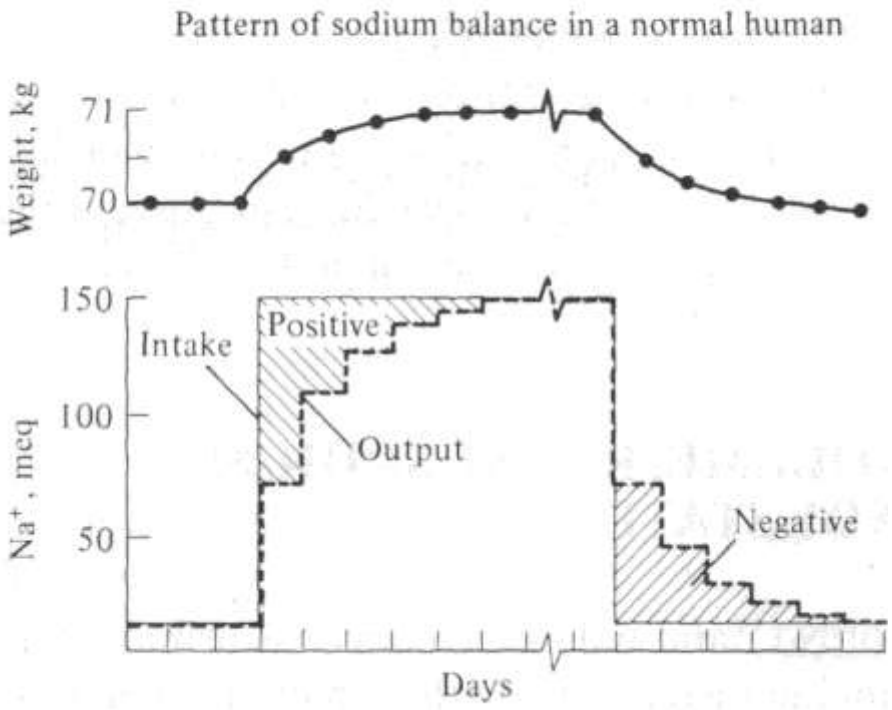
≈ 140 mmol/L
(≈ 9 g NaCl)

≈ 140 mmol/L

Na^+ and the maintainance of the internal environment



Body sodium balance in humans



Check box Na^+ accumulation:

Extracellular?

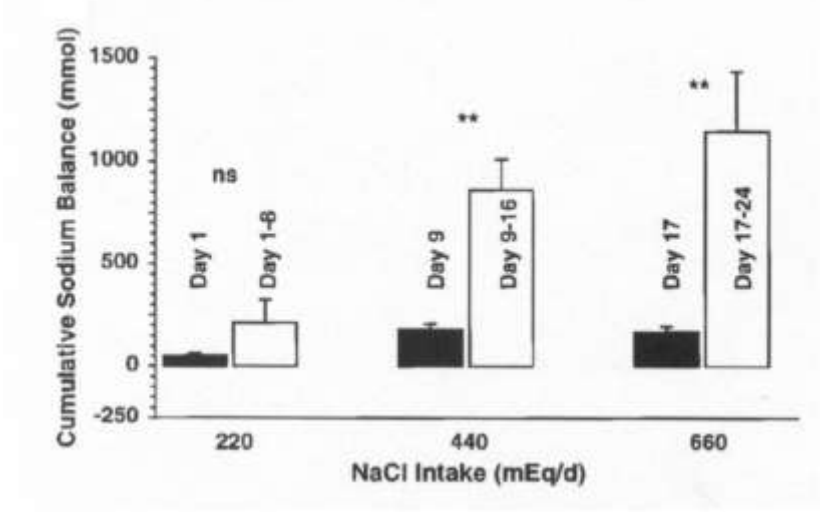
Commensurate water retention?

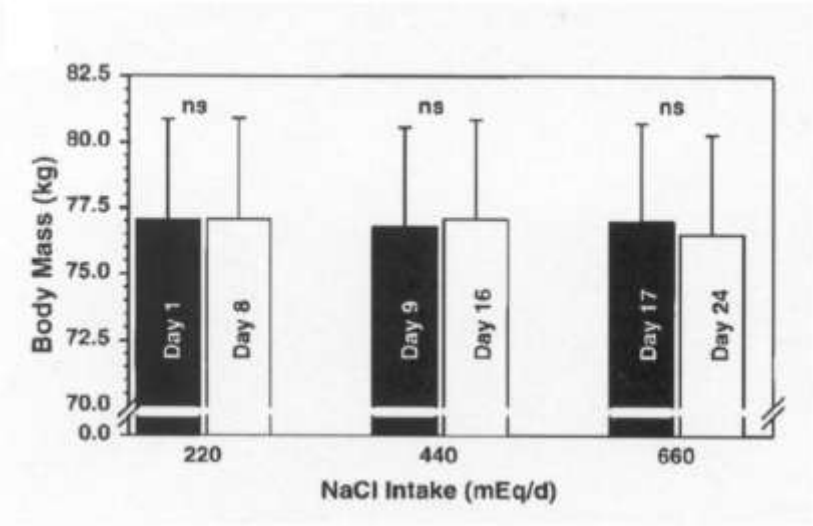
$TBNa^+$ maintained within narrow limits?

Increase in $TBNa^+$ = Increase in BP?

Maxwell & Kleeman: Clinical Disorders of Fluid and Electrolyte Metabolism, McGraw Hill, 1972

Startling data from balance studies in humans.





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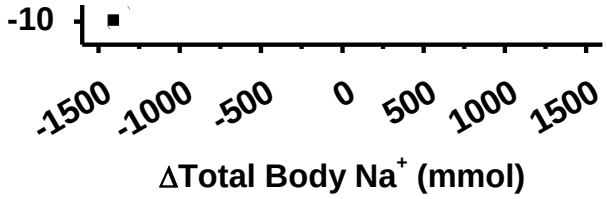

Heer M, et al.: *Am J Physiol Renal Physiol* 278 (4):F585-F595, 2000.

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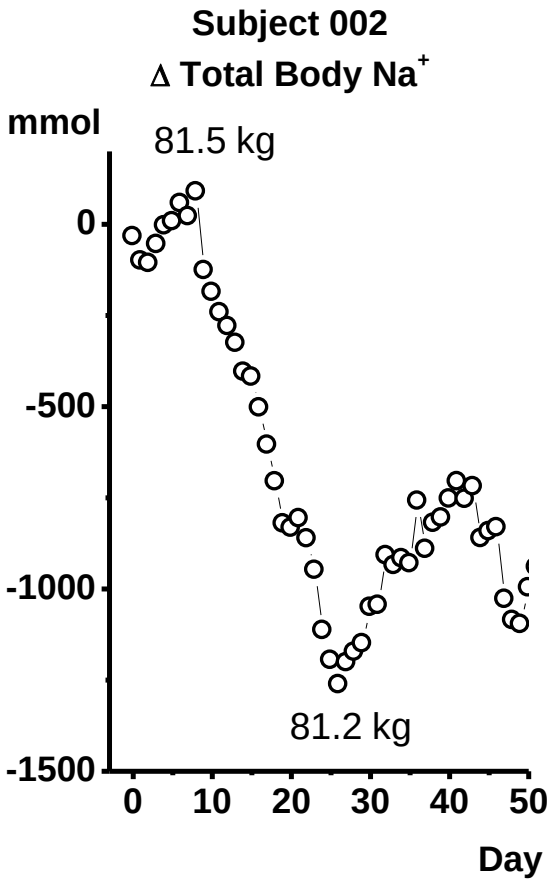

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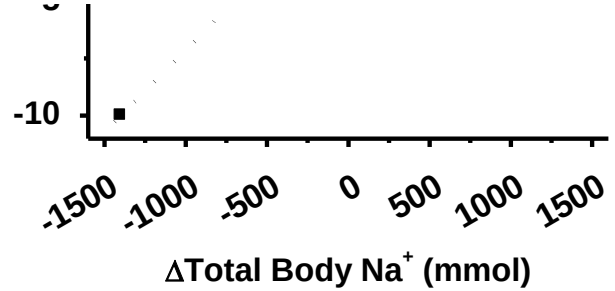
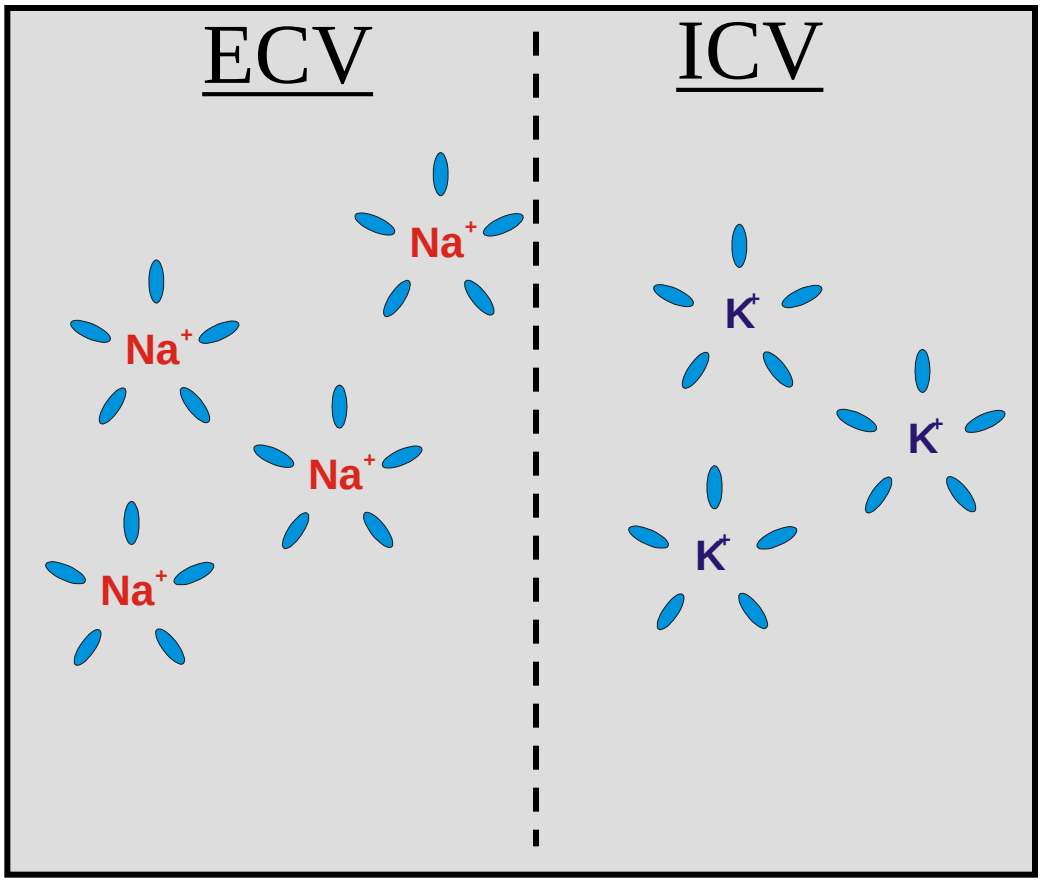


Am J Kidney Dis 40 (3): 508-16, 2002

Can we accumulate Na^+ in abundance over water?



Osmotically neutral Na^+ / K^+ Exchange

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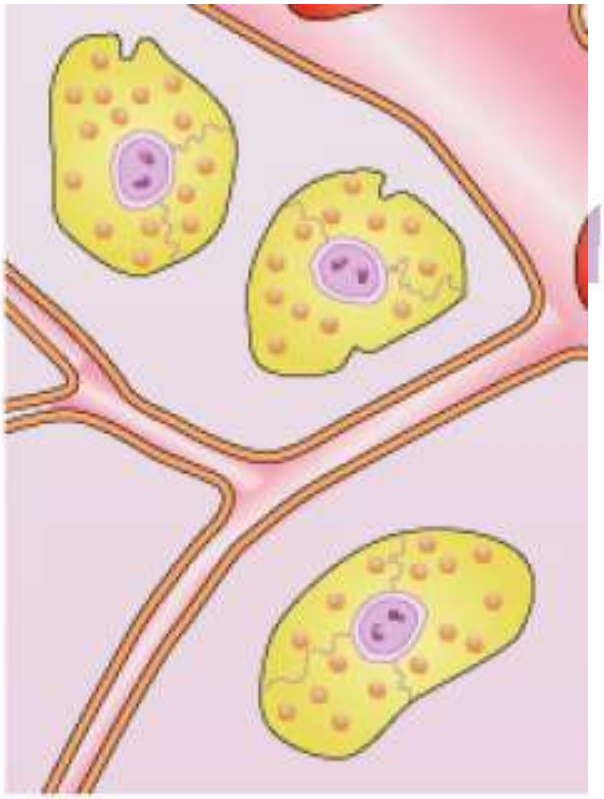
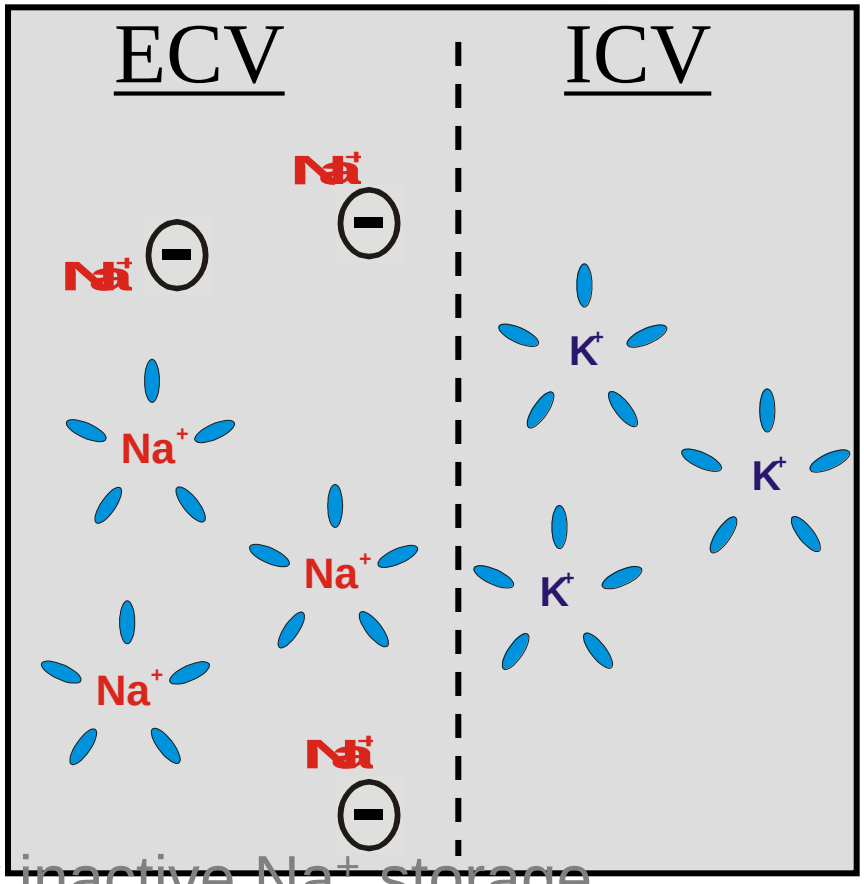




Osmotically inactive Na^+ storage

A view inside the body: chemical analysis.

skinning →

Dessication:

SKW

→

Ashing:

Na^+, K^+

↘

Dessication:

wet weight
minus
dry weight:

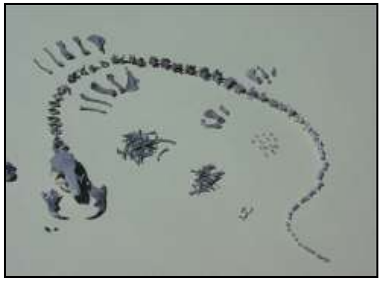
TBW

↙ ↘

Rest Carcass Na^+, K^+
- Internal organs
- Retroperitoneum
- Muscle

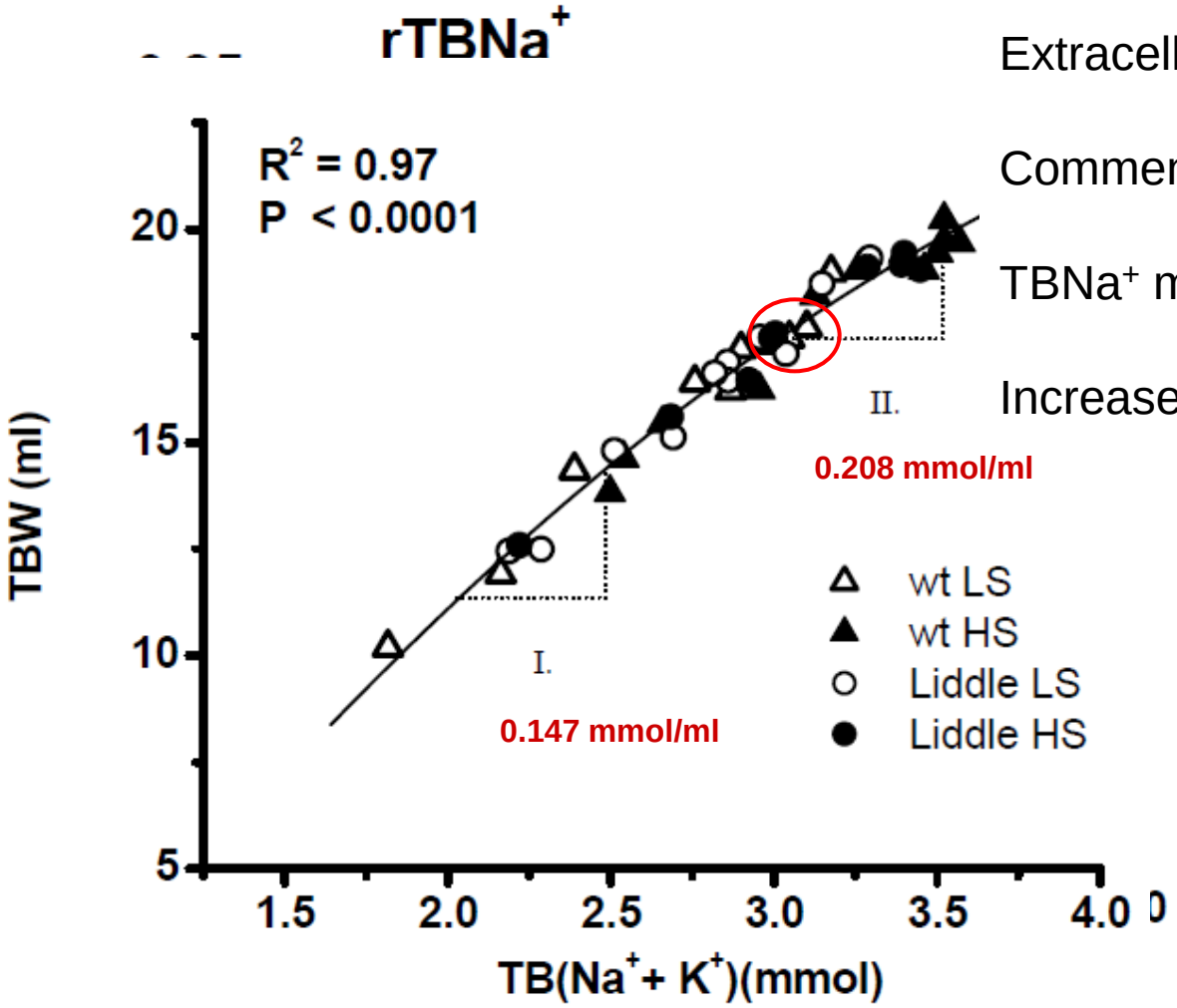
Skeleton:

Na^+, K^+



Startling data from animal experiments.

Liddle‘s syndrome



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Extracellular?

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$TBNa^+$ maintained within narrow limits?

Increase in $TBNa^+$ = Increase in BP?

Bench to bedside

rising incidence of arterial hypertension worldwide, leading to secondary end organ damage

association of elevated RR and high salt intake

Pimenta E, Gaddam KK, Oparil S, Aban I, Husain S, Dell'Italia LJ, Calhoun DA. Effects of dietary sodium reduction on blood pressure in subjects with resistant hypertension: results from a randomized trial. *Hypertension.* 2009 Sep; 54(3):475-81

RR_{syst} -23 mmHg !!!

renal failure: **associated with reduced salt removal,**

dialysis: **accompanied by elevated blood pressure**

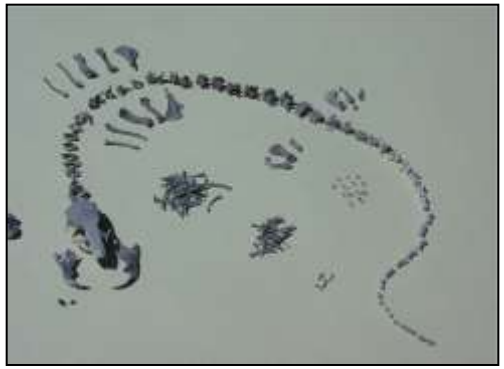
high risk of cardio-vascular events

therefore: recommendation for dialysis patients to moderatly lower their dietary salt intake (WHO 6 g NaCl/ day)

but: difficulty to maintain salt restricted diet at home

persisting high blood pressure values

Tissue specific Na^+ content in humans



alternative technique?

$^{23}Na^+$-knee coil/ 3 Tesla MRT

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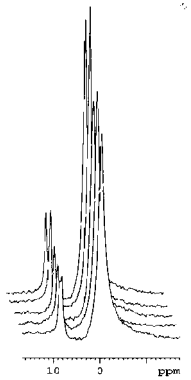
$^{23}Na^{+}$- MRI

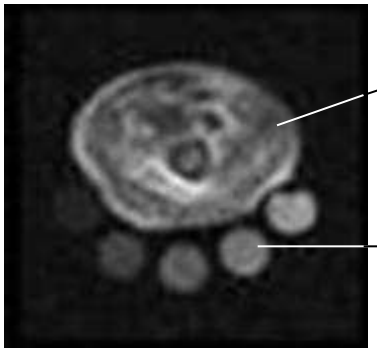
$^{23}Na^{+}$-knee coil



ideal tool for clinical investigations

duration of measurement: ca. 35-45 min,
no contrast medium needed

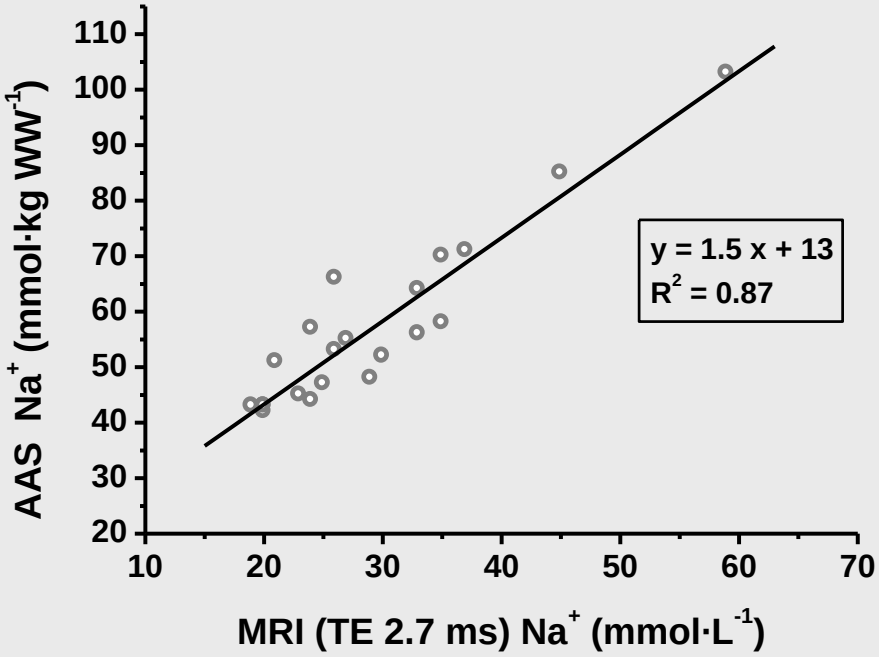
3-Tesla MRI



Cross section of lower leg

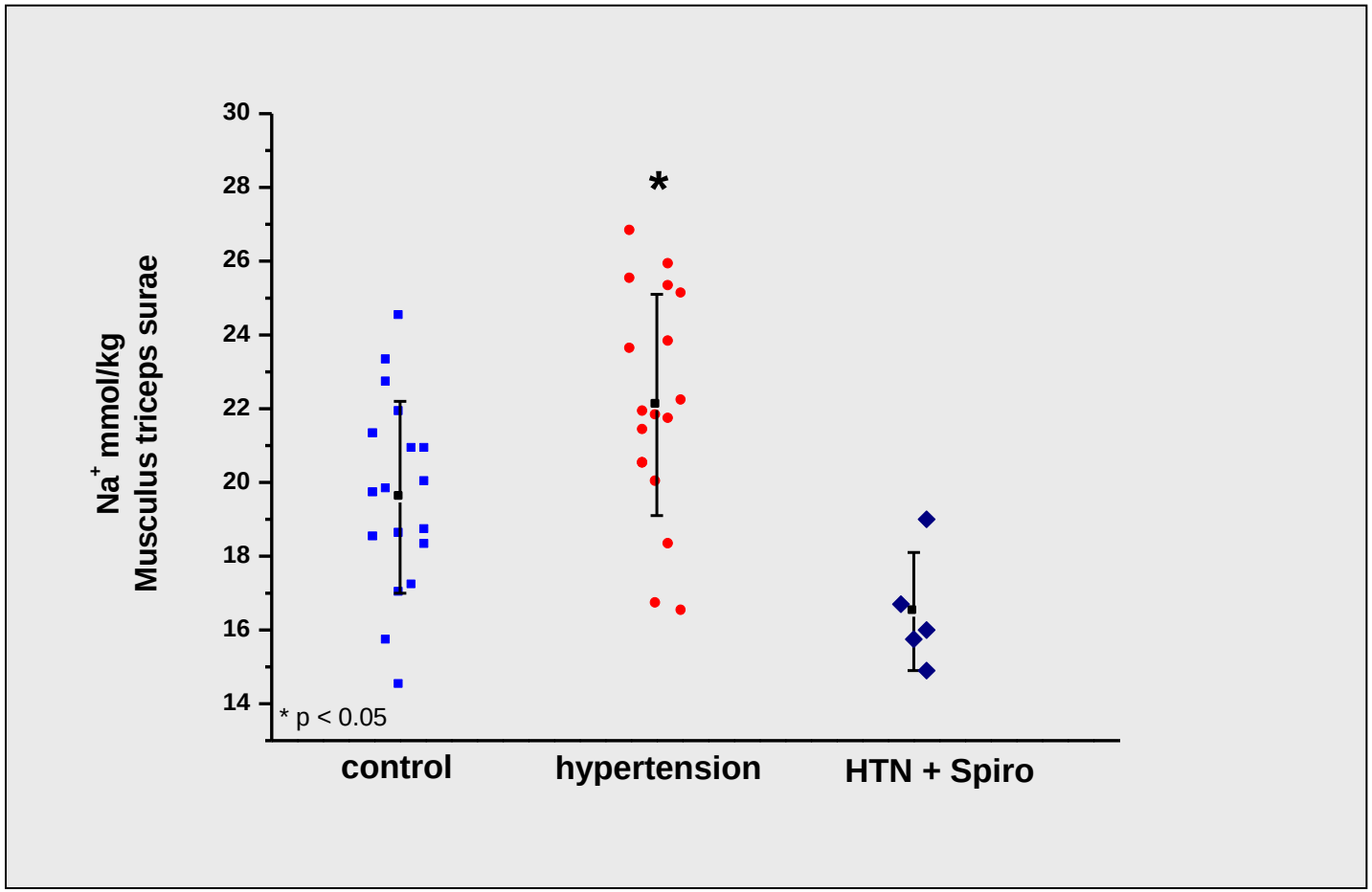
NaCl calibration tubes

Human tissue specific Na^+ content



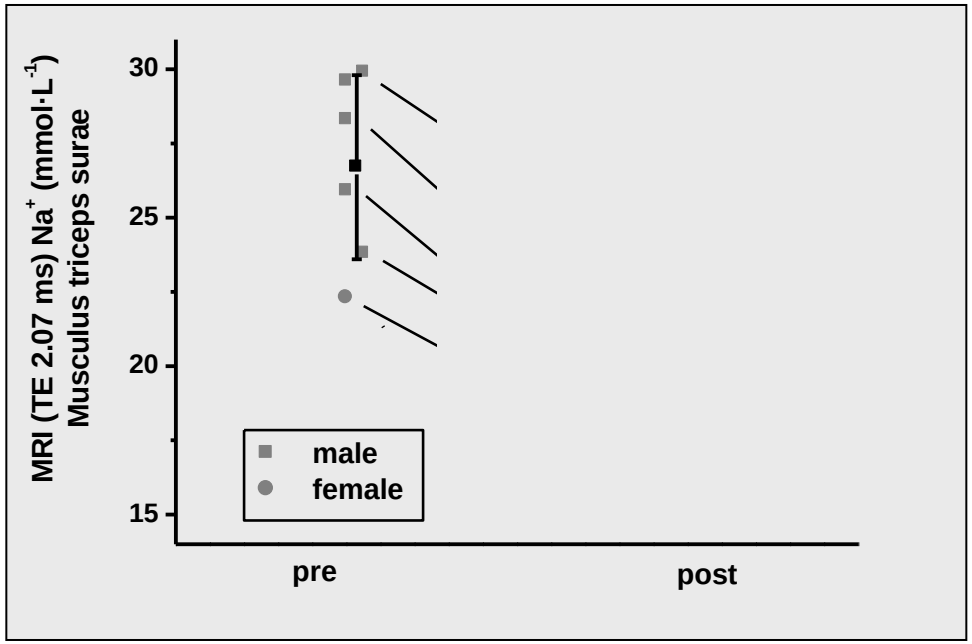
Kopp C. et al., submitted *Hypertension*

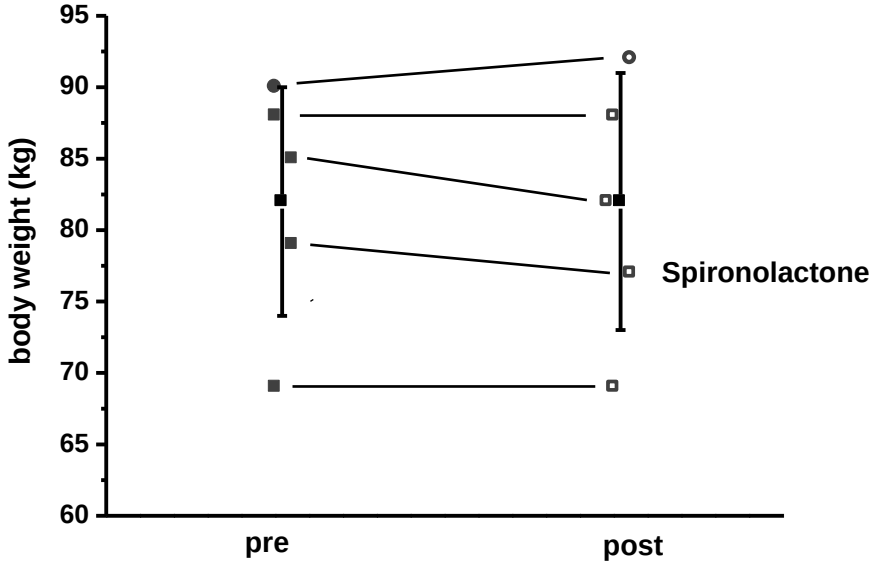
Therapy resistant hypertension



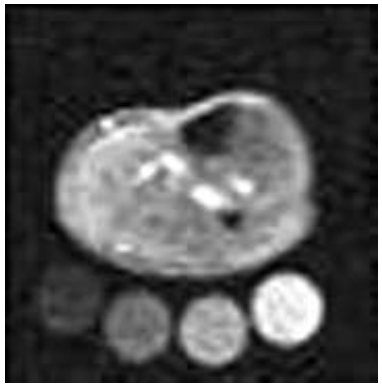
Kopp C. et al., submitted *Hypertension*

Hyperaldosteronism (Conn syndrome)

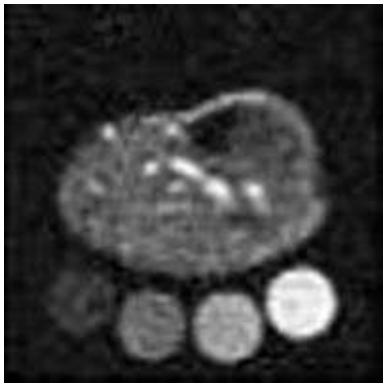




pre



post



Where is the salt?

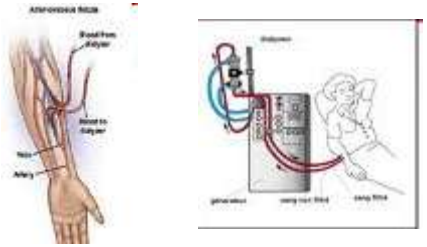
Na^+ MRI: diagnostic tool

Kopp C. et al., submitted *Hypertension*

Nürnberg

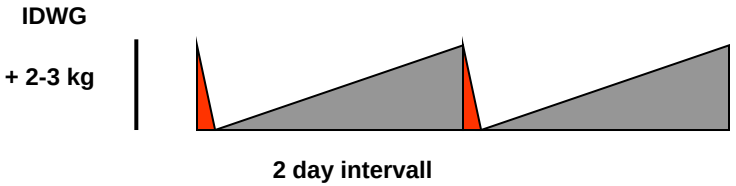
Dialysis therapy

CIHD: chronic intermittend hemodialysis



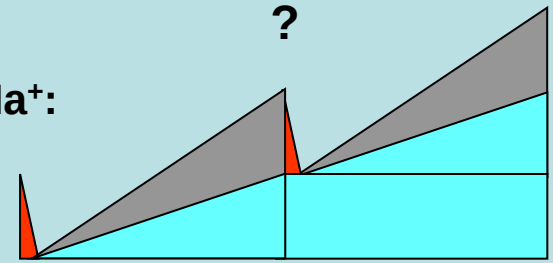
duration of treatment: 4h / 3x per week

IDWG: interdialytic weight gain ~ ultrafiltration rate



IDWG of 2-3 kg corresponds to daily intake of 10-15 g NaCl

TBNa⁺:



- **no change in serum Na^+ concentration**
- **Na^+ removal estimated by IDWG**

→ **Na^+ MRI**

^{23}Na MRI dialysis study

DS Nr.	gender	age (yrs)	bw (kg) pre dialysis	diabetes	smoker	duration CIHD (yrs)	RR meds (fold)	HD time (h)	IDWG (kg)	net filtration (ml)
1	male	21	109,3	no	yes	3	3	8	4,8	5000,0
2	male	66	88,6	no	no	1	3	4,5	2,1	2100
3	male	55	95,7	no	no	2	3	6	0,7	700
4	male	58	87,5	no		4	3	5	2,5	2500
5	male	29	108					6	3,5	3500
6	male	75	120	yes		2	2	5,5	2,5	2500
7	female	42	58,4	no		9	4	4,5	2,9	2900
8	female	30	53,7	no		8	2	4	-0,3	-300
9	female	61	70,4	no	yes	5	1	4,5	2,4	2400
10	male	82	75,3	no	yes	4	3	4,75	2,8	2800
11	male	63	79,3	no	yes	5,5	4	5	3,3	3300
12	female	50	77,3	no	no	0,5	1	4,5	0,3	300
13	female	67	57,3	no	no	6,5	1	4,25	-0,7	-300
14	male	68	56,3	no	no	20	3	5	1,3	1300
15	male	30	78,2	no	no	0,1	4	4,25	0,7	700
16	female	69	76,8	yes	no	3,5	3	4	0,8	800
17	male	74	83,2	yes	no	0,5	4	4,25	0,2	200
18	male	50	92,3	no	no	2		4	1,3	1300
19	male	62	86	no	yes	2,5	2	4,75	2,4	2400
20	female	74	52,5	no	yes	1,25	5	4	2	2000
21	male	64	90,8	yes	no	2,5	2	4,5	1,3	1600
22	male	66	63,2	no	no	6,2	3	4,75	2,2	2200
23	male	65	75,6	no	no	0,5	4	4,5	3,1	2700
mean value		**57,4348**	**79,8130**			**4,0705**	**2,8571**	**4,8043**	**1,8304**	**1852,1739**
std		16,6592	18,2920			4,3507	1,1084	0,8981	1,3425	1312,8282

^{23}Na MRI dialysis study

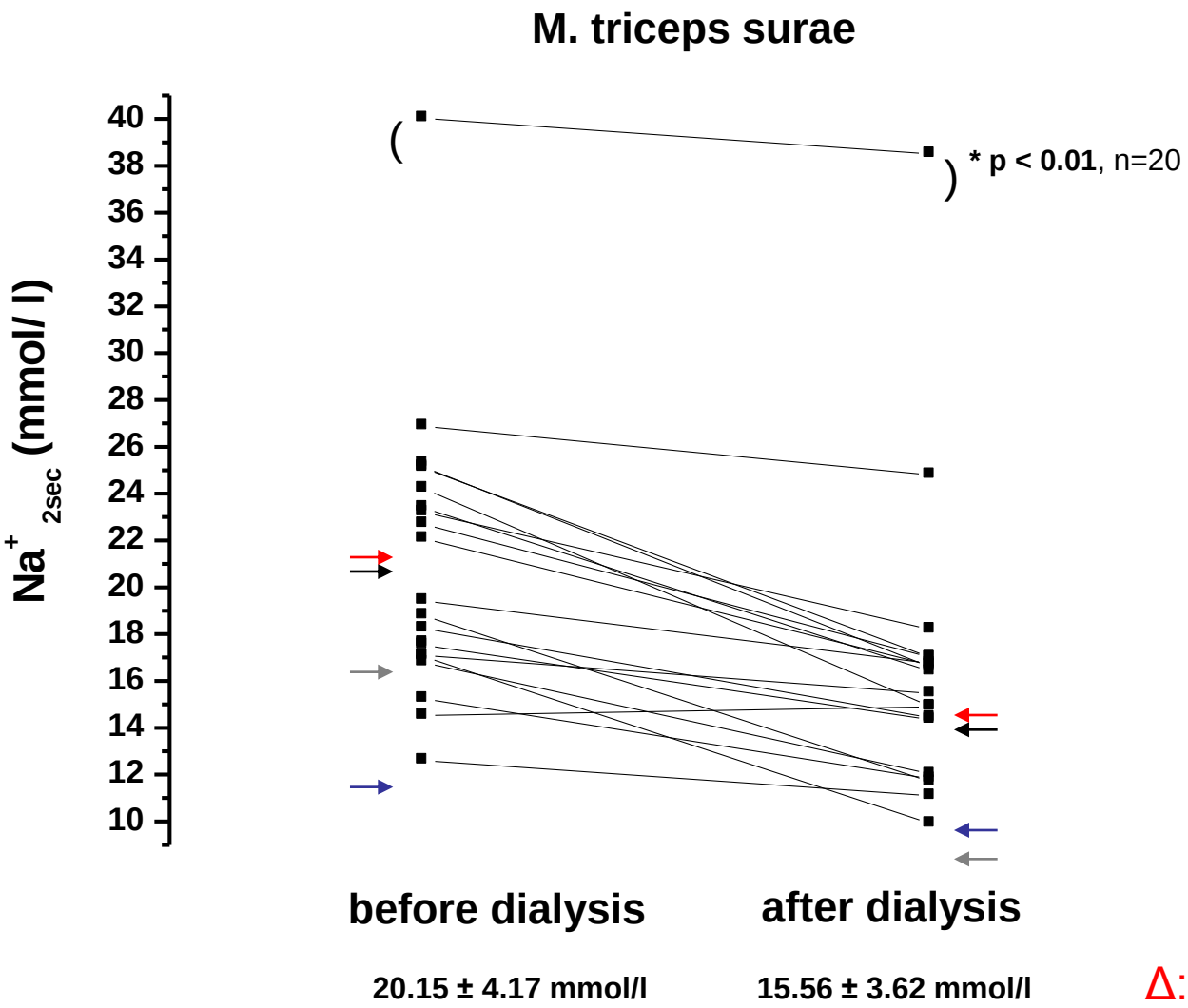
conventional MRI:

$^{23}Na^{+}$- MRI:

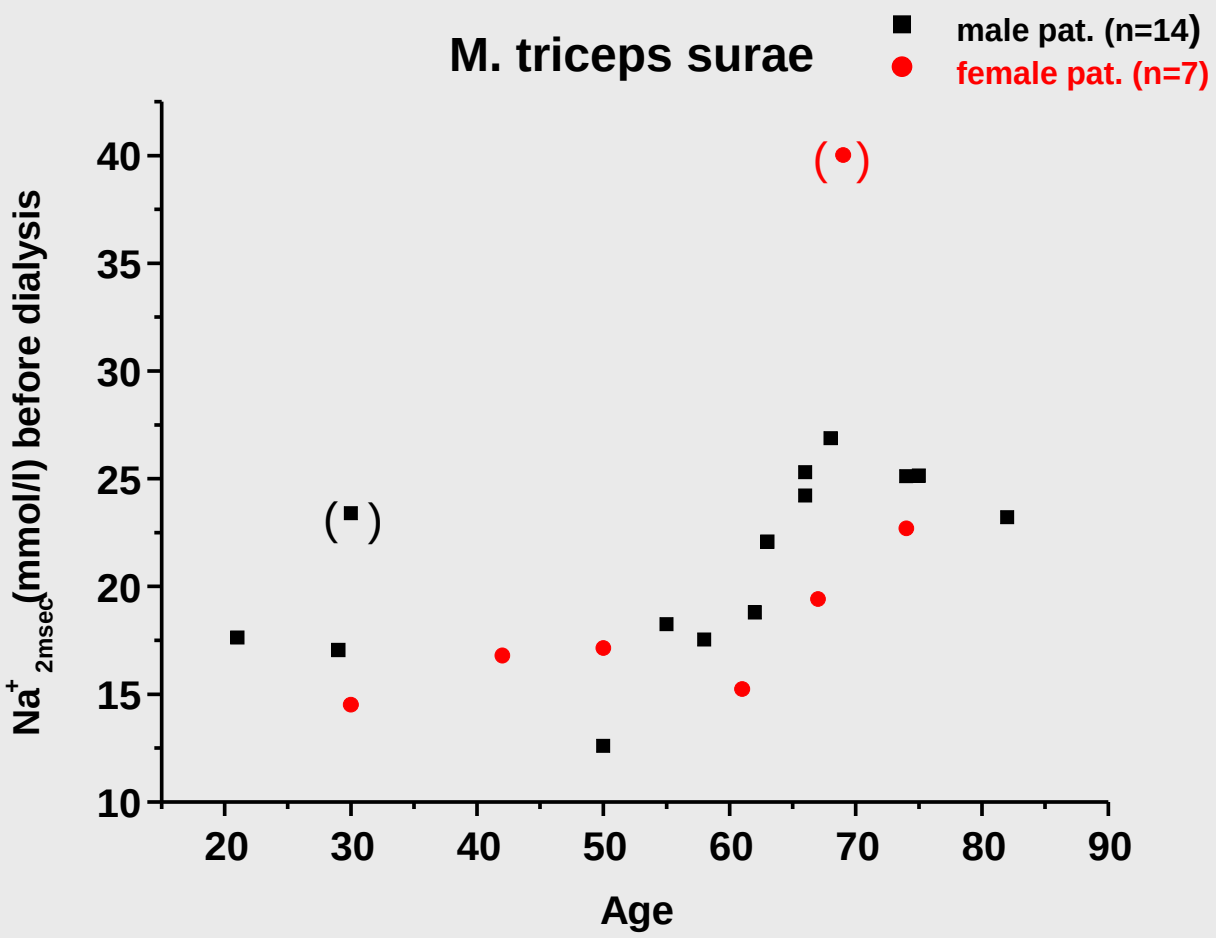
pre dialysis

post dialysis

Na^+_{2msec} in muscle before/ after dialysis



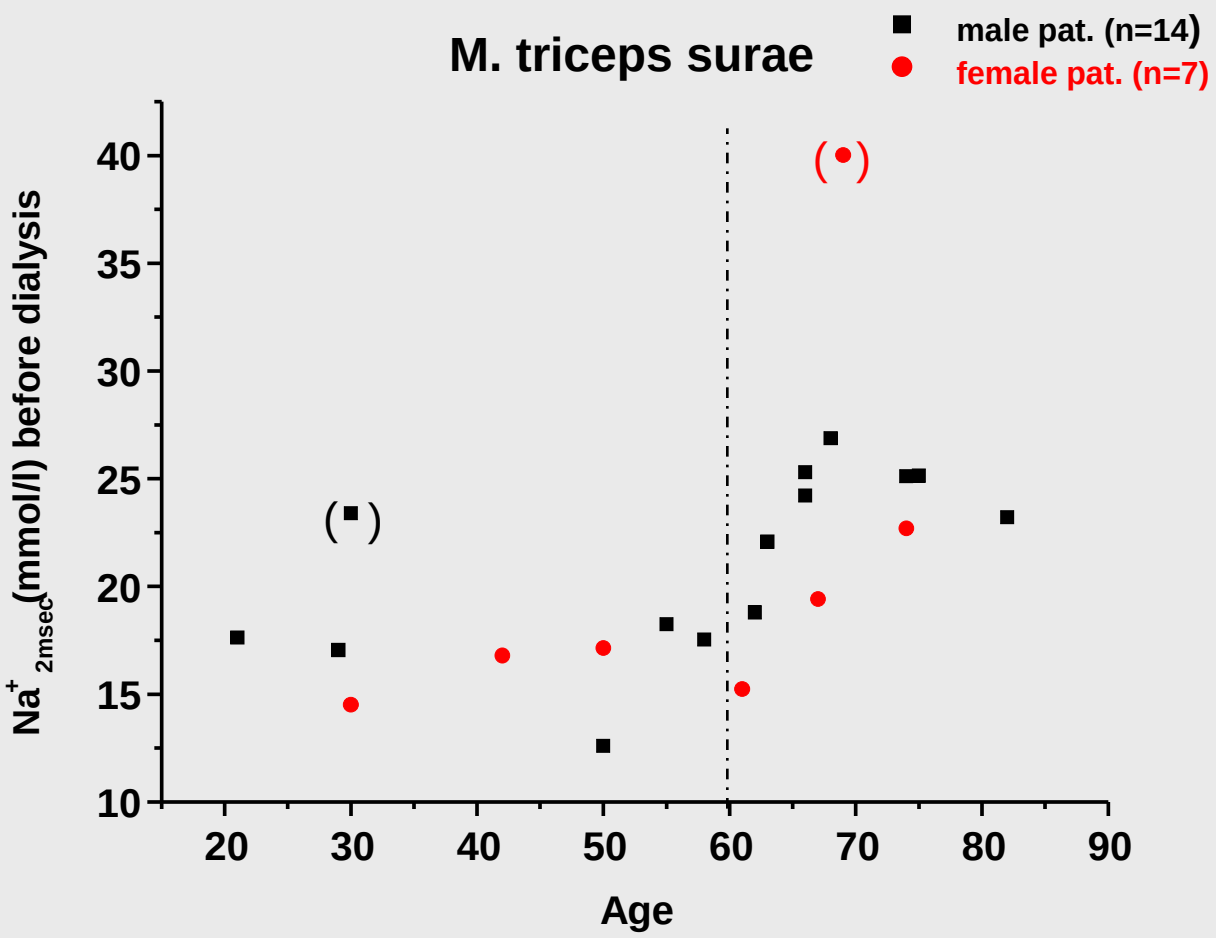
gender dependency of initial Na^+_{2msec} in muscle



Male (58,8 ± 19,1 yrs): **21,23 ± 4,21 mmol/l**

Female (54,0 ± 16,5 yrs): **17,64 ± 3,0 mmol/l,** $p < 0.1$

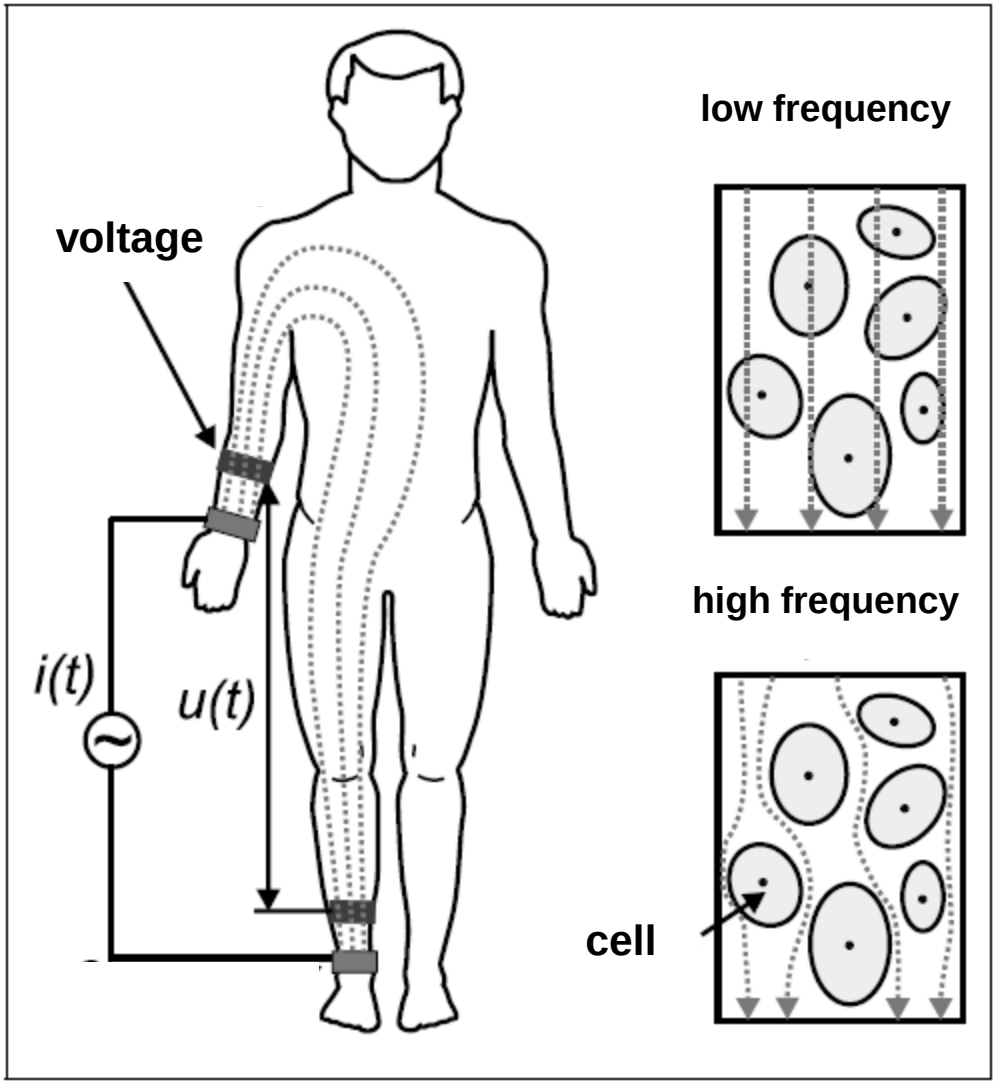
gender dependency of initial Na^+_{2msec} in muscle



Age dependency of initial Na^{+}_{2msec} in muscle

Subjects < 60 yrs:	Subjects > 60 yrs:
controls (**n= 10**, **age 37.8** ± 9.2 a)	**controls** (**n= 15**, **age 66.5** ± 3.6 a)
17.6 ± 2.6 mmol/l	19.8 ± 2.7 mmol/l
patients (**n= 8**, **age 40.6** ± 13.7 a)	**patients** (**n= 10, age 69.2** ± 6.5 a)
17.1 ± 3.1 mmol/l	**24.8 ± 5.9** mmol/l ***p < 0.05**
<u>after dialysis</u>:	<u>after dialysis</u>:
13.6 ± 2.2 mmol/l	19.2 ± 7.5 mmol/l

Body composition measurement (BCM)



measurements

- resistancy
- impedance
- reactance

parameter

- age
- gender
- height
- body weight

frequency: 5 kHz – 1MHz

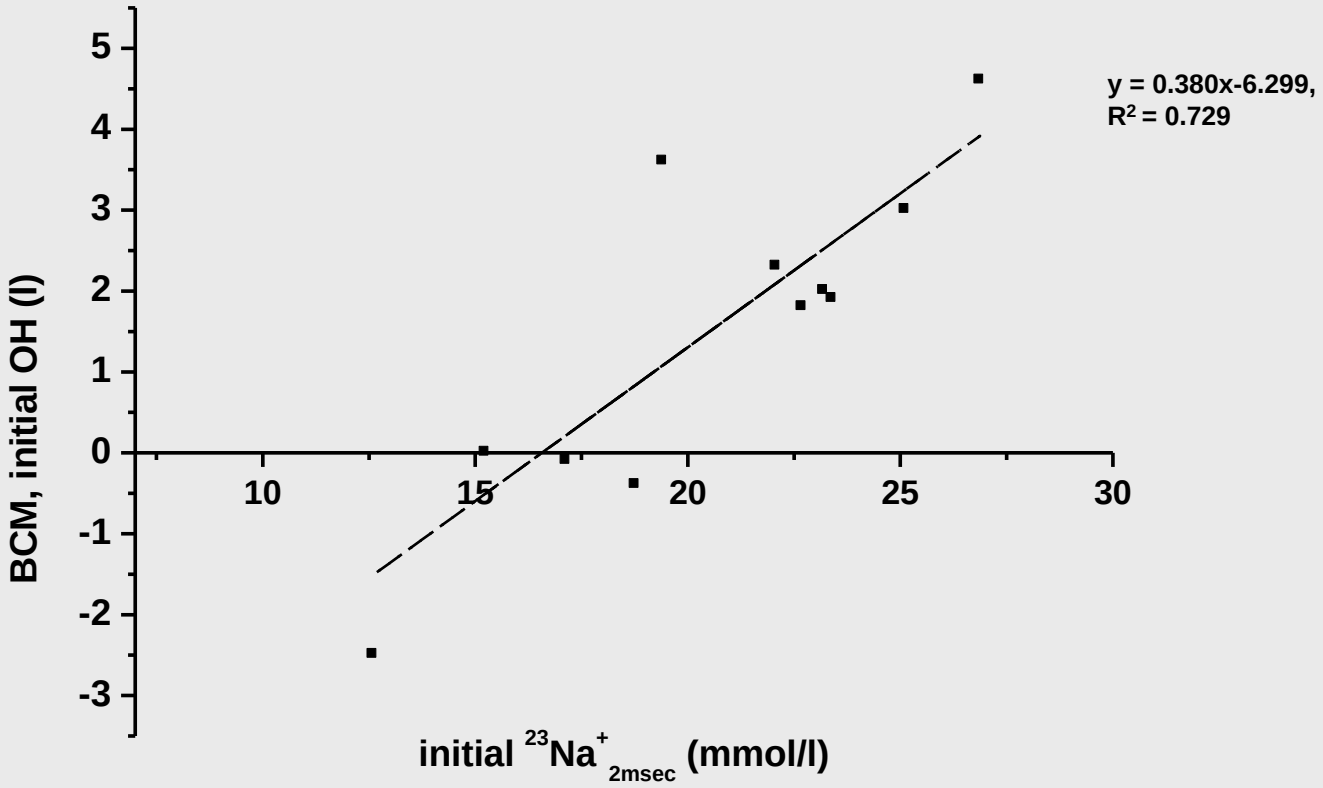
BCM and hemodialysis

	OH (l)	TBW (l)	ECW (l)	ICW (l)	E/I	LTM (kg)	LTI (kg/m²)
DS1 pre HD	0	25,2	12,7	12,5	1,01	19,9	7,5
DS2 pre HD	2	36,2	18,2	18	1,01	36,3	13,7
DS3 pre HD	2,3	38,2	18,9	19,7	0,96	39,9	13,5

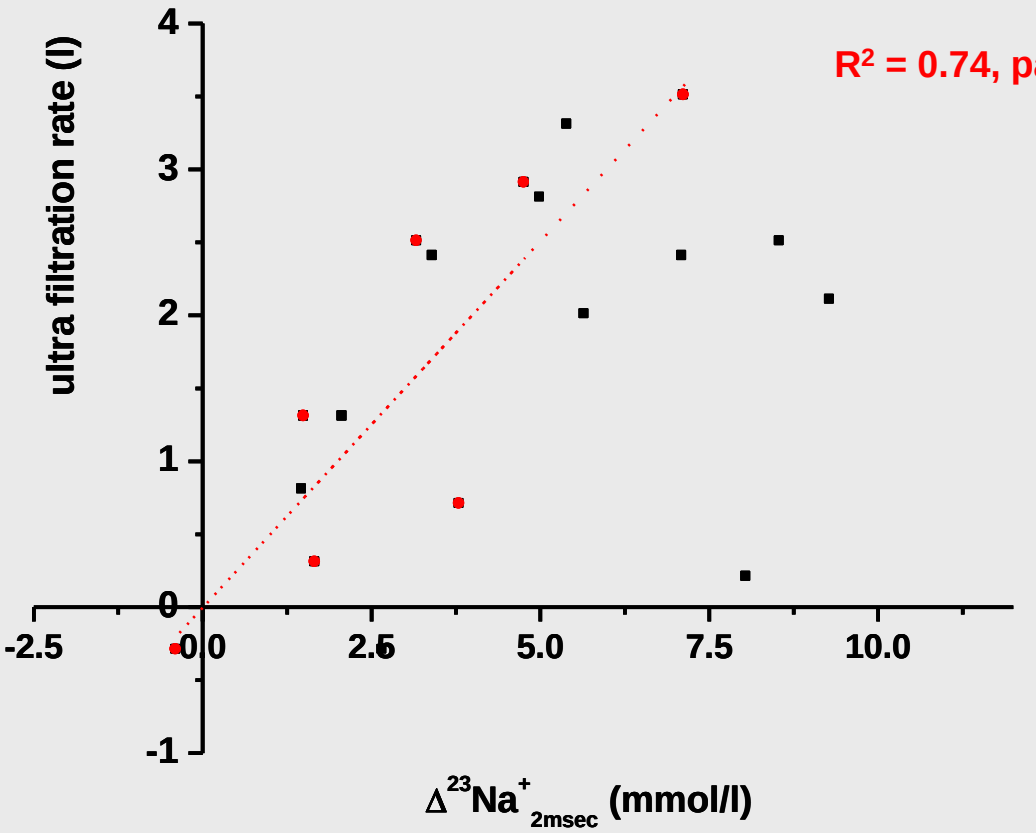
	OH (l)	TBW (l)	ECW (l)	ICW (l)	E/I	LTM (kg)	LTI (kg/m²)
DS1 post HD	-2,2	23,7	10,7	12,9	0,83	21	7,9
DS2 post HD	0,5	33,8	16,4	17,4	0,94	34,3	12,9
DS3 post HD	-0,4	36,2	16,3	19,9	0,82	40,2	13,6

Bioimpedance and muscle sodium content

Na^+- content in M.triceps surae determines overhydration



Ultrafiltration rate and Na^+ removal



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<u>after dialysis</u>:	<u>after dialysis</u>:
13.6 ± 2.2 mmol/l	19.2 ± 7.5 mmol/l

estimation of total Na^+ removal

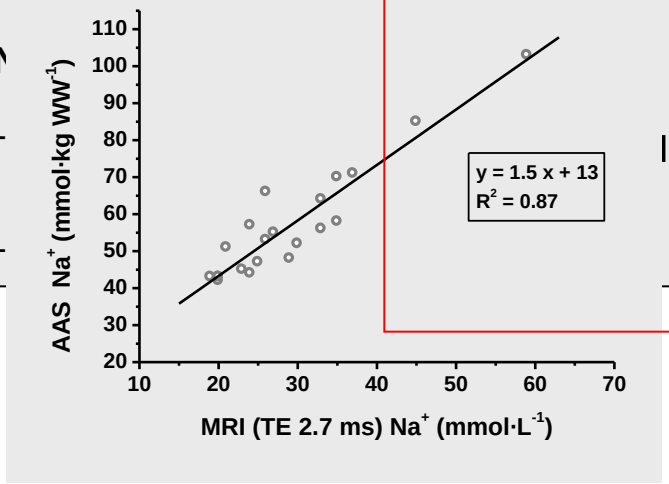
Subjects < 60 yrs:

	$^{23}Na^+$ muscle (mmol/kg)	ultra-filtration (l)	LTM (kg)
pre	38.7		
post	33.4		**~ 43.6**
Delta	**5.3**	**~ 1.55**	

^{23}N

LT l

/ 1



Subjects > 60 yrs:

	$^{23}Na^+$ muscle (mmol/kg)	ultra-filtration (l)	LTM (kg)
pre	50.2		
post	41.8		**~ 43.6**
Delta	**8.4**	**~ 1.77**	

$^{23}Na^+$ content muscle **=**

LTM (kg) * $^{23}Na^+$(mmol/kg) = **313.6 mmol**

/ 140 mmol/l **~ 2,24 l**

water free sodium removal?

Conclusion

water free sodium retention	osmotically neutral Na^+ /K^+ exchange osmotically inactive Na^+ storage
^{23}Na MRI	diagnostic tool
^{23}Na MRI and dialysis	gender/ age dependency

Open questions concerning dialysis treatment!

group and cooperation partners

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Institut für Physiologie, Universität Regensburg
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Deutsches Zentrum für Luft- und Raumfahrt, DLR Köln
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Institut für Pathologie, Wien
Institut für molekulare Zellbiologie, Niederlande

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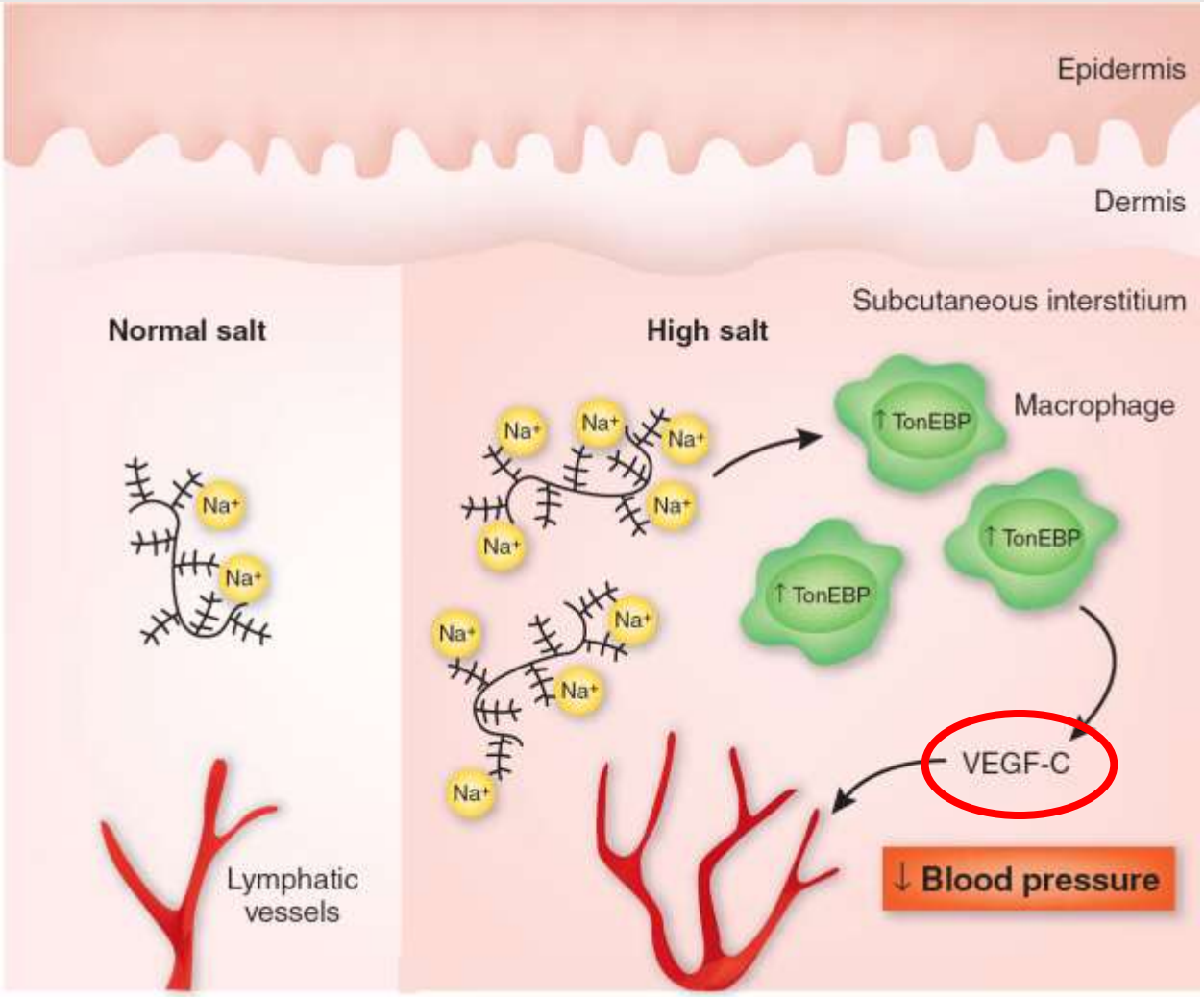
MPS cells and blood pressure regulation



Marvar P.J., Gordon F.J., Harrison D.G., *Nat Med* 15 (5), pp 487-488, **2009**

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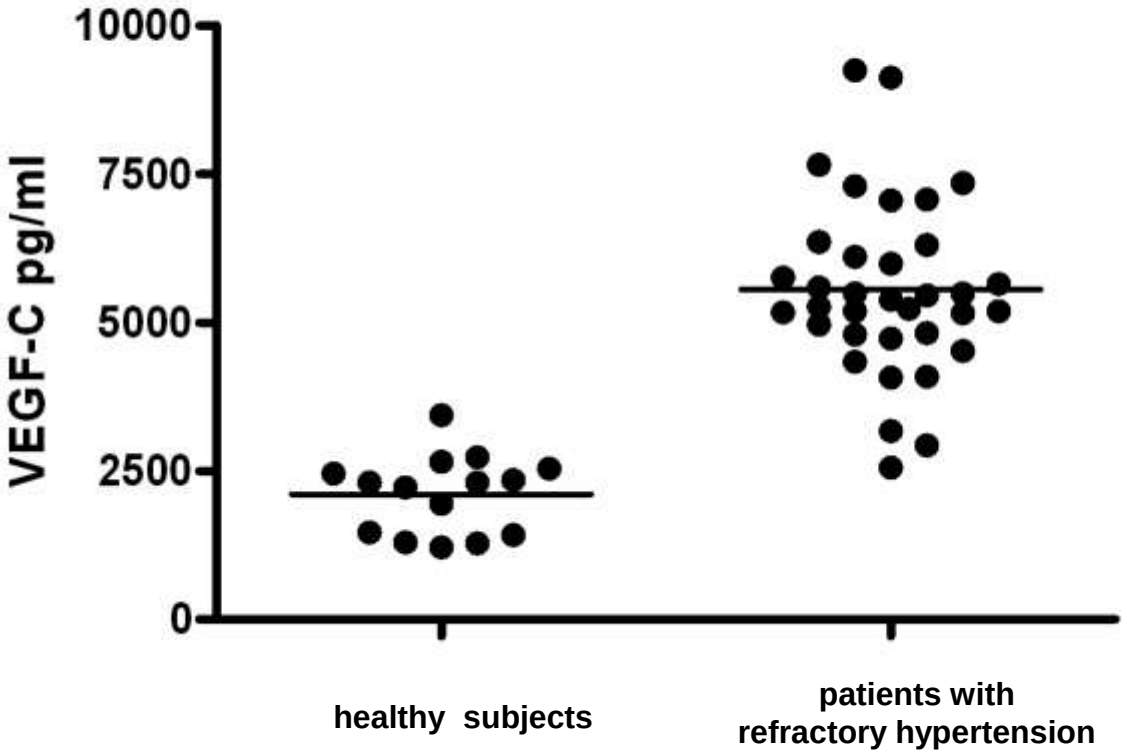
Clinical relevance: VEGF-C and RR?



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