THE DILEMNA OF PTH LEVELS.

Dosage Parathormone

Seconde ou Troisième génération

GLEM

28 mars 2012

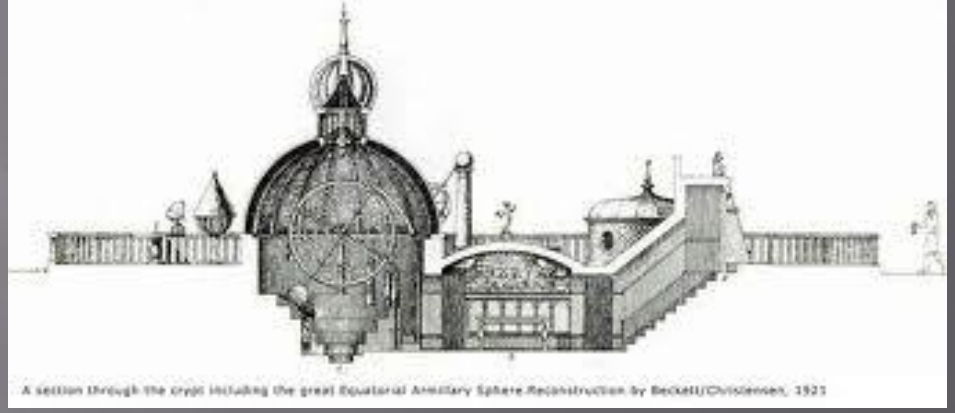
Quelques questions ?

- Connaissez vous le nom de la firme qui fait votre dosage PTH ?
- Connaissez vous le nom du Test ?
- Connaissez vous son index de conversion apr rapport au Nichols ?
- Avez-vous lu le rapport de l'Affsaps 2009 ?
- ……

Plan

- Introduction .
- KDIGO .
- Test de 2eme et 3 eme génération.
- Correlation intra centre.
- Discussion sur la bonne pratique et peut être recommandation de GLEM ?

PARATHORMONE
2eme et 3eme génération


A section through the crypt including the great Equatorial Armillary Sphere.Reconstruction by Beckett/Christensen, 1921

Tyge Tycho Brahé
1546 - 1601

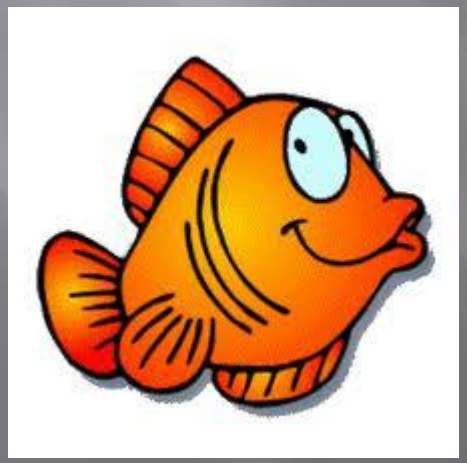

Stjärneborg. excavations in 1951.

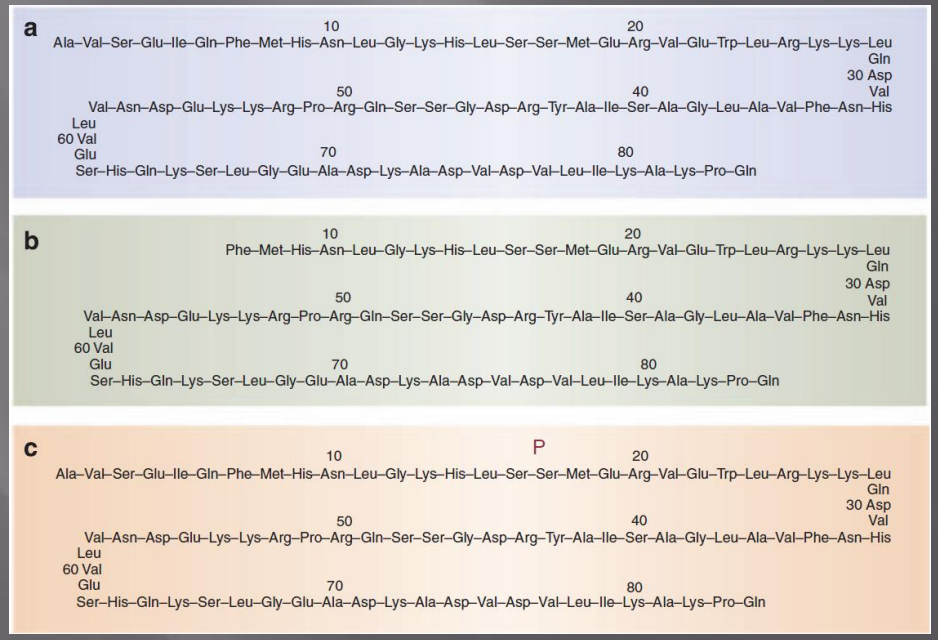
Ivar Sandstrom

- Sweedish Medical Student
- Discovered Parathyroid gland In 1880
- Last major organ Identified in humans

Changement à Hornu

Le 1er avril 2011 le Laboratoire passe du dosage Diasorin I PTH au dosage Diasorin Whole PTH





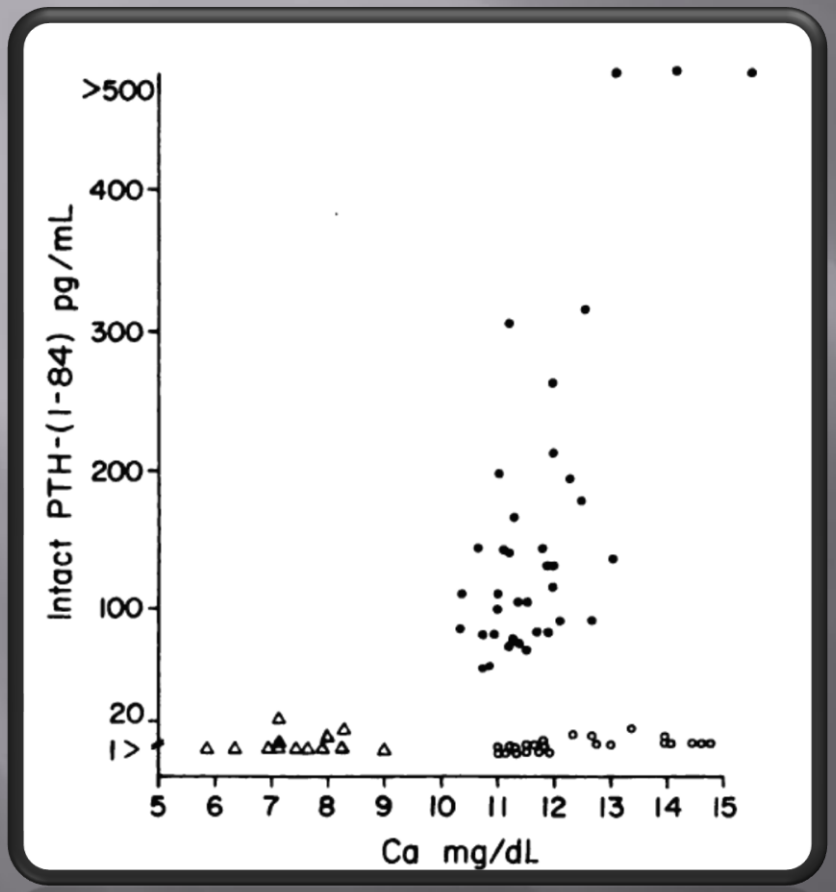
Changement à Hornu

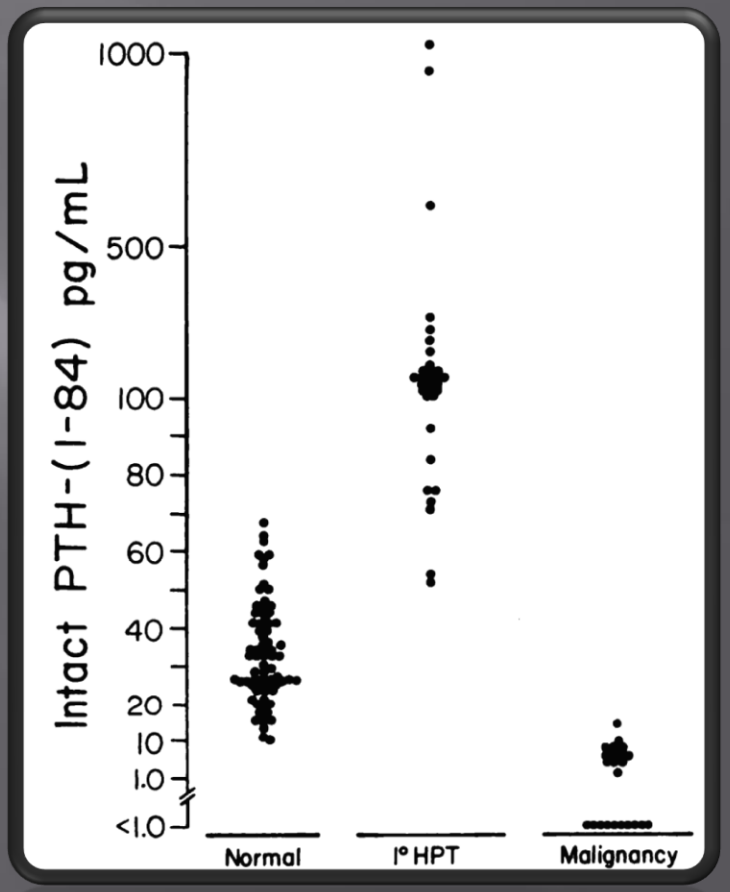
Cela ne vous dérange pas si on change de kit de dosage de PTH ?

Heu, …, vous pouvez nous faire la correlation entre les mesures ?

Highly Sensitive Two-Site Immunoradiometric Assay of Parathyrin, and Its Clinical Utility in Evaluating Patients with Hypercalcemia

Samuel R. Nussbaum,[1] Richard J. Zahradnik,[3] Jeffrey R. Lavigne,[3] George L. Brennan,[3] Kathleen Nozawa-Ung,[3] Lance Y. Kim,[1] Henry T. Keutmann,[1] Chiu-An Wang,[2] John T. Potts, Jr.,[1] and Gino V. Segre[1]





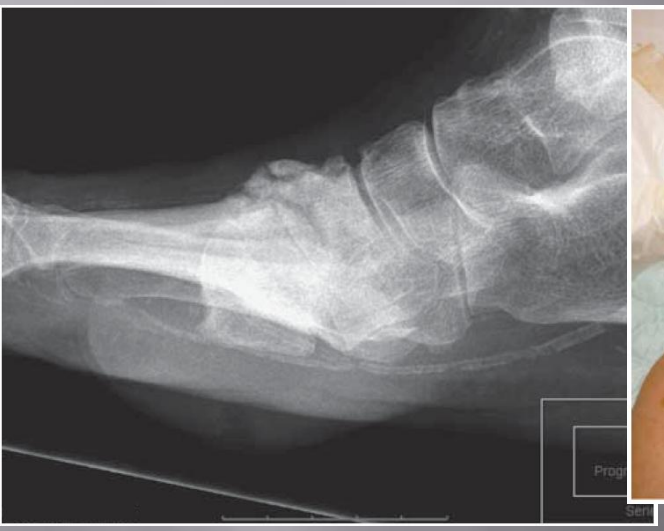
CLIN. CHEM. 33/8, 1364–1367 (1987)

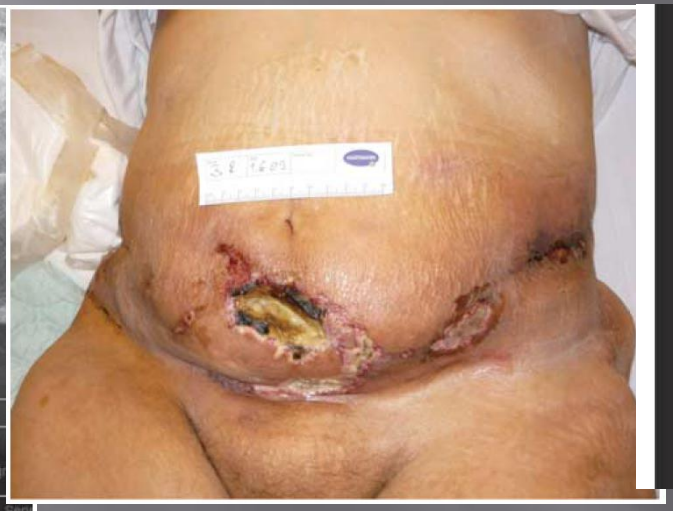
2eme génération…

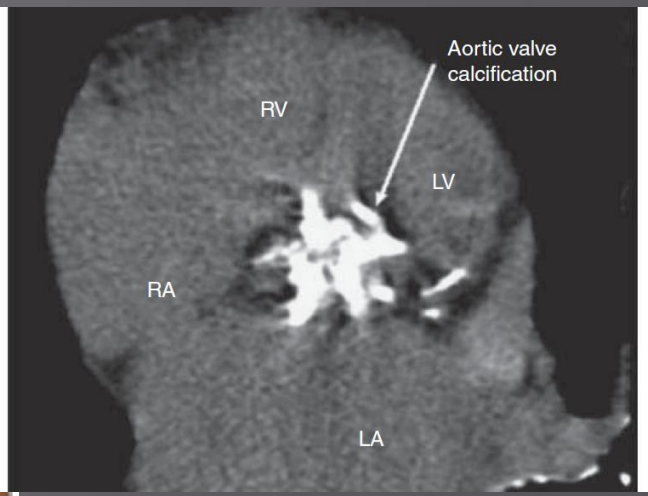
Name of the assay	Manufacturer	Intra-assay CV (%)	Inter-assay CV (%)	Reference range (manufacturer) (pg/mL)	Reference population	Automated	2nd or 3rd generation
Intact PTH Architect	Abbott (Abbott Park, IL)	<6.1	<6.4	15.0–68.3	143 plasma samples from apparently healthy adults	Yes	2nd
Access PTH intact	Beckman-Coulter (Brea, CA)	<2.6	<5.8	12–88	289 paired samples (serum and plasma EDTA) from apparently healthy men and women aged 19–67 years old. Exclusion of individuals with abnormal calcium, creatinine and 25-OH vitamin D levels.	Yes	2nd
N-tact PTH SP IRMA	DiaSorin (Stillwater, MN)	<3.6	<4.9	13–54	129 serum samples from apparently healthy fasting young adults	No	2nd
Liaison N-tact	DiaSorin (Stillwater, MN)	<5.0	<6.2	17.3–72.9	105 healthy adults.	Yes	2nd
Intact PTH Vitros 5600	Ortho Clinical Diagnostics (Rochester, NY)	<2.0	<7.5	7.5–53.5	EDTA, heparin plasma or serum from 240 patients presenting normal calcium, TSH, creatinine and vitamin D levels.	Yes	2nd
Elecsys 2010	Roche (Mannheim, Germany)	<2.7	<6.5	15–65	Not specified	Yes	2nd
Total intact PTH IRMA	Scantibodies (Shantee, CA)	<4.8	<6.8	14–66	165 EDTA plasma samples from apparently healthy blood donors according to the National Clinical Chemistry Laboratory Standards (NCCLS) recommendations	No	2nd
Immulite 2000Xpi Intact PTH	Siemens Healthcare Diagnostics (Deerfield, IL).	<5.7	<8.8	12–65	Serum from 255 apparently healthy patients	Yes	2nd

Nephrol Dial Transplant (2011) 0: 1–7

Parathormone et Maladie rénale chronique







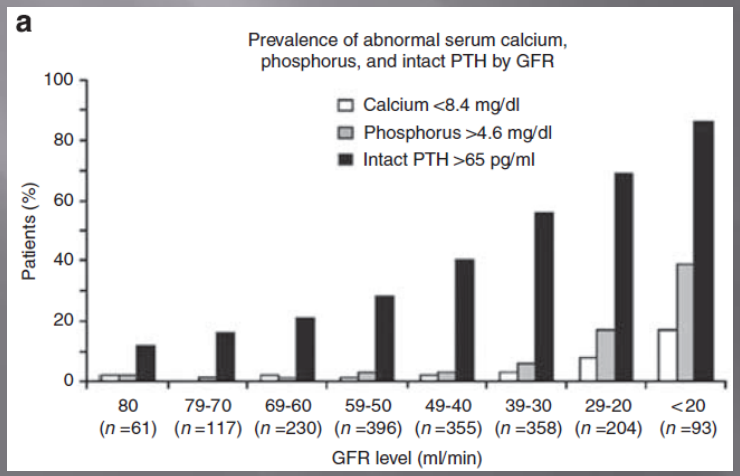


Table 16 | Relationship between fractures and PTH in patients with CKD–MBD

Author, year	*N*	Relationship between fractures and PTH
Coco (2000)[90]	1272	High risk with low PTH
Stehman-Breen (2003)[204]	4952	No relation
Block (2004)[205]	40,538	Weak direct association, *P*=0.035
Danese (2006)[89]	9007	Higher risk with low or high PTH
Jadoul (2006)[206]	12,782	RR=1.7 if PTH > 900
Mitterbauer (2007)[207]	1774	No relation

CKD–MBD, chronic kidney disease–mineral and bone disorder; PTH, parathyroid hormone; RR, relative risk.

Vincent M. Brandenburg[1], Markus Ketteler[2] and Mariano Rodriguez[3]

Kidney International Supplements (2011) **1**, 116–121

The Spectrum of Renal Osteodystrophy

Edited by

TILMAN DRÜEKE
Associate Professor, Division of Nephrology; Director of Research, Inserm Unit 507, Necker Hospital, Paris, France

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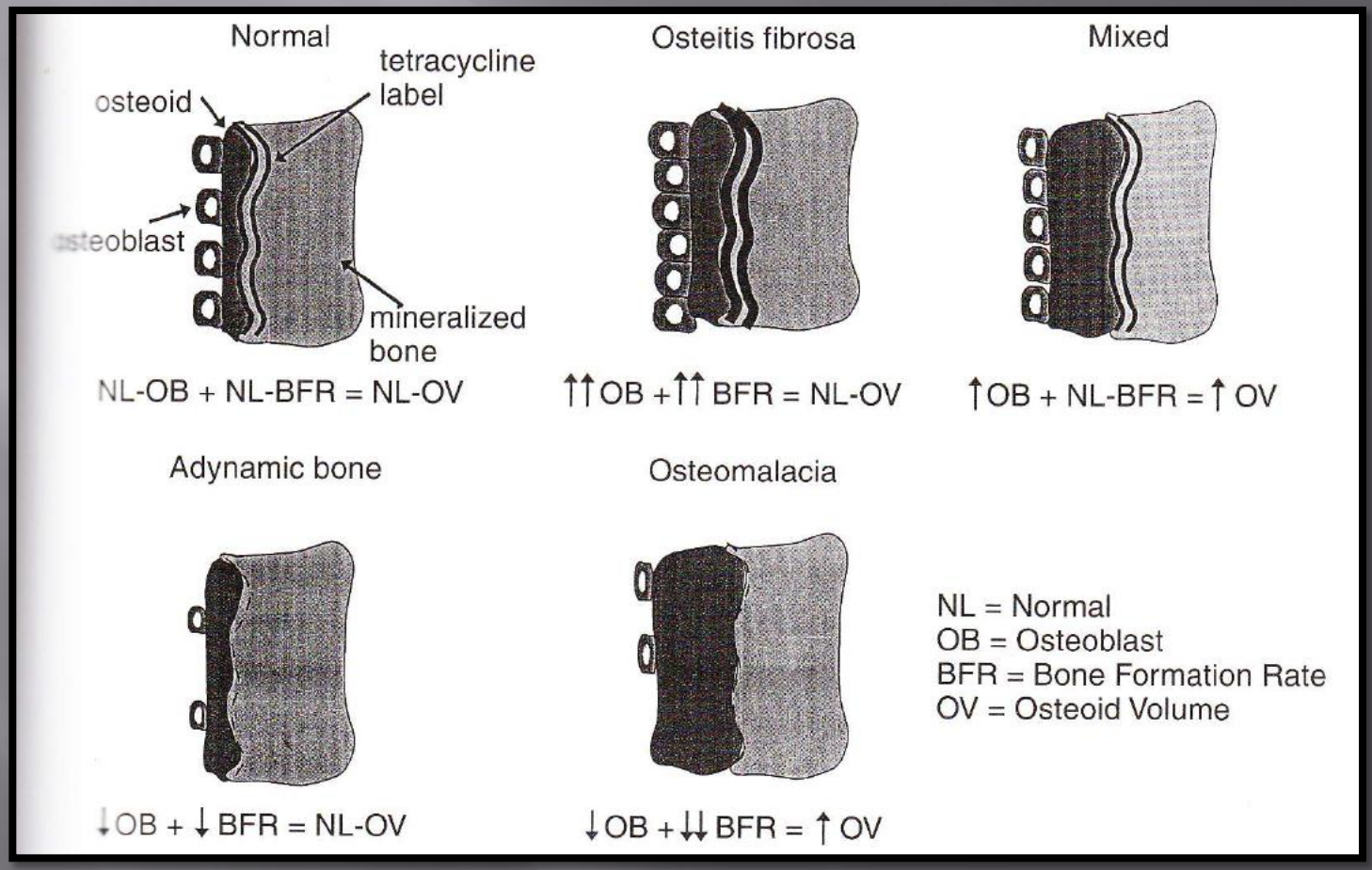


CKD - BMD

Vincent M. Brandenburg[1], Markus Ketteler[2] and Mariano Rodriguez[3]

Kidney International Supplements (2011) **1**, 116–121

CKD – BMD: Parathormone

Ces Recommandations de Bonnes Pratiques Cliniques sont basées sur toute l'information disponible en mars 2009, la dernière mise à jour de la revue de la littérature datant de décembre 2008. Elles visent à informer et constituer une aide à la prise de décisions. Elles ne visent pas à définir un traitement standard et ne doivent pas être comprises en tant que telles ni interprétées comme la prescription d'un seul type de prise en charge.

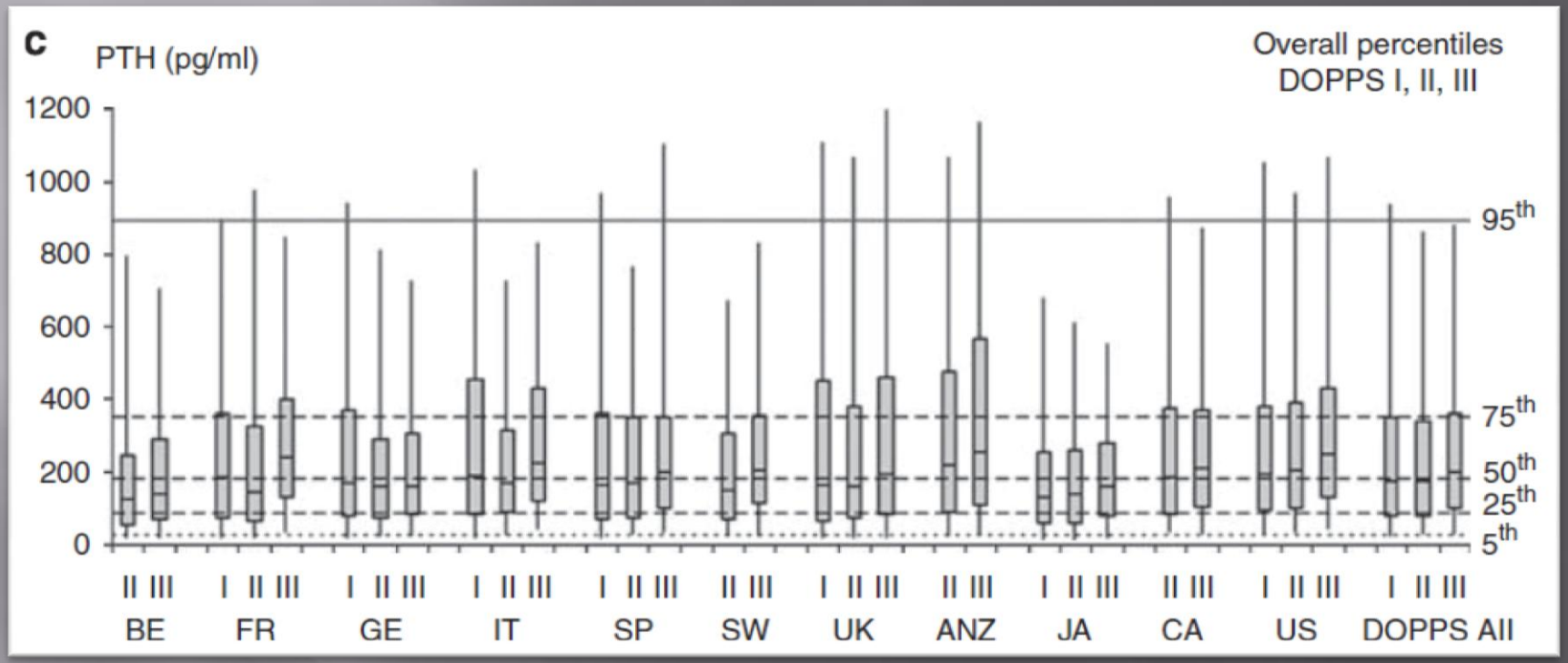
Classement des recommandations et des preuves

Classement de la solidité des recommandations	Solidité	Formulation	Classement de la qualité des preuves	Qualité des preuves
Niveau 1	Forte	"Nous recommandons… doit"	A	Elevée
			B	Modérée
Niveau 2	Faible	"Nous suggérons… pourrait"	C	Basse
			D	Très basse

[a] En outre, le GT peut formuler des recommandations ungraded (voir chapitre 2 concernant les recommandations).

Kidney International 2009; 76 (Suppl 113): S1-S130.

DOPPS Study


c
PTH (pg/ml)
Overall percentiles
DOPPS I, II, III
1200
1000
800
600
400
200
0
95th
75th
50th
25th
5th
II III
I II III
BE
FR
GE
IT
SP
SW
UK
ANZ
JA
CA
US
DOPPS All

KDIGO CKD BMD

Chapter 3.1: Diagnosis of CKD–MBD: biochemical abnormalities

3.1.1. We recommend monitoring serum levels of calcium, phosphorus, PTH, and alkaline phosphatase activity beginning in CKD stage 3 (1C). In children, we suggest such monitoring beginning in CKD stage 2 (2D).

3.1.2. In patients with CKD stages 3–5D, it is reasonable to base the frequency of monitoring serum calcium, phosphorus, and PTH on the presence and magnitude of abnormalities, and the rate of progression of CKD (not graded).

KDIGO CKD BMD

Chapter 3.2: Diagnosis of CKD–MBD: bone

3.2.3. In patients with CKD stages 3–5D, we suggest that measurements of serum PTH or bone-specific alkaline phosphatase can be used to evaluate bone disease because markedly high or low values predict underlying bone turnover (2B).

Chapter 3.3: Diagnosis of CKD–MBD: vascular calcification

3.3.1. In patients with CKD stages 3–5D, we suggest that a lateral abdominal radiograph can be used to detect the presence or absence of vascular calcification, and an echocardiogram can be used to detect the presence or absence of valvular calcification, as reasonable alternatives to computed tomography-based imaging (2C).

KDIGO CKD BMD

Chapter 4.2: Treatment of abnormal PTH levels in CKD–MBD

4.2.1. In patients with CKD stages 3–5 not on dialysis, the optimal PTH level is not known. However, we suggest that patients with levels of intact PTH (iPTH) above the upper normal limit of the assay are first evaluated for hyperphosphatemia, hypocalcemia, and vitamin D deficiency (2C).

It is reasonable to correct these abnormalities with any or all of the following: reducing dietary phosphate intake and administering phosphate binders, calcium supplements, and/or native vitamin D (not graded).

4.2.2. In patients with CKD stages 3–5 not on dialysis, in whom serum PTH is progressively rising and remains persistently above the upper limit of normal for the assay despite correction of modifiable factors, we suggest treatment with calcitriol or vitamin D analogs (2C).

4.2.3. In patients with CKD stage 5D, we suggest maintaining iPTH levels in the range of approximately two to nine times the upper normal limit for the assay (2C).

We suggest that marked changes in PTH levels in either direction within this range prompt an initiation or change in therapy to avoid progression to levels outside of this range (2C).

4.2.4. In patients with CKD stage 5D and elevated or rising PTH, we suggest calcitriol, or vitamin D analogs, or calcimimetics, or a combination of calcimimetics and calcitriol or vitamin D analogs be used to lower PTH (2B).

- We recommend that, in patients with hypercalcemia, calcitriol or another vitamin D sterol be reduced or stopped (1B).

4.2.5. In patients with CKD stages 3–5D with severe hyperparathyroidism (HPT) who fail to respond to medical/pharmacological therapy, we suggest parathyroidectomy (2B).

KDIGO CKD BMD

Table 12 | Suggested frequencies of serum calcium, phosphorus, and PTH measurements according to CKD stage

	Progressive CKD stage 3	CKD stage 4	CKD stages 5 and 5D
Calcium and phosphorus	6–12 months	3–6 months	1–3 months
PTH and alkaline phosphatases	Baseline	6–12 months	3–6 months
Calcidiol	Baseline	Baseline	Baseline

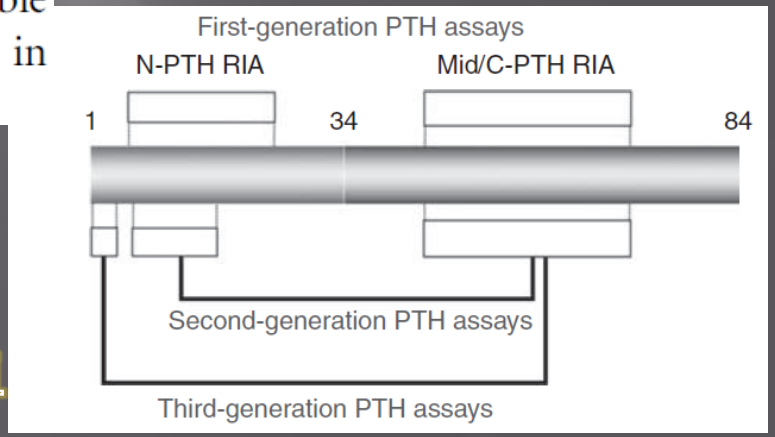
3.1.2 In patients with CKD stages 3–5D, it is reasonable to base the frequency of monitoring serum calcium, phosphorus, and PTH on the presence and magnitude of abnormalities, and the rate of progression of CKD (not graded).

3.1.4 In patients with CKD stages 3–5D, we recommend that therapeutic decisions be based on trends rather than on a single laboratory value, taking into account all available CKD–MBD assessments (1C).

KDIGO CKD BMD

3.1.6 **In reports of laboratory tests for patients with CKD stages 3–5D, we recommend that clinical laboratories inform clinicians of the actual assay method in use and report any change in methods, sample source (plasma or serum), and handling specifications to facilitate an appropriate interpretation of biochemistry data (1B).**

Therefore, the Work Group felt that the widely available second-generation PTH assays should continue to be used in routine clinical practice at present.



Votre laboratoire indique t il le nom du test utilisé ?

KDIGO CKD BMD

Table 17 | Positive predictive value for iPTH and b-ALP to predict bone turnover in patients with CKD stage 5

		High bone turnover			Low bone turnover		
Author, year	*N*	Cutoff	PPV	Sensitivity	Cutoff	PPV	Sensitivity
McCarthy (1989)[225]	41	>1200[a]	79	92	<490[a]	76	93
Hutchison (1993)[146]	30	>200	88	83	<65	78	88
Torres (1995)[215]	119	>450	100	43	<120	89	48
Wang (1995)[216 b]	175	>200	58	88	<150	83	91
Qi (1995)[226 b]	79	>250	80	89			
Couttenye (1996)[227]	103				<150	65	81
					b-ALP	75	78
Urena (1996)[219]	42	>200	92	72	<150	51	70
		b-ALP	90	84	b-ALP	58	70
Gerakis (1996)[218]	114	>200	78	87	<65	45	69
Fletcher (1997)[202 b]	73	>100	89	81			
		b-ALP	97	70			
Carmen Sanchez (2000)[221]	57	>250	92	57	<150	97	92
Coen (2002)[108]	107				<150	54	81
Bervoets (2003)[222]	84				<237	47	78
					b-ALP	57	83
Lehmann (2008)[228]	132	>161	89	75			
		b-ALP	91	71			
Barreto (2008)[229]	97	>300	62	69	<150	83	50

b-ALP, bone-specific alkaline phosphatase; iPTH, intact parathyroid hormone; *N*, number of subjects; PPV, positive predictive value.

[a]C-terminal assay.

[b]Calculated from sensitivity, specificity, and prevalence.

KDIGO CKD BMD

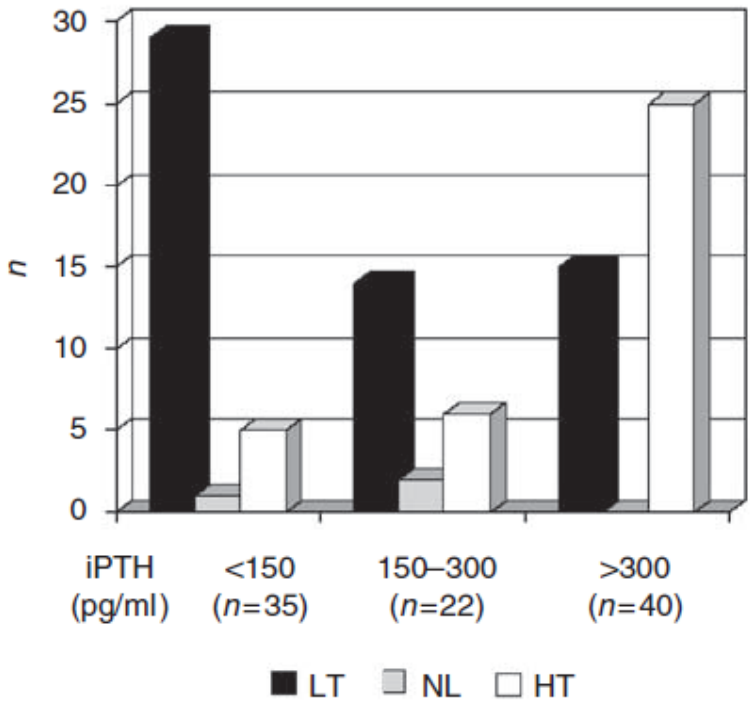


Figure 15 | Comparison of PTH levels to underlying bone histology in chronic hemodialysis patients. Intact PTH levels <150 pg/ml presented a 50% sensitivity, an 85% specificity, and an 83% positive predictive value for the diagnosis of low bone turnover (LT). In contrast, iPTH levels > 300 pg/ml presented a 69% sensitivity, a 75% specificity, and a 62% positive predictive value for the diagnosis of high bone turnover (HT). iPTH, intact parathyroid hormone; n, number of patients; NL, normal bone turnover. Reprinted with permission from Barreto *et al.*[229]

VISER

2 à 9 * valeur max PTH.

a

10 20
Ala–Val–Ser–Glu–Ile–Gln–Phe–Met–His–Asn–Leu–Gly–Lys–His–Leu–Ser–Ser–Met–Glu–Arg–Val–Glu–Trp–Leu–Arg–Lys–Lys–Leu
Gln
30 Asp
50 40 Val
Val–Asn–Asp–Glu–Lys–Lys–Arg–Pro–Arg–Gln–Ser–Ser–Gly–Asp–Arg–Tyr–Ala–Ile–Ser–Ala–Gly–Leu–Ala–Val–Phe–Asn–His
Leu
60 Val
Glu
70 80
Ser–His–Gln–Lys–Ser–Leu–Gly–Glu–Ala–Asp–Lys–Ala–Asp–Val–Asp–Val–Leu–Ile–Lys–Ala–Lys–Pro–Gln

b

10 20
Phe–Met–His–Asn–Leu–Gly–Lys–His–Leu–Ser–Ser–Met–Glu–Arg–Val–Glu–Trp–Leu–Arg–Lys–Lys–Leu
Gln
30 Asp
50 40 Val
Val–Asn–Asp–Glu–Lys–Lys–Arg–Pro–Arg–Gln–Ser–Ser–Gly–Asp–Arg–Tyr–Ala–Ile–Ser–Ala–Gly–Leu–Ala–Val–Phe–Asn–His
Leu
60 Val
Glu
70 80
Ser–His–Gln–Lys–Ser–Leu–Gly–Glu–Ala–Asp–Lys–Ala–Asp–Val–Asp–Val–Leu–Ile–Lys–Ala–Lys–Pro–Gln

c

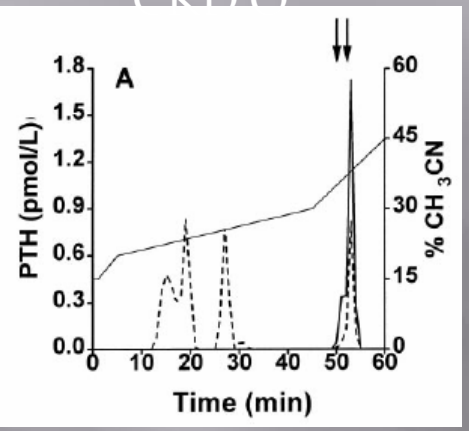
P
10 20
he–Met–His–Asn–Leu–Gly–Lys–His–Leu–Ser–Ser–Met–Glu–Arg–Val–Glu–Trp–Leu–Arg–Lys–Lys–Leu
Gln
30 Asp
50 40 Val
-Lys–Arg–Pro–Arg–Gln–Ser–Ser–Gly–Asp–Arg–Tyr–Ala–Ile–Ser–Ala–Gly–Leu–Ala–Val–Phe–Asn–His
70 80
eu–Gly–Glu–Ala–Asp–Lys–Ala–Asp–Val–Asp–Val–Leu–Ile–Lys–Ala–Lys–Pro–Gln

Influence of Glomerular Filtration Rate on Non-(1-84) Parathyroid Hormone (PTH) Detected by Intact PTH Assays

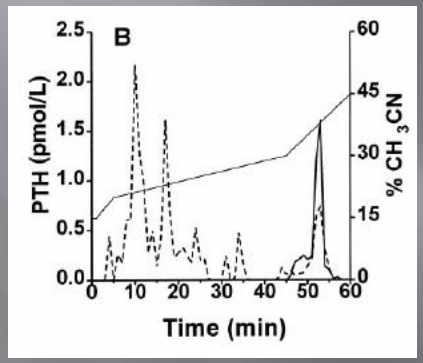
Clinical Chemistry 46:5
697–703 (2000)

Jean-Hugues Brossard,[1,3] Raymond Lepage,[2,4] Héloïse Cardinal,[1,3] Louise Roy,[1,3]
Louise Rousseau,[1] Claude Dorais,[1] and Pierre D'Amour[1,3*]

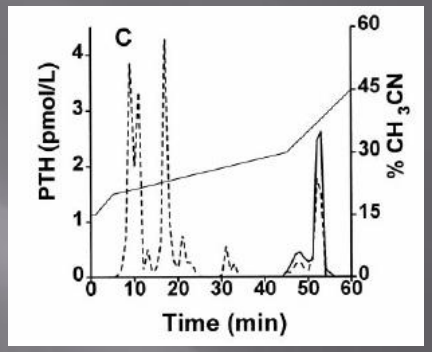
CKD 0



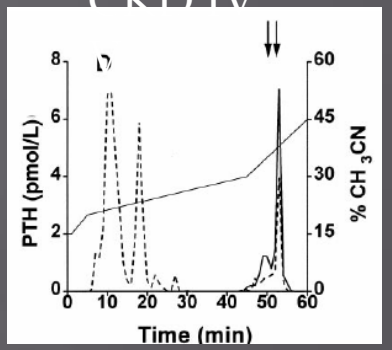
CKD I -

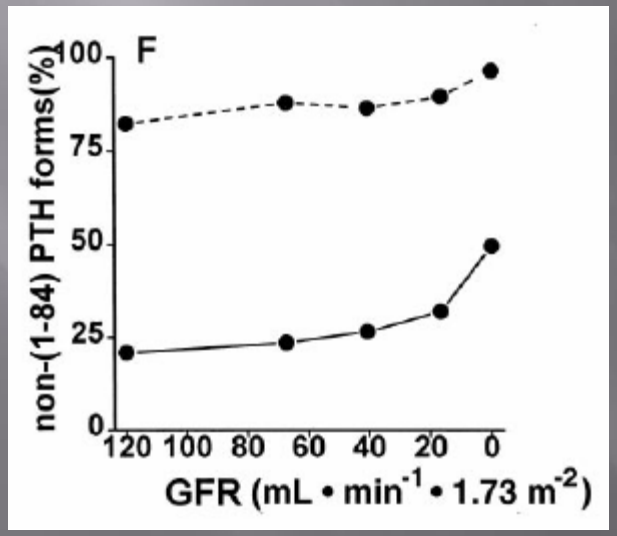


CKD III

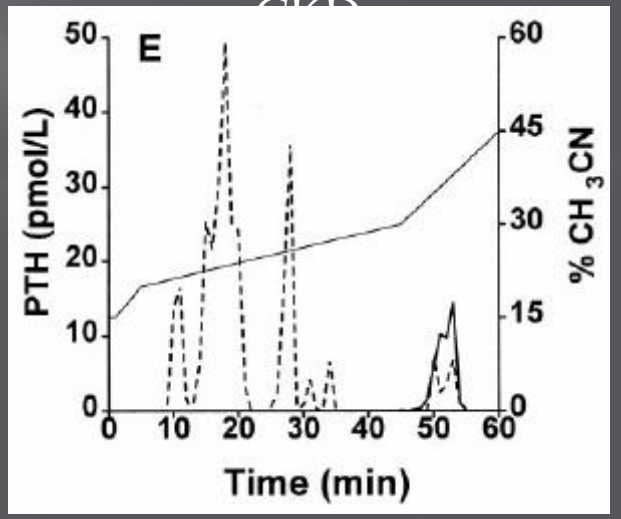


CKD IV





CKD



A non-(1–84) circulating parathyroid hormone (PTH) fragment interferes significantly with intact PTH commercial assay measurements in uremic samples

Clinical Chemistry 44:4
805–809 (1998)

Raymond Lepage,[4] Louise Roy,[1,3] Jean-Hugues Brossard,[1,3] Louise Rousseau,[1,3]
Claude Dorais,[1,3] Claude Lazure,[2] and Pierre D'Amour[1,3*]

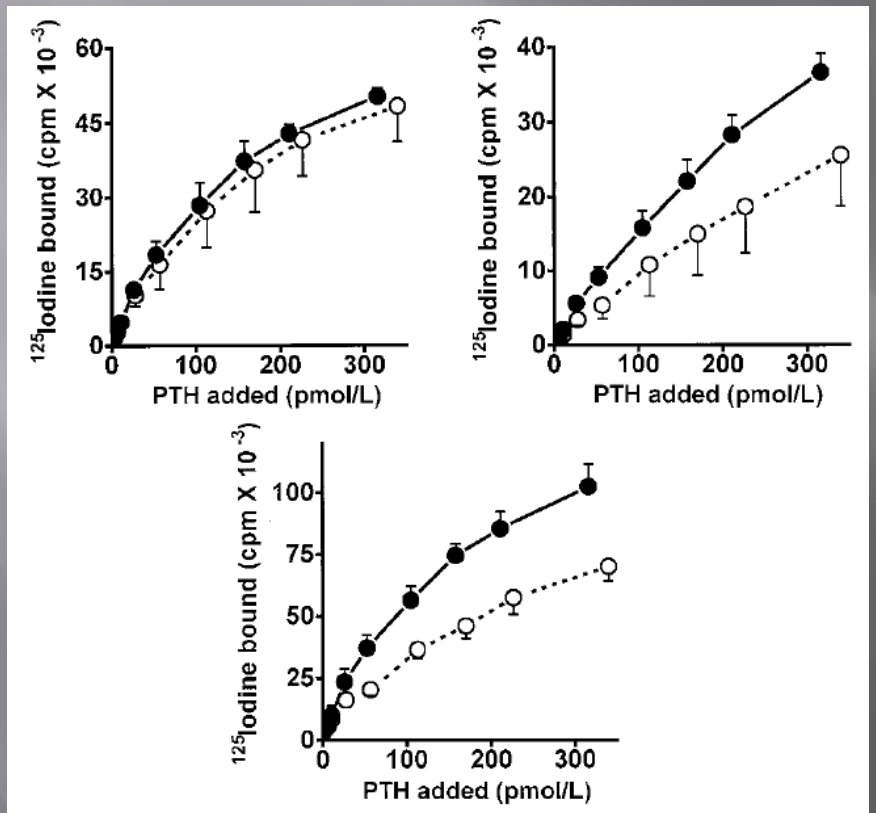
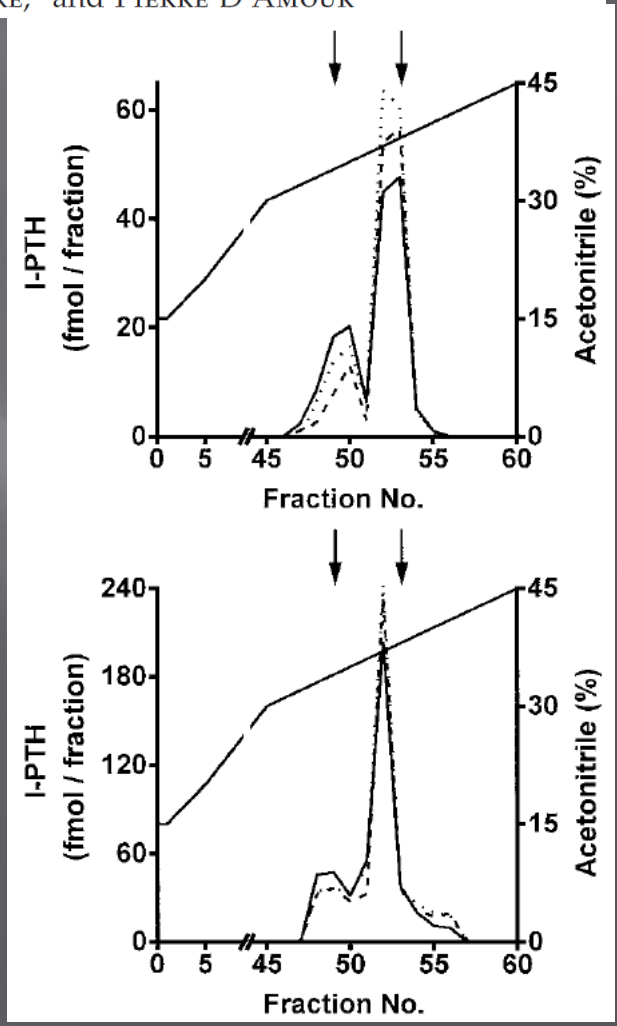


Fig. 3. Immunoreactivity of hPTH(1–84) (*solid lines*) and hPTH(7–84) (*broken lines*) in the Nichols, Incstar, and DSL assays.



The Spectrum of Renal Osteodystrophy

Edited by

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ISIDRO B. SALUSKY, M.D.
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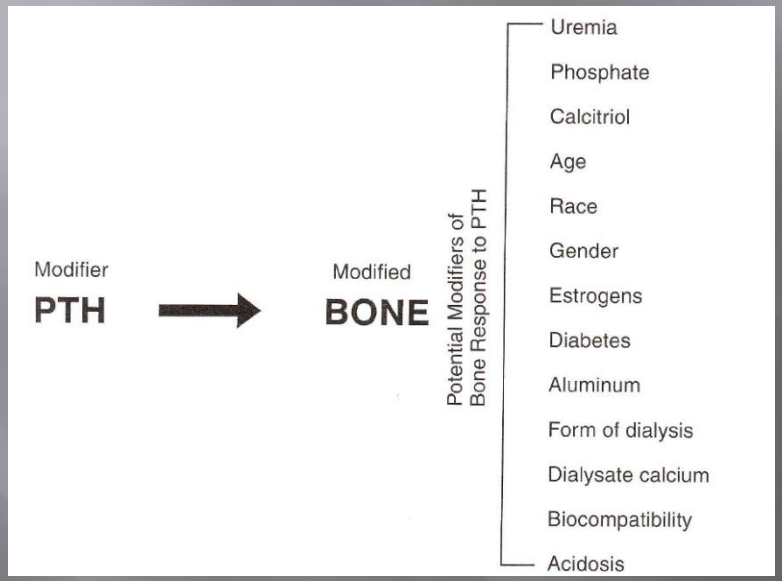
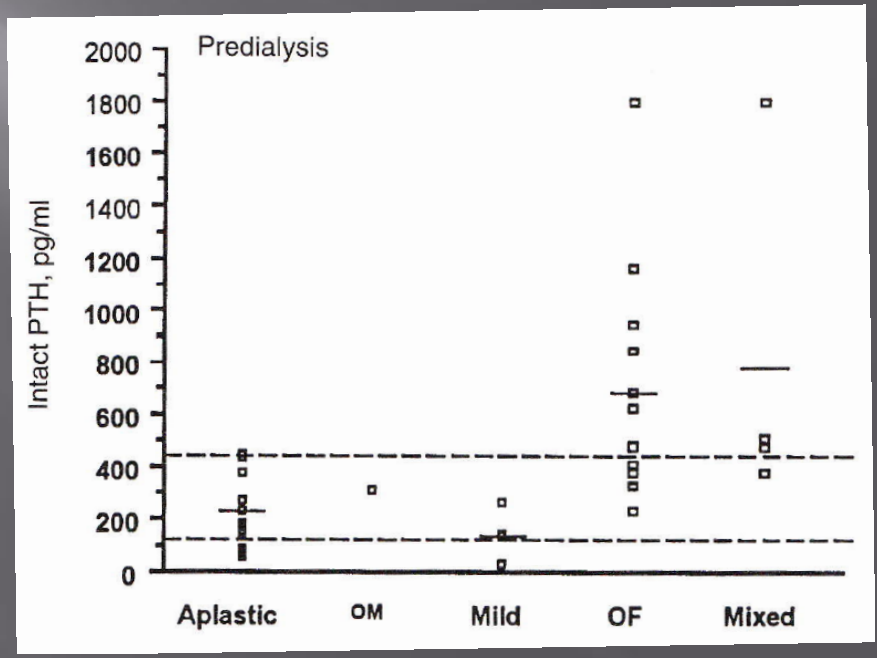




3 eme génération

- Ne tient compte que d'une seul hormone
- Ne tient pas compte de l'hormone 7-84 … peut être inhibitrice !

third generation assays, parathyroid = 23

Double dosage ?

Improved assessment of bone turnover by the PTH-(1-84)/ large C-PTH fragments ratio in ESRD patients

Marie-Claude Monier-Faugere, Zhaopo Geng, Hanna Mawad, Robert M. Friedler, Ping Gao, Tom L. Cantor, and Hartmut H. Malluche

Division of Nephrology, Bone and Mineral Metabolism, Department of Internal Medicine, University of Kentucky, Lexington, Kentucky, and Scantibodies Inc., Santee, California, USA

OH, USA). Plasma intact PTH levels were determined with the IRMA assay for intact PTH (Nichols Institute Diagnostics, San Juan Capistrano, CA, USA). The reference range is 15 to 65 pg/mL. The intra-assay and interassay coefficients of variation were 3.4 and 5.6%, respectively. Plasma PTH-(1-84) was determined with the IRMA assay using a radiolabeled detection antibody specific for the first amino acid from the N-terminal site (Whole PTH™; Scantibodies, Inc., Santee, CA, USA) [11, 12]. The reference range of the assay is 7 to 36 pg/mL based on over 120 normal controls [12]. Intra-assay and interassay coefficients of variation were <5 and <7%,

	Low bone turnover	High or normal bone turnover
Number of patients	28	23
Age *years*	50 ± 3	39 ± 3[a]
Patients on HD/CAPD	16/12	16/7
Male/female	18/10	11/12
Diabetic patients	8/20	4/18
Duration on dialysis *months*	26 ± 4	25 ± 4
Serum calcium *mg/dL*	9.3 ± 0.2	9.0 ± 0.2
Ionized calcium *mEq/L*	4.85 ± 0.11	4.70 ± 0.08
Serum phosphorus *mg/dL*	6.1 ± 0.4	7.1 ± 0.5
Serum bone-specific alkaline phosphatase *μg/L*	19.8 ± 3.45	35.1 ± 4.39[a]
Serum osteocalcin *ng/mL*	21.5 ± 4.8	34.5 ± 5.1

Abbreviations are: HD, hemodialysis; CAPD, chronic ambulatory peritoneal dialysis.

[a] Different from low bone turnover, $P < 0.01$, student t test

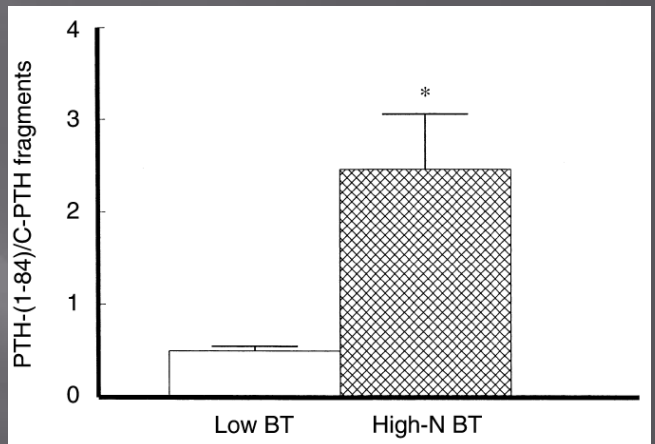


Fig. 2. Mean value of the PTH-(1-84)/C-PTH fragments ratio in 51 patients on chronic maintenance dialysis with low bone turnover (low BT) and high or normal bone turnover (high-N BT). The asterisk indicates significant difference between high or normal and low bone turnover ($P < 0.01$).

Kidney International, Vol. 60 (2001), pp. 1460–1468

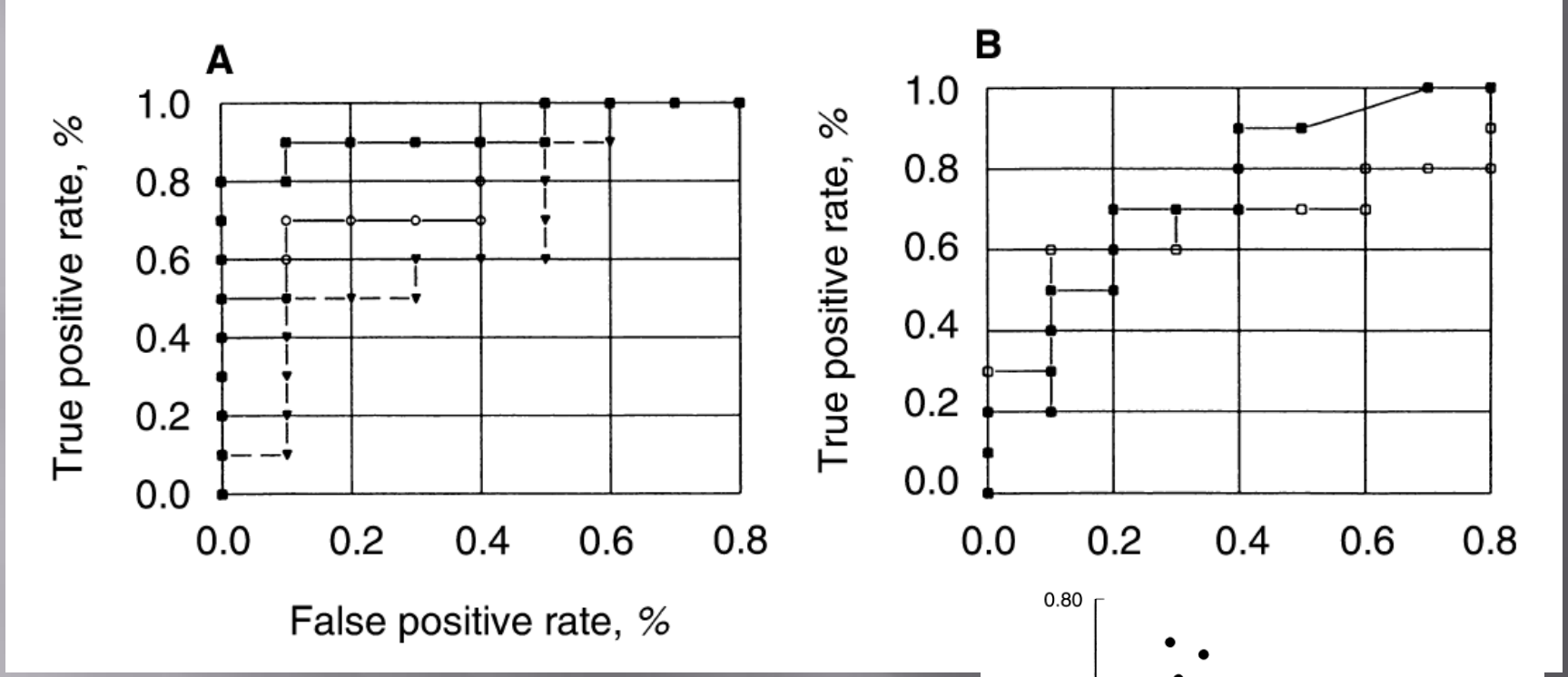


Fig. 4. Receiver-operator characteristics (ROC) curves for the prediction of bone turnover in chronically dialyzed patients. (*A*) Symbols are: plasma PTH-(1-84)/C-PTH fragment ratio (■), plasma PTH-(1-84) (○), and plasma intact PTH (▼). (*B*) Symbols are: serum bone-specific alkaline phosphatase (■) and serum osteocalcin (□).

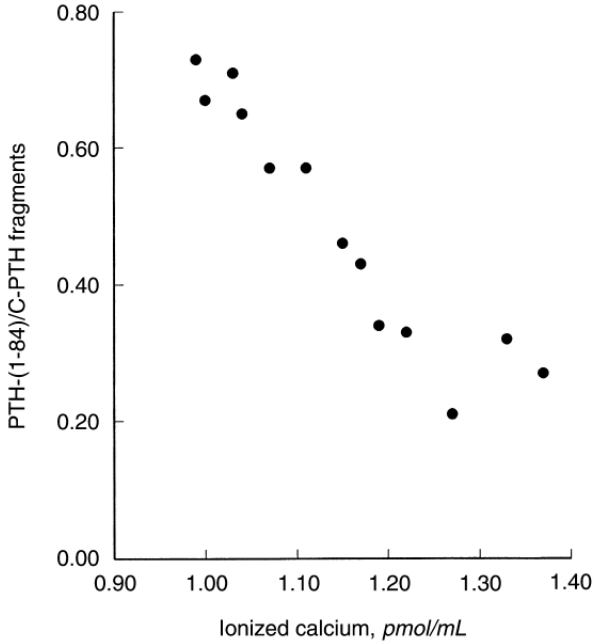


Fig. 8. Relationship between ionized calcium levels and PTH-(1-84)/C-PTH fragments ratio in a patients on dialysis during calcium gluconate infusion.

Nephrol Dial Transplant (2008) 23: 1650–1658

Third-generation parathyroid hormone assays and all-cause mortality in incident dialysis patients: the CHOICE study

Table 4. Associations of PTH with all-cause mortality in patients with PTH measurement within 6 months of starting dialysis from the CHOICE cohort, recruited 1995–1998, reported as hazard ratios (95% confidence intervals)

	Model 1[a] ($n = 515$)	Model 2[b] ($n = 475$)	Model 3[c] ($n = 455$)
Total PTH <150 ($n = 115$)	0.96 (0.70–1.30)	1.01 (0.71–1.43)	0.97 (0.66–1.43)
Total PTH 150–300 ($n = 298$)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
Total PTH >300 ($n = 102$)	0.98 (0.66–1.47)	1.24 (0.80–1.90)	1.41 (0.89–2.23)
1–84 PTH <80 ($n = 96$)	1.01 (0.73–1.40)	1.07 (0.74–1.56)	1.13 (0.75–1.71)
1–84 PTH 80–160 ($n = 308$)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
1–84 PTH >160 ($n = 111$)	1.05 (0.71–1.55)	1.27 (0.83–1.94)	1.62 (1.03–2.54)*
7–84 PTH <70 ($n = 117$)	0.98 (0.71–1.35)	1.05 (0.74–1.49)	1.03 (0.70–1.52)
7–84 PTH 70–140 ($n = 303$)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
7–84 PTH >140 ($n = 95$)	1.04 (0.69–1.56)	1.30 (0.84–2.03)	1.51 (0.94–2.42)
Ratio < 1.0 ($n = 194$)	1.0 (ref.)	1.0 (ref.)	1.0 (ref.)
Ratio 1.0–1.3 ($n = 171$)	0.88 (0.65–1.19)	0.84 (0.60–1.18)	0.95 (0.65–1.38)
Ratio ≥ 1.4 ($n = 150$)	0.99 (0.72–1.35)	0.92 (0.65–1.30)	1.04 (0.71–1.53)

*$P < 0.05$

[a]Adjusted for demographic characteristics: age, sex and race.

[b]Adjusted for demographic and clinical characteristics: baseline modality, ICED category, baseline diabetes mellitus, baseline employment, smoking, late referral time, intravenous vitamin D use and BMI (kg/m^2).

[c]Adjusted for demographic, clinical and laboratory characteristics: albumin, hemoglobin, calcium, phosphate and log C-reactive protein.

Michal L. Melamed[1], Joseph A. Eustace[2,4], Laura C. Plantinga[2,3], Bernard G. Jaar[2,3,5], Nancy E. Fink[2,3,5], Rulan S. Parekh[2,3,5], Josef Coresh[2,3,5], Zan Yang[6], Tom Cantor[6] and Neil R. Powe[2,3,5]

Contrôle du marché (CM) Afssaps 2007- 2008 des dosages de parathormone (PTH)

Experts : Yvonne FULLA (coordonnateur), Philippe CHANSON , Didier CHEVENNE, Denis FOUQUE, Pascal HOUILLIER, Xavier PARENT, Jean-Claude SOUBERBIELLE, Chantal VALAT. Afssaps : Gaëlle LE BRUN, Muriel DURAN CORDOBES, Francis POISSON

- Les trousses de 1ère génération qui regroupent les premiers dosages reposant sur une technique par compétition (RIA) et qui ne sont plus commercialisés pour la pratique clinique
- Les trousses de 2ème génération qui sont constituées des premiers dosages en sandwich (immunométriques). Elles reconnaissent le fragment 1-84 à 100% et le fragment 7-84 entre 50 et 100%
- Les trousses de 3ème génération qui représentent également des dosages immunométriques mais qui reconnaissent le fragment 1-84 à 100% ainsi qu'une autre molécule, appelée amino-PTH (N-PTH), dont la structure n'est pas encore clairement identifiée, et ne reconnaissent pas le fragment 7-84

Allegro intact PTH - société Nichols Institute

standard 79/500

préparation 95/646

afssaps

Agence française de sécurité sanitaire des produits de santé

Direction de l'Evaluation des Dispositifs Médicaux
Département Surveillance du Marché
Unité Evaluation et Contrôle du Marché - DIV

DIASORIN	LIAISON N TACT PTH	Intacte	1Ac anti 1-34 PTH 1 Ac anti 39-84 PTH	52%
	N-TACT-PTH SP IRMA	Intacte	1Ac polyclonal anti 1-34 PTH 1 Ac polyclonal anti 39-84 PTH	Non précisé

DIASORIN	LIAISON N TACT PTH	17.3-72.9 pg/ml (n=105)
	N-TACT-PTH SP IRMA	13-54 pg/ml (n=129)

DIASORIN	LIAISON N TACT PTH	PTH 1 – 84 : 100% PTH 39 – 84 (200 000 pg/ml) : 0,1% PTH 53 - 84 (200 000 pg/ml) : 0,1% PTH 39 – 68 (200 000 pg/ml) : 0,1% PTH 44 – 68 (200 000 pg/ml) : 0,1% PTH 1 –34 (200 000 pg/ml) : 0,1% PTH 13 - 34 (200 000 pg/ml) : 0,1% PTH 7 – 84 (200 000 pg/ml) : 52%
	N-TACT-PTH SP IRMA	PTH 1 – 84 : 100% PTH 39 – 84 < 0,1% PTH 53 – 84 < 0,1% PTH 39 – 68 < 0,1% PTH 44 – 68 < 0,1% PTH 1 – 34 < 0,1% PTH 13 – 34 < 0,1%

DIASORIN	LIAISON N TACT PTH	pg/ml x 0,106 = pmol/l (pg/ml)	**non précisé**
	N-TACT-PTH SP IRMA	non précisé (pg/ml)	**non précisé**

afssaps
Agence française de sécurité sanitaire des produits de santé
Direction de l'Evaluation des Dispositifs Médicaux
Département Surveillance du Marché
Unité Evaluation et Contrôle du Marché - DIV

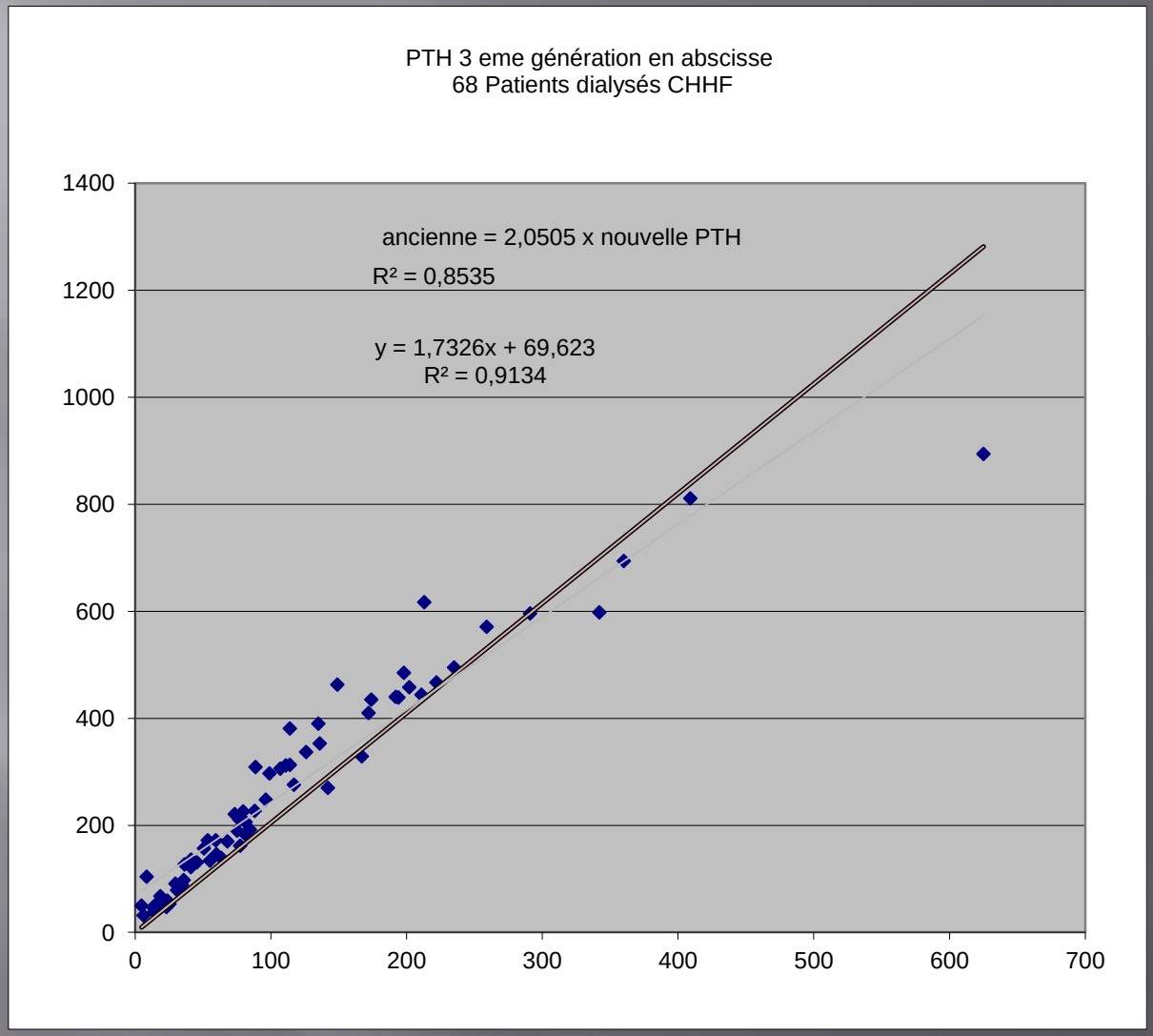
Liaison N tact Pth = 0.75 Allegro +2.6 (KI 2006 70 345-350)

PTH 3eme génération au CHHF

- → Analyse en hémodialyse.
- → Analyse en prédialyse.
- → (?) Analyse à fonction rénale normale (non en notre possession).
- → (?) Analyse dossier avec hyperparthyroïdie primaire (non en notre possession)

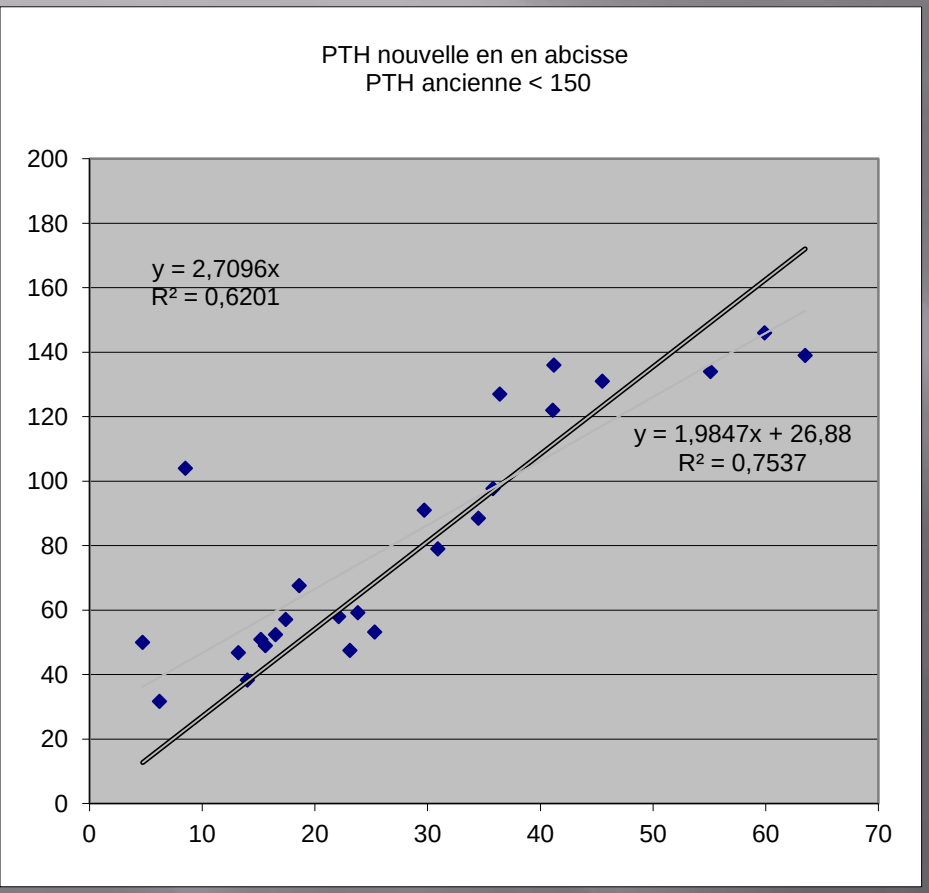
3eme génération et hémodialyse

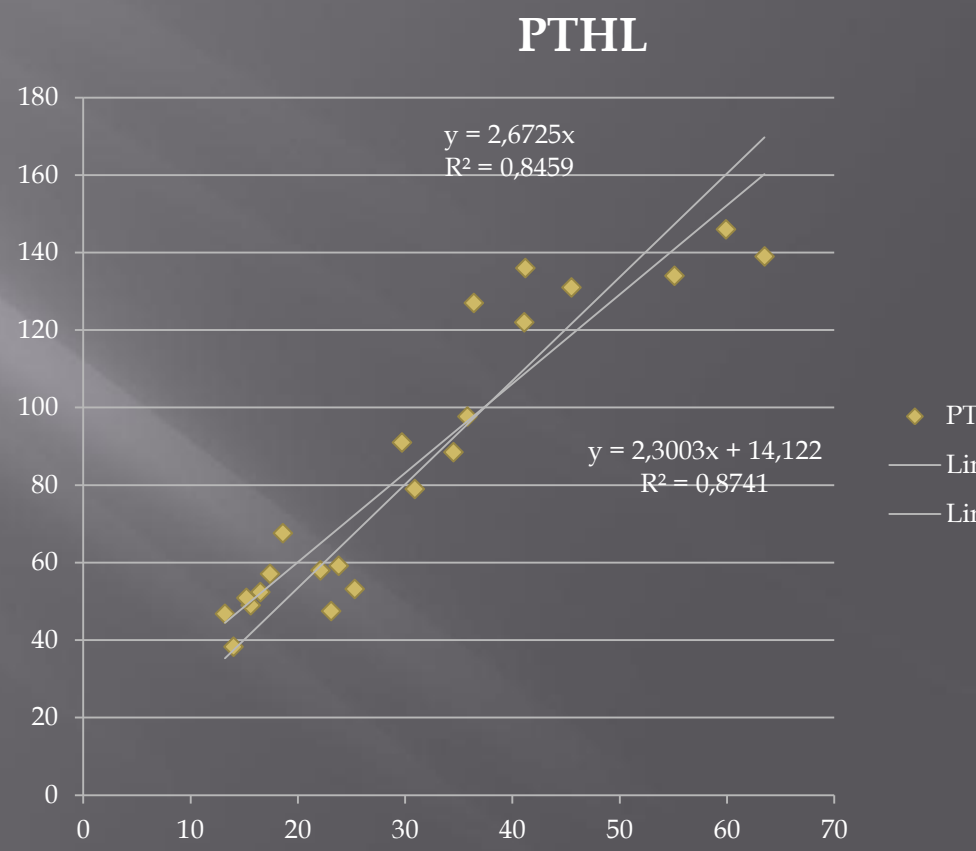
- Prélèvement lors du grand bilan 30/11 au 02/12/2011 concernant les patients en hémodialyses centre (Site Hornu: n=65) et en auto – dialyse (n=6).
- Site Hornu 2 patients exclu car PTH 3eme génération sous le seuil de détection.



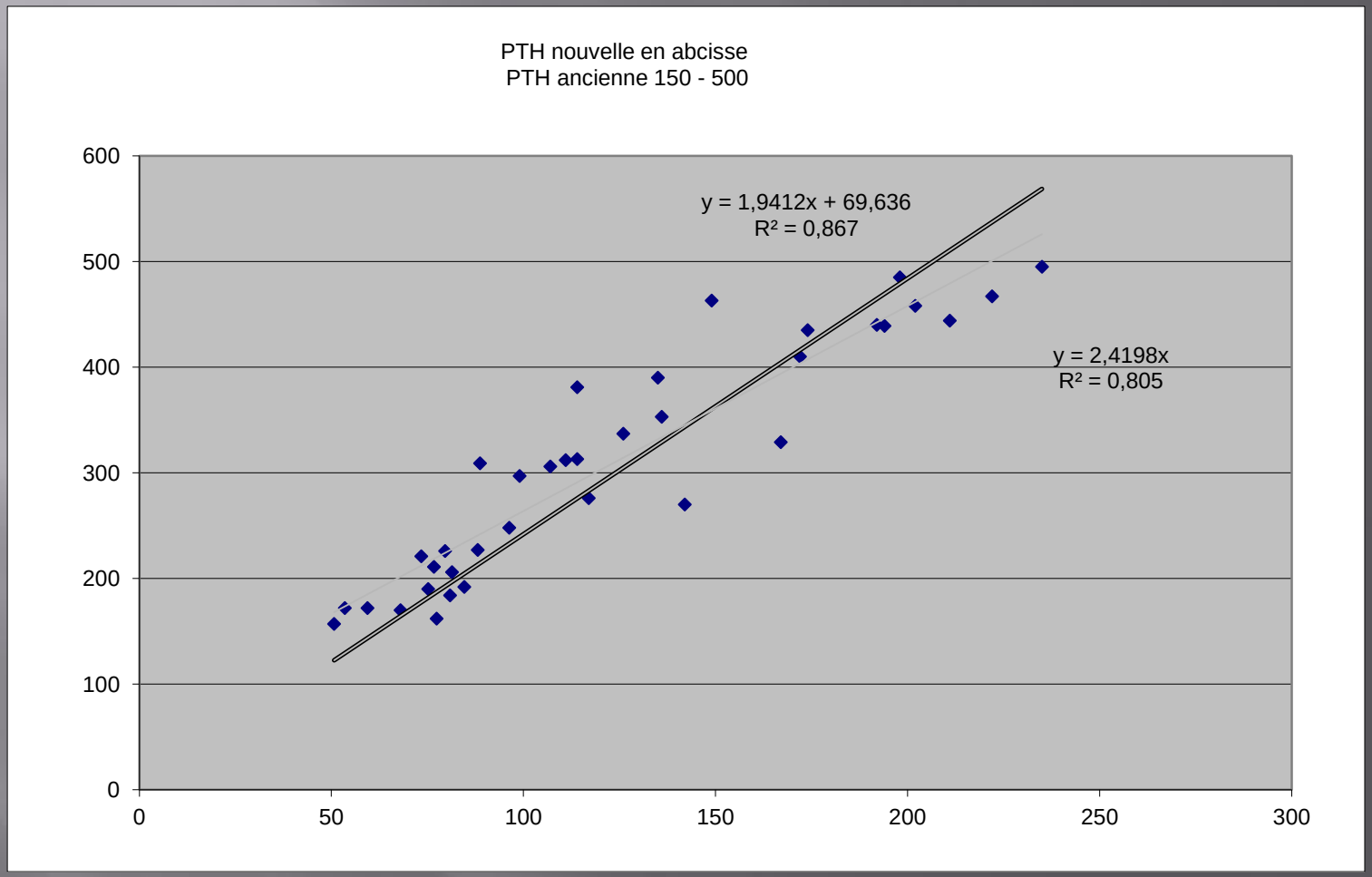
Limite PTH basse: 46 ou 73

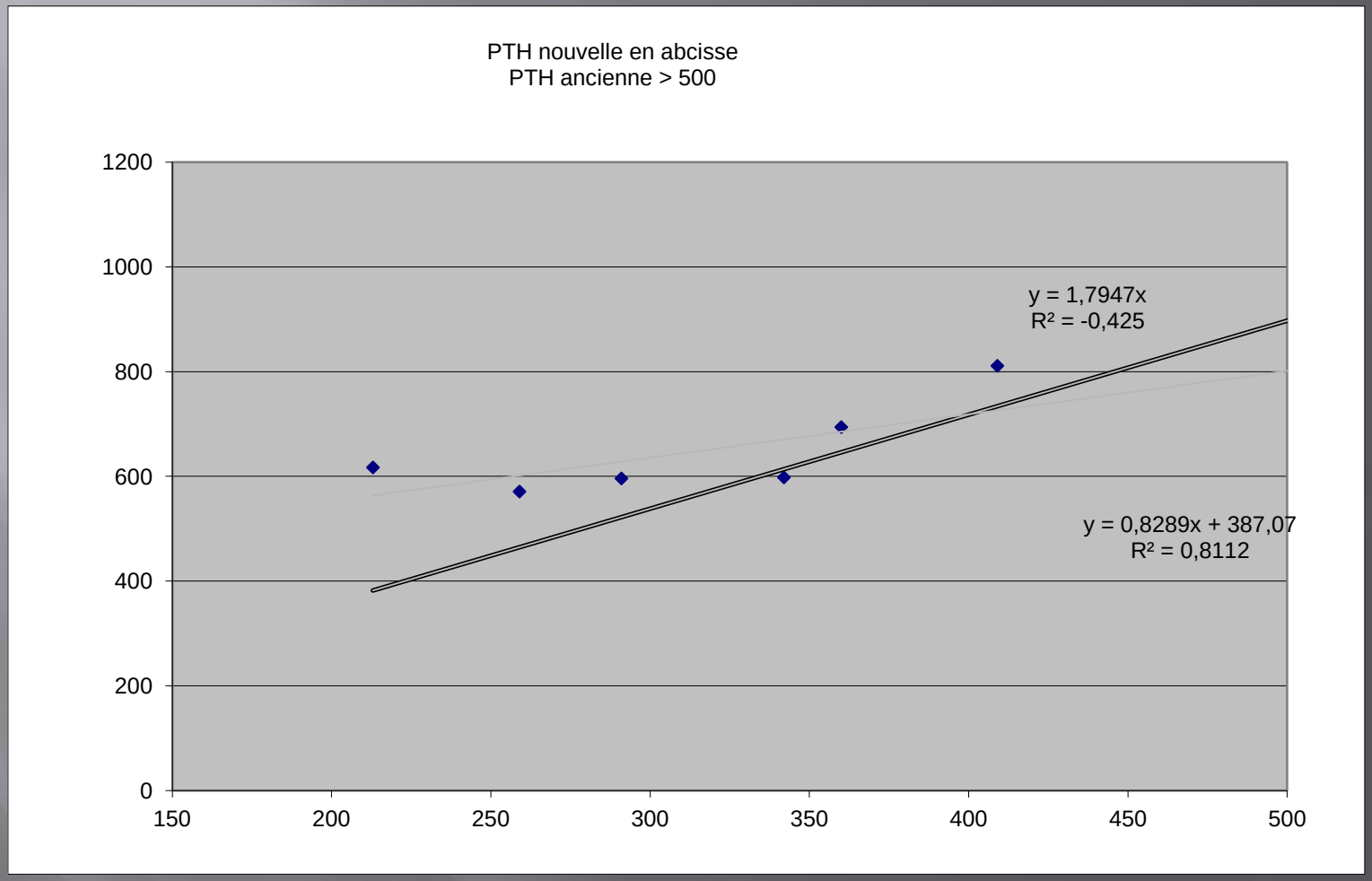
CKD – BMD: Low Turnover



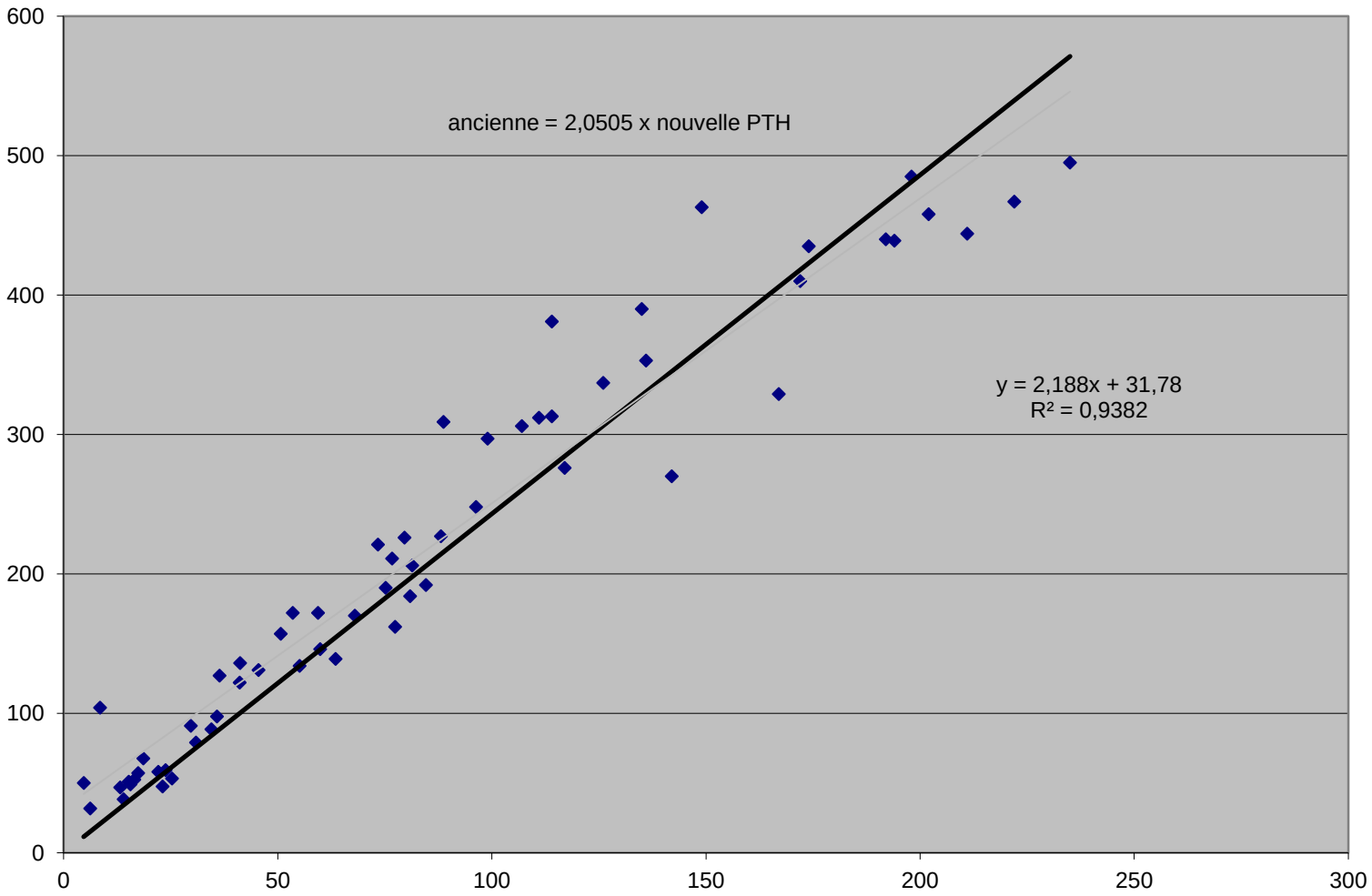


Limite PTH basse: 51 ou 54


PTH nouvelle en abcisse
PTH ancienne 150 - 500
y = 1,9412x + 69,636
R² = 0,867
y = 2,4198x
R² = 0,805
600
500
400
300
200
100
0
0
50
100
150
200
250
300


PTH nouvelle en abcisse
PTH ancienne > 500
1200
1000
800
600
400
200
0
150
200
250
300
350
400
450
500
y = 1,7947x
R² = -0,425
y = 0,8289x + 387,07
R² = 0,8112

PTH nouvelle en abcisse
PTH ancienne 0 - 500

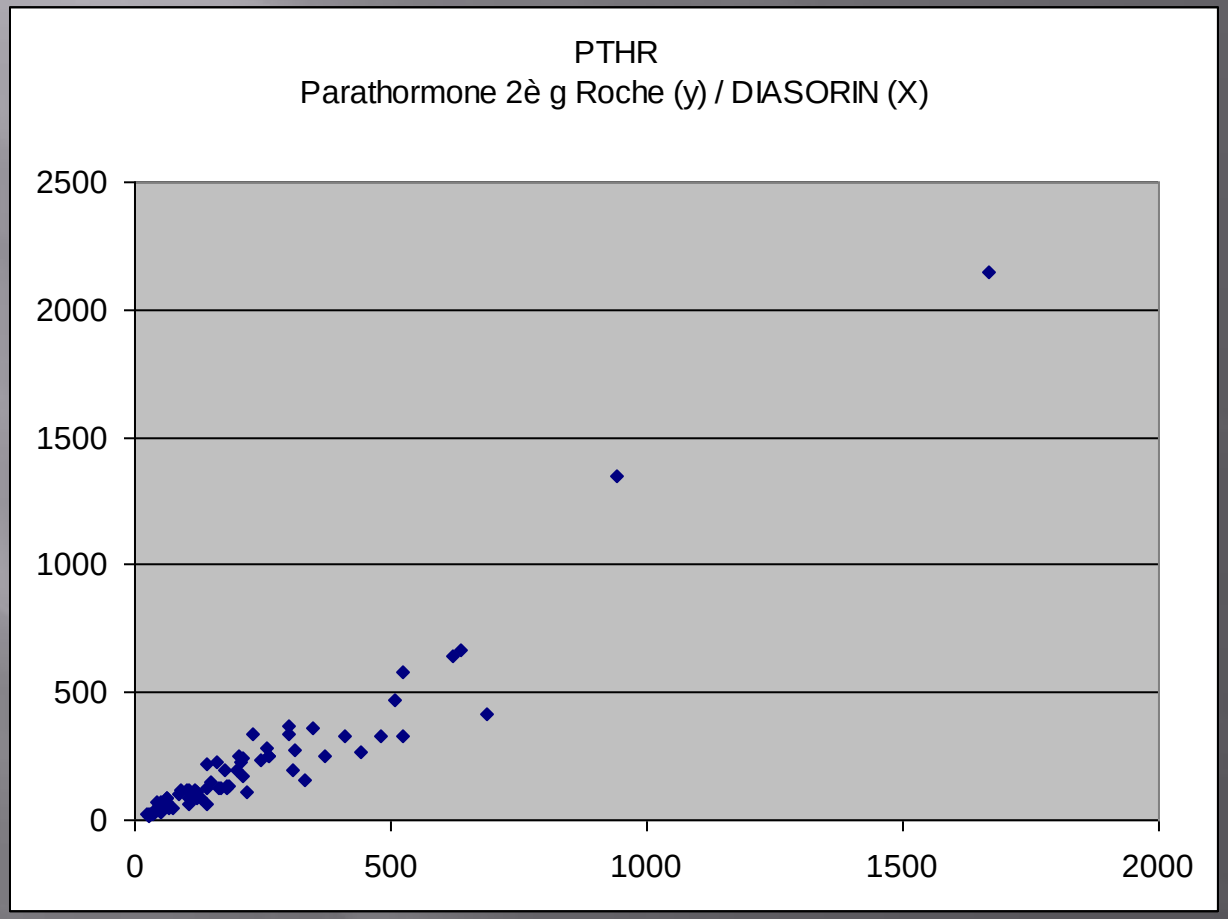


Quelle(s) formule(s)

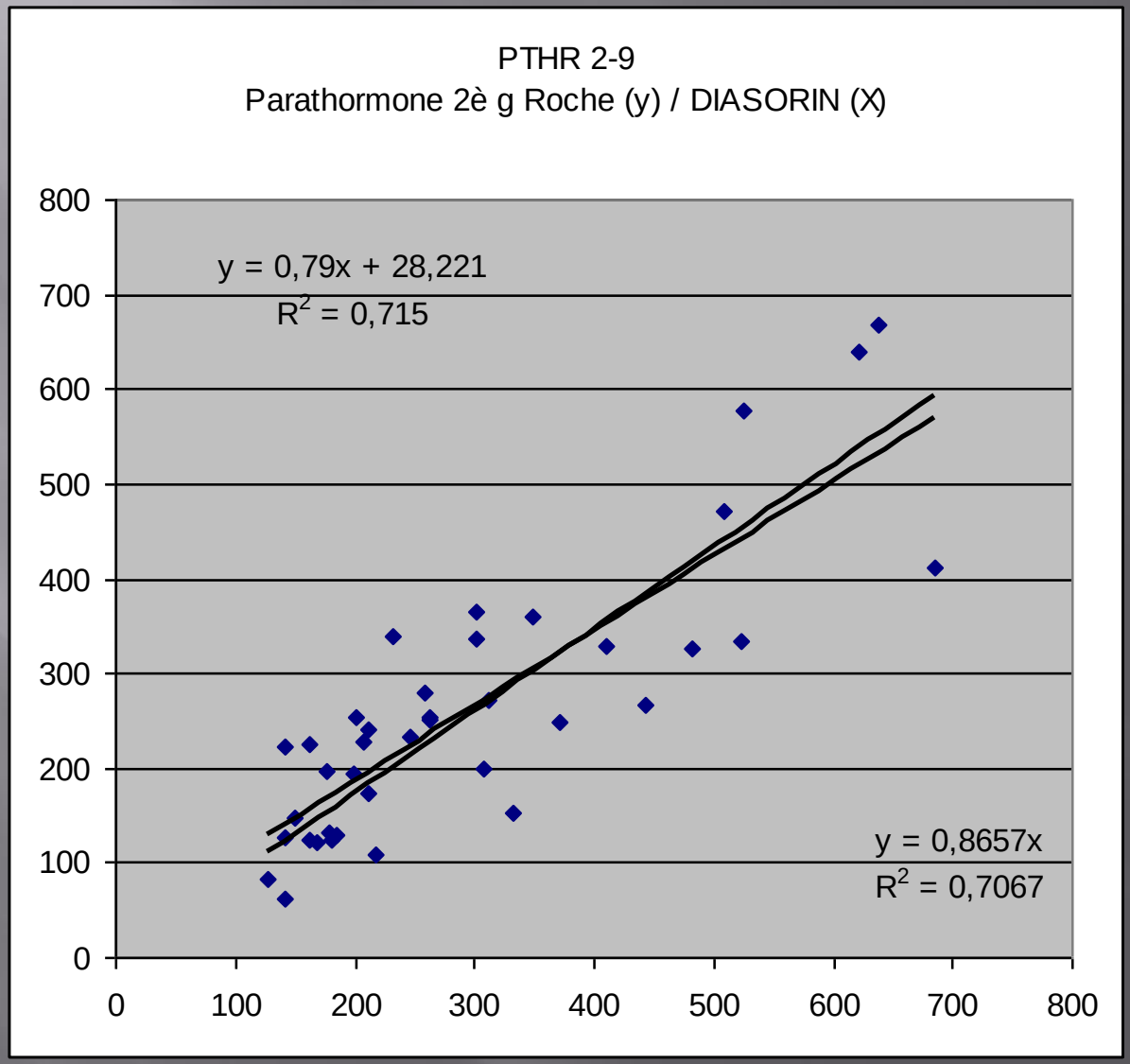
VALEUR PTH ancienne	Formule	r2
< 150	2.71*PTH3	0.62
< 150	1.985*PTH3+26.88	0.75
10 -150	2.672*PTH3	0.85
10-150	2.30*PTH3+14.1	0.87
0 -500	2.43 * PTH3	0.92
0- 500	2.188*PTH3 + 31.78	0.938
150- 500	1.94*PTH3 + 69.6	0.867
150- 500	2.419*PTH3	0.805
> 500	0.8289*PTH3+387.07	0.811
> 500	1.795*PTH3	-0.42

- Pour Critère 300 – 800 (+ critère Ca/P/Vit D avant).
  - Facteur correctif 2.05 suffisant.
- Pour critère > 800
  - Considérer un PTH 3eme génération > 450 par sécurité.

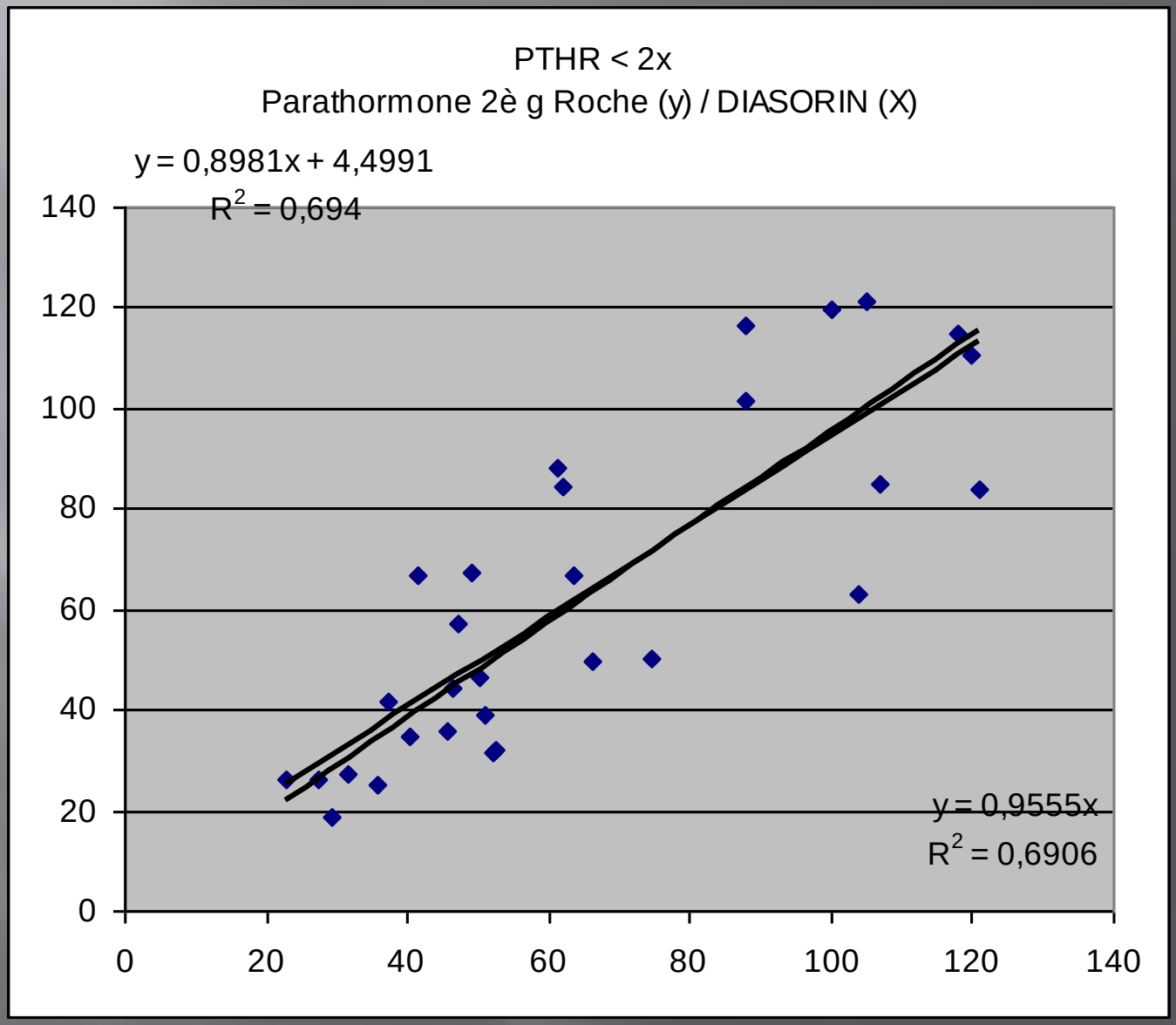
Corrélation entre 2 eme génération



Corrélation entre 2 eme génération



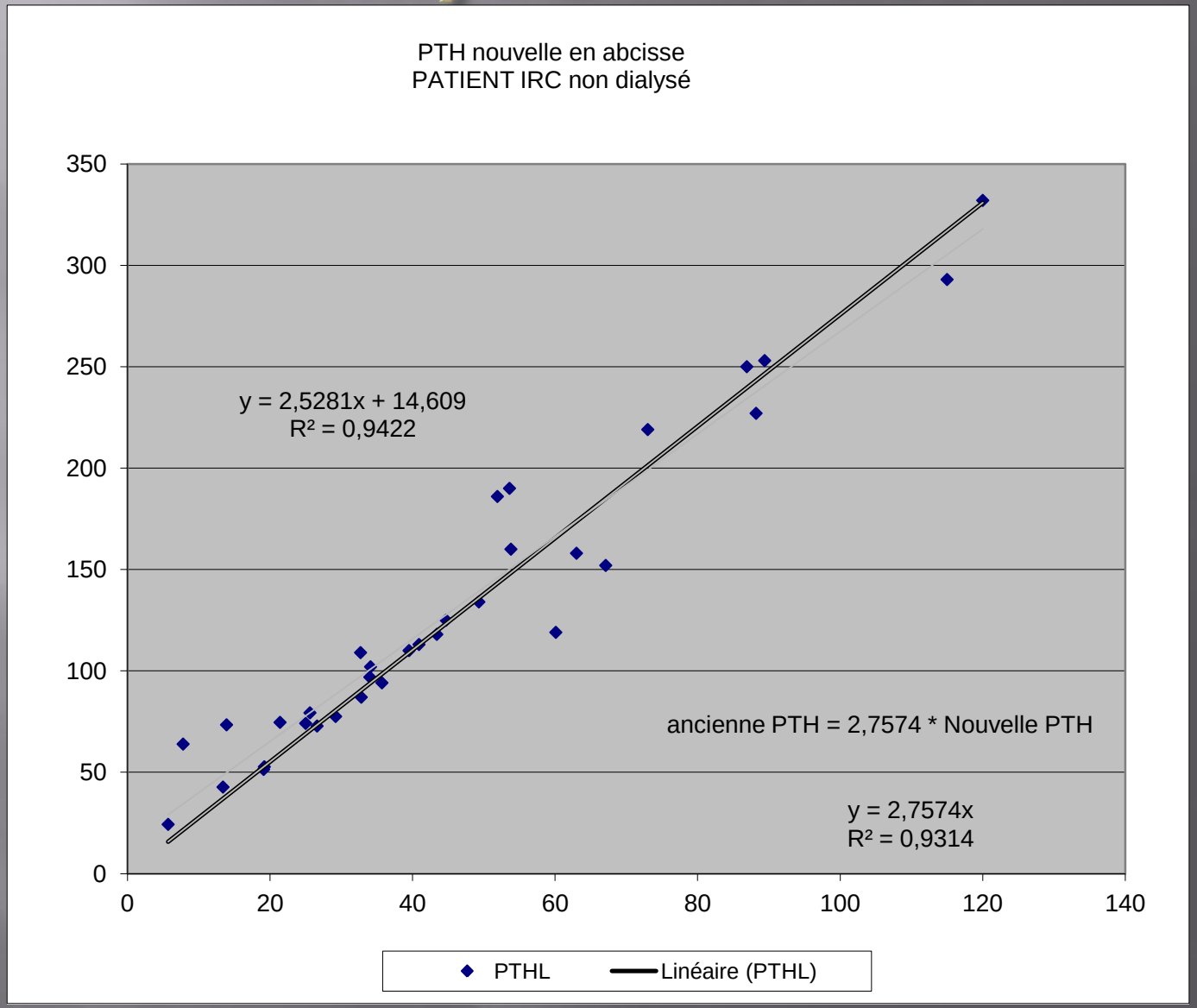
Corrélation entre 2 eme génération



Patient en prédialyse

- Analyse 30 novembre au 10 décembre 2010
- Nombre d'analyse: 33
- Nombre de patient: 20.
- Age 40 à 87 ans.

Analyse « brute »

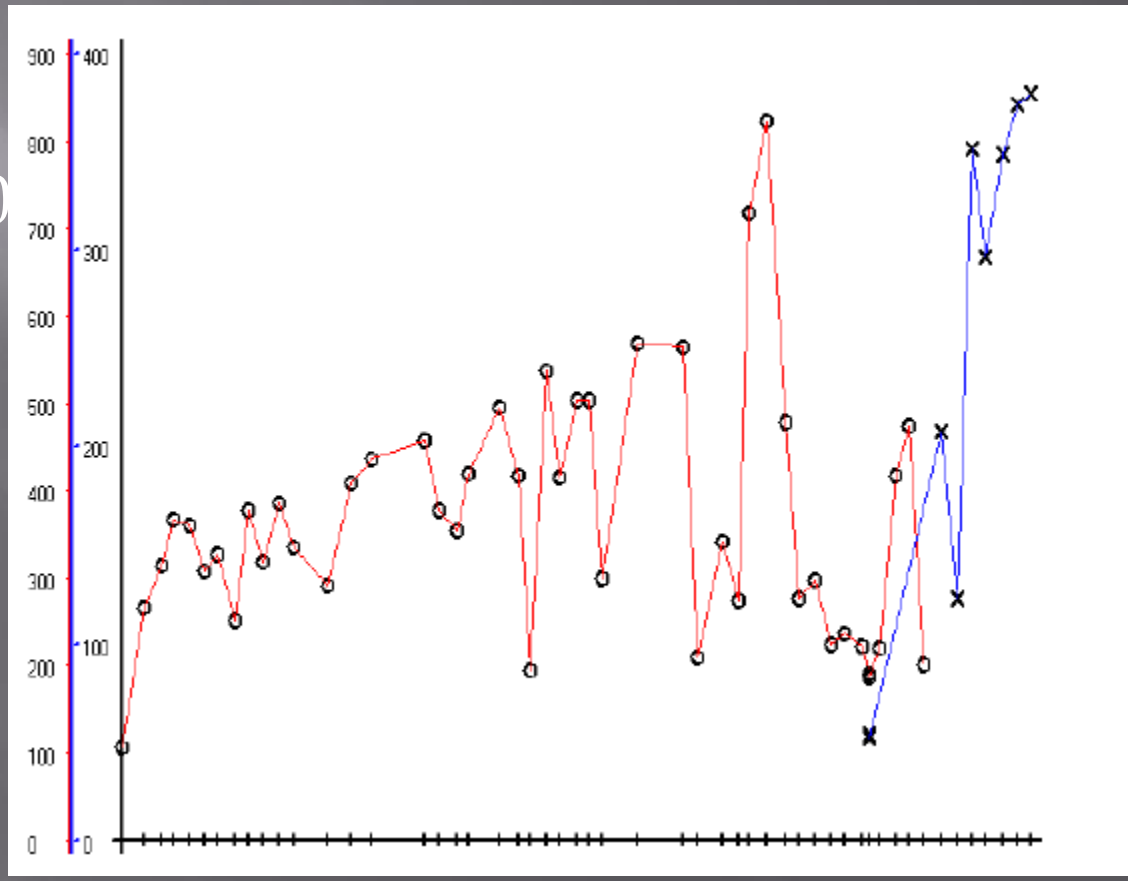


Extrèmes

Patient	Facteur Correctif
A	3,54
	3,58
B	4,26
C	5,28
	8,19

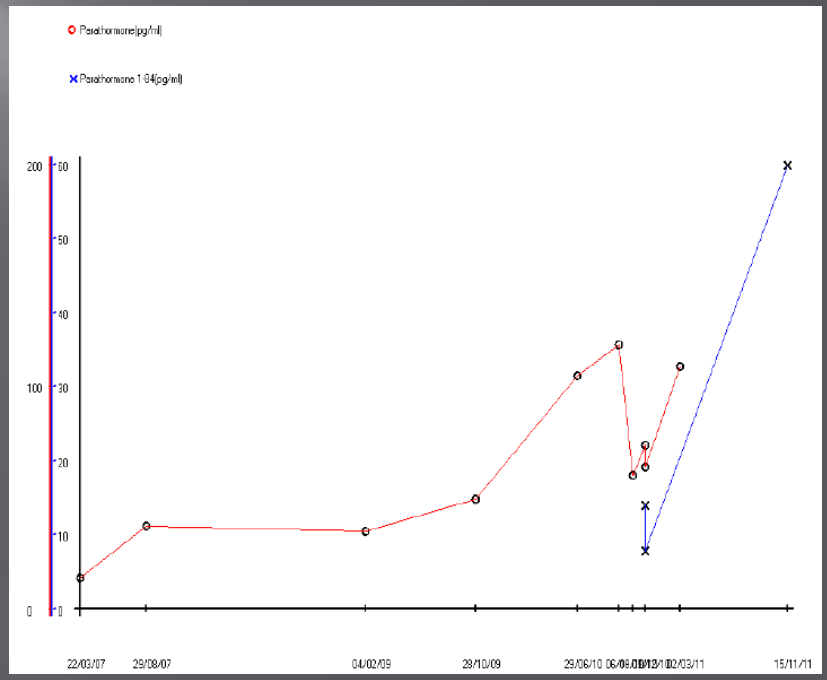
Patient A

- Homme diabetique
- Clerance MDRD < 20 depuis 2007.
- Rapport Prot./Créat. : 1,61
- Mimpara 30 mg.
- PTH2/PTH 3: 190/53.6 et 186/51.9



Patient B

- Femme 61 ans: créatinine 0.95 mg/dL
- HTA sévère avec ATCDT CV.
- PTH2/PTH3: 24.3 / 5.7
- Pas de Protéinurie.

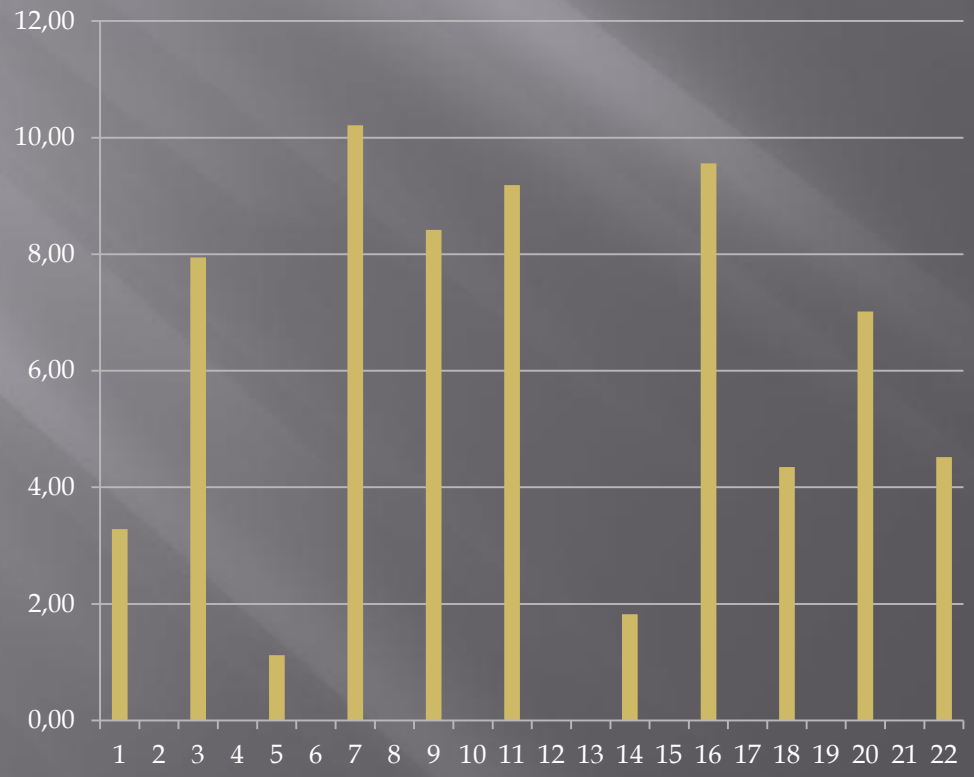


Patient C

- Femme: 40 ans
- IRC: créatinine:
- HSF : syndrome nephrotique vrai
- PTH2/PTH3: 63.9 / 7.8 et 73.4 / 13.9

Variation du rapport PTH 2 / PTH 3 entre deux dosages consécutifs.

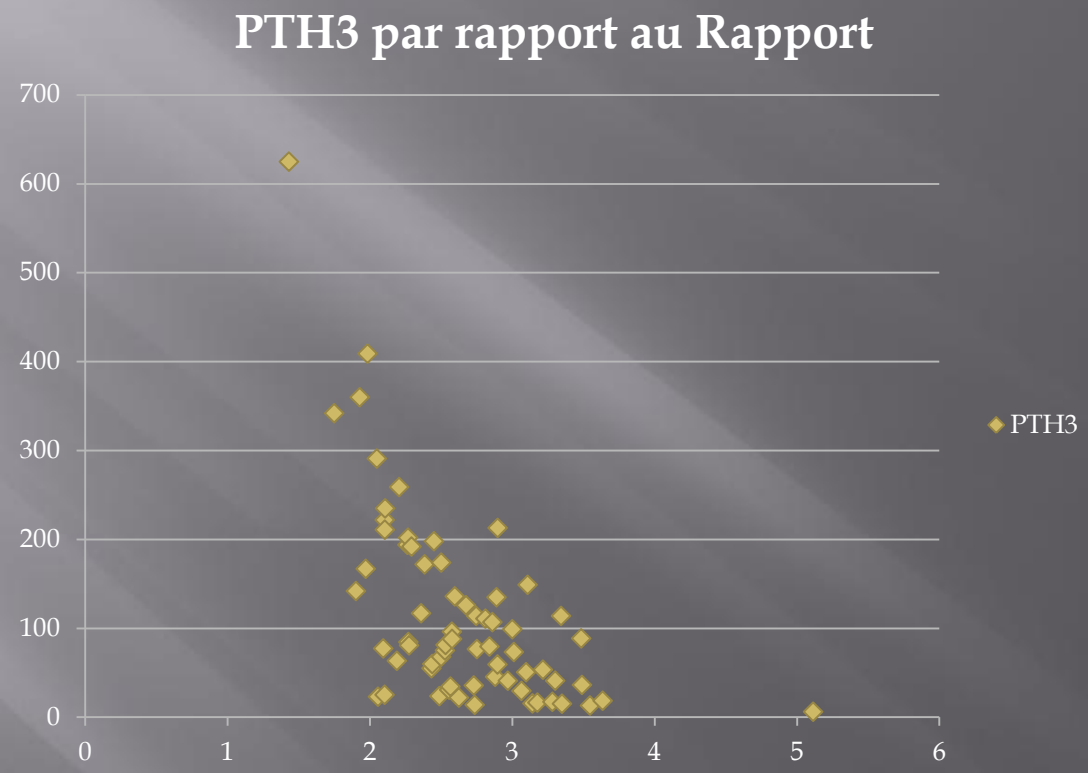
- 12 patients en prédialyses ont bénéficié d'un double dosage.Patient C éliminé il reste:



Conclusion prédialyse

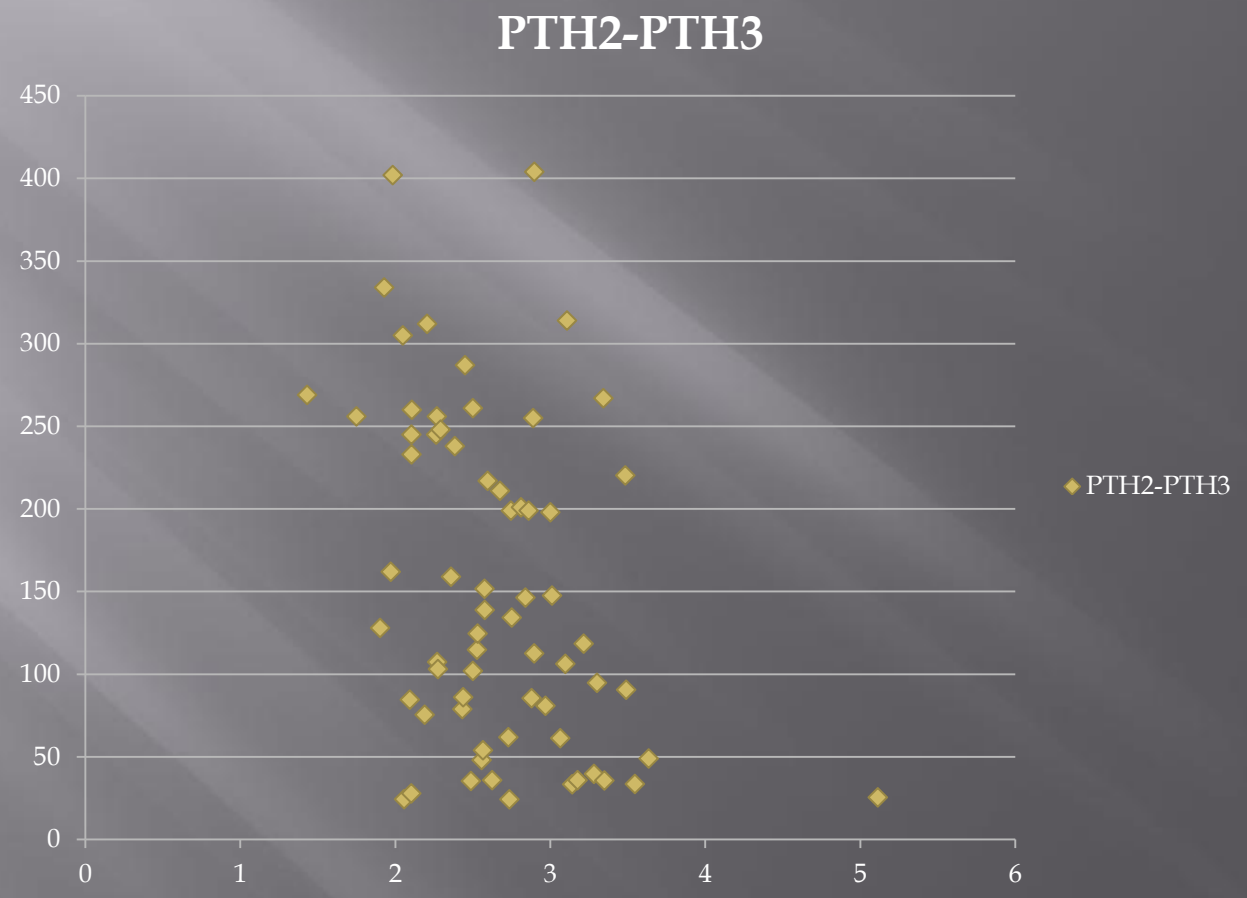
- Multiplier la valeur de la 3eme génération par 2.75 pour la corréler à la 2eme génération.
- Dispersion maximum 10 %

Autres analyses ?

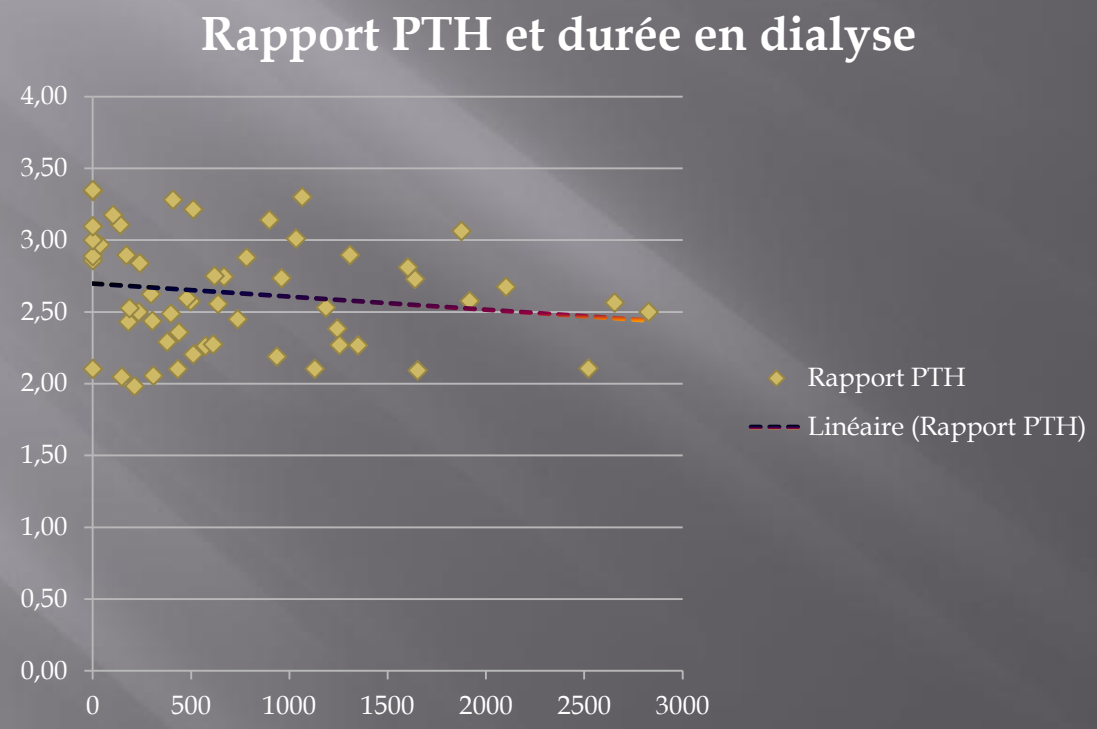


- Analyse de la relation entre la PTH3 (whole 1-84) par rapport à son dosage. Donc plus le dosage i PTH 1-84 est éléevé moins le rapport ancienne sur nouvelle est élevé… est ce que cela témoigne d'une diminution du taux de 7-84 //? Relation à la clearance ?

Analyse fragement 7 – 84 et rapport PTH2/PTH3



Relation entre la durée en dialyse et le Rapport PTH2/PTH3



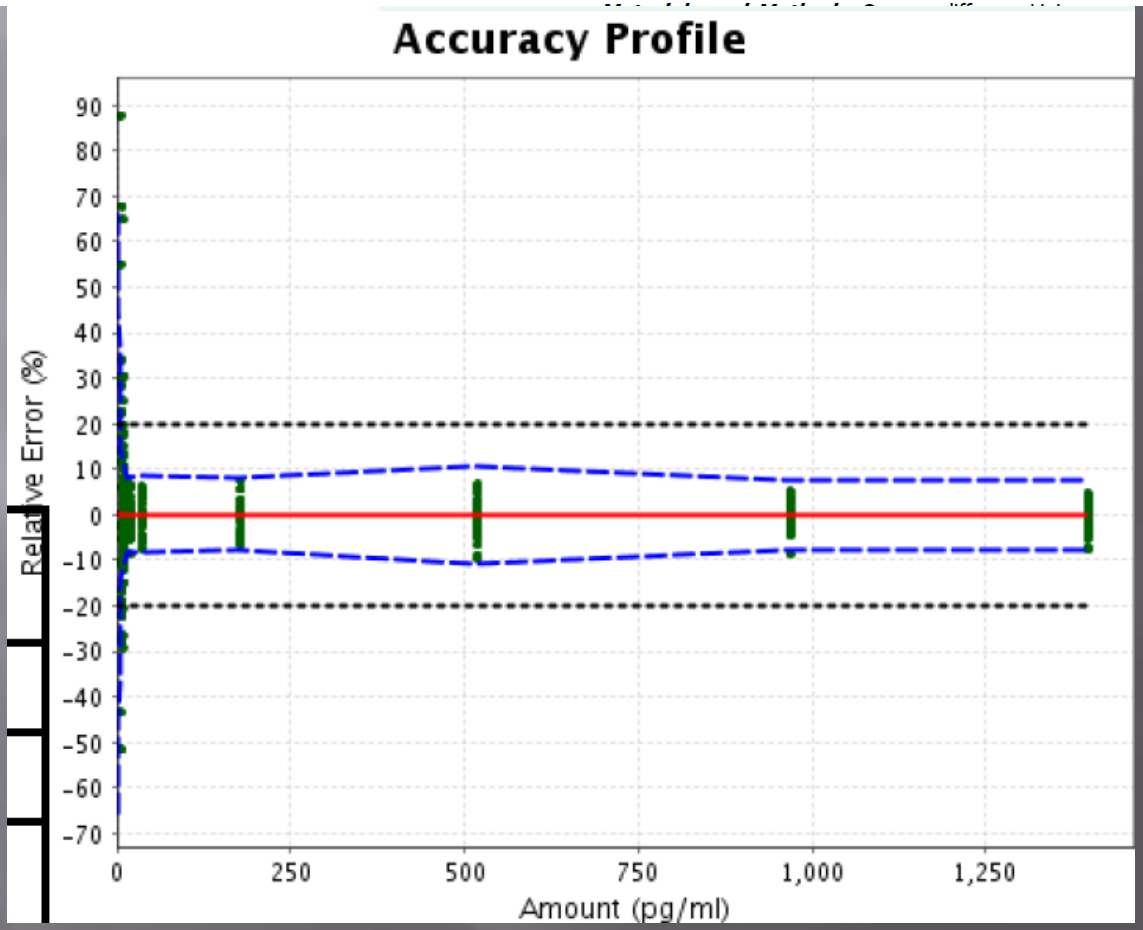
Mons Borrinage donnée de 5 Laboratories

- LABO1: 2eme génération
- LABO2: 3 eme génération
- LABO3: 2eme génération (10-65)
- LABO4: 2eme génération (10-65)
- LABO5 : 2eme génération (17-73)

Profil de sécurité

EVALUATION OF DIASORIN LIAISON 1-84 PTH ASSAY,A NEW AUTOMATED IMMUNOASSAY FOR THE DETERMINATION OF 3rd GENERATION PTH.

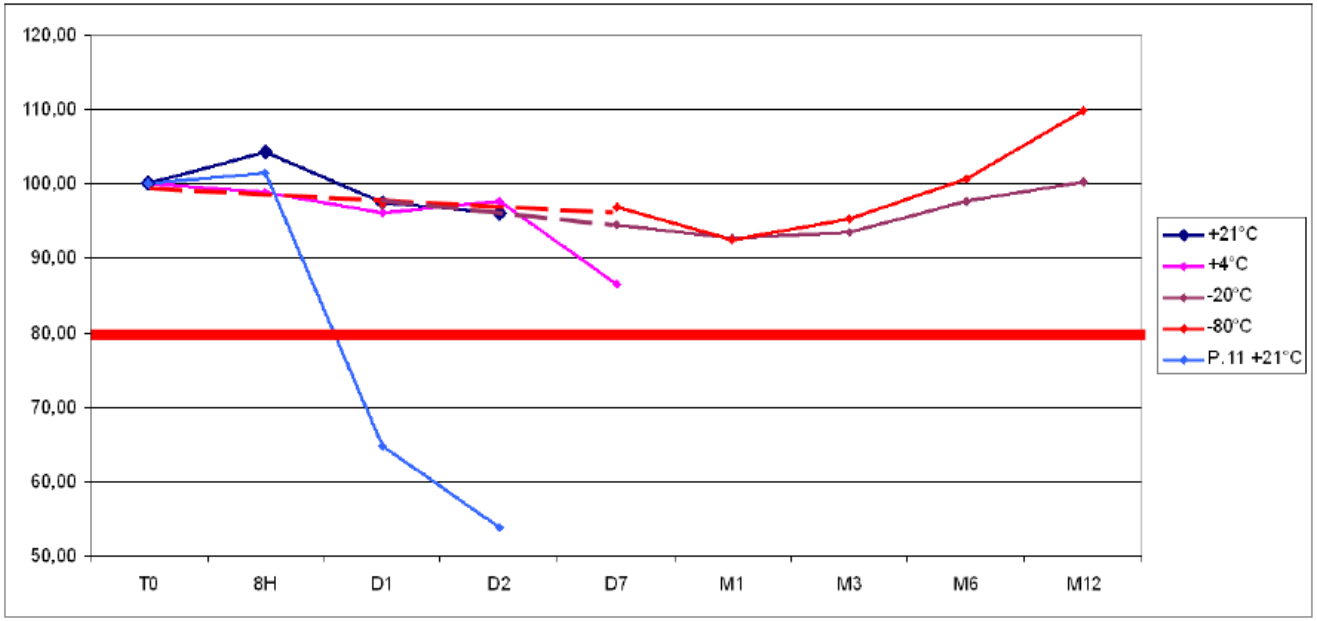
E CAVALIER (1), AO ROUSSELLE (1), AC BEKAERT (1),A CARLISI (1), JP CHAPELLE (1), P DELANAYE (2)
Departments of (1) Clinical Chemistry, and (2) Nephrology Dialysis and Transplantation,
University of Liège, CHU Sart-Tilman, Belgium



NEW INSIGHTS ON THE STABILITY OF THE (1-84) PTH AS ASSAYED BY AN AUTOMATED 3rd GENERATION PTH ASSAY.

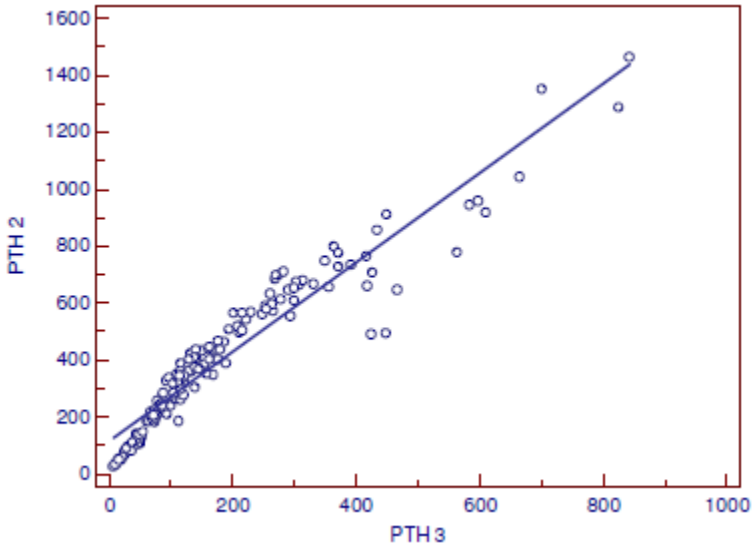
E CAVALIER (1), A CARLISI (1), AC BEKAERT, O ROUSSELLE (1), JP CHAPELLE (1), P DELANAYE (2)
Departments of (1) Clinical Chemistry, and (2) Nephrology Dialysis and Transplantation,
University of Liège, CHU Sart-Tilman, Belgium

Stability in plasma EDTA



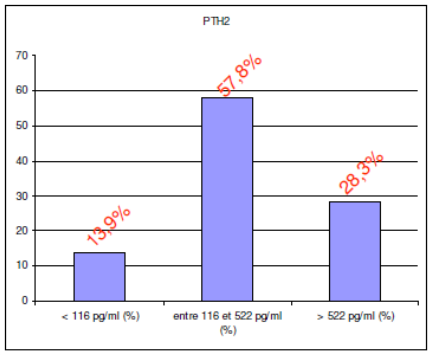
Mesure de la PTH chez le patient hémodialysé avec une trousse de 2ème ou de 3ème génération: impact pour le Clinicien.

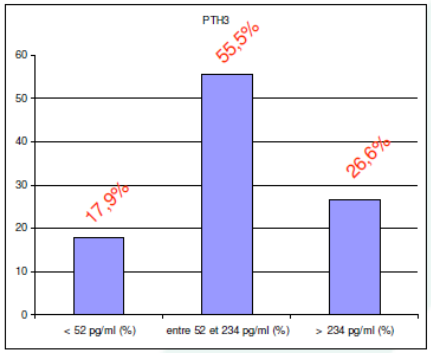
Etienne Cavalier (1), Jean-Marie Krzesinski (2), Pierre Delanaye (2),
Départements de (1) Chimie Médicale et (2) Néphrologie Dialyse et Transplantation
Université de Liège, CHU de Liège, Liège, Belgique



$PTH_2 = 1{,}57 PTH_3 + 117$

$r = 0.953$





Conclusions:
Doser la PTH (1-84) uniquement sans les fragments, a plusieurs avantages: diminution des variabilités inter-méthode, standardisation possible de tous les kits, meilleure compréhension physiopathologique.
Cependant, la classification KDIGO et les variations longitudinales ne sont pas fort différents entre les 2 trousses.

Profil de sécurité

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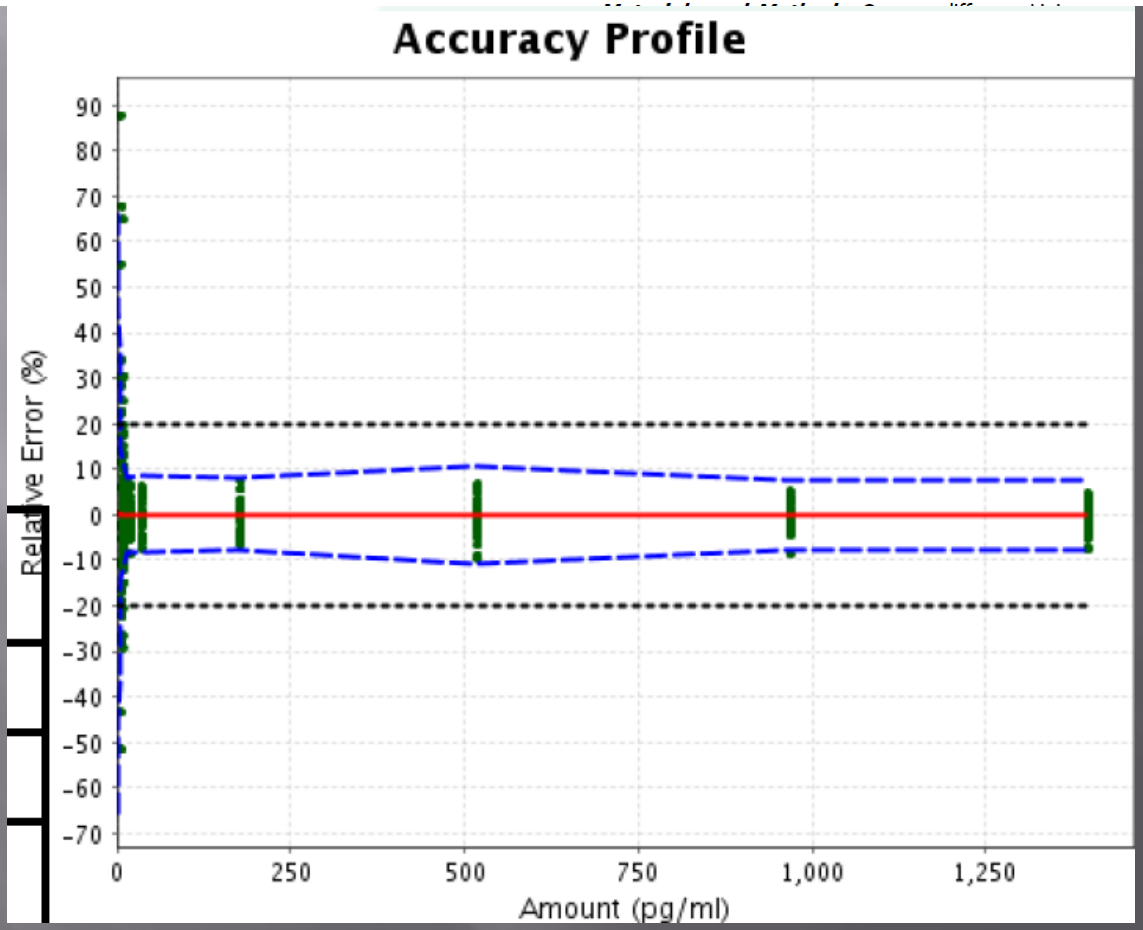

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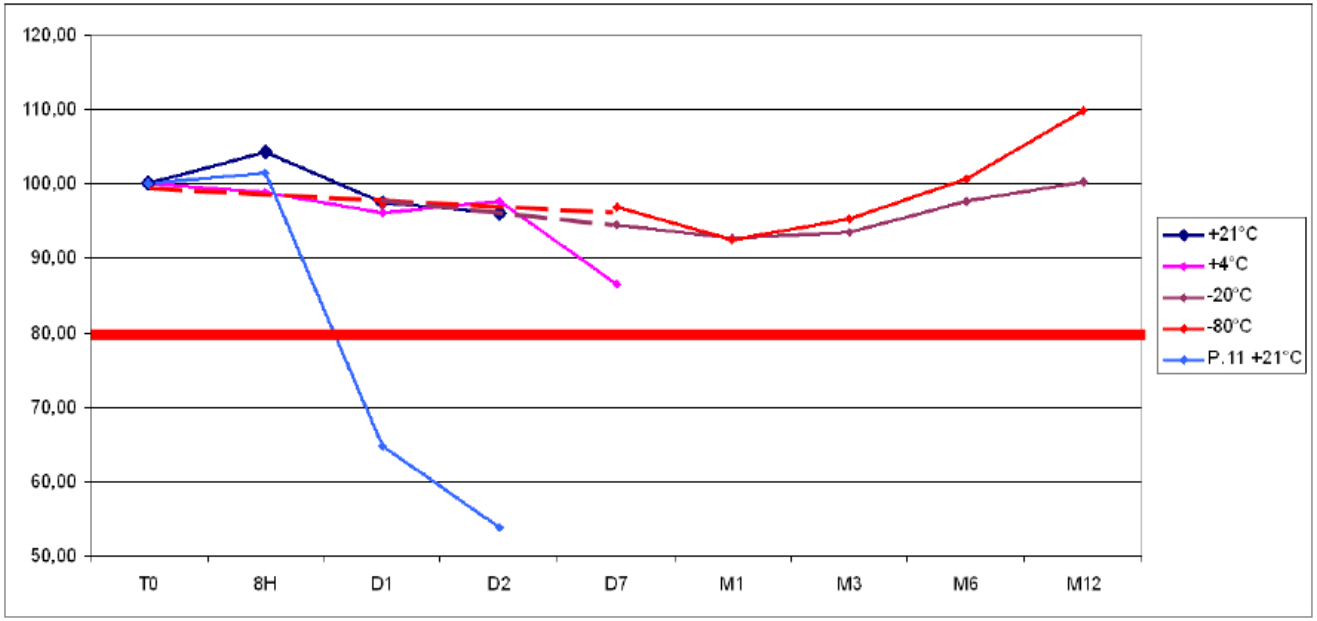

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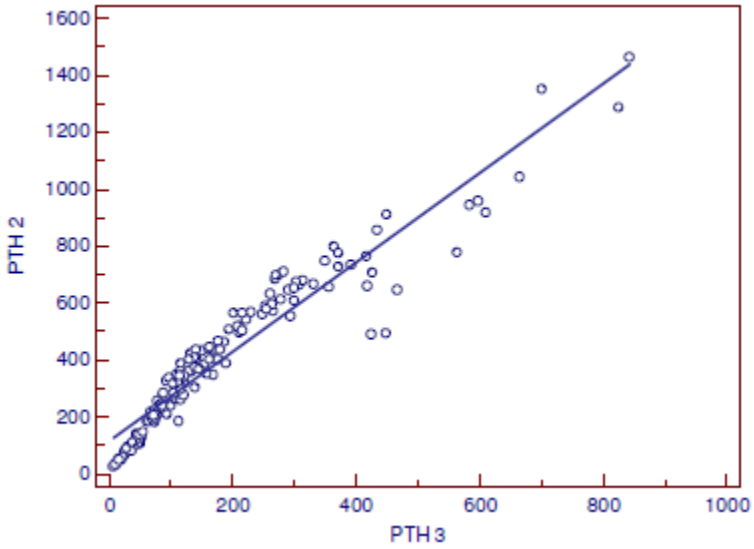
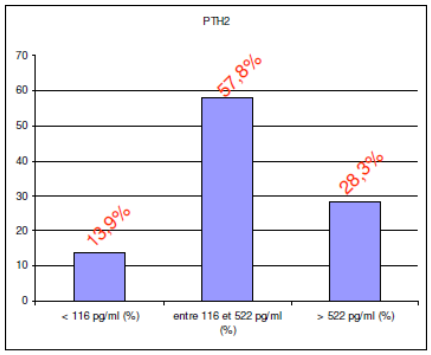
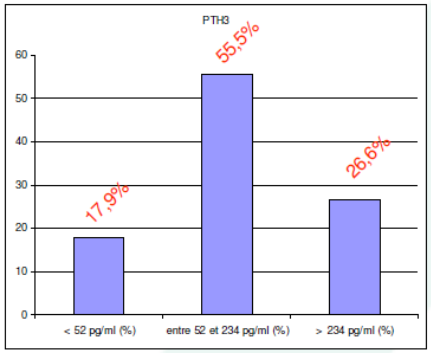


$PTH_2 = 1{,}57 PTH_3 + 117$

$r = 0.953$





Conclusions:
Doser la PTH (1-84) uniquement sans les fragments, a plusieurs avantages: diminution des variabilités inter-méthode, standardisation possible de tous les kits, meilleure compréhension physiopathologique.
Cependant, la classification KDIGO et les variations longitudinales ne sont pas fort différents entre les 2 trousses.

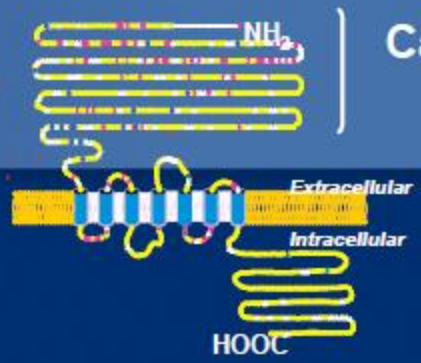
PTH 2eme génération		PTH 3eme génération	
Pour	Contre	Pour	Contre
• Suggestion KDIGO • Integre 1-84 et 7-84 PTH. • Etude majoritairement faite avec 2eme génération.	• Mesure plusieurs PTH. • Discrimination HPT I ? • Avenir du test ?	•Ne mesure qu'une PTH •Corrélation suffisante par rapport à la 2eme génération au niveau des critères. •Probablement test retenu pour l'avenir.	• Peu d'étude de corrélation clinique et pathologique. • Suggestion KDIGO • N'integre pas la 7-84 PTH inhibiteur • Cut off de l'os adynamique trop flou.

Abstraction faite des différences économiques du test….

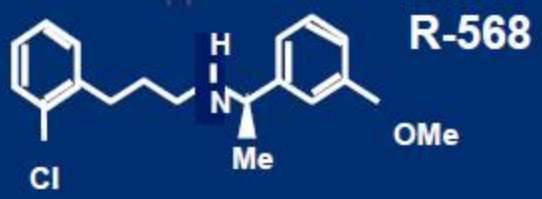
Commentaire laboratoire ?

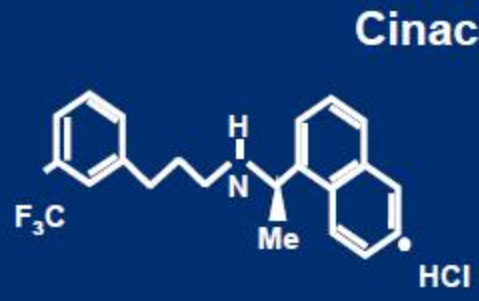
Patient	Commentaire
tous	PTH 3eme génération Diasorin
DY	Correlation ancienne PTH (……..) pour facteur correctif (r2 =)
Prédialyse	Correlation ancienne PTH 2.75.(r2 =)
Autres ?	Autres ?

History of Calcimimetics



- 1993: Brown and Hebert cloned the calcium sensing receptor
- Dec. 1993: IND filed by NPS for R-568
- March 1996: Amgen licensed R-568 from NPS
- May 1998: IND filed by Amgen for AMG 073 (cinacalcet HCl)
- Dec. 2001: Phase 3 clinical trials initiated
- Sep 2003: New Drug Application filed with FDA
- Mar 2004: Sensipar® approved and launched in the US





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Current Clinical Trial Data Suggest a Benefit of Cinacalcet on Outcomes Including CV Hospitalization 6 & 12 Month Pooled Data

Clinical Outcome	Hazard Ratio* (95% CI)	*P* Value for Hazard Ratio	Cinacalcet HCl (events per 100 subject-years)	Control (events per 100 subject-years)
Parathyroidectomy	0.07 (0.01–0.55)	0.009	0.3	4.1
Fracture	0.46 (0.22–0.95)	0.04	3.2	6.9
Cardiovascular Hospitalization	0.61 (0.43–0.86)	0.005	15.0	19.7
All-Cause Hospitalization	1.03 (0.87–1.22)	0.74	67.0	71.0
Mortality	0.81 (0.45–1.45)	0.47	5.2	7.4

*Control used as reference group

HR = hazard ratio

Cunningham, et al. Kidney International, 2006

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Evaluation of Cinacalcet Therapy to Lower Cardiovascular Events (EVOLVE): Rationale and Design Overview

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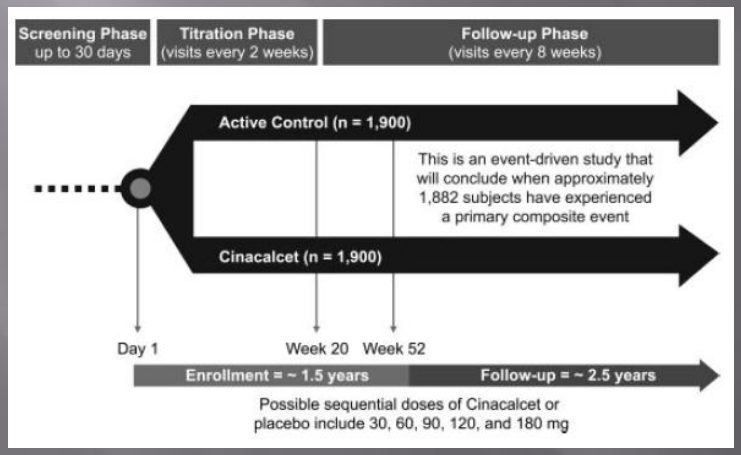

Clin J Am Soc Nephrol 2: 898-905, 2007. doi: 10.2215/CJN.04381206

Roman Pais
Dr Lheureux B

- Nouveau dosage PTH depuis: 03/03/2011
- LIAISON PTH 1-84.
- Correlation:
- Mieux correlation

Remerciement

- Laboratoire Centre Hospitalier Hornu Frameries
- Infirmière dialyse qui suivent les recommandations de prélèvements.
- Patients prédialyses volontaires…

- Amgen
  - Sponsor de cette réunion
  - Certains articles fournis et discussion de leur expérience.