

# Diagnostik des Hyperparathyreoidismus

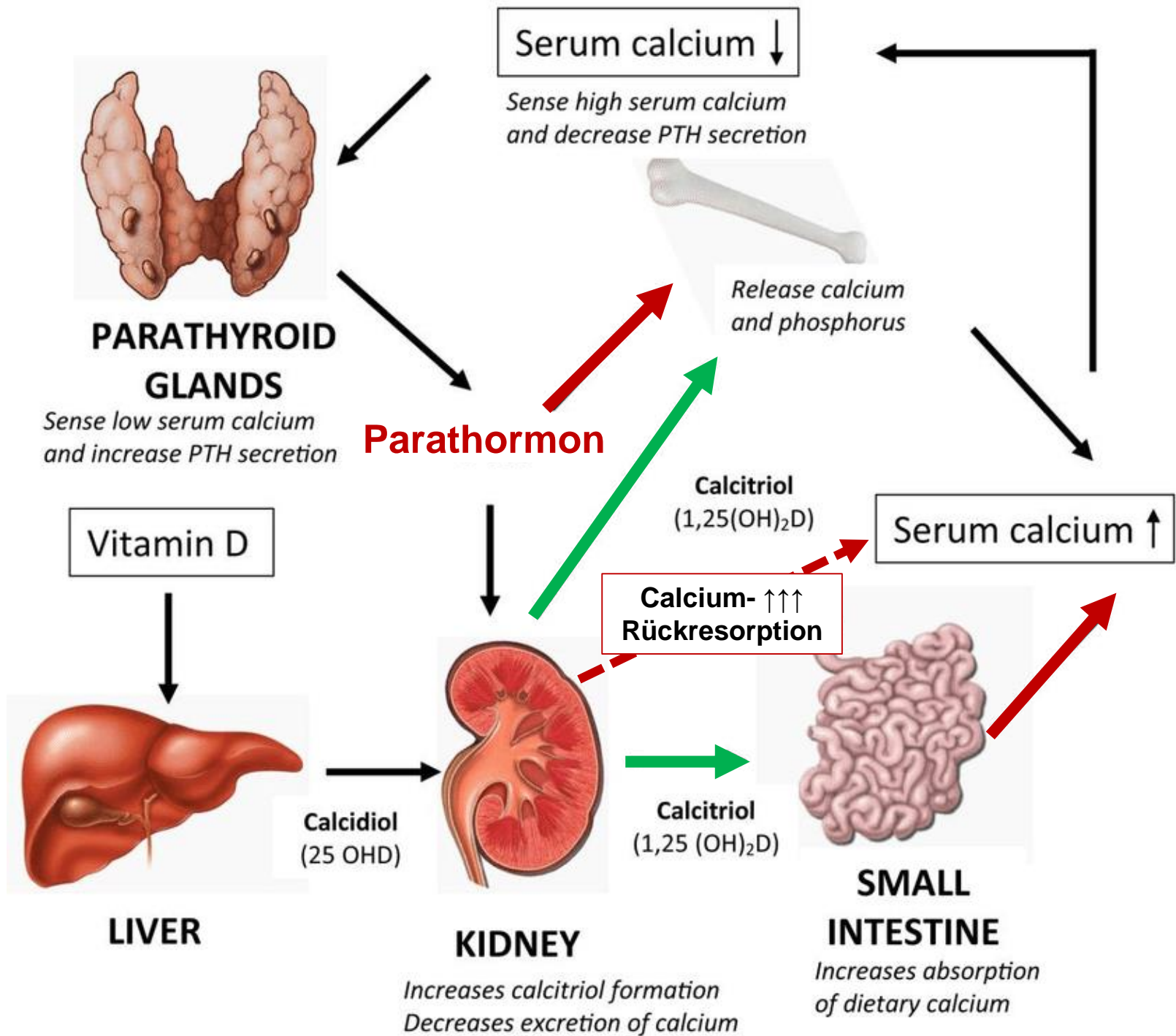


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*Endokrinologie /// Diabetologie /// Innere Medizin*

*Innovationspark Springorum  
Facharztpraxis und Labor  
Springorumallee 2 - 44795 Bochum*

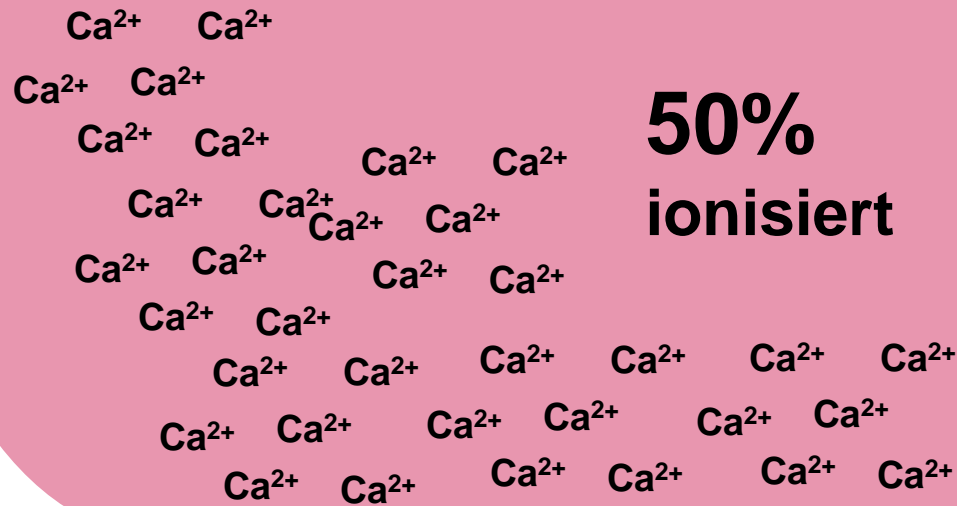
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# Calcium-Bindung im Blut

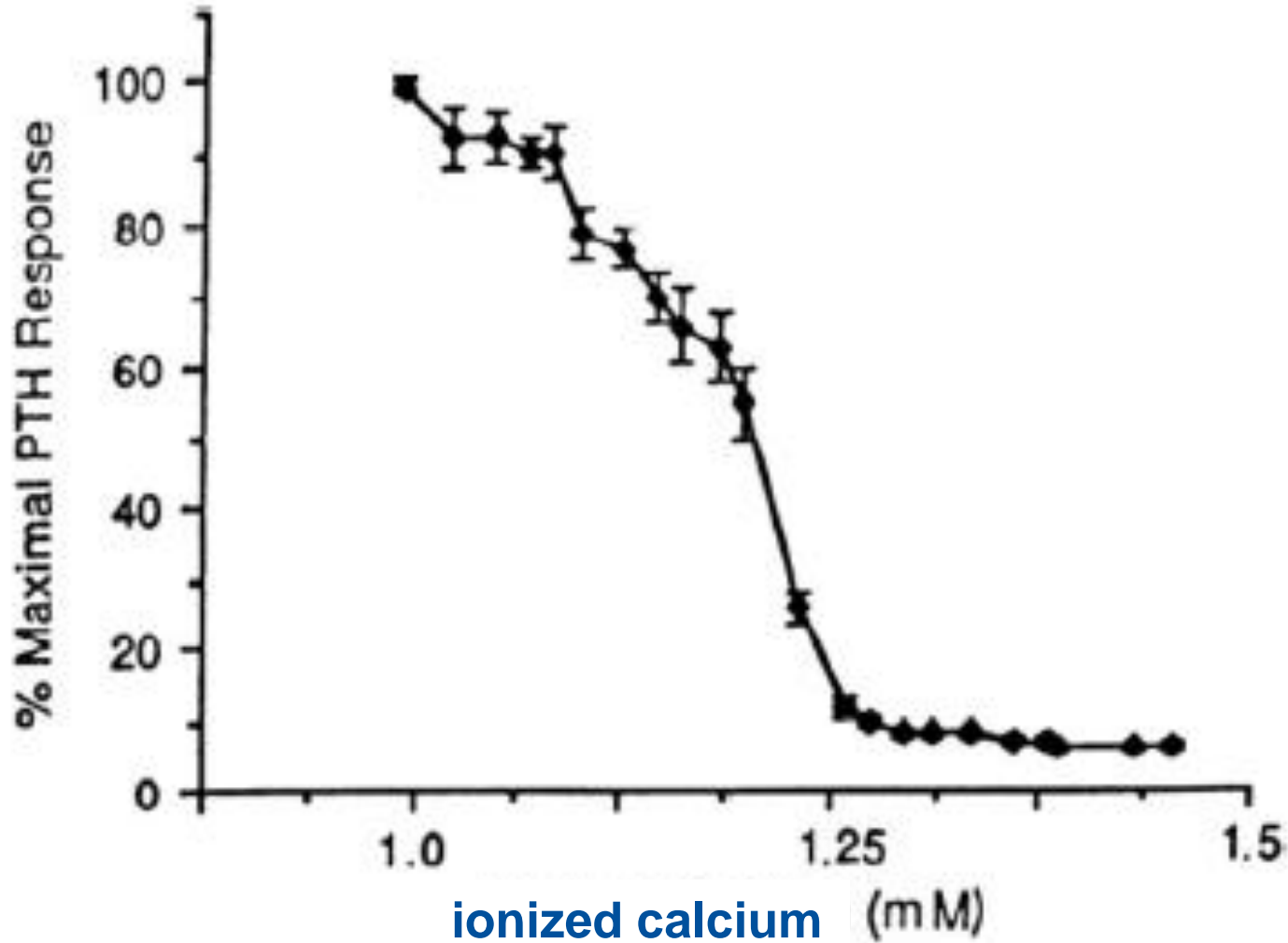
35% Albumin

15%  
komplex  
gebunden  
(Bicarbonat,  
Lactat, Citrat,  
Phosphat)

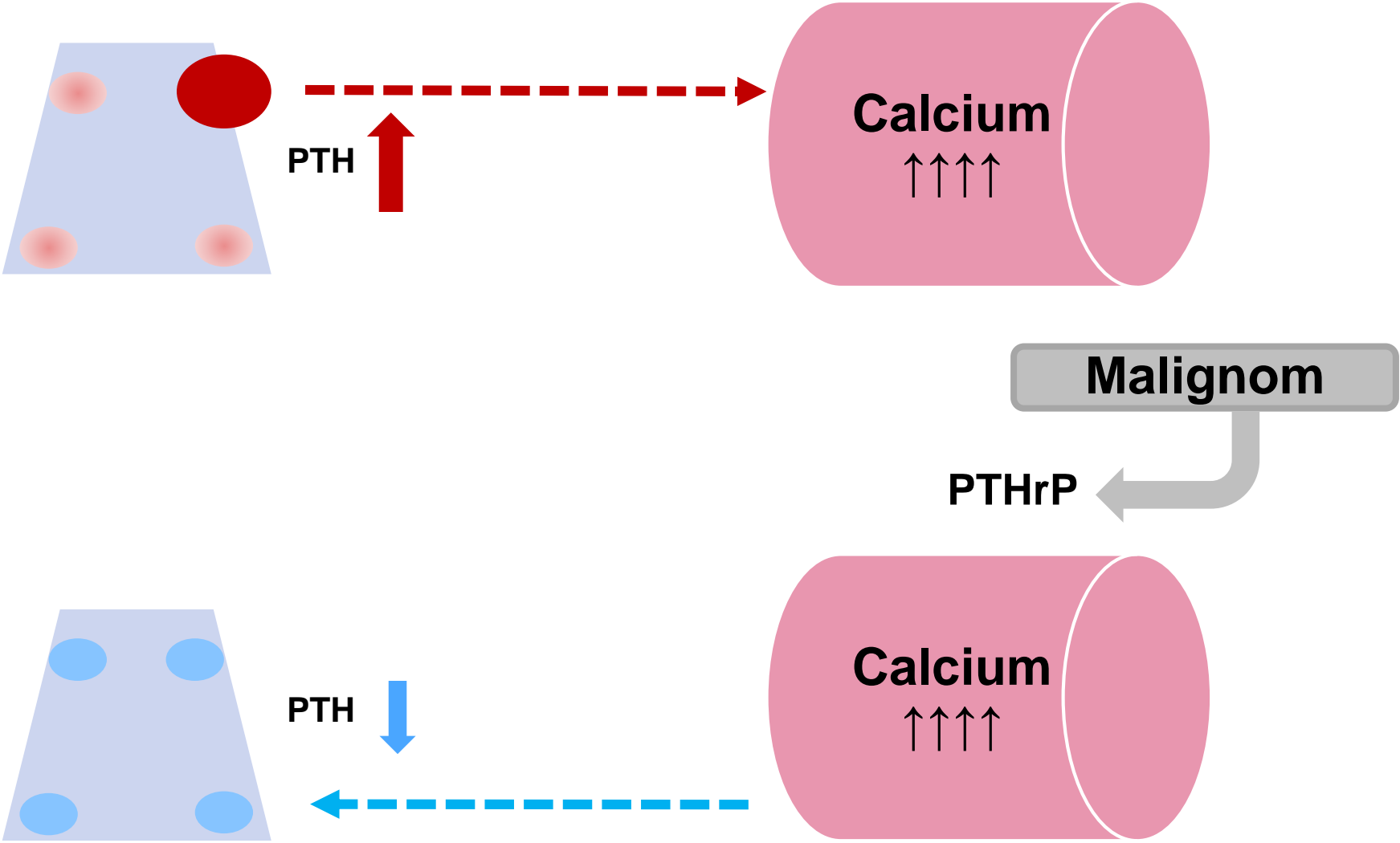


# Beziehung zwischen Calcium und Parathormon bei Gesunden

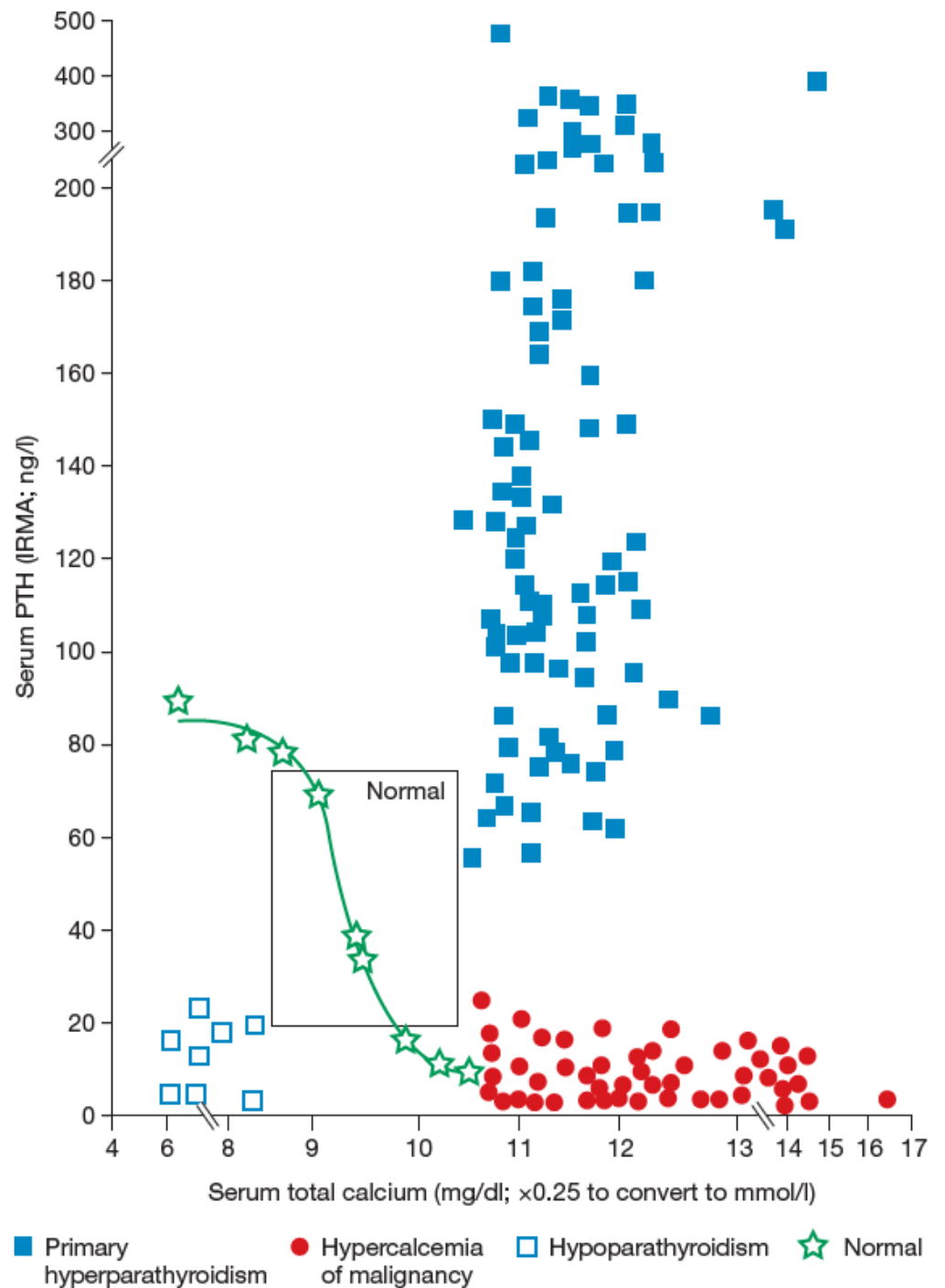
PTH



# Differenzialdiagnose der Hypercalcämie



# Beziehung zwischen Calcium und PTH



*Nature Clinical Practice Nephrology,*  
2007, 3, 397-404

# Diffenzialdiagnose Hypercalcämie

		Ursache	PTH	Calcium	Phosphat
prim.	HPT	NSD-Adenom	↔↑	↑	↔↓

$\text{Ca}^{2+}\uparrow\uparrow\uparrow$

1%

aller  
Krankenhaus-Pat.

80%

Primärer / tertiärer  
Hyperparathyreoidismus

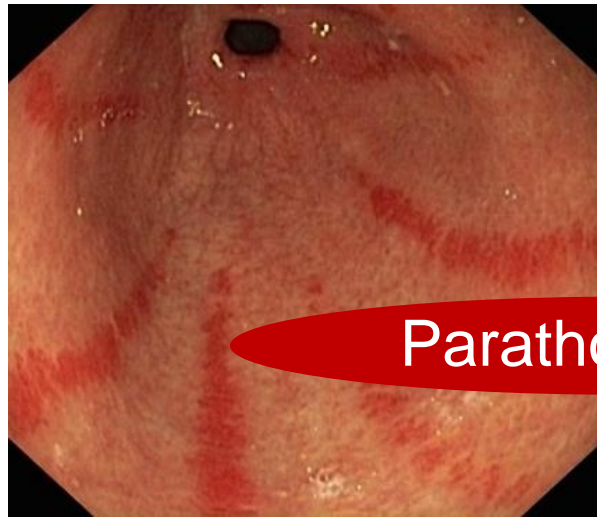
20%

Tumorhyperkalzämie



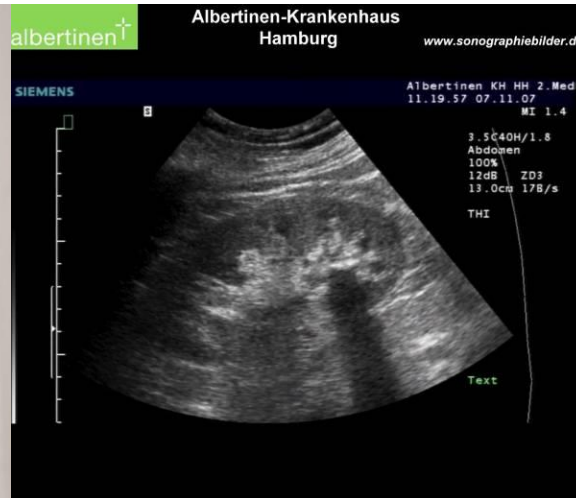
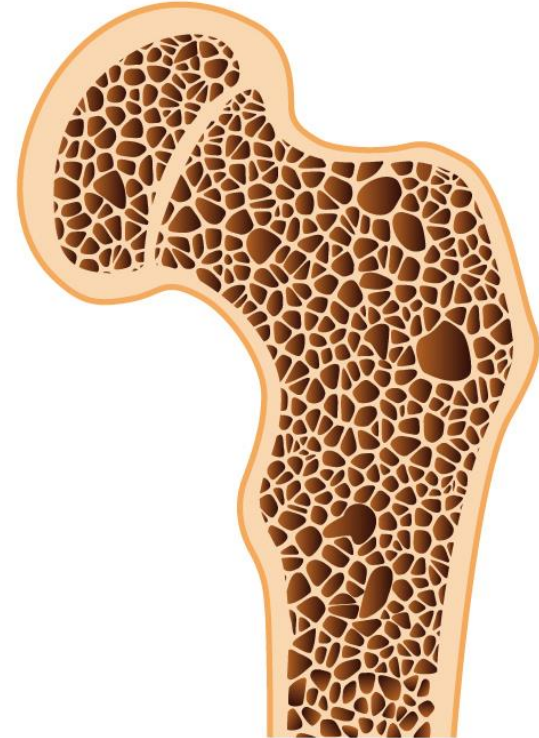
# Seltene Ursachen der Hypercalcämie

- Vitamin **D** Intoxikation
- **Granulomatöse** Erkrankungen
- **Medikamente**
  - Thiazid-Diuretika
  - Lithium
  - Teriparatid
  - Vitamin A in exzessiver Dosis
  - Theophyllin-Intoxikation
- **Hyperthyreose**
- **Akromegalie**
- **Phäochromozytom**
- Nebennierenrinden**insuffizienz**
- Immobilisation
- Parenterale Ernährung
- Milch-Alkali-Syndrom



Parathormon  $\uparrow\uparrow$

Calcium  $\uparrow\uparrow$   
anorg. Phosphat  $\downarrow$



# Diagnose des pHPT

Calcium im Serum ↑

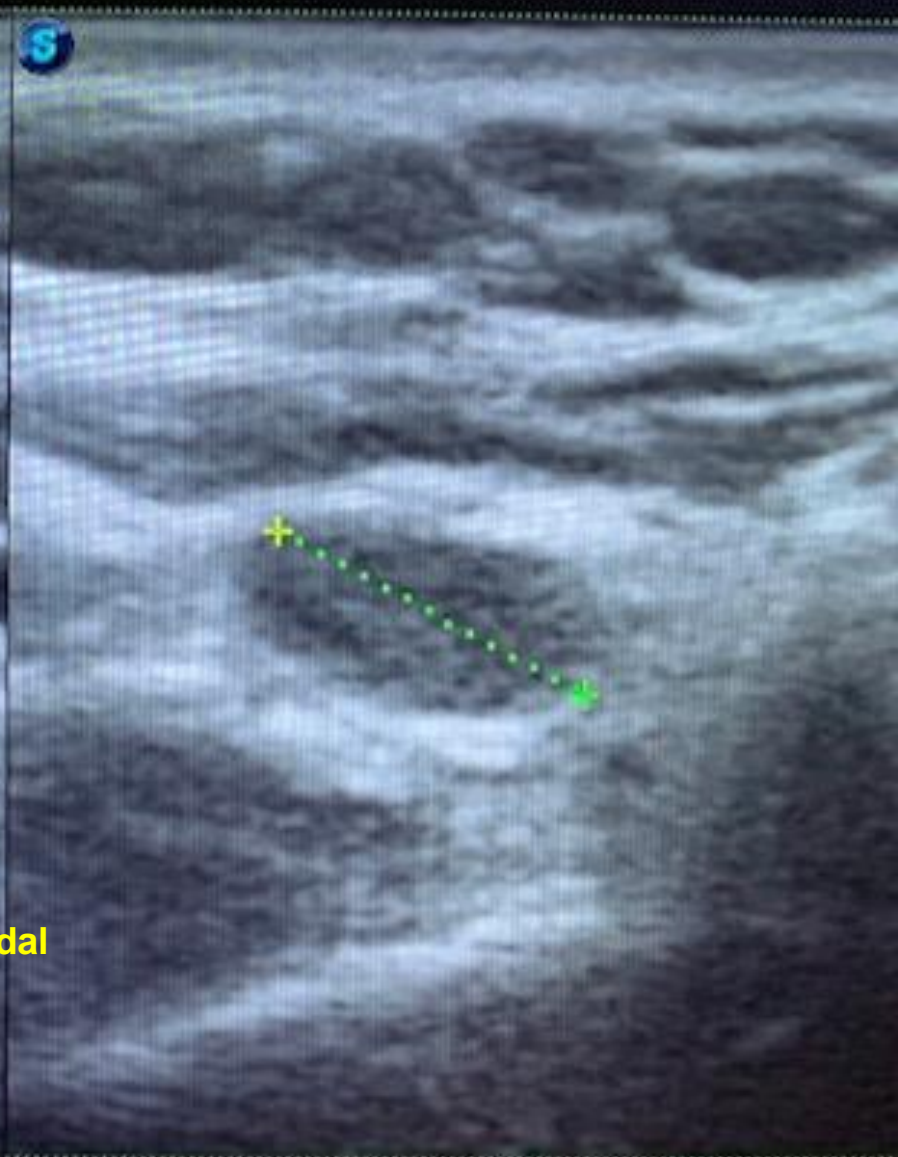
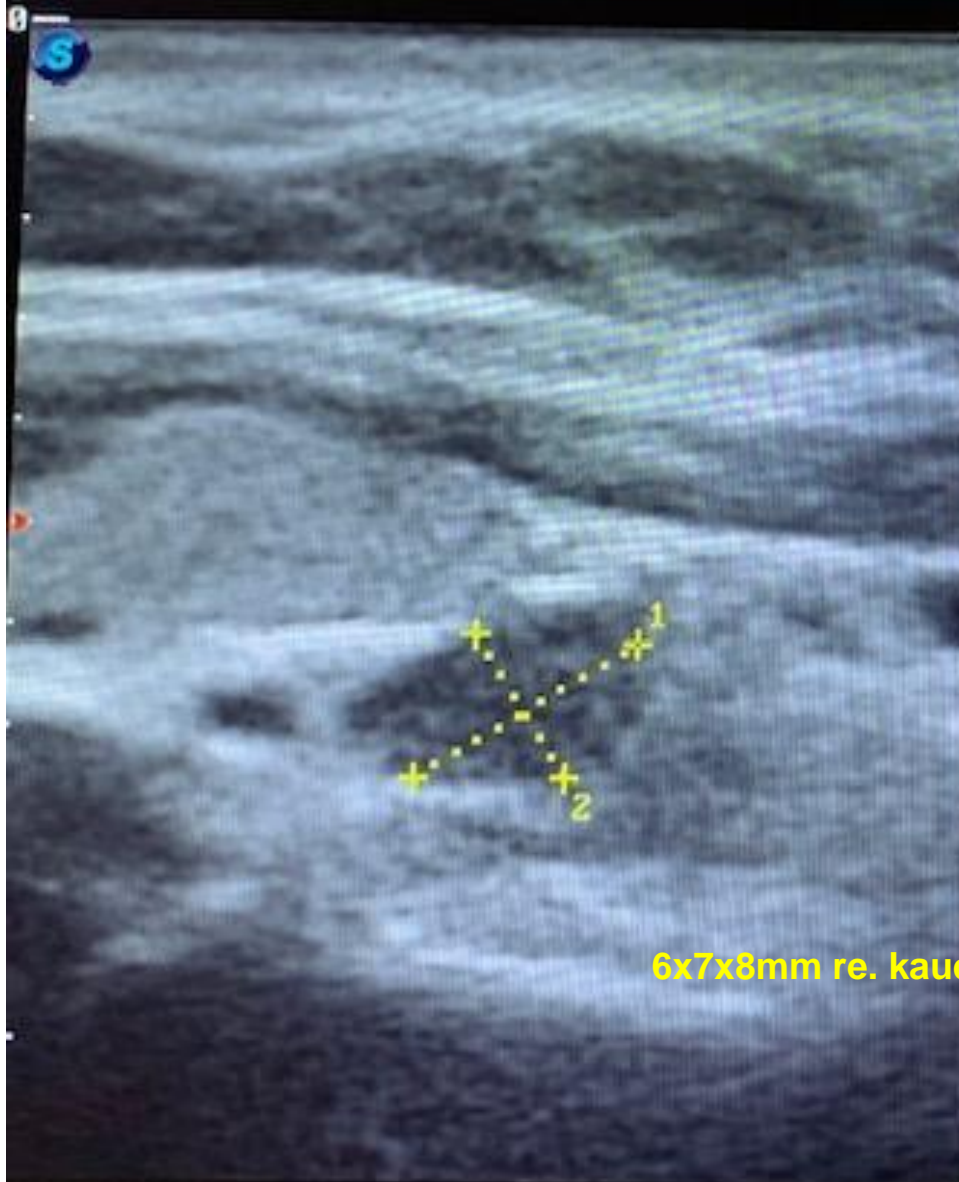
anorgan. Phosphat ↓

Parathormon ↑

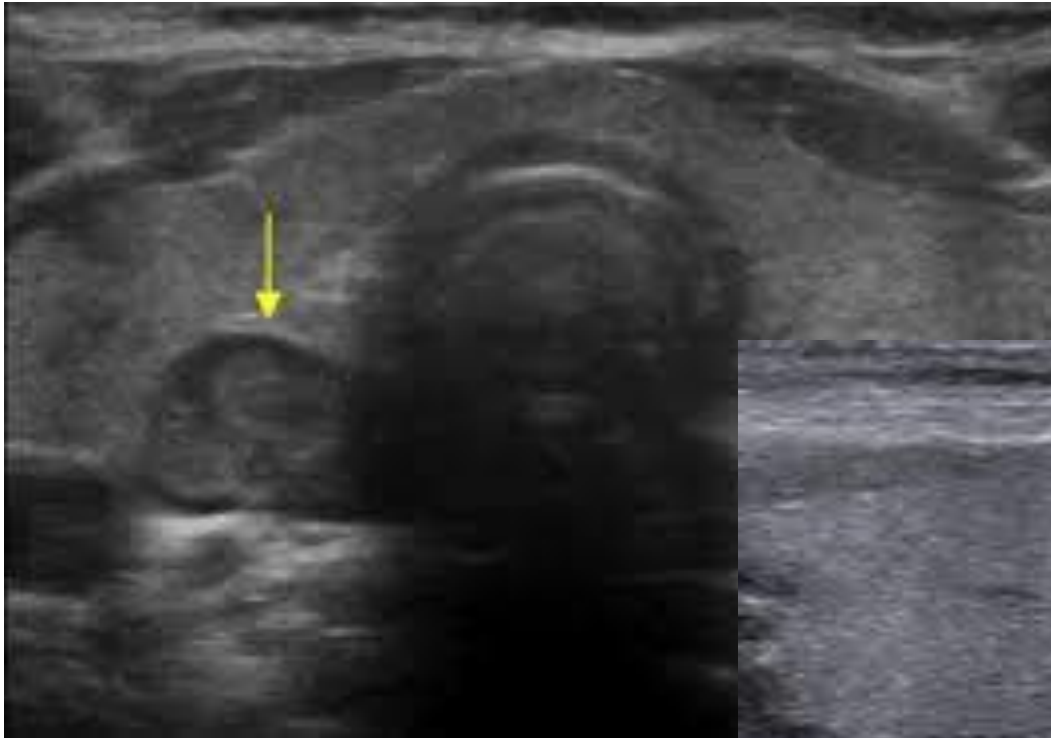
Calcium im 24-Urin ↑

Knochendichtemessung (DEXA)





# Primärer Hyperparathyreoidismus

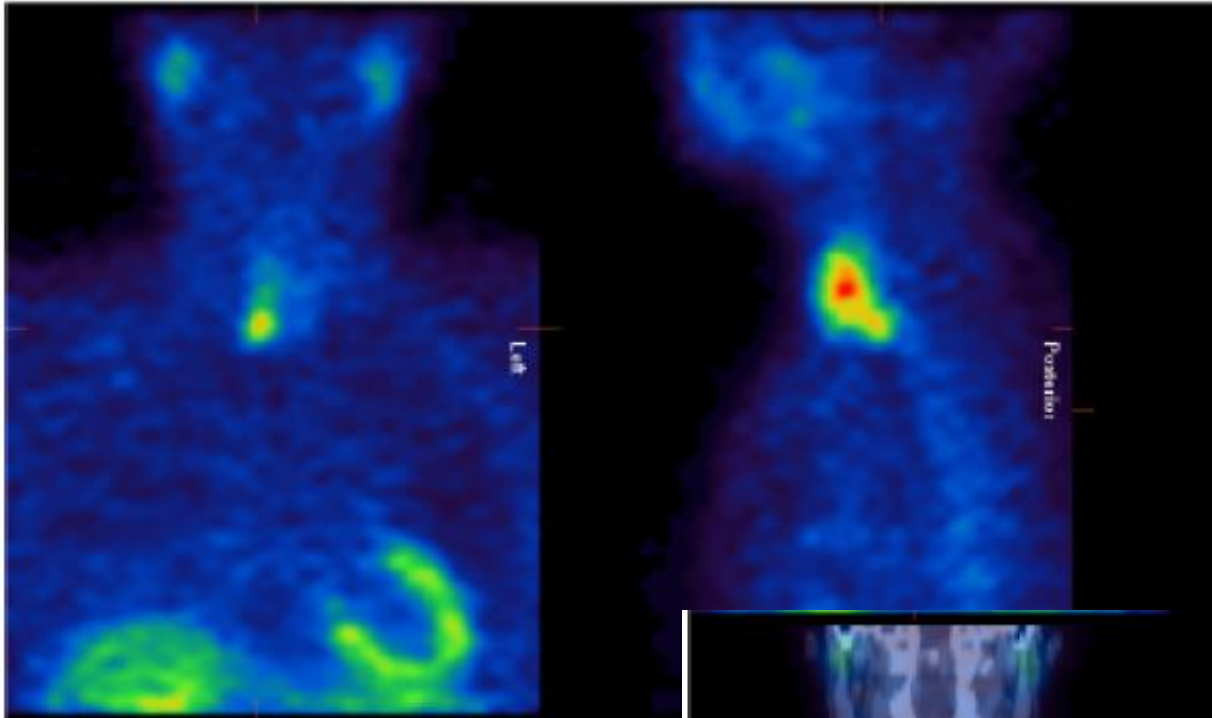


## Sonographie

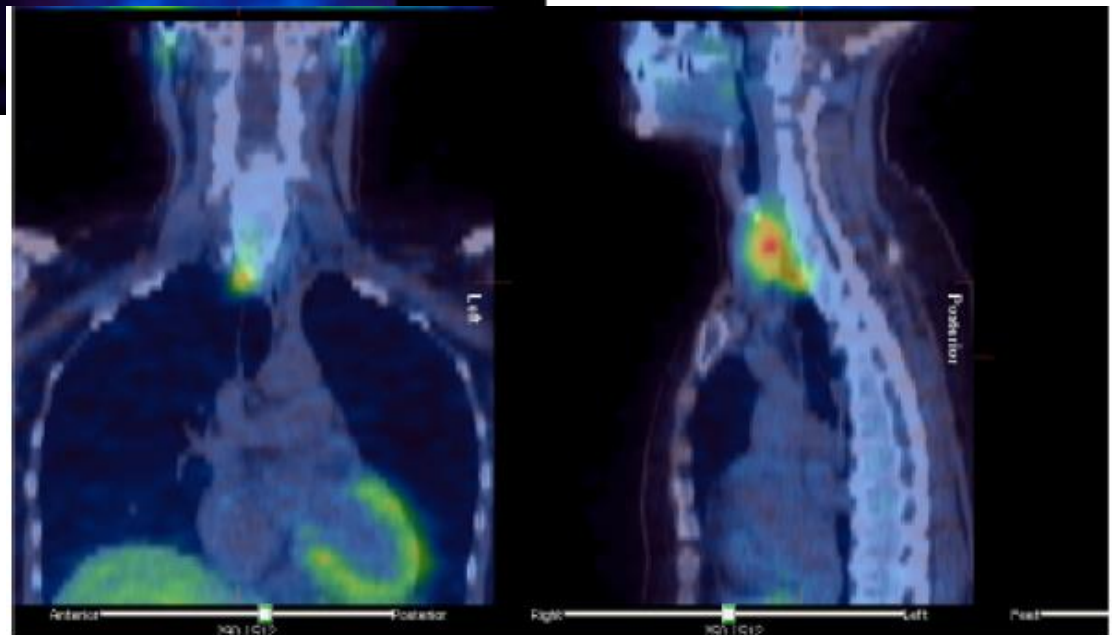
Sensitivität 76-87%

Spezifität 93-97%

# 99mTC-sestaMIBI-scintigraphy with SPECT



and low-dose CT



# Indikation einer <sup>99m</sup>Sesta-MIBI-Szintigraphie

Sensitivität            90%

Spezifität              97%

Sensitivität / Spezifität steigt mit.....

- Adenomgröße 18mm
- Hohe Calciumspiegel (ionisierendes Calcium >1,49 mmol/l)

Wash-out in Nebenschilddrüsenzellen langsamer als in Thyreozyten

## <sup>99m</sup>Sesta-MIBI-Szintigraphie + <sup>99m</sup>Technetium-Szintigraphie

Sensitivität            79%

Spezifität              91%

*Kunstman JW et al. JCEM 2013, 98:902–12*  
*Singer MC et al, Laryngoscope, 2013, 123:298–301*  
*Cheung K et al., 2012, Ann Surg Oncol 19:577–83*

# Akute medikamentöse Calciumsenkung

## Forcierte Diurese (5l/die)

physiologische NaCl  
+ Furosemid

## Bisphosphonate

Pamidronsäure 15-90 mg i.v. / 2h

Zoledronsäure 4mg i.v. / 15 min

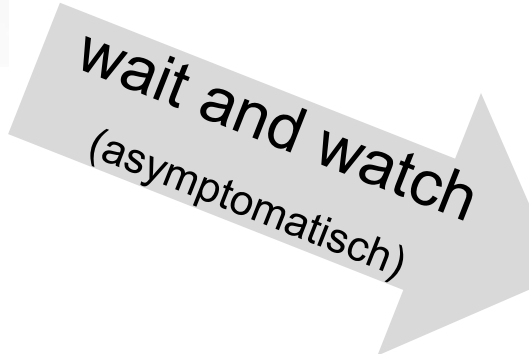
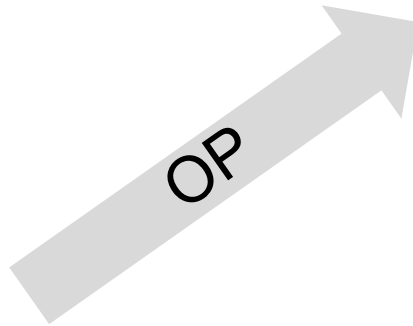
**Glucocorticoide**

**Hämodialyse**



# Hypercalcämie

„What to do?“

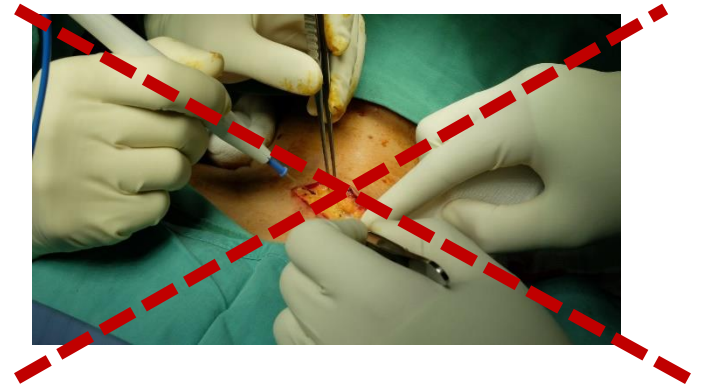


# OP-Indikation eines asymptomatischen primären Hyperparathyreoidismus (pHPT)

Alter	<50 Jahre
Calcium im Serum	+0,25mmol/l (+1,0 mg/dl) über Ref.-W.
Knochendichte (DXA)	T-Score <-2,5
Frakturen	Vertebrale Frakturen
Nierenfunktion	Kreatinin-Clearance <60 ml/min
24-h-Calcium im Urin	>400 mg/d (>10 mmol/d)

# Hypercalcämie

„What to do?“



OP-Risiko ↑↑↑



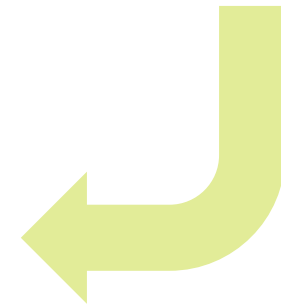
## Cinacalcet (Mimpara®)

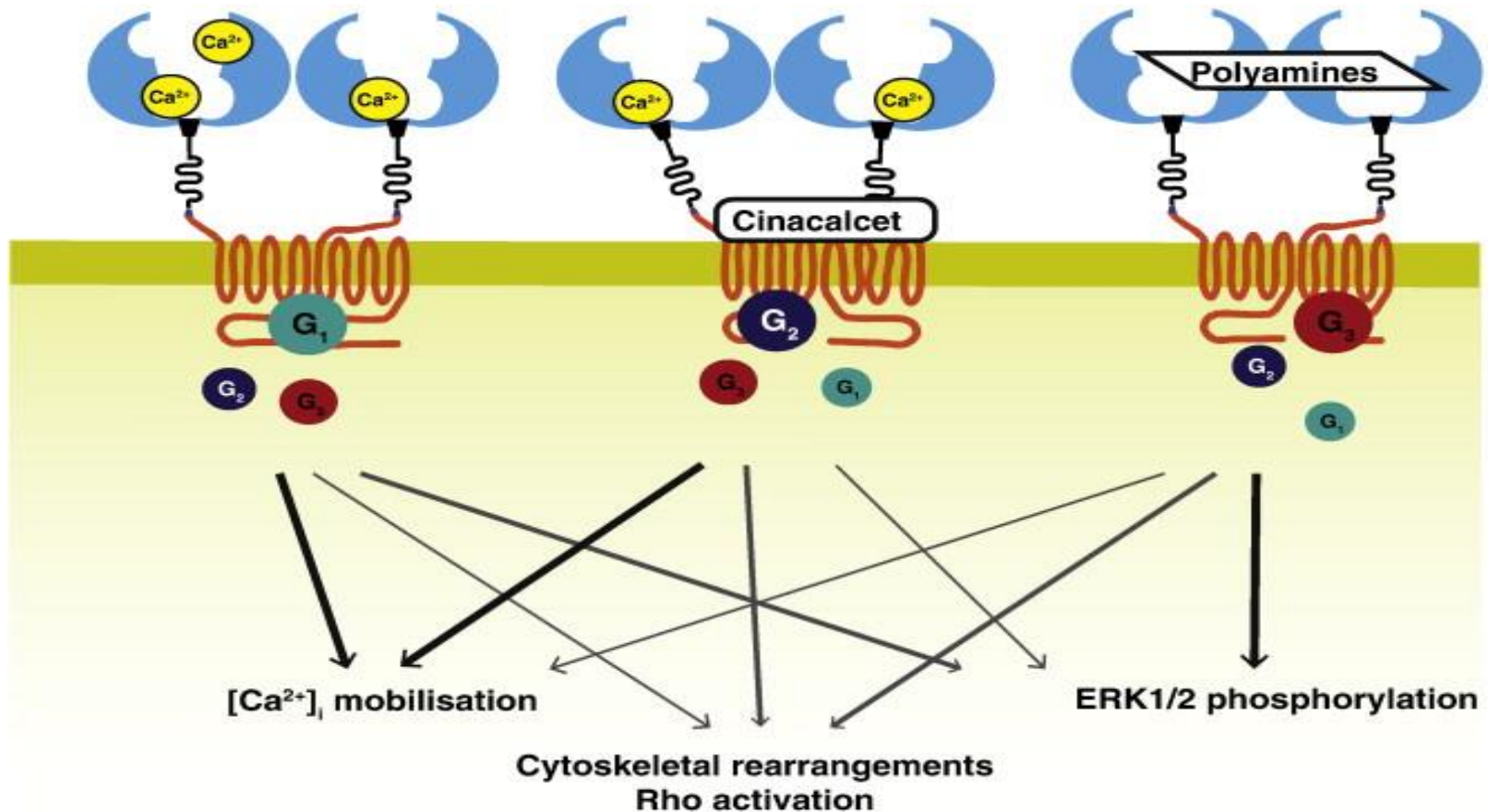
allosterischer Modulator des calciumsensitiven Rezeptors

Erhöhung der Empfindlichkeit des Rezeptors für Calcium

höhere Calciumspiegel werden als tatsächlich vorhanden suggeriert

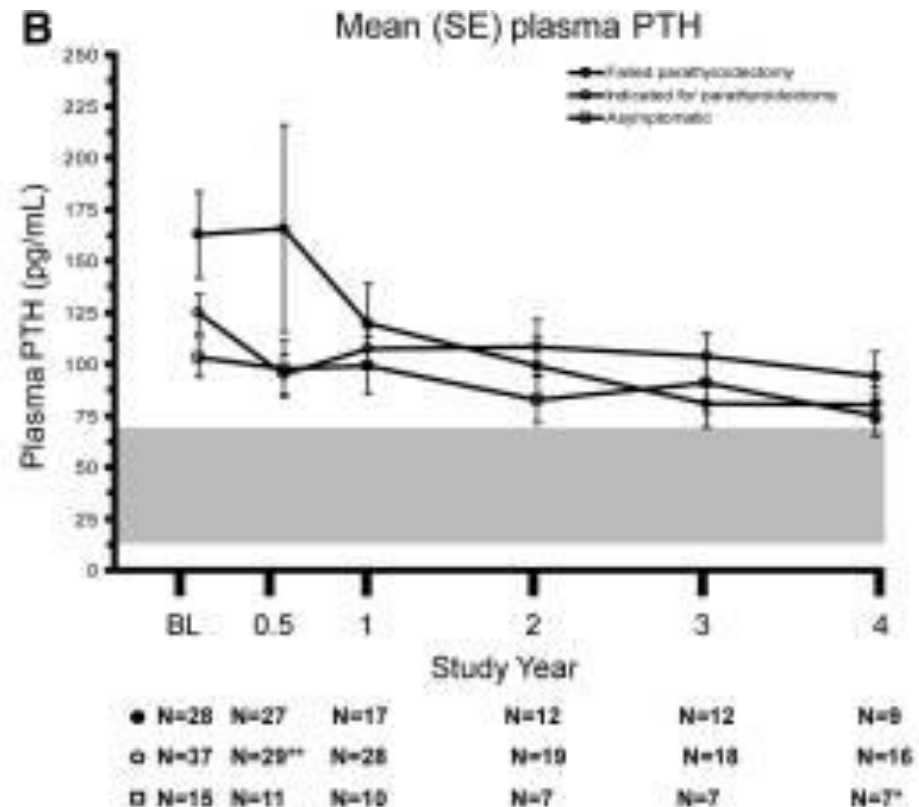
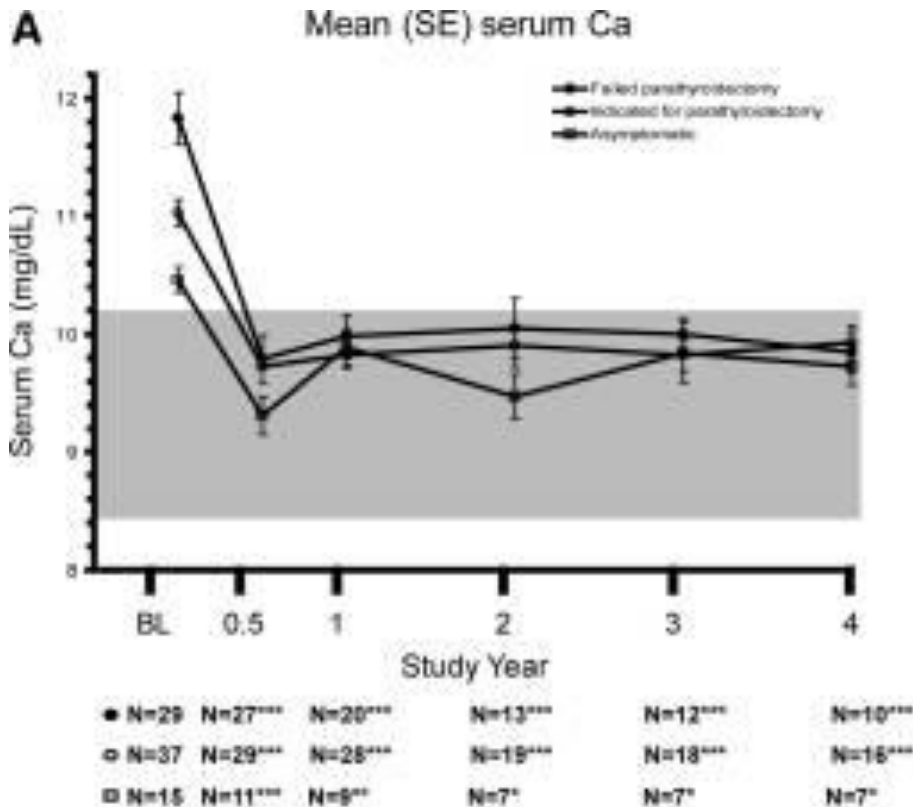
Freisetzung von Parathormon ↓↓↓





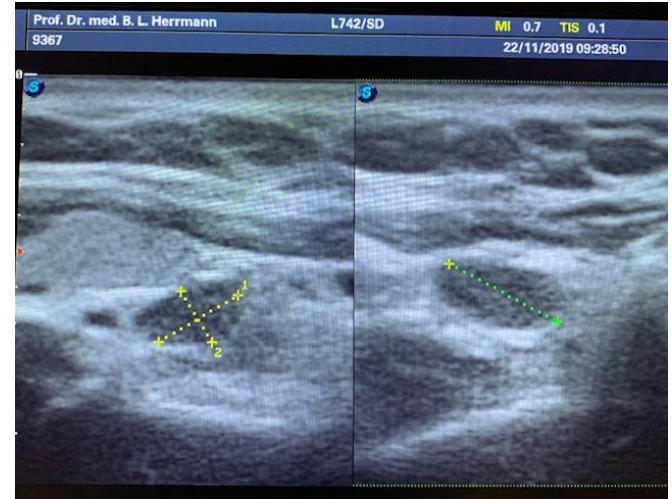
Physiological ligand biased signalling of the calcium sensing receptor (CaSR). The receptor conformation is dependent on the amount and type of ligands bound. Different effector molecules bind preferentially to the different receptor states. This results in differential activation of the downstream signalling pathways. Arrow thickness correlates with the direction of the bias signaling. Adapted from

# Cinacalcet (Mimpara®) senkt Calcium- und Parathormonspiegel



# Fallbeispiel

- 17 Jahre
- Z.n. 4 Nierenkoliken
- Z.n. Lithotripsie
- Calcium 3.11 mmol/l (2.13–2.56)
- Phosphat 2.8 mg/dl (3.1–5.3)
- Parathormon 111 pg/ml (16-87)
- Hypercalciurie



Zwei kaudalen NSD-Adenomen  
re. 3x4x4mm und links 5x9x18mm

???

OP:

3-Drüsen-Nebenschilddrüsen-Adenom-Entfernung (rechts-kranial,  
rechts-kaudal und links-kaudal 12/2018)

**Multiple Endocrine Neoplasie Typ-1 (autosomal dominant)**

c. 1403\_1410dupAGGAGCCG heterozygot (p. Trp471Arggfs\*91)

## MEN 1

Pituitary adenoma

Parathyroid hyperplasia

Pancreatic tumors

## MEN 2A

Parathyroid hyperplasia

Medullary thyroid carcinoma

Pheochromocytoma

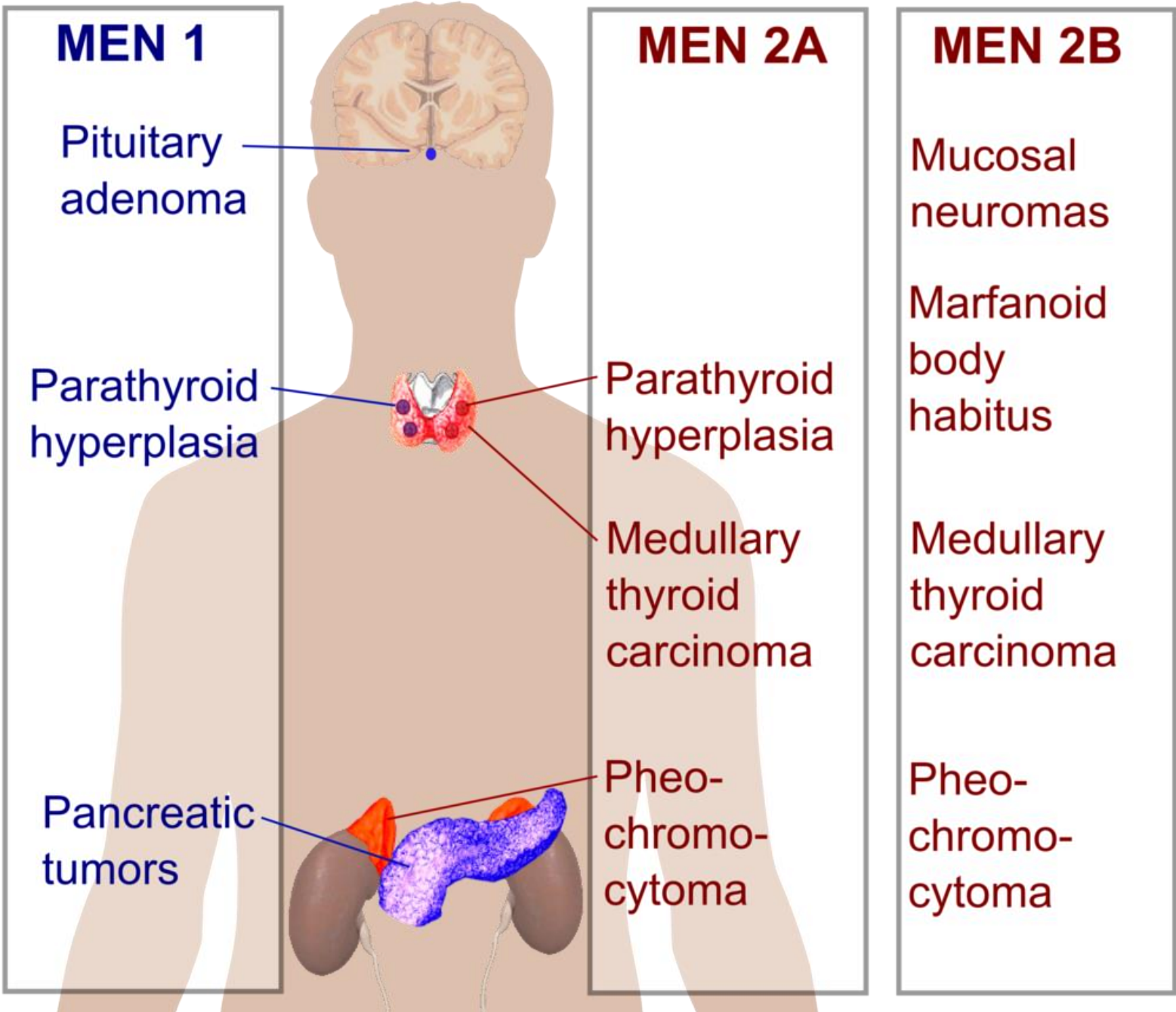
## MEN 2B

Mucosal neuromas

Marfanoid body habitus

Medullary thyroid carcinoma

Pheochromocytoma



# MEN-1

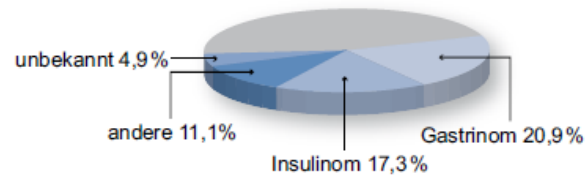
## Erkrankung nach Entstehungsort:

Nebenschilddrüse 89,2 %	Pankreas/Darm 54,2 %	Hypophyse 44,9 %	andere 34,4 %
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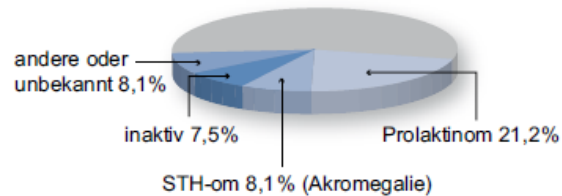
### Nebenschilddrüsen 89,2 %



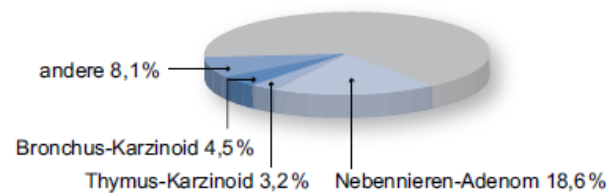
### Pankreas/Darm 54,2 %



### Hypophyse 44,9 %



### andere 34,4 %





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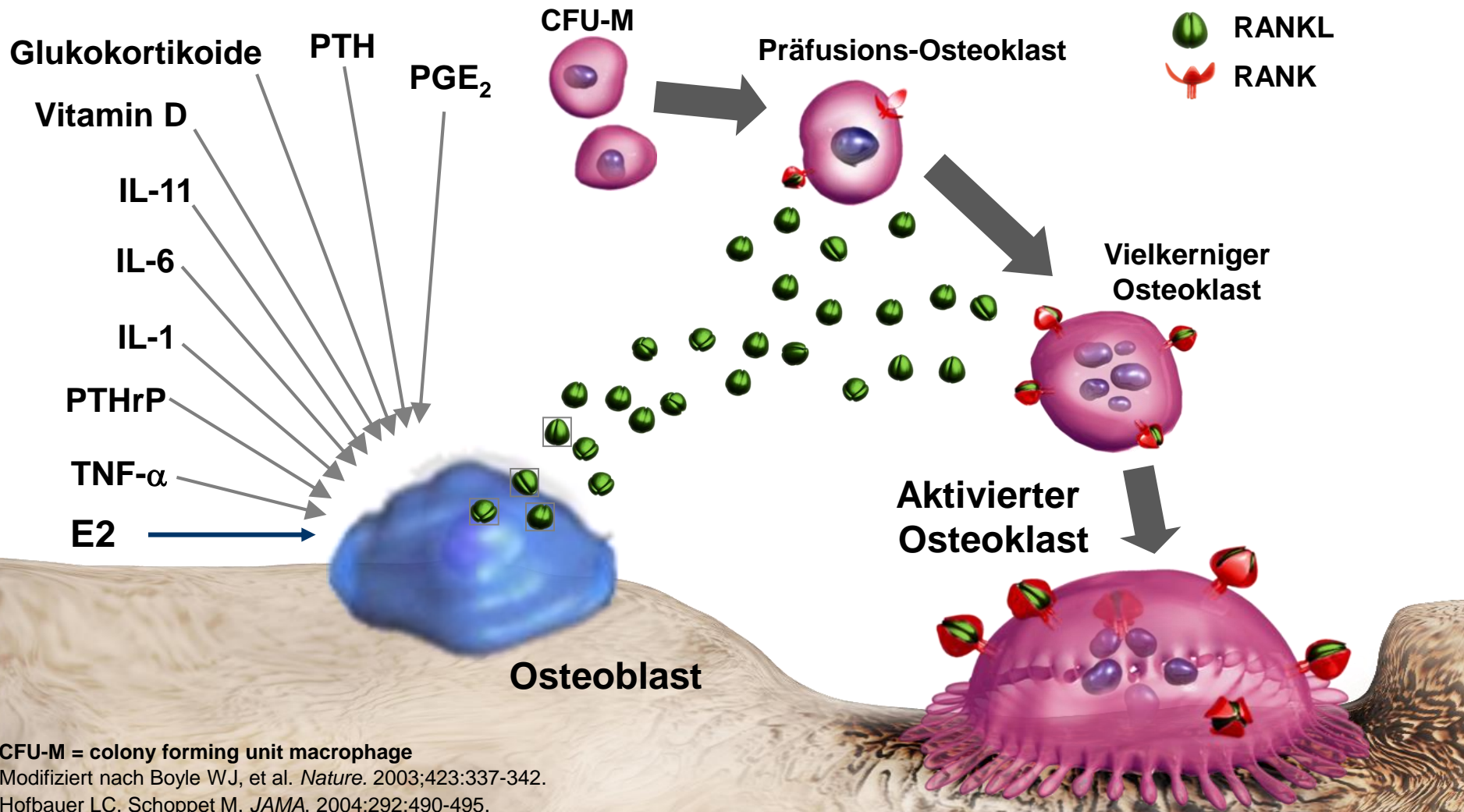
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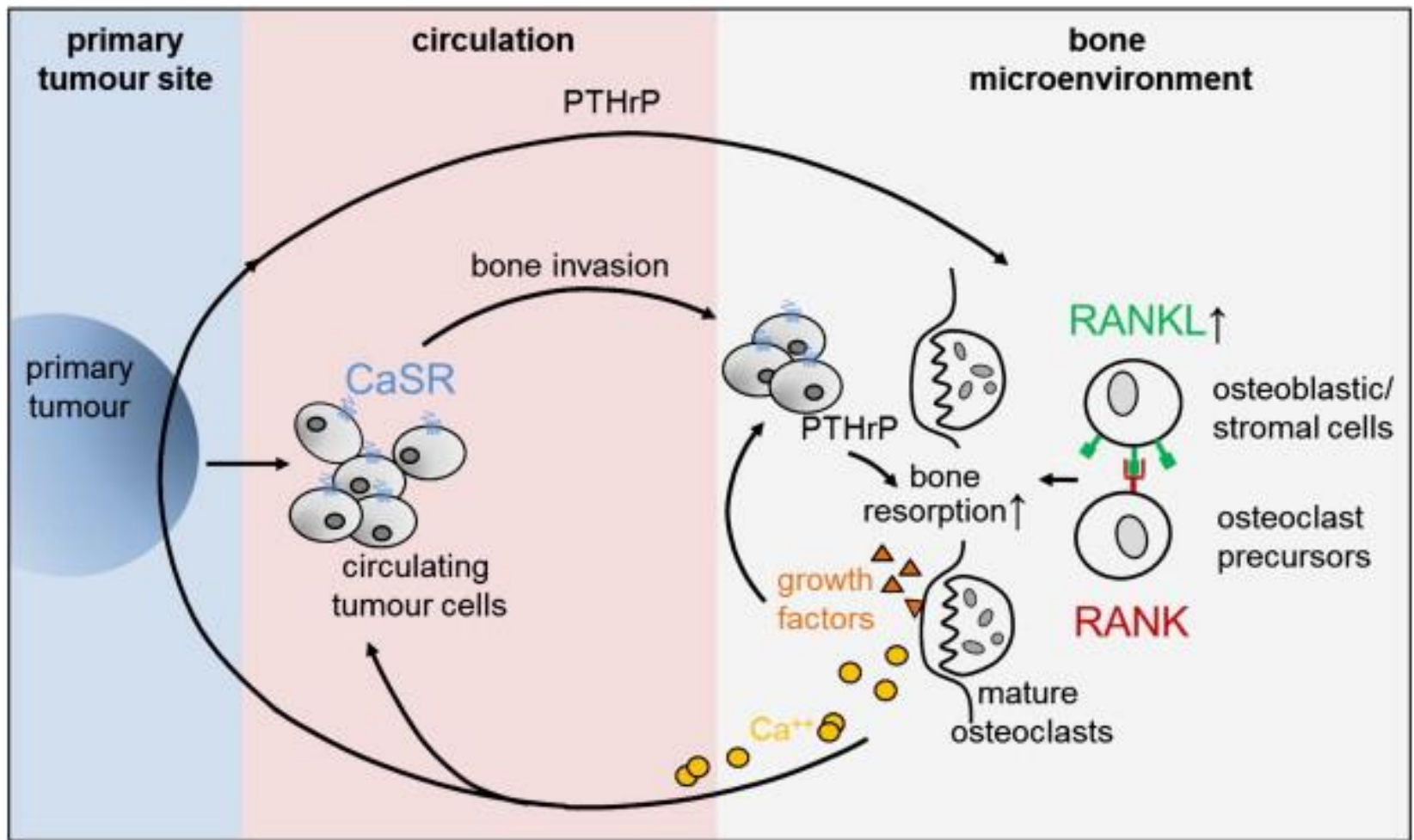
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# Die Knochenzellen „sprechen miteinander“





The vicious circle of bone metastasis in breast and prostate cancer. Breast and prostate tumours produce parathyroid hormone related peptide (PTHrP) which up-regulates receptor activator for NFκB ligand (RANKL) on osteoblastic and stromal cells. Upon binding of RANKL to its receptor on osteoclast precursor cells, i.e. Receptor activator for nuclear factor κB (RANK), maturation and differentiation of osteoclast precursors to activated osteoclasts is initiated and bone resorption stimulated. During bone resorption, large amounts of calcium (Ca<sup>2+</sup>) as well as diverse growth factors are released. Calcium promotes further PTHrP production in the tumour, thereby supporting the vicious circle. Acting via the calcium sensing receptor (CaSR), Ca<sup>2+</sup> is considered to act as a chemoattractant factor and to facilitate tumour cell migration into the bone. Growth factors enable tumour cell survival and growth in the bone microenvironment and in consequence the manifestation of bone metastases which in turn increases the rate of bone turnover, thus feeding the vicious circle.