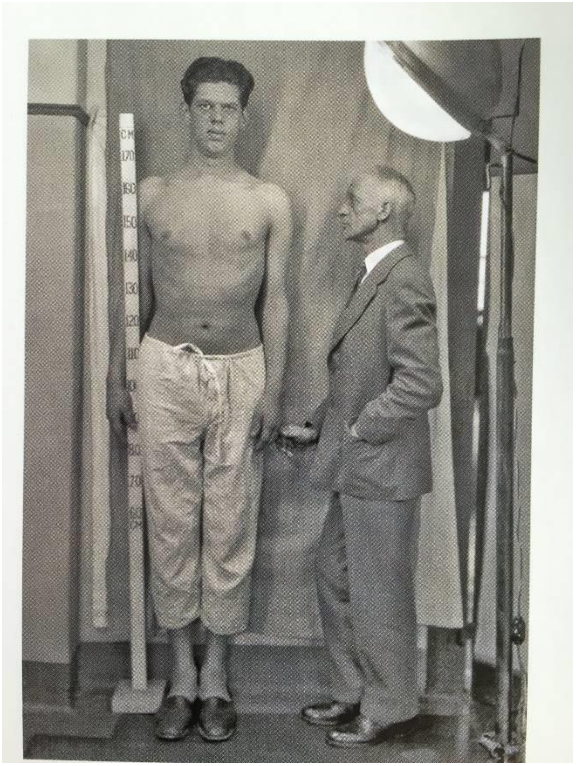
Update Akromegalie DGIM 2015



Burkhard L. Herrmann

Endokrinologie /// Diabetologie /// Innere Medizin

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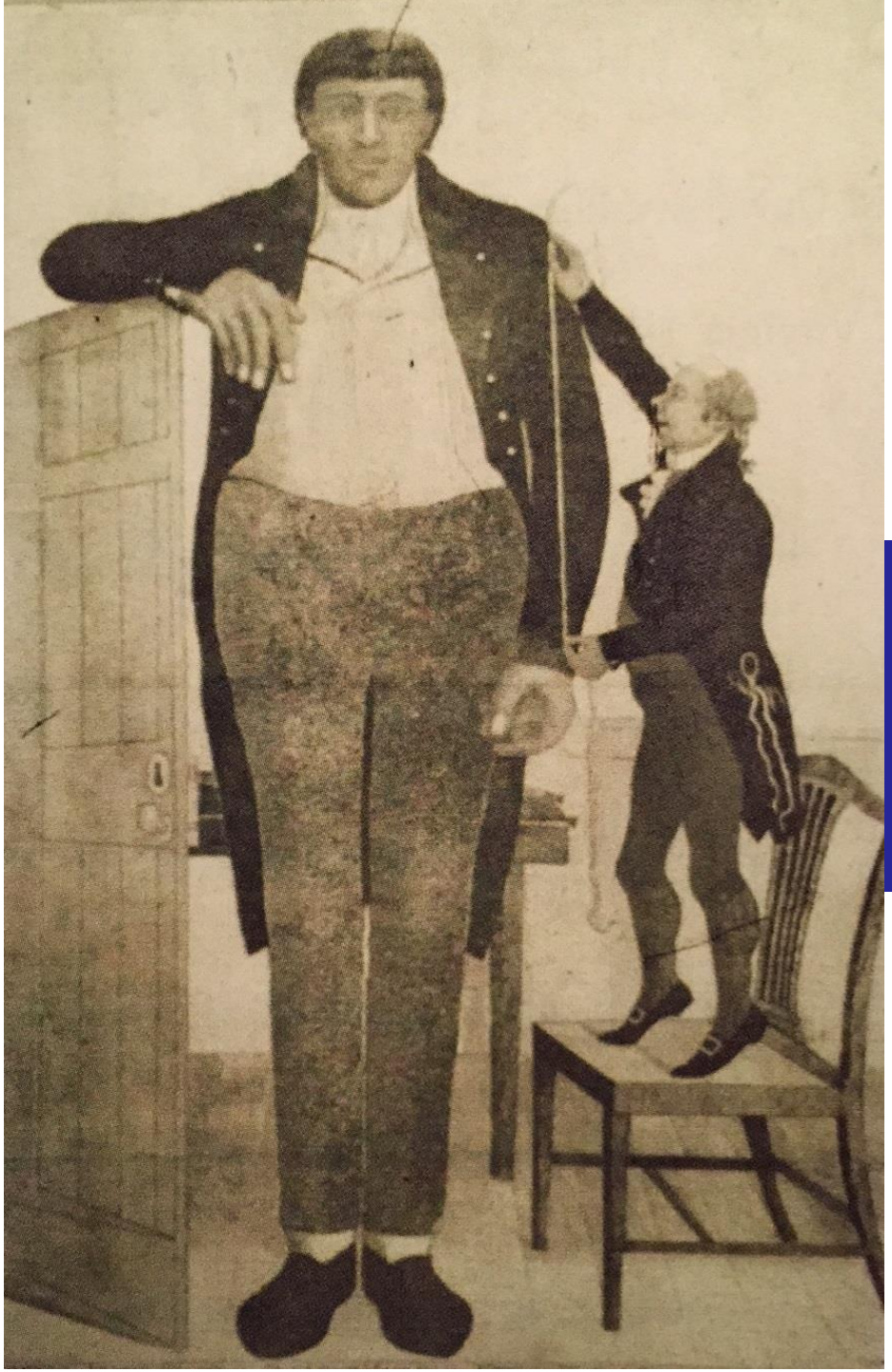
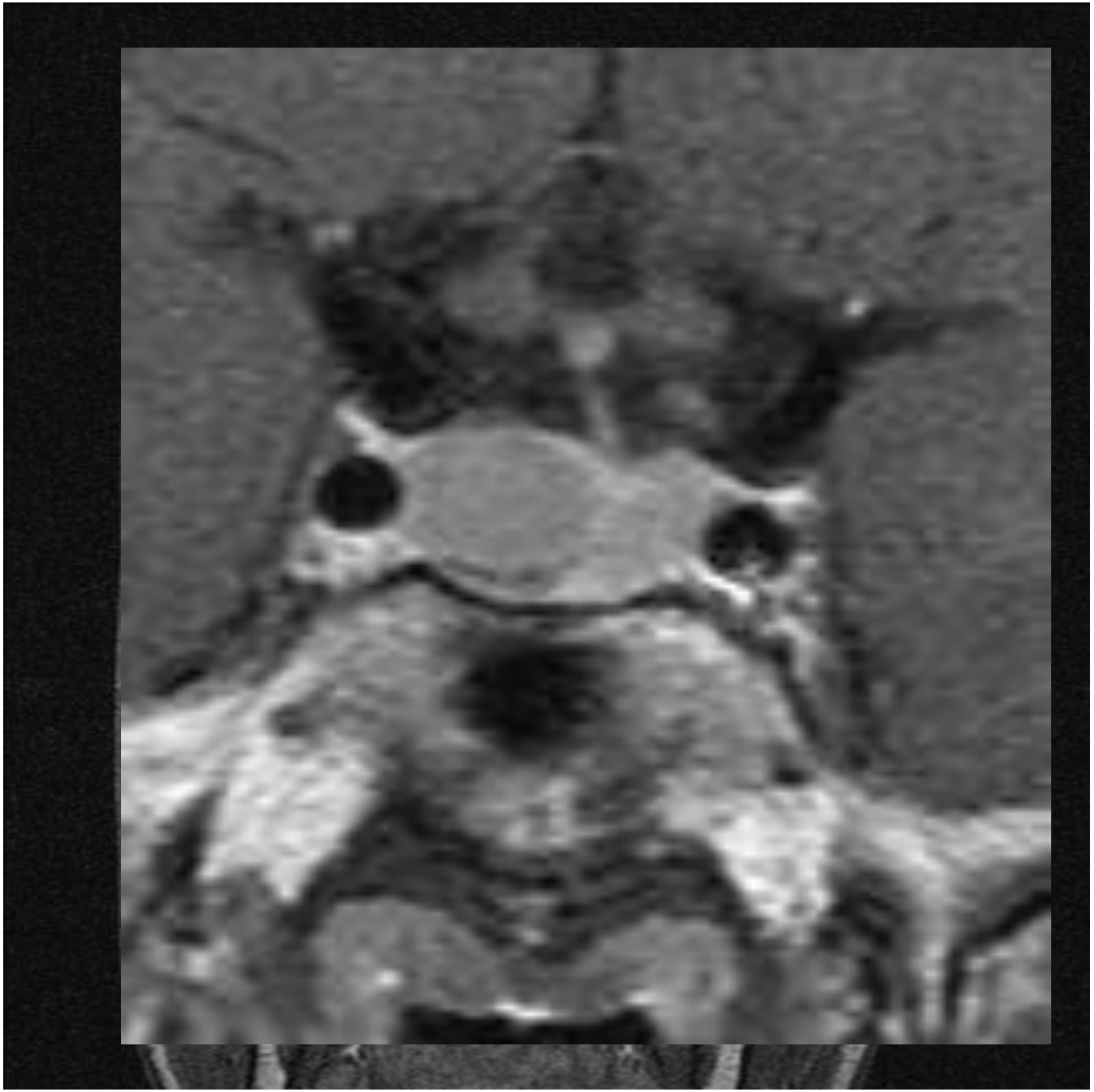
www.endo-bochum.de



Ätiologie der Akromegalie



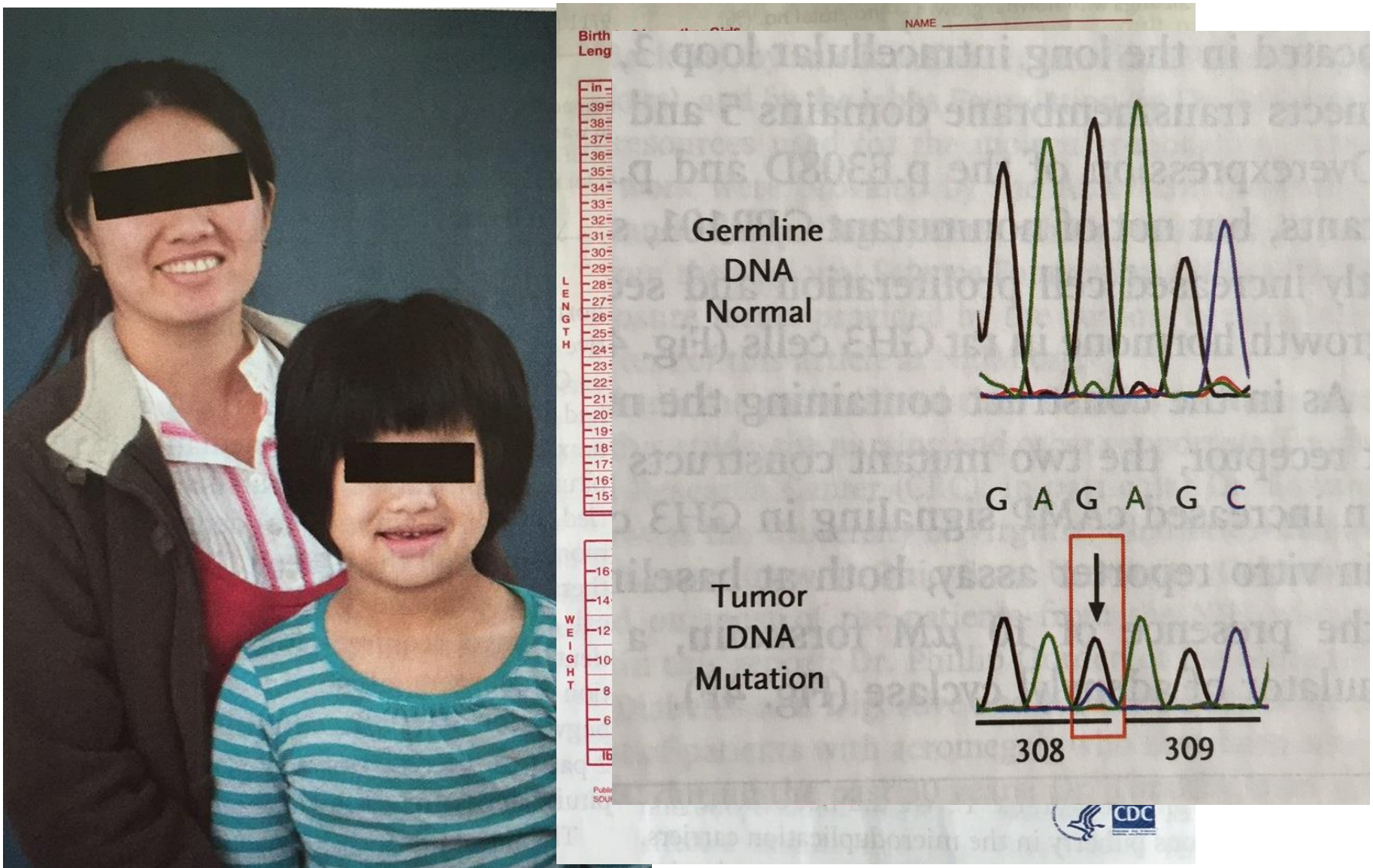
Etiology of Acromegaly

Table 1. Etiology of acromegaly.

Hormone excess	
GH	
	Pituitary – sporadic
	Pure somatotropinomas:
	Densely granulated
	Sparsely granulated
	Mixed GH-cell and PRL-cell adenomas
	Mammosomatotroph cell adenomas
	Acidophil stem cell adenomas
	Pluri-hormonal somatotropinomas
	Ectopic GH-secreting pituitary adenomas (sphenoid sinus, temporal bone and nasopharynx)
	Somatotroph carcinomas
	McCune Albright syndrome
	Pituitary – familial
	Isolated familial somatotropinoma (IFS)
	Multiple endocrine neoplasia type 1 (MEN-1)
	Carney Complex (CNC)
	Extra-pituitary
	Ectopic pancreatic islet cell tumor; non-Hodgkin's lymphoma
GHRH	
	Hypothalamic
	Hamartomas, gliomas and gangliocytomas
	Ectopic
	Carcinoid tumors, pancreatic cell tumors, small-cell lung carcinomas, pheocromocytomas, medullary thyroid carcinomas, adrenal adenomas, breast and endometrial carcinomas.

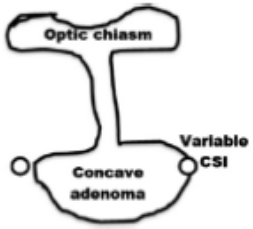
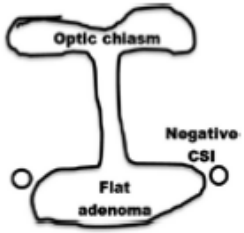
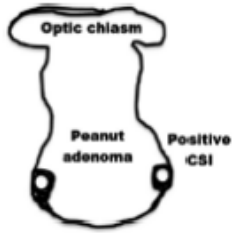
... M. Gadelha, Arq Bras Endocrinol Metab vol.49 no.5 São Paulo Oct. 2005

Gigantism and acromegaly due to Xq26 microduplications and GPR101 mutation



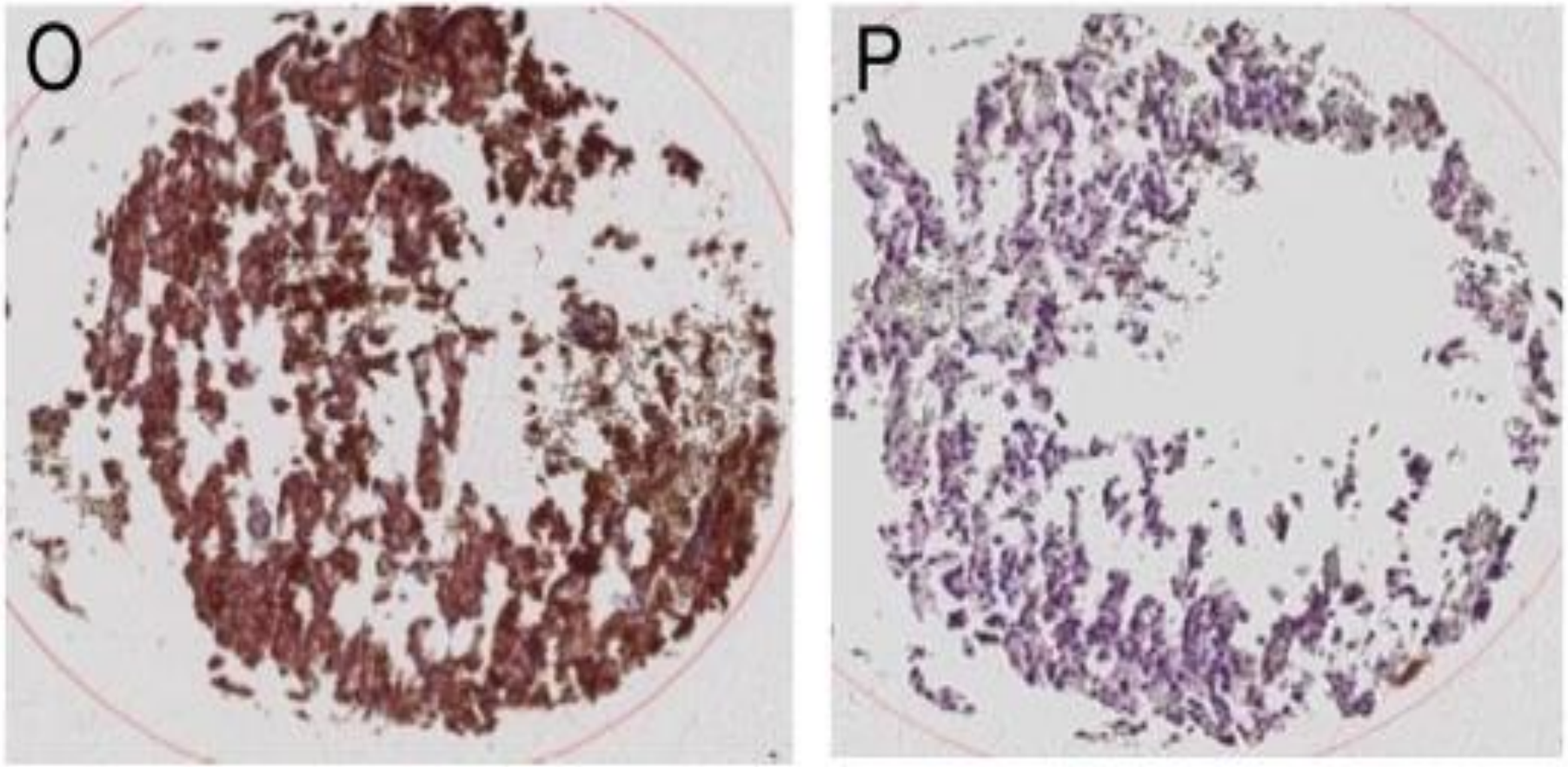
NEJM 2014 Dec 18;371(25):2363-74.

Akromegaly Types

	1	2	3
Frequency order	1	3	2
Tumor			
Shape and CSI	Concave 	Flat 	Peanut 
Size	Micro- or macroadenomas	Macroadenomas	Macroadenomas
Invasiveness by MRI	Intermediate	Never	Always
Aggressive behavior	Intermediate	No	Yes
Suprasellar extension	Intermediate	Rare	Common
Sphenoid sinus extension	Common	Rare	Intermediate
Optic chiasm compression	Rare	Rare	Common
Granulation	Dense	Both	Sparse
Immunoreactivity			
GH	Strong	Weak	Weak
α-Subunit	Positive	Positive or Negative	Negative
Ki-67 index $< 3\%$	90%	33%	42%
SSTR2	58%	30%	22%
p16	0.0%	0.2%	0.5%
p21	38%	15%	4%
Biochemistry			
IGF-1 levels at diagnosis	Lower	Intermediate	Higher
Prolactin at diagnosis	Intermediate	Lower	Higher
Management and outcomes			
No. of medications	2 or less	2 or less	2 or more
No. of surgeries	1	1 or 2	2 or more
Disease control	Frequent	Intermediate	Rare
IGF-1 levels at follow-up	Normal	Intermediate	Elevated

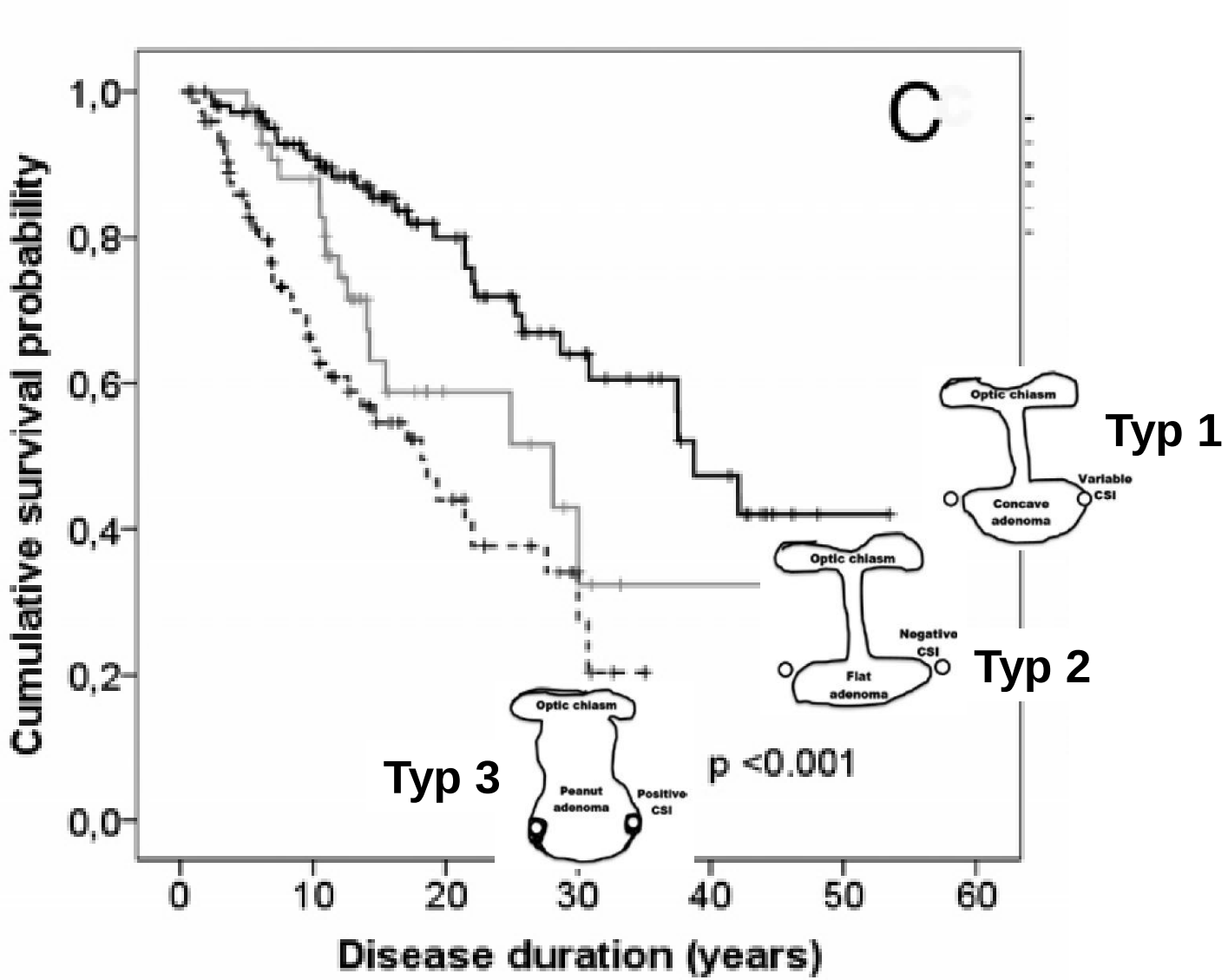
Cuevas-Ramos D, …. Melmed S, JCEM Jan 2015

Reduzierte SSTR-2-Aktivität in Typ 3 Tumoren

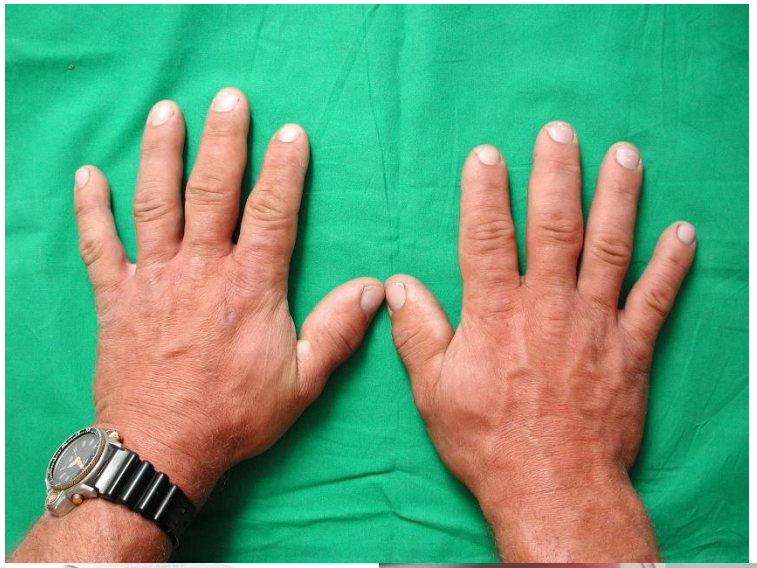


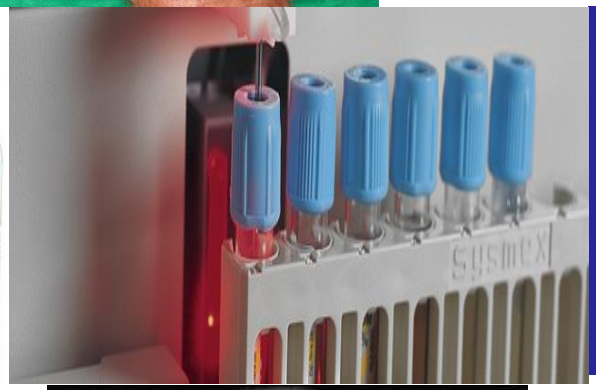
Cuevas-Ramos D, …. Melmed S, JCEM Jan 2015

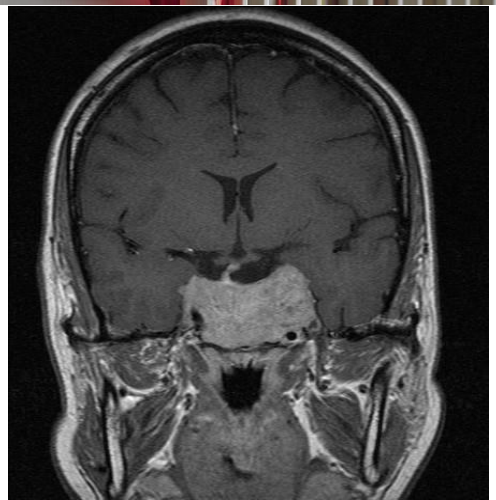
Reduzierte Überlebensrate bei Typ 3 / Peanuts-Tumoren



Cuevas-Ramos D, …. Melmed S, JCEM Jan 2015



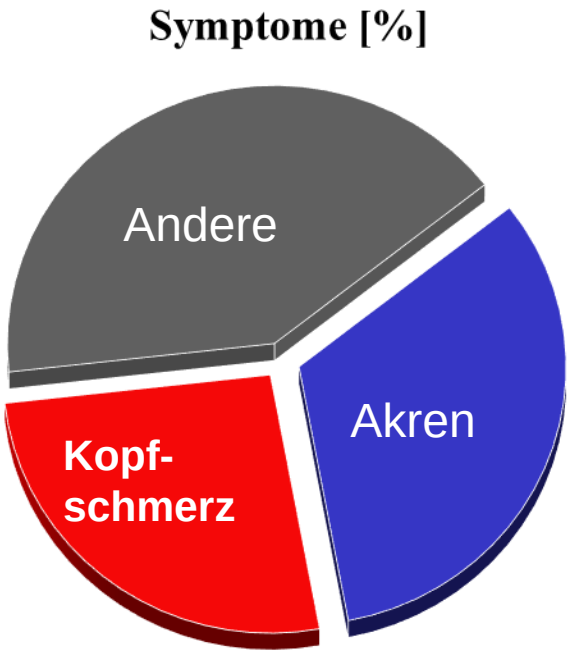




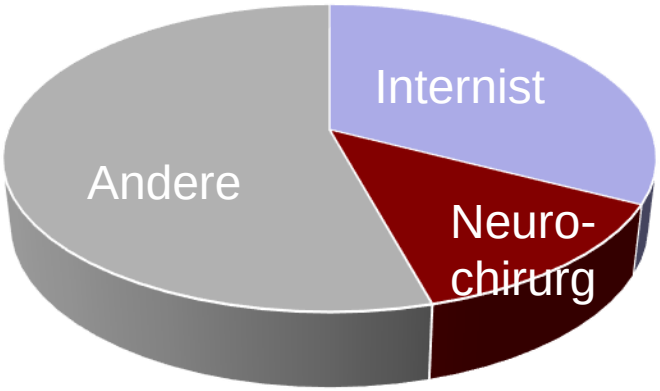
Diagnose der Akromegalie

“Die unentdeckte Akromegalie”

N=313, w=181, Alter 48.8±12.0 Jahre



Zeit bis zur Diagnose 24 Mo
(range 6-48 Mo)



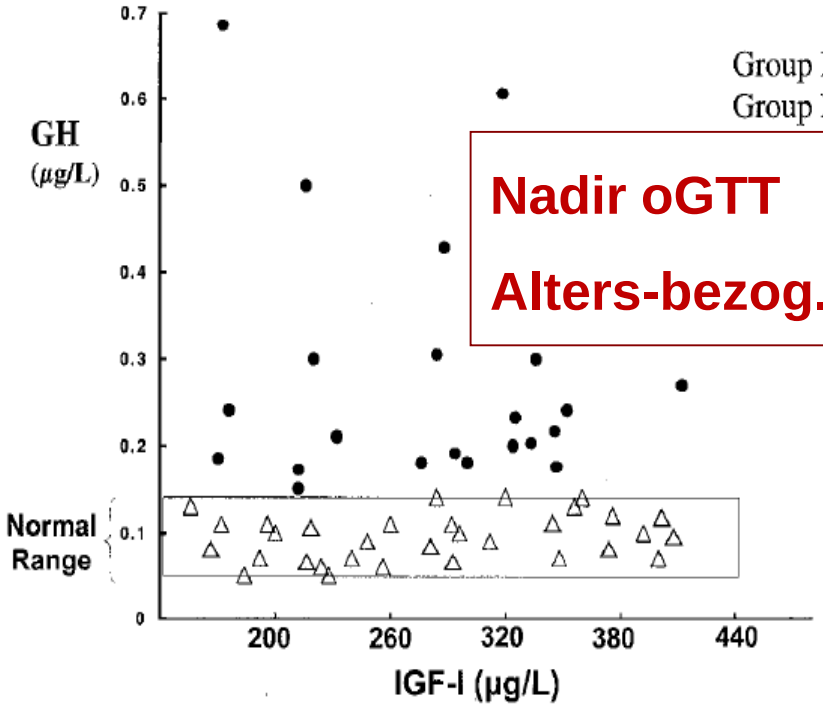
1. Vorstellung

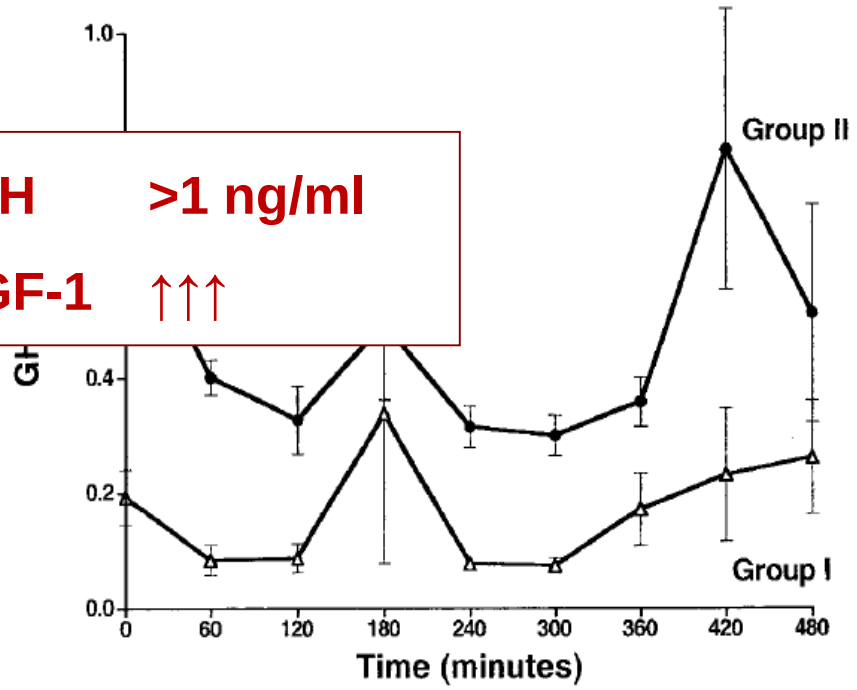
46% zur OP (35% Akro-assoz.)

13% Kopf / Kehlkopf
9% Nase
6% Schilddrüse
5% Carpaltunnel-Syndrom

Keskin et al. J Endocrinol Invest. 2015 Feb 26

Definition der Krankheitsaktivität



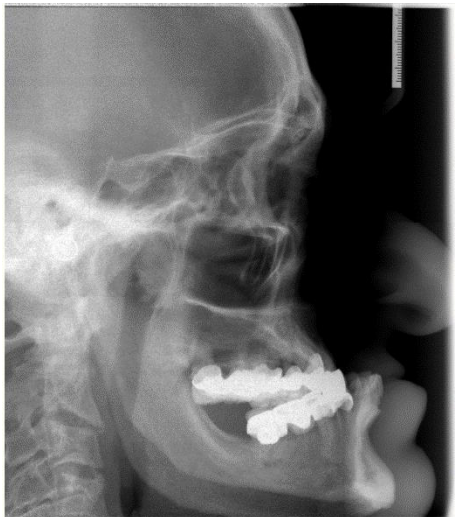


Nadir oGTT GH >1 ng/ml

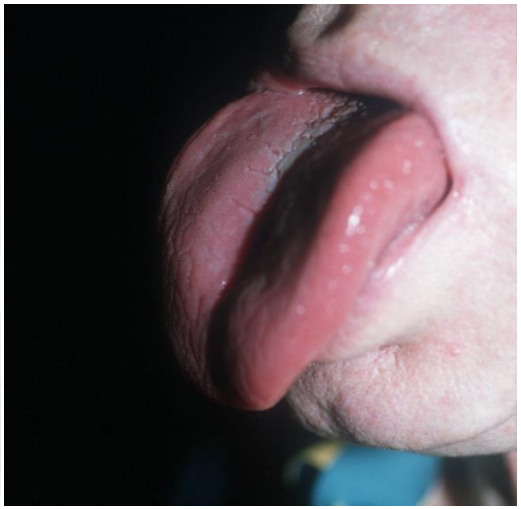
Alters-bezog. IGF-1 ↑↑↑

FIG. 1. Nadir GH levels after oral glucose and IGF-I levels in post-operative patients in remission as defined by normal IGF-I levels. △, Remission group I, nadir GH levels within the range of healthy subjects (≤0.14 μg/liter). ●, Remission group II, nadir GH levels were above the normal range (>0.14 μg/liter).

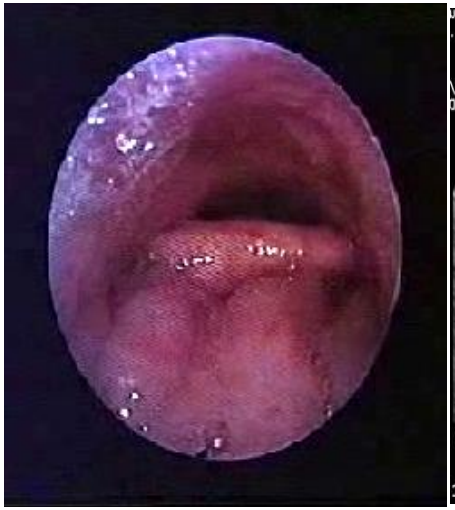
Freda et al. JCEM 2004
Melmed et al. Pituitary 2013
Katznelson et al, JCEM 2014



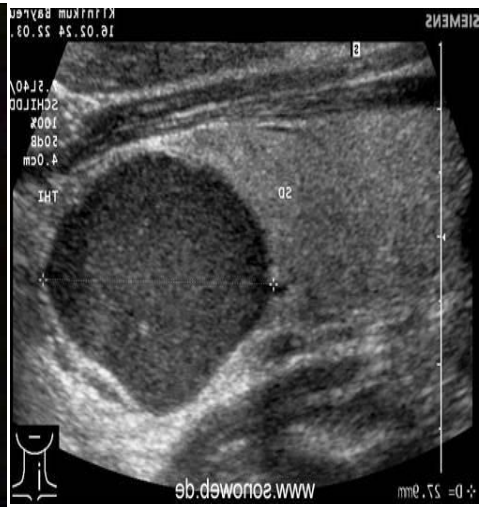
Herrmann BL et al., ECED 2009



Herrmann BL et al., EJE 2005



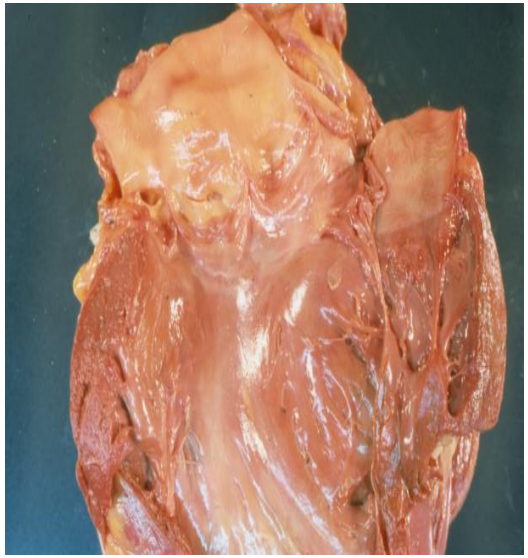
Attal et Chanson JCEM 2010



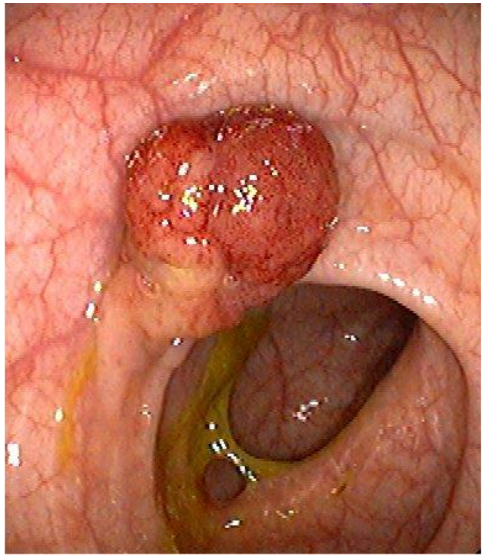
Herrmann BL et al., ECED 2004

Komplikationen der Akromegalie

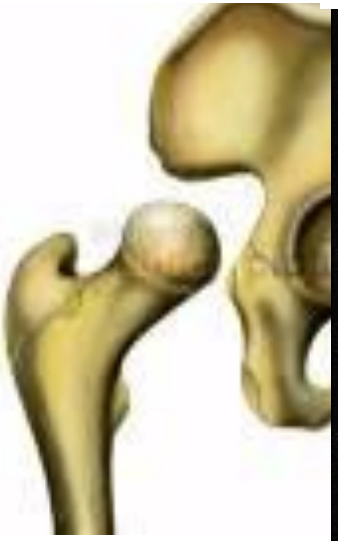
Isgaard et al. Endocrine 2015



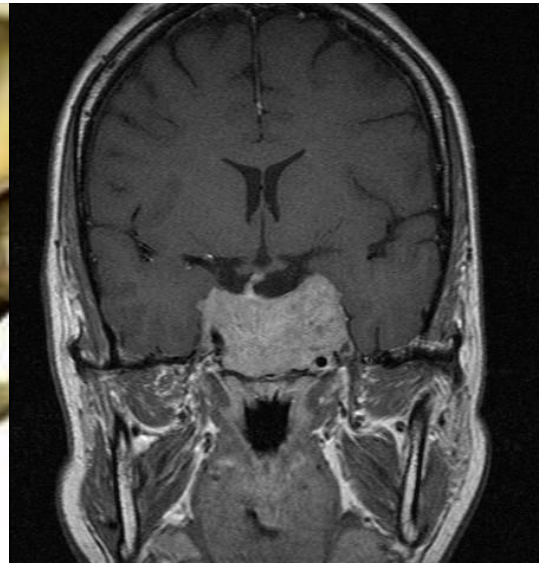
Yamamoto et al., Pituitary 2014



Anthony, Curr Op Endoc



Sarkar et al., Clin N Neuros 2014



Regelmäßige Untersuchungen

kardiologisch

endokrinologsich

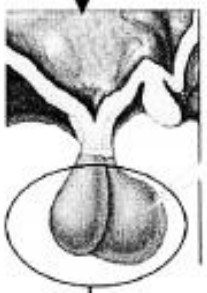
gastro-enterologisch

Diagnosis	During long-term follow-up
Blood pressure measurement	Every 6 months or when change of treatment (if hypertensive)
Echocardiography	Annually
ECG	Annually
Epworth scale or sleep study	Annually
Echo Doppler of peripheral arterial and venous system	Annually particularly in gigantism
OGTT	Fasting blood glucose every 6 months (particularly in uncontrolled disease and during SRL therapy); HbA_{1c} every 6 months if diabetes present
Total testosterone, SHBG and prolactin (males)	Annually (free testosterone when doubts in interpretation of total testosterone)
LH, FSH, 17β-estradiol and prolactin (females)	Annually (or when pregnancy is desired)
AcroQoL	Annually
DEXA	Every 2 years if patient with osteopenia/osteoporosis
Thoracic and lumbar spine X-ray	Every 2–3 years if osteoporosis risk factors, kyphosis or symptoms
Colonoscopy	Every 10 years (more frequently if IGF-I remains persistently elevated or if abnormal colonoscopy or family history of colonic cancer)
Genetic screening for markers of familial acromegaly (if suspicion)	

Melmed et al. Pituitary 2013

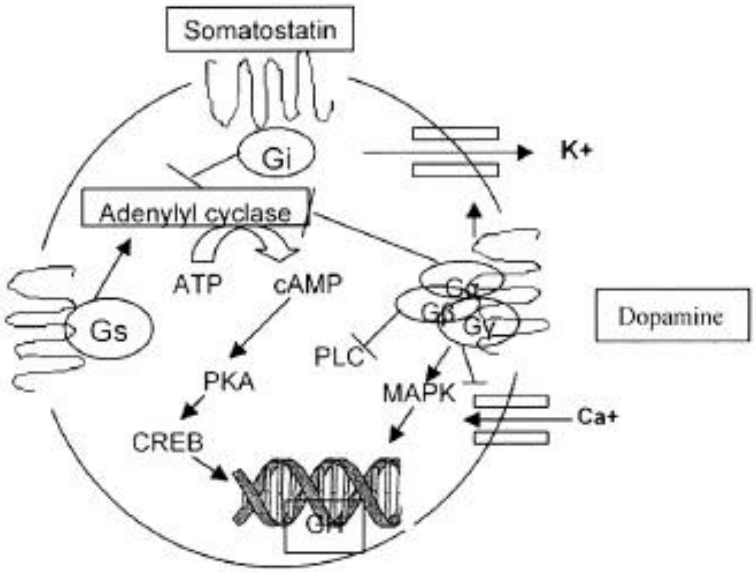
Therapie der Akromegalie

Radiotherapie
Operation
Dopaminagonisten
Somatostatin-Analogues



Somatotroph

GHRH



GH-Rezeptor-Antagonist

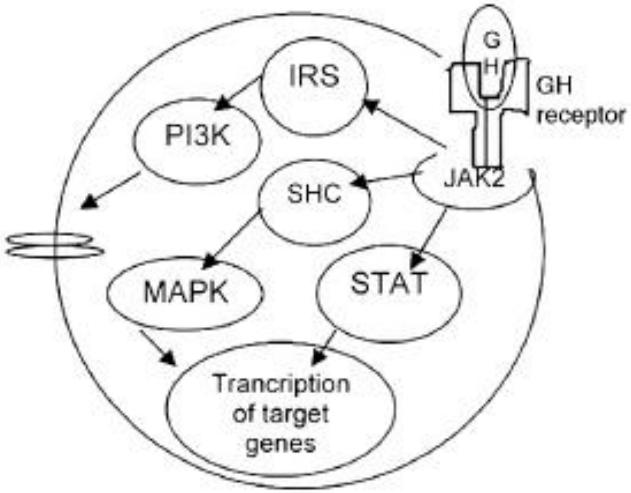
GH

Liver

IGF-1

Circulation

glucose



Sabino et al., Cancer Biology & Therapy 2010

Acromegaly: An Endocrine Society Clinical Practice Guideline 2014

4.0 Surgery

Indications

4.1 We recommend transsphenoidal surgery as the primary therapy in most patients. (1|⊕⊕⊕◯)

4.2 We suggest that repeat surgery be considered in a patient with residual intrasellar disease following initial surgery. (2|⊕⊕◯◯)

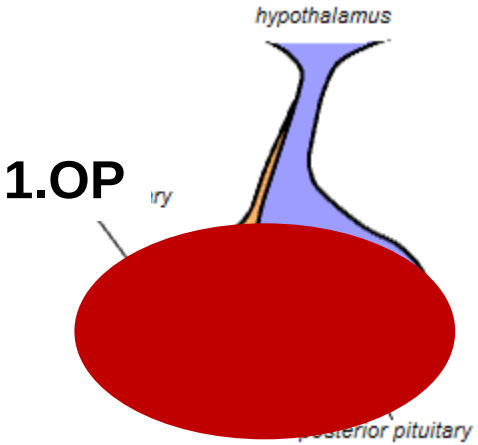
Preoperative medical therapy

4.3 We suggest against the routine use of preoperative medical therapy to improve biochemical control after surgery. (2|⊕⊕◯◯)

4.4 For patients with severe pharyngeal thickness and sleep apnea, or high-output heart failure, we suggest medical therapy with somatostatin receptor ligands (SRLs) preoperatively to reduce surgical risk from severe comorbidities. (2|⊕◯◯◯)

Surgical debulking

4.5 In a patient with parasellar disease making total surgical resection unlikely, we suggest surgical debulking to improve subsequent response to medical therapy. (2|⊕⊕◯◯)



Katznelzon et al. JCEM 2014

Acromegaly: An Endocrine Society Clinical Practice Guideline 2014

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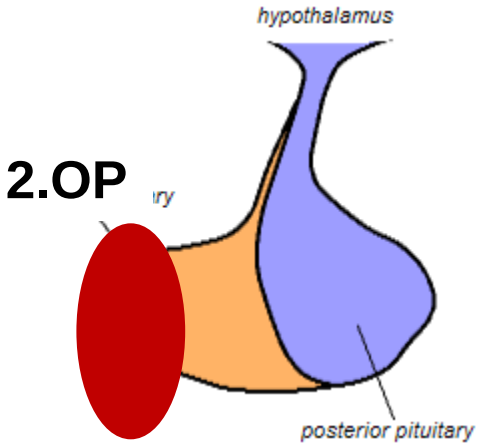

Katznelzon et al. JCEM 2014

Acromegaly: An Endocrine Society Clinical Practice Guideline 2014

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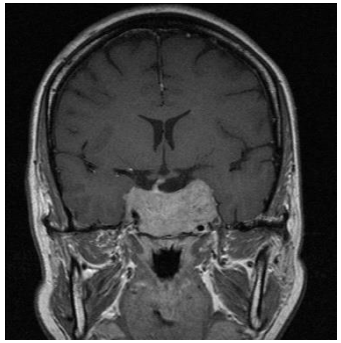
Fougner et al. Eur. J Endo 2014

SSA

OP

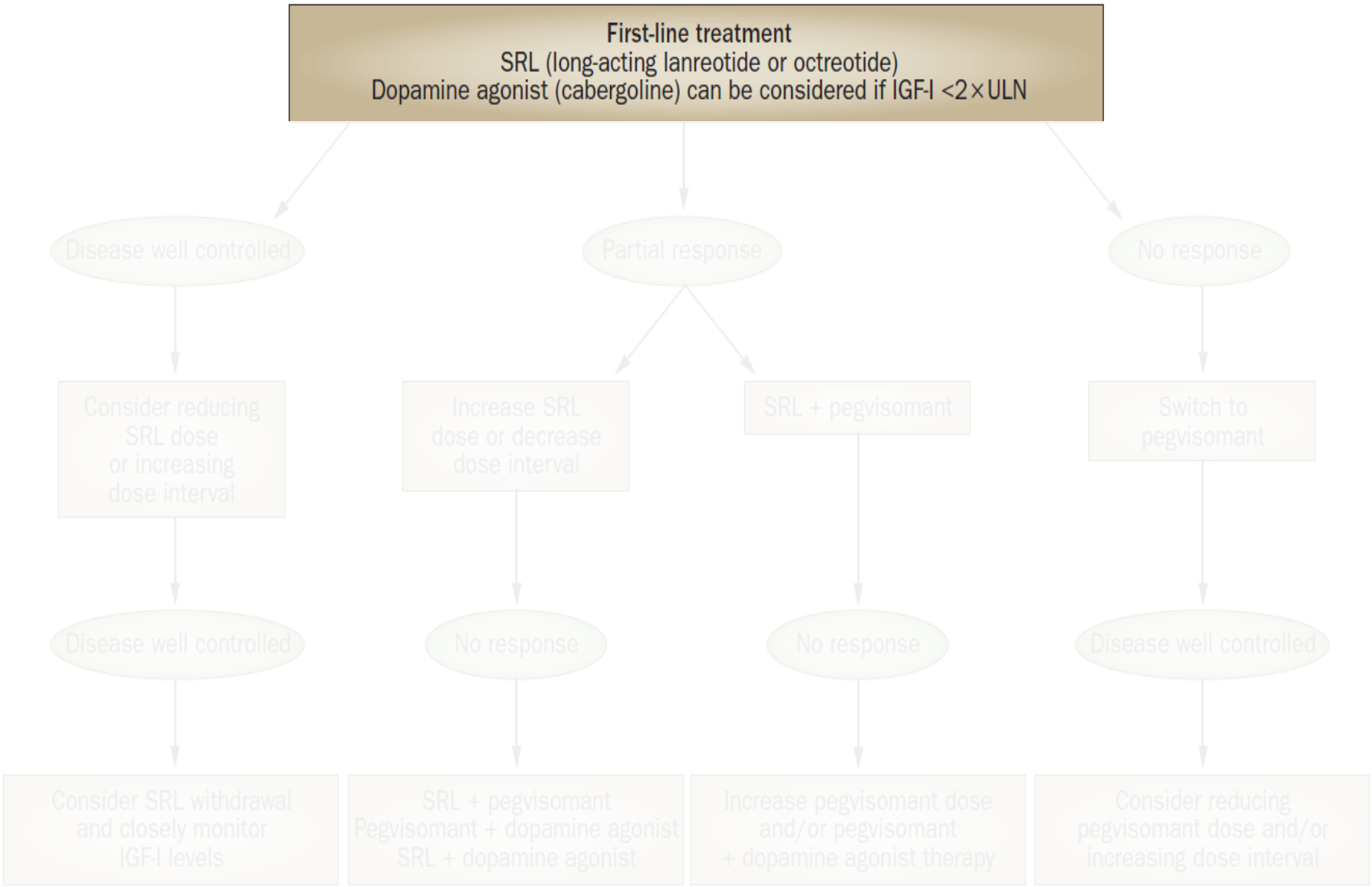


SSA

Karavitaki et al., Clin Endo 2008

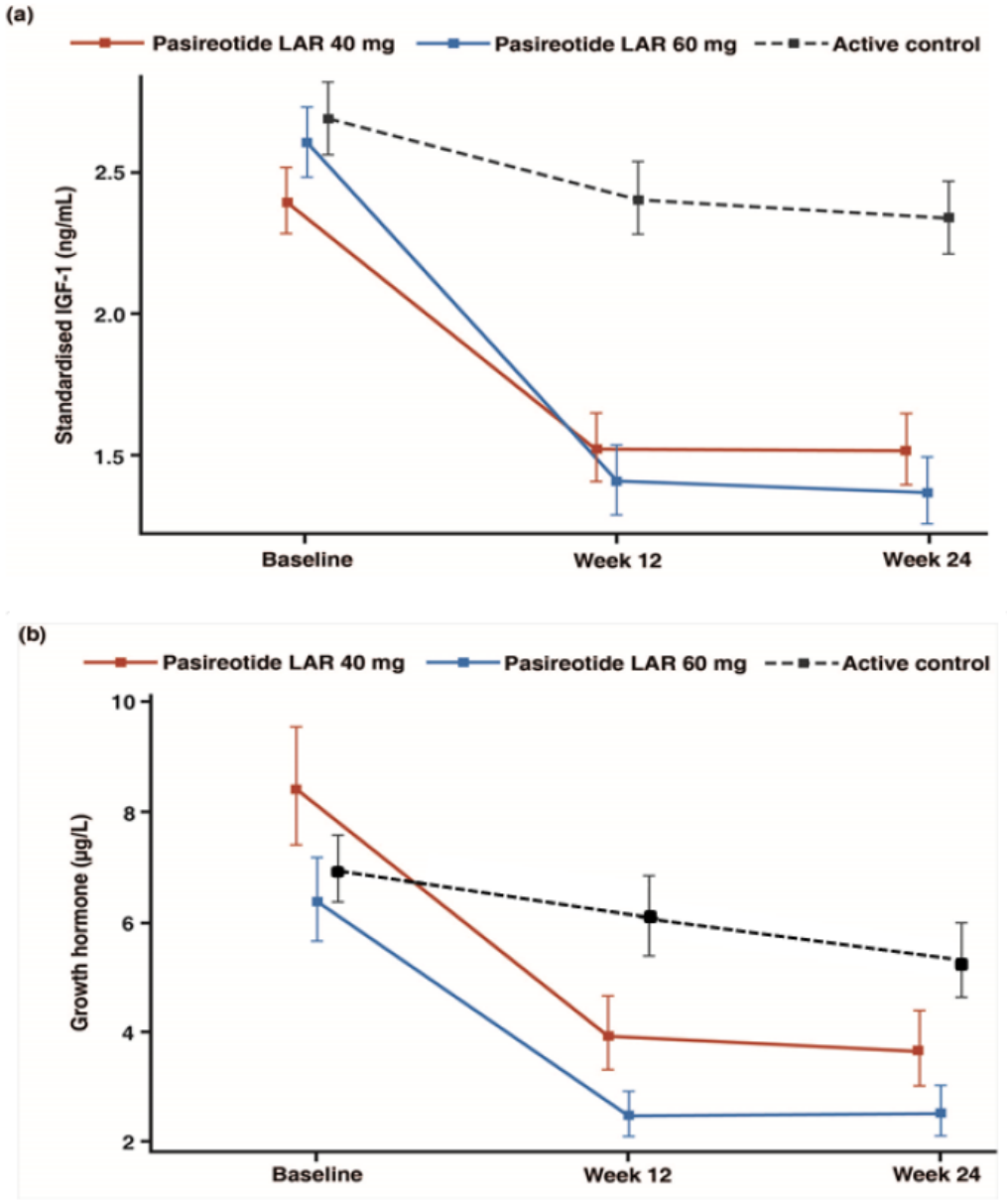
Katznelzon et al. JCEM 2014

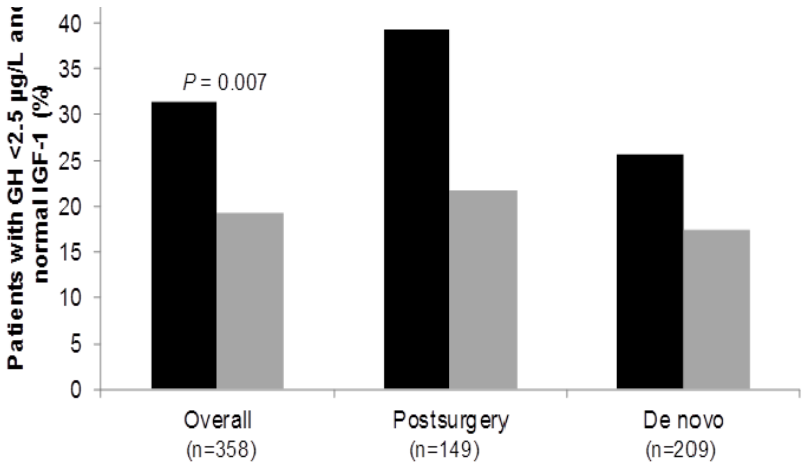
Medikamentöse Therapie der Akromegalie



Giustina et al, Nature Reviews / Endocrinology 4/2014

Pasireotide in Acromegaly



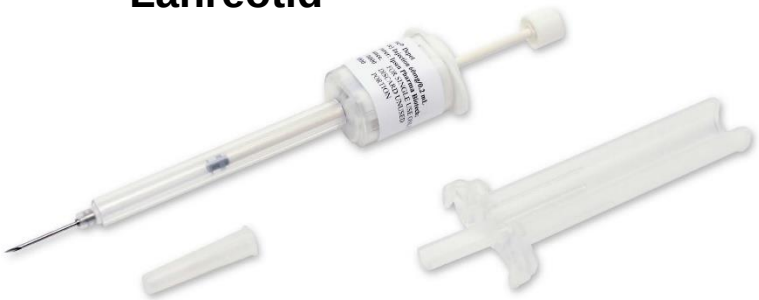


Petersenn S et al., Pituitary 2014
Gadelha M et al., Lancet Diabetes Endocrinol 2014
Samson S, Neuroendocrinology 2015

Medikamentöse Applikationsformen

Cabergolin

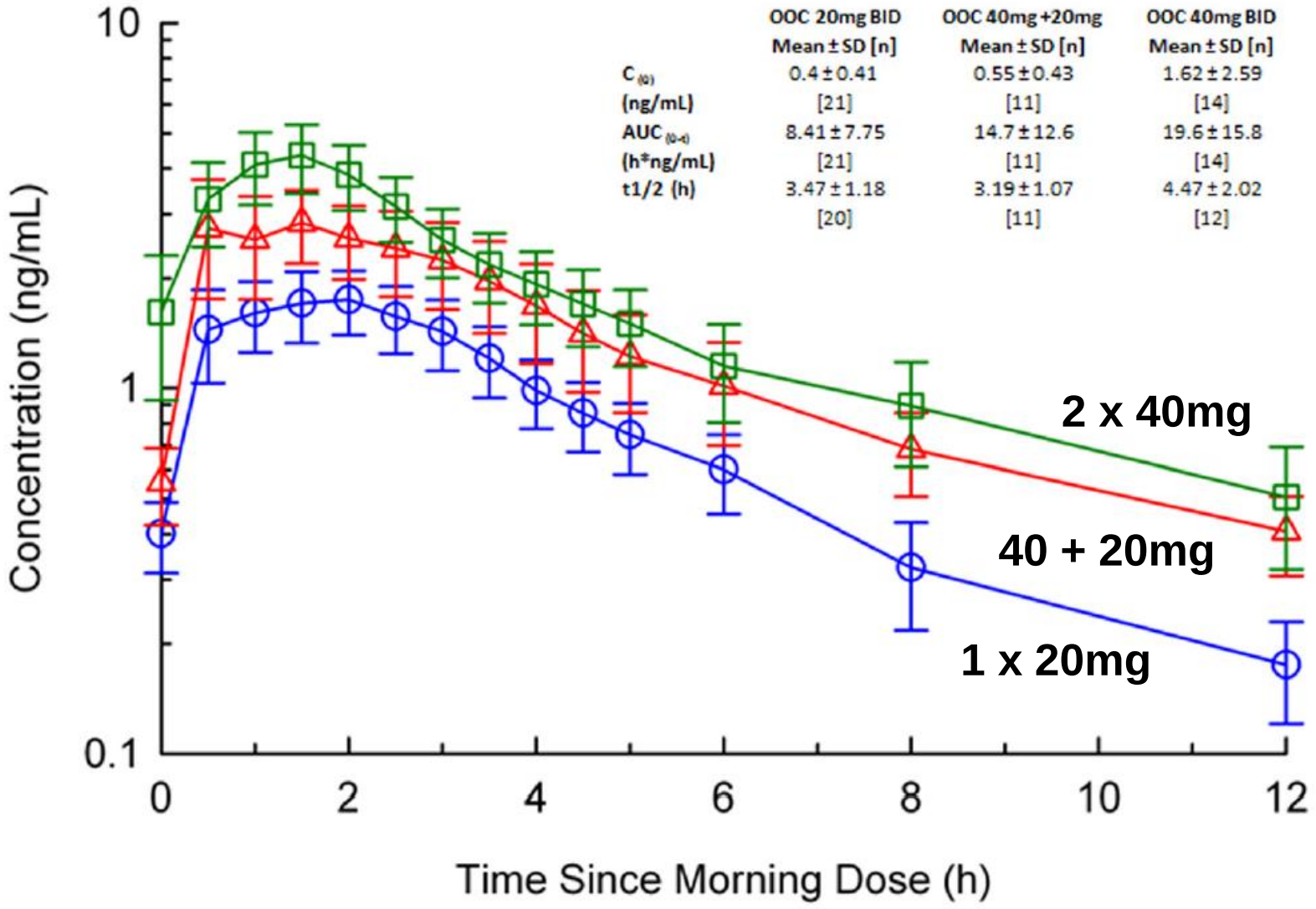
Lanreotid



Octreotid

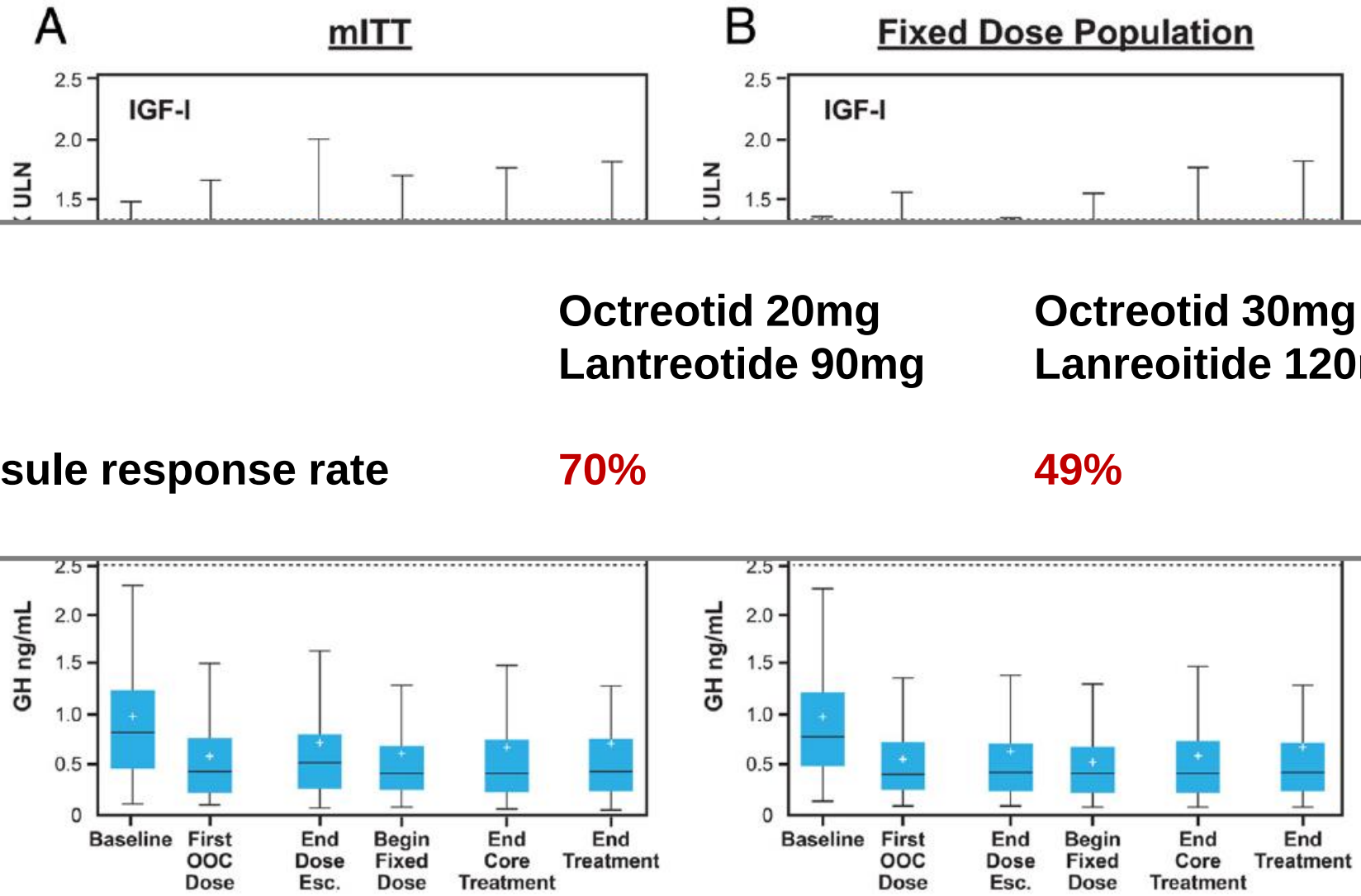
Pegvisomant

Orales Octreotid



Trainer et al., JCEM 2/2015

Orales Octreotid



	Octreotid 20mg Lantreotide 90mg	Octreotid 30mg Lanreoitide 120mg
capsule response rate	70%	49%

Trainer et al., JCEM 2/2015

Outcome der Akromegalie

Variables affecting **mortality in acromegaly** assessed by multivariate analysis

Study	Variable	*P* value
Holdaway *et al*.	GH post-treatment	0.001
(2004) (12)[a]	IGF-I post-treatment[b]	0.02[b]
	Age	0.006
	Years delay before diagnosis	0.035
	Hypertension at follow-up	0.043
Kauppinen-Makelin	Age	<0.001
et al. (2005) (13)[c]	GH post-treatment	0.007
	Male gender	0.015
	Microadenoma[d]	0.045

Holdaway et al., EJE 2008 Aug;159(2):89-95

www.akromegalie-register.de

DEUTSCHES AKROMEGALIE REGISTER

HOME KONTAKT IMPRESSUM INTERN

Standort: **Öffentlich** » Startseite »

- **Startseite**
- Aktuell
- Aufgaben und Ziele
- Was ist Akromegalie?
- Behandlungszentren
- Anmeldung als Zentrum
- Publikationen
- Links und Adressen

Teilnehmende Zentren
Adressen >>, Übersicht >>

Herzlich willkommen beim Deutschen Akromegalie-Register

Das Deutsche Akromegalie-Register wird geführt von der Arbeitsgemeinschaft Hypophyse und Hypophysentumore/DGE (AG Hypophyse), einer wissenschaftlichen Arbeitsgruppe der Deutschen Gesellschaft für Endokrinologie (DGE),

Deutsche Gesellschaft für Endokrinologie
Hormone und Stoffwechsel

und unterstützt von NOVARTIS Pfizer IPSEN

Letzte Änderung 15.10.2014

Für Ärzte

Initiative Akromegalie
Erkennen. Therapieren. Optimieren.

Download PDF »

Aktuelle Informationen zur modifizierten Register-Datenbank
mehr lesen »

Für Patienten und Ärzte

Awareness-Kampagne
Frühdiagnose erhöht die Heilungschancen - Machen Sie mit und fragen Sie Ihren Arzt!

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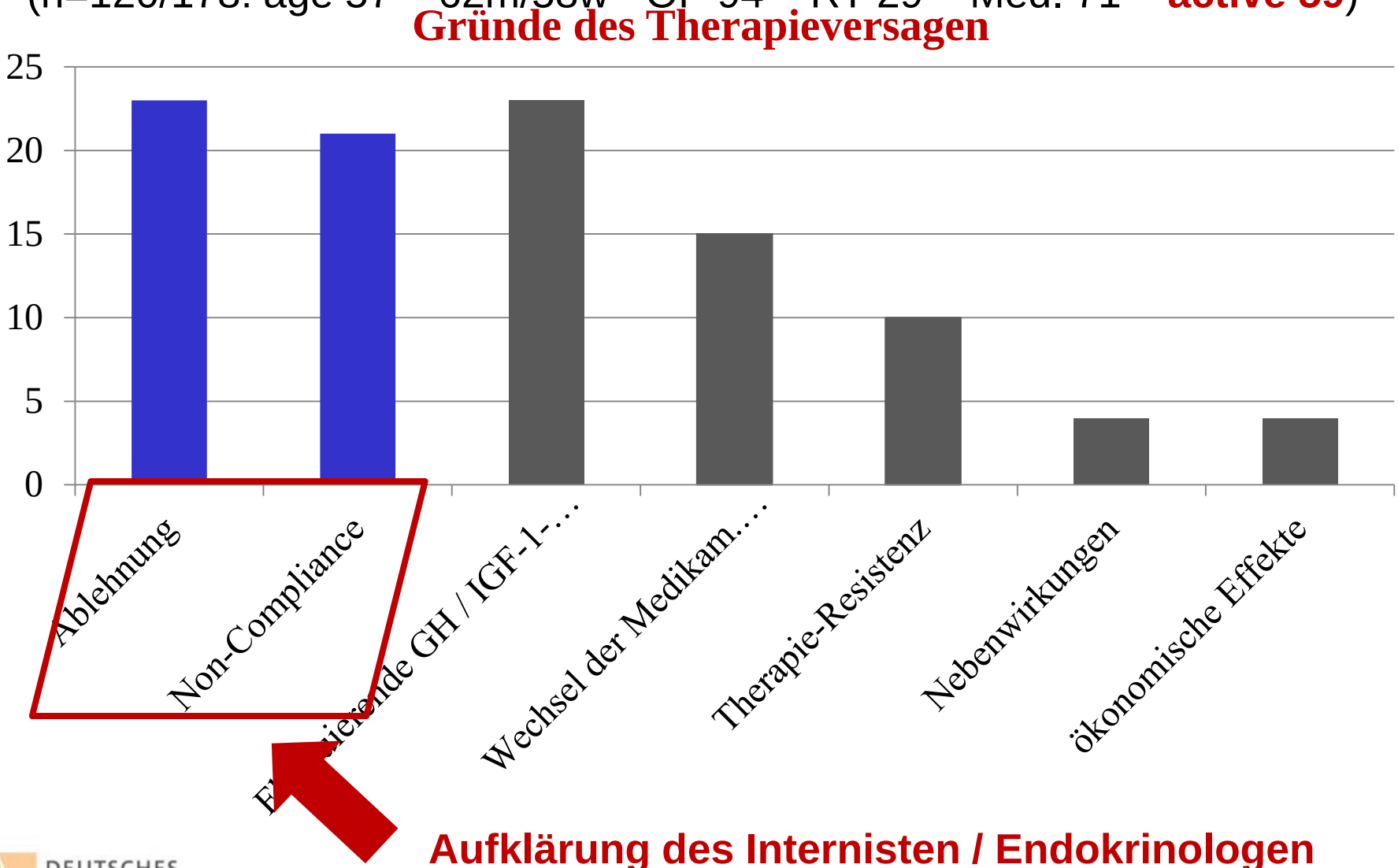
Akromegalie in den Medien

siehe Spiegel-online am 4.10.2014
Artikel lesen »

Failure to achieve disease control in acromegaly: cause analysis by a registry-based survey

(n=120/178: age 57 – 62m/58w - OP 94 – RT 29 – Med. 71 – **active 59**)

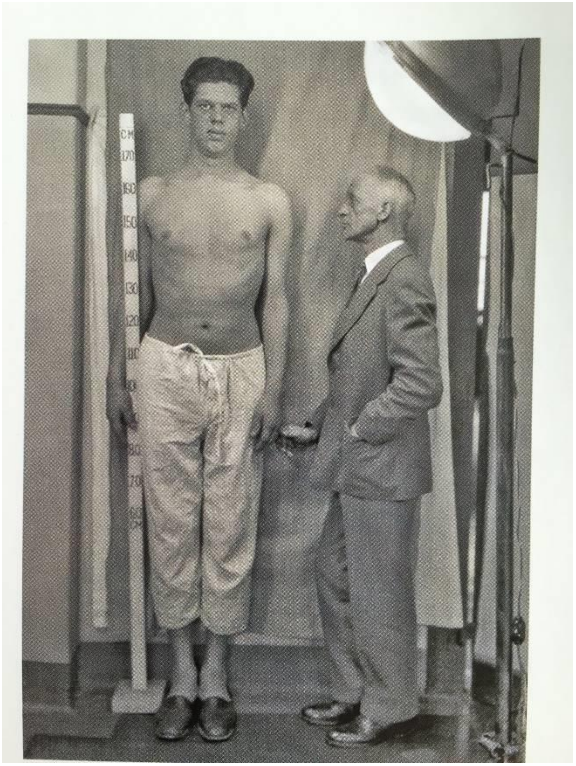


Aufklärung des Internisten / Endokrinologen

DEUTSCHES AKROMEGALIE REGISTER

Schöfl C et al., EJE Jan 2015

Update Akromegalie DGIM 2015



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Endokrinologie /// Diabetologie /// Innere Medizin

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