p-NET beeldvorming

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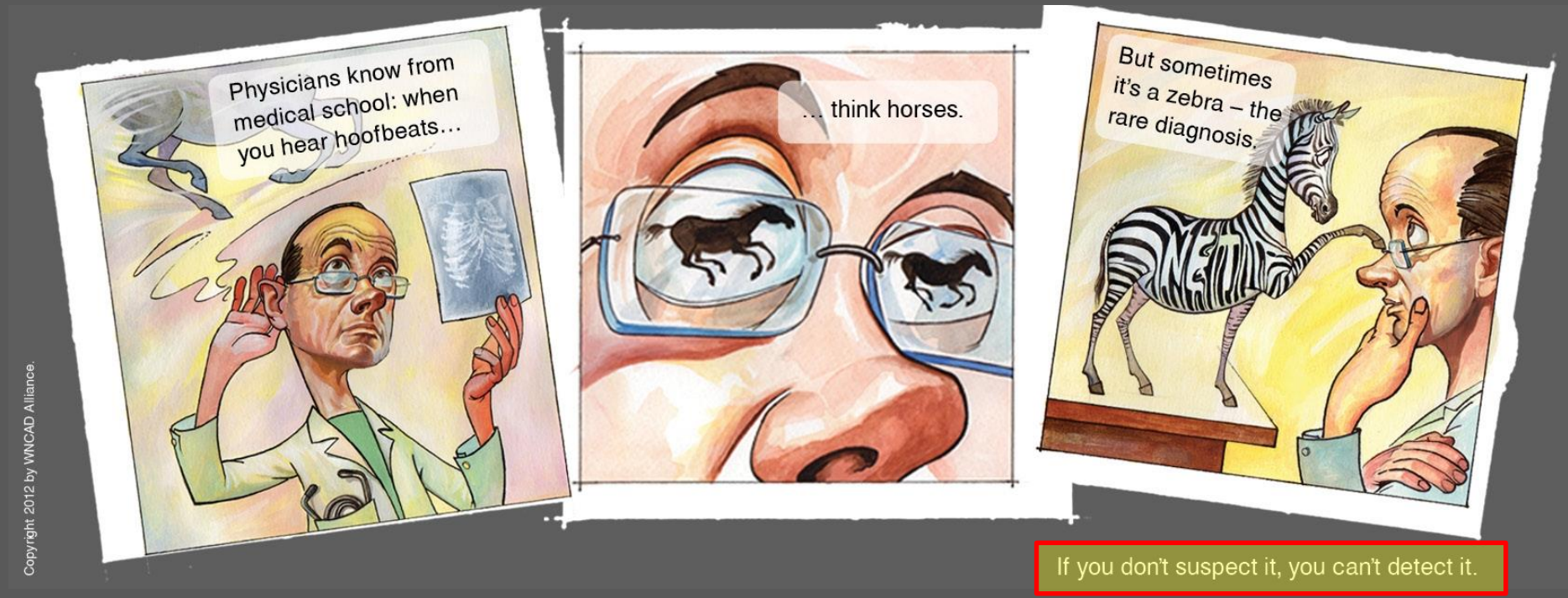

If you don't suspect it, you can't detect it.

p-NET: epidemiologie

- **3% van alle pancreastumoren**
  - 3 à 4 / miljoen / jaar
- op elke leeftijd (uitzonderlijk bij kinderen), *typisch* ontdekt tussen 40 – 60j
- M = V

- +/- 10% van de p-NETs: in het kader van één van deze syndromen, en dan vnl op jongere leeftijd:
  - Wermer syndroom: **multiple endocriene neoplasieën type 1** (**MEN-1**) (60% heeft p-NET)
  - **von Hippel-Lindau syndroom** (16% p-NET)
  - ziekte van Von Recklinghausen: **neurofibromatose type 1** (1% p-NET)
  - ziekte van Bourneville: **tubereuze sclerose** (uitzonderlijk p-NET)
  - (Oncol Res Treat 2016;39:643)

neuroendocrine neoplasms

Table 1. Site-specific relative frequency of neuroendocrine neoplasms in the body

Organ system	Proportion, %
Gastroenteropancreatic system	70
Respiratory system	25
Other primary sites	5

Table 2. Site-specific distribution of well and poorly differentiated neuroendocrine neoplasms (NENs) in relation to their relative frequency

Organ	Well differentiated NENs	Poorly differentiated NENs
Pituitary	common	very rare
Thyroid	common	very rare
Parathyroid	common	very rare
Thymus	common	rare
Lung	rare	common
Pancreas	common	very rare
Esophagus	very rare	common
Stomach	common	rare
Small bowel	common	rare
Appendix	common	very rare
Colon	very rare	common
Rectum	common	rare
Urogenital organs	very rare	common
Skin	very rare	common

Klöppel G, Visc Med 2017;33:324–330

2017 WHO classifications of neuroendocrine neoplasms of the pancreas

- well-differentiated NENs
  - NET **G1**: Ki67 **< 3%**
  - NET **G2**: Ki67 **3-20%**
  - NET **G3**: Ki67 **> 20%** (*NET-G3 has similar molecular features of NET G1/G2 rather than those of NE**C**-G3*)
- poorly differentiated NENs
  - NE**C** **G3**: Ki67 **> 20%**

Hijioka e.a. JOP. J Pancreas (Online) 2017 Dec 28; S(3):216-220.

Table 2. Genetic mutations and molecular abnormalities.

Molecular abnormalities	Well-diff.NET (NET G1/2)	NET-G3	NEC G3
Authors	Jiao et al. [39] Raj et al. [11]	Hijioka et al. [8] Tang et al. [13] Konukiewitz et al. [44]	Yachida et al. [44, 45] Hijioka et al. [8] Tang et al. [13] Shida et al. [50]
KRAS	0%	0%	29-49%
Rb1	0%	0%	55-89%
P53	3%	0%	18-100%
mTOR (PTEN, TSC2) Or p-mTOR	7-18%	NA	67%
Bcl2	18%	NA	50-100%
MEN1	44-61%	75%	33%
DAXX/ATRX	18-41%	75%	20%

NEC neuroendocrine carcinoma; NET neuroendocrine tumor

- MiNEN (mixed neuroendocrine-nonneuroendocrine neoplasm)

beeldvorming: rol

- diagnose
  - localisatie, identificatie, uitgebreidheid
    - primaire tumor
    - metastasen, klieren
- behandeling opvolgen: therapierespons, recidieven opsporen
- behandeling (cfr Nucleaire Geneeskunde)

- keuze van BV-techniek afhankelijk van context (tumor status)
  - CT (meestal eerste keuze)
  - PET-CT
  - MR
  - echografie: cfr “echo-endo”
  - angiografie
- **multidisciplinaire samenwerking is cruciaal**

p-NET

- **functionele tumoren:**
  - meestal < 1 cm
  - klinisch: symptomen tgv de *geproduceerde hormonen*

- **niet functionele tumoren:**
  - meestal >> cm
  - klinisch: symptomen tgv *massa-effect*

From: **Evolving Patterns in the Detection and Outcomes of Pancreatic Neuroendocrine Neoplasms: The Massachusetts General Hospital Experience From 1977 to 2005**

Arch Surg. 2007;142(4):347-354. doi:10.1001/archsurg.142.4.347

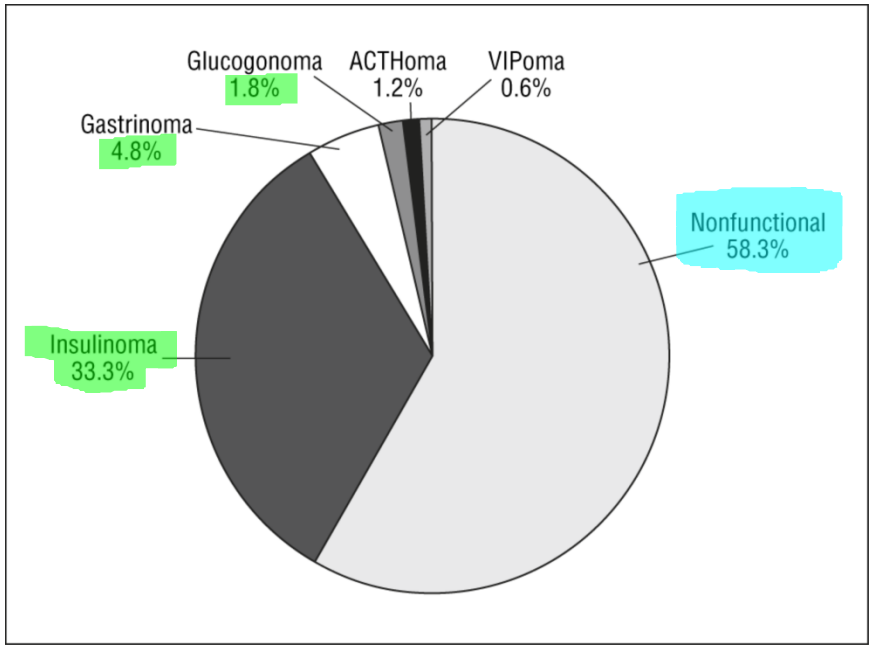

Figure Legend:

Classification of 168 resected pancreatic neuroendocrine neoplasms. Of the nonfunctional neoplasms, 87.8% were discovered incidentally. ACTH indicates adrenocorticotropic hormone; VIP, vasoactive intestinal polypeptide.

From: **Evolving Patterns in the Detection and Outcomes of Pancreatic Neuroendocrine Neoplasms: The Massachusetts General Hospital Experience From 1977 to 2005**

Arch Surg. 2007;142(4):347-354. doi:10.1001/archsurg.142.4.347

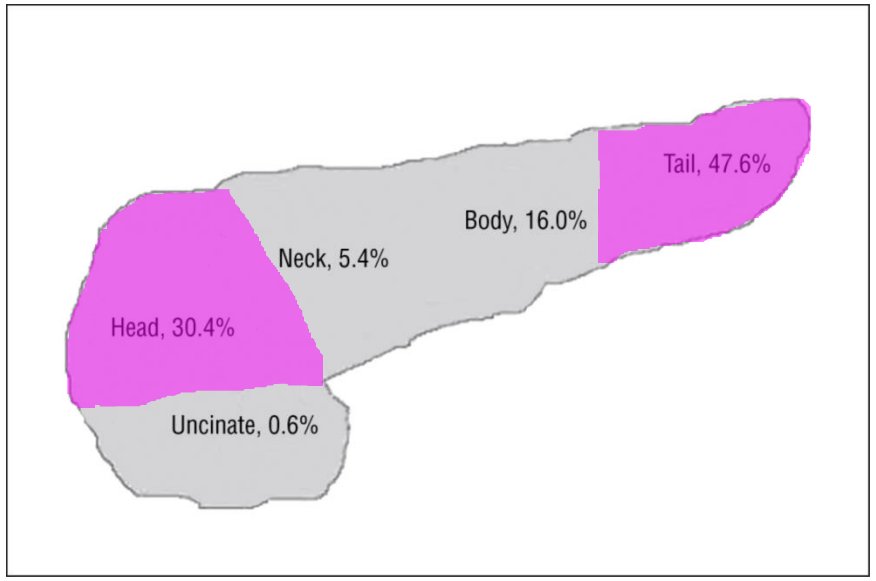

Figure Legend:

Location of 168 pancreatic neuroendocrine neoplasms.

p-NET: CT

- multifase **CT:** aanvaarde 1ste keuze beeldvorming
  - sensitiviteit: 69–94%

- **<u>functionele p-NET:</u>**
  - **klein** (1–2 cm) goed omschreven, **hypervasculair**
    - *als* grotere tumor (vb. glucagonoma): vaak degeneratie: heterogeen
- **<u>niet-functionele p-NET:</u>**
  - **groter** (gemiddeld: 4 cm)
  - meestal goed afgelijnd: 90% “**hypervasculaire rand**”
  - heterogene aankleuring
    - cystisch-degeneratieve zones, necrose, fibrose
    - helemaal <u>cystisch:17% </u>van alle p-NETs, groter en vaker symptomatisch (typisch in MEN-1)

p-NET: MR

- = CT-morfologie
- **hypo-intense noduli op T1-wi** (zonder- en mét vetsaturatie)
- **hoge SI op T2-wi**
- beter contrast in weke weefsels ⇒ betere detectie en typering
- sensitiviteit: 74–94%, specificiteit: 78–100%
- **diffusie** gewogen beelden en “apparent diffusion coefficient “ mapping
  - hulp om niet-hypervasculaire NETs te visualiseren
  - inverse correlatie tussen Ki-67 index en ADC waarde

Choi respons evaluatie criteria

Response	Definition
CR	Disappearance of all lesions No new lesions
PR	A decrease in size ⩾10% or a decrease in tumour attenuation (HU) ⩾15% on CT No new lesions No obvious progression of non-measurable disease
SD	Does not meet criteria for CR, PR, or PD No symptomatic deterioration attributed to tumour progression
PD	An increase in tumour size ⩾10% and does not meet criteria of PR by tumour attenuation on CT New lesions

Abbreviations: CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; HU = Hounsfield unit.

Nuclear Medicine
^{18}FDG PET-CT

- p-NET's: don't typically demonstrate sufficient uptake *unless they are poorly differentiated*
- **^{18}FDG PET-CT = complementary technique to ^{68}Ga PET-CT** (which shows *poor uptake in poorly differentiated tumors*)

Nuclear Medicine

gallium labeled somatostatin analogs

^{68}Ga PET-CT

- ^{68}Ga-DOTA-1-Nal-octreotide (**DOTANOC**)
  - higher affinity for receptor subtypes 2, 3, and 5

- ^{68}Ga-DOTA-tyrosine-3-octreotide (**DOTATOC**)
  - higher affinity for receptor subtype 2
- ^{68}Ga- DOTA-tyrosine-3-octreotate (**DOTATATE**)
  - higher affinity for receptor subtype 2

Nuclear Medicine

^{177}Lu-DOTATATE therapie

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FDA approves lutetium Lu 177 dotatate for treatment of GEP-NETS

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On January 26, 2018, the Food and Drug Administration approved lutetium Lu 177 dotatate (LUTATHERA, Advanced Accelerator Applications USA, Inc.) a radiolabeled somatostatin analog, for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

Approval was based on data from NETTER-1 (NCT01578239), a randomized, multicenter, open-label, active-controlled trial in 229 patients with progressive, well-differentiated, locally advanced/inoperable or metastatic somatostatin receptor-positive midgut carcinoid tumors. Patients were randomized (1:1) to receive either lutetium Lu 177 dotatate (7.4 GBq [200 mCi] every 8 weeks for up to 4 administrations; maximum cumulative dose of 29.6