PET Scan in Practice for CHI

- Basics, strength and weakness -

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Topics in today's presentation

1. Basics
   - Mechanisms of PET-Imaging
   - What is special on DOPA as PET-tracer?
2. 10 years experience: - role of DOPA/PET in CHI
3. Limits and Weaknesses of DOPA-PET in CHI

"The truth is rarely pure and never simple."

Oscar Wilde

^{18}F-DOPA-PET in CHI

- Started 2001 in Turku, Finnland (T. Otonkonski, 2003)
- Superior performance compared to older localisation methods (PVS, Calc.-stimulation)
  - Non-invasive, faster
  - Less radiation than PVS
  - Higher sensitivity + specifity

The Berlin way

Creation of:

- high resolution PET-scans with a spatial resolution of 2 mm
- high resolution enhanced 3-phase CT-images (64 lines)
- serial scans after 20, 30 and 40 minutes

Chronology:

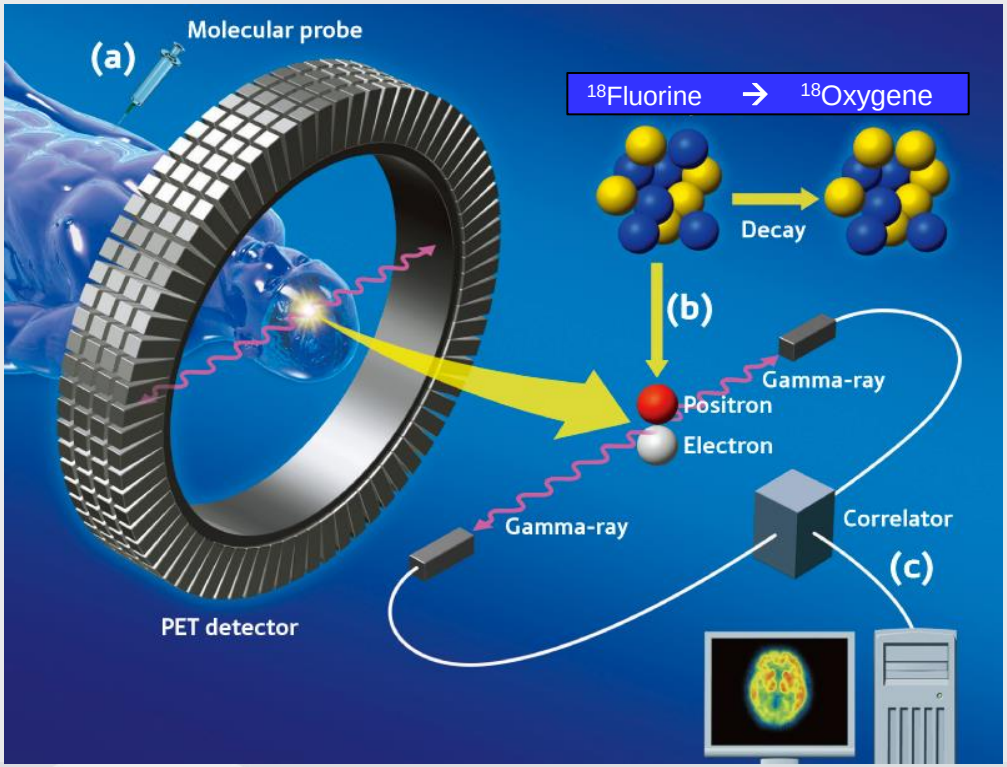
- First investigation at DTZ: 19th of December 2003
- Total number of investigations : about 175 (in collaboration with Charité)

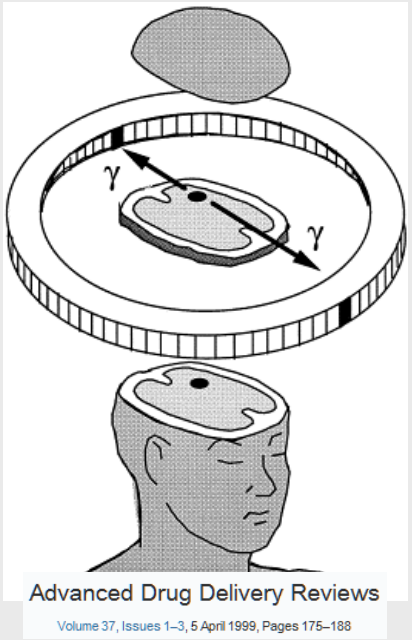
In collaboration with:

PET

= Positron-Emission-Tomography

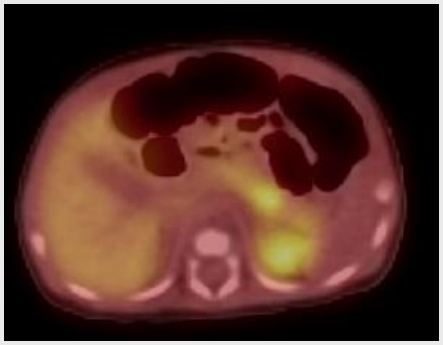
- High spatial resolution(1 – 3 mm)
- Visualization of metabolic processes
- "true" 3D-imaging

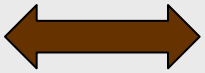




What do we expect from the DOPA-PET ?

- Just Differentiation?





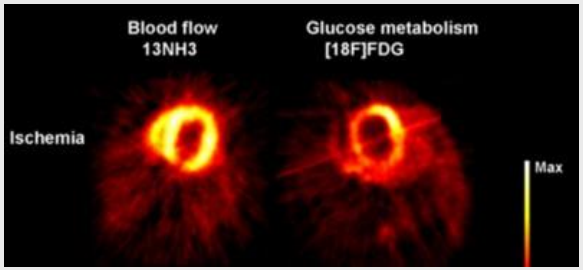
- Added value for the surgeon?
  - Image guided surgery, Potential reduction of surgical trauma

Localization is the key to differentiated therapy

- Focal ➔ surgery with possible cure
- Diffuse ➔ long-term therapy, limited surgical possibilities

Added value of PET-imaging?

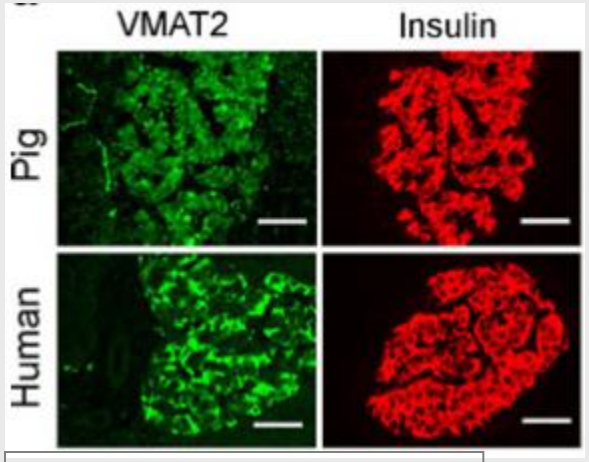
- Tracer metabolism is the key to understand PET images
  - ^{18}F-Glucose-PET shows where sugar is burned in the body (malignant tumors, inflammation)



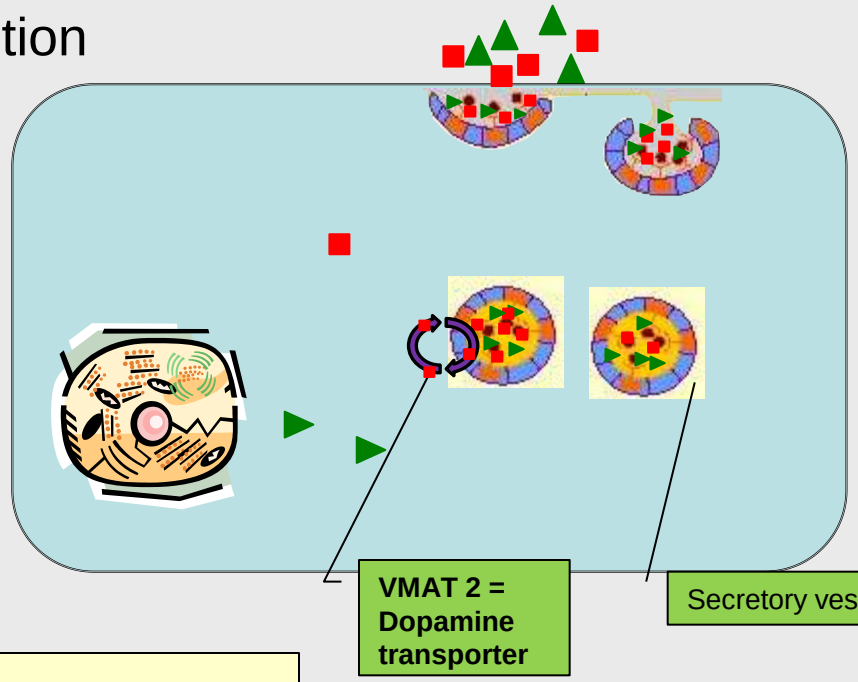
  - **^{18}F-DOPA is successful in visualization of CHI…(?)**
    - …but why…?
    - is there a metabolic link between DOPA and Insulin?

Dopamine regulates Insulin-secretion

- Highly-specific dopamine transporter in human beta-cells (VMAT2)
- Same amount of dopamie and insuline in the secretory vesicles
- Dopamine is secreted together with insuline
- Dopamine reduces insuline-secretion of surrounding beta-cells
- Neurotransmitter-like mode of action



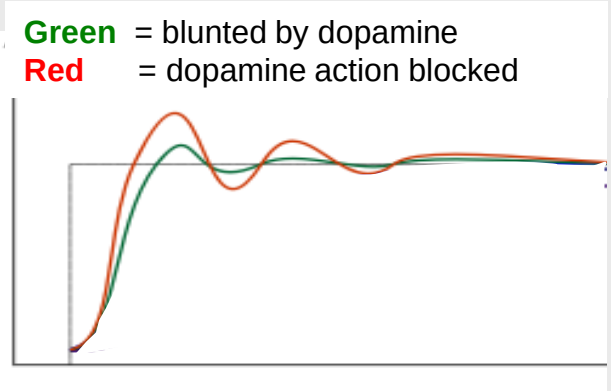
Schäfer, MKH; Diabetologia 2013

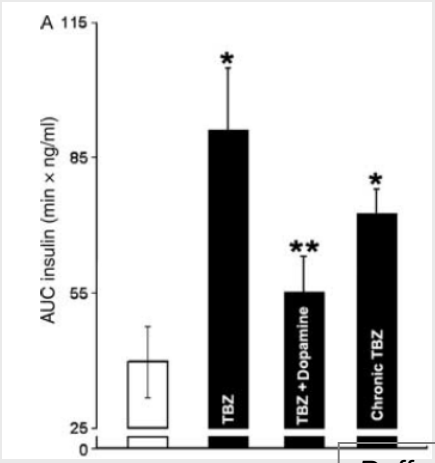


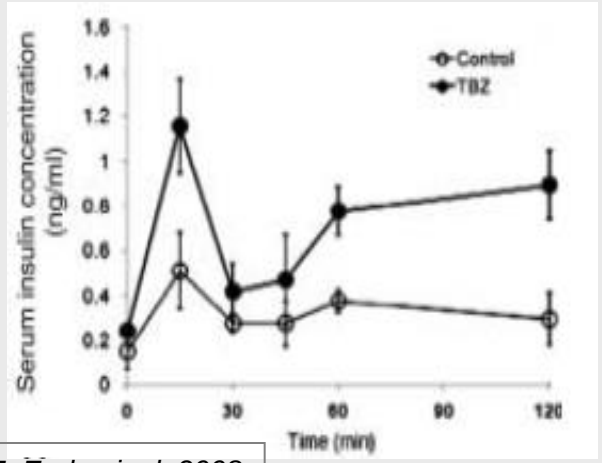
➔ **DOPA-content is linked to insulin secretion…!**

"Hey - I'm doing the job…"

- Without attenuation too much insulin would be released (always behind the blood sugar) resulting in hypoglycaemias
- Blunting of secretion curve by paracrine regulation.





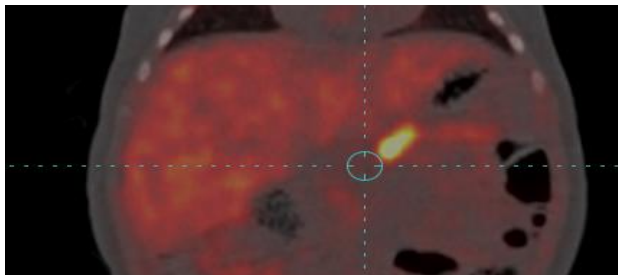


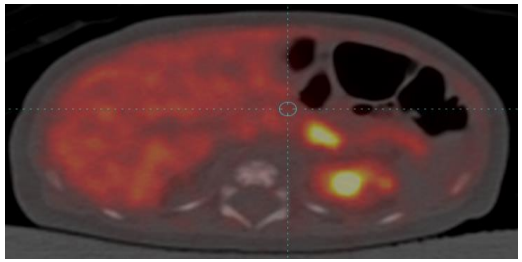
Raffo; J. Endocrinol. 2008

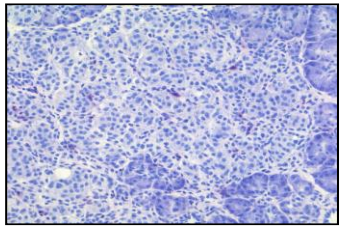
- Dopamine is the way ß-cells tell their neighbourhood that they are active *("Hey - I'm doing the job…")*

→ relevant effect on blood sugar (and PET images?)

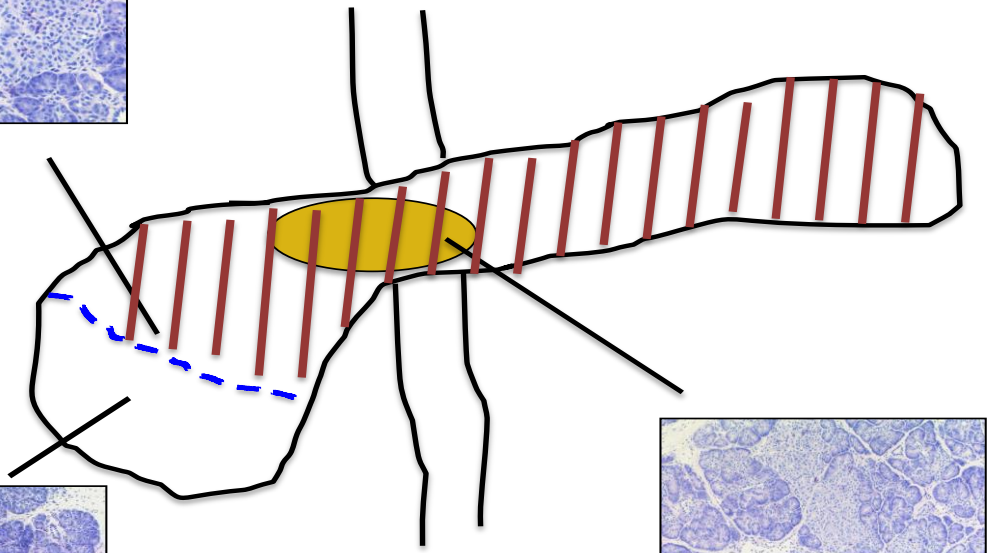
Limits of DOPA-PET: Giant foci

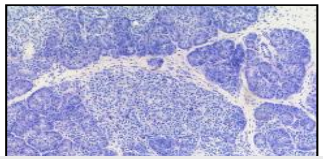






3 patients in Berlin…

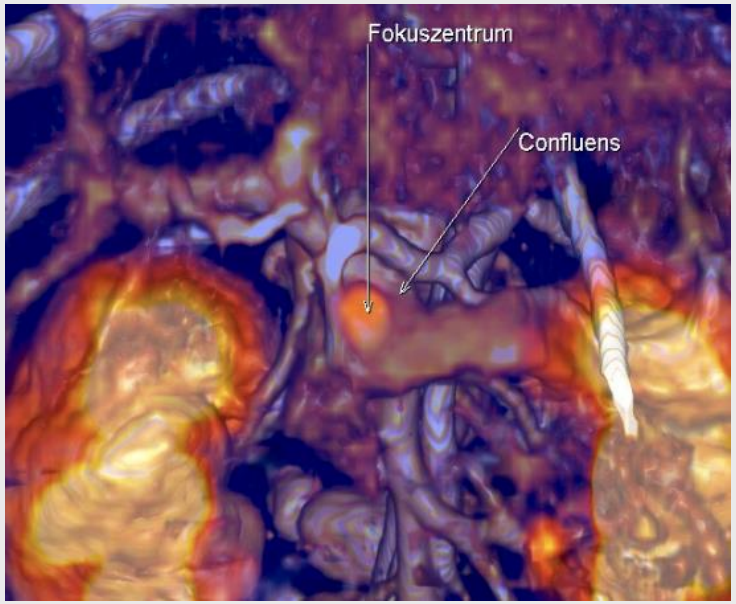




DOPA-PET is specific in focal CHI

- A diagnosis of a focal ^{18}F-DOPA-Pet is true in 95 – 98% of surgical treated patients
- Only few false-positive PET focal diagnoses

Focal CHI, 3 mo.

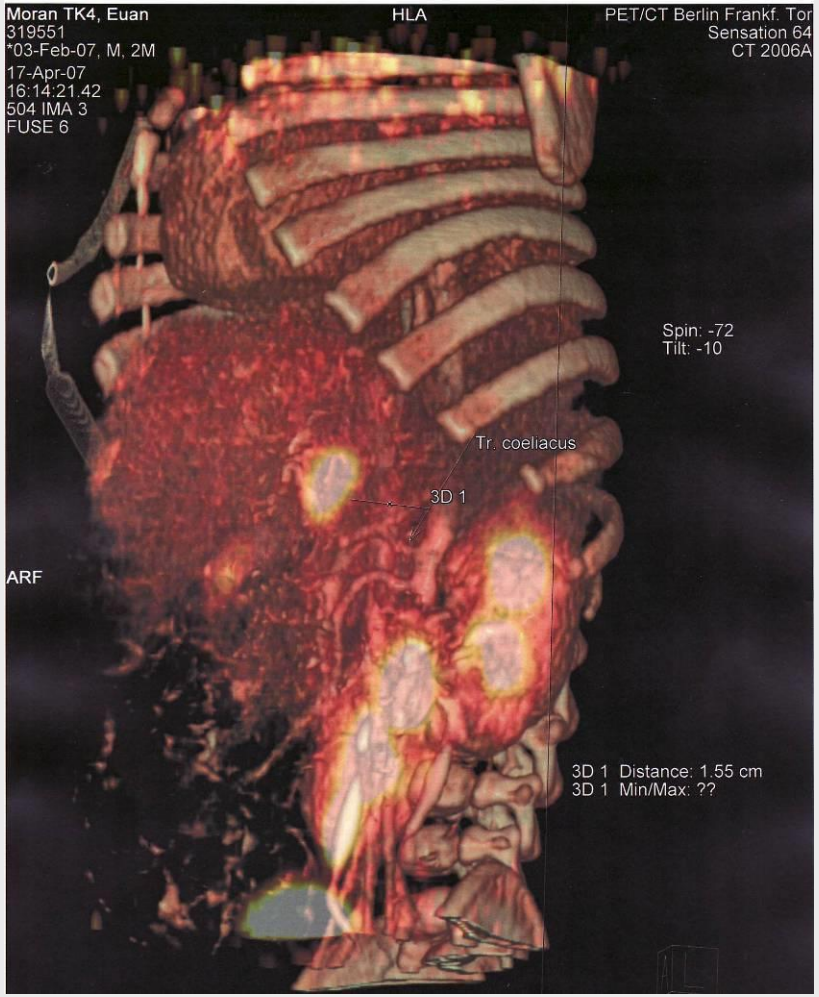


Non-focal CHI, 4 mo.

Sensitivity is moderate – good

- Focal CHI has been found in up to 20% of surgically treated patients with non-focal-PET result
  - Histology available in only a small part of patients with non-focal-PET results
  - Those receiving surgical therapy were selected by individual criteria based on experience of PET examiner and paediatrician.
  - Individual differences of tracer metabolism

3D-Reconstruction in focal form

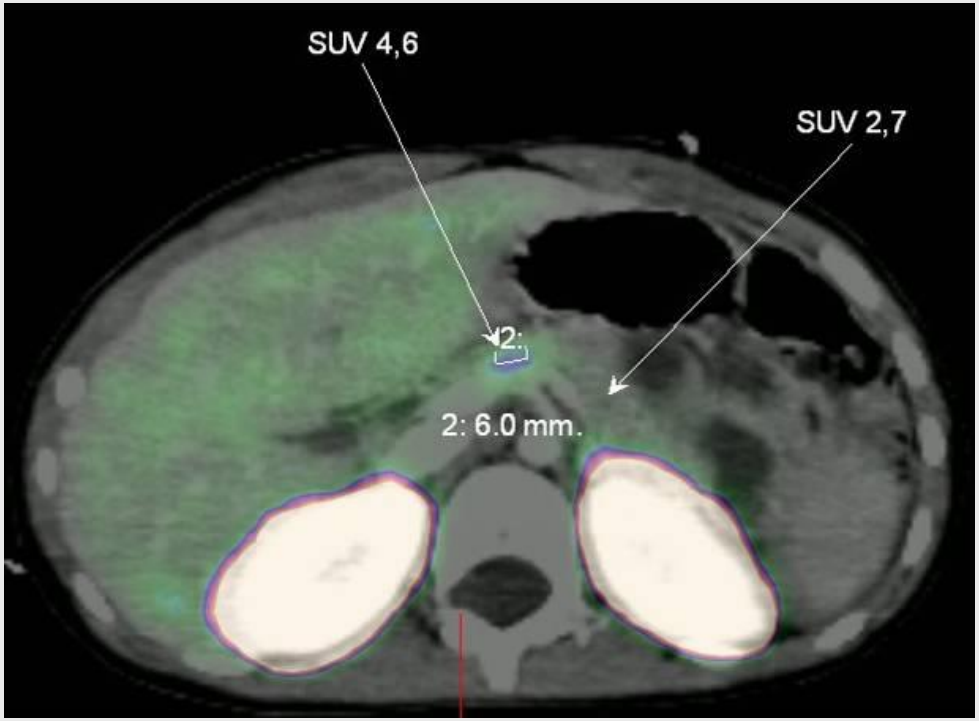


Known problems in identifying a focus

- Very small foci
- Very large foci (might be seen as diffuse)
- "Hidden behind other DOPA-accumulating structures"
  - Kidneys
  - Gallbladder
- Very low DOPA-uptake

Importance of DOPA metabolism in CHI

- Varialbe intensity of focus enhancement
  - Some patients show very low enhancement



6 mo. old CHI patient

Prior DOPA-PET scan: "*showed nearly no uptake in the pancreas*"

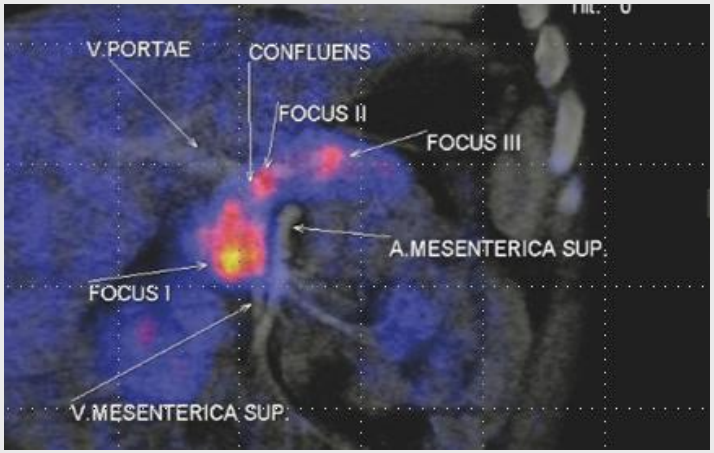
- Extreme weak uptake of tracer on re-examination
- Maximum sensitivity showed a **small focus** in corpus.

➢ Very special DOPA-metabolism in this patient

If you don't see it… – doesn't mean it isn't there

Position and size of focal lesions?

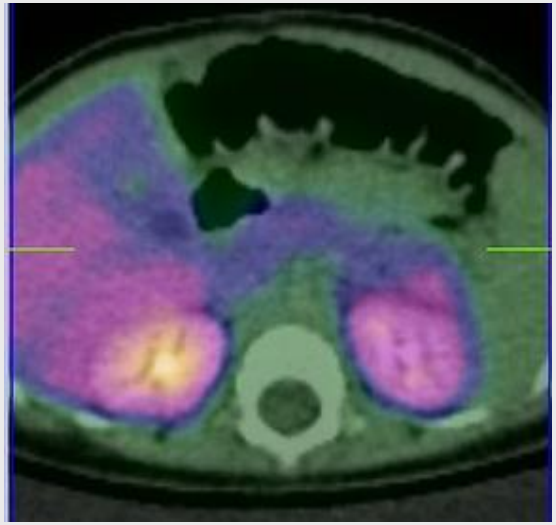
- Size and position of focal lesions are accurate in 71 – 88% *(Treglia, Pediatr. Radiol 2012)*
  - Different surgical strategies in different places
  - PET pictures and situation in the operation theatre not always identical
  - No established technique of image-guided CHI surgery



Localization of the focus using intersection points between confluens and focus

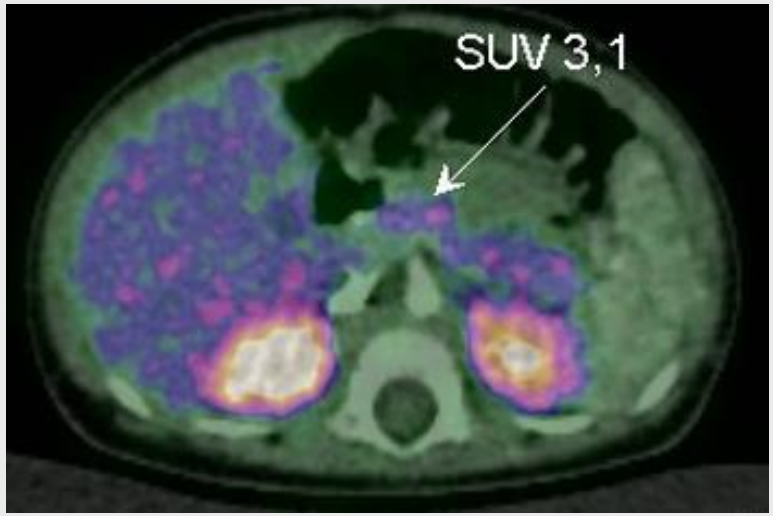
Intermediate or mosaic forms of CHI?

- Objective histologic criteria missing
- No data on sensitivity or specifity available
- **All** PET-pictures are altered electronically:



Diffuse CHI?

4 wk. old boy, CHI



Intermediate or multifocal CHI?

Same patient – pictures taken with 10 min. time difference

PET and Clinic always correlated…?

Lasting ^{18}F-DOPA PET Uptake after Clinical Remission of the Focal Form of Congenital Hyperinsulinism

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Takako Matsumoto[d] Hironori Nishibori[e] Michiya Masue[f]

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Horm Res Paediatr 2011;76:286–290

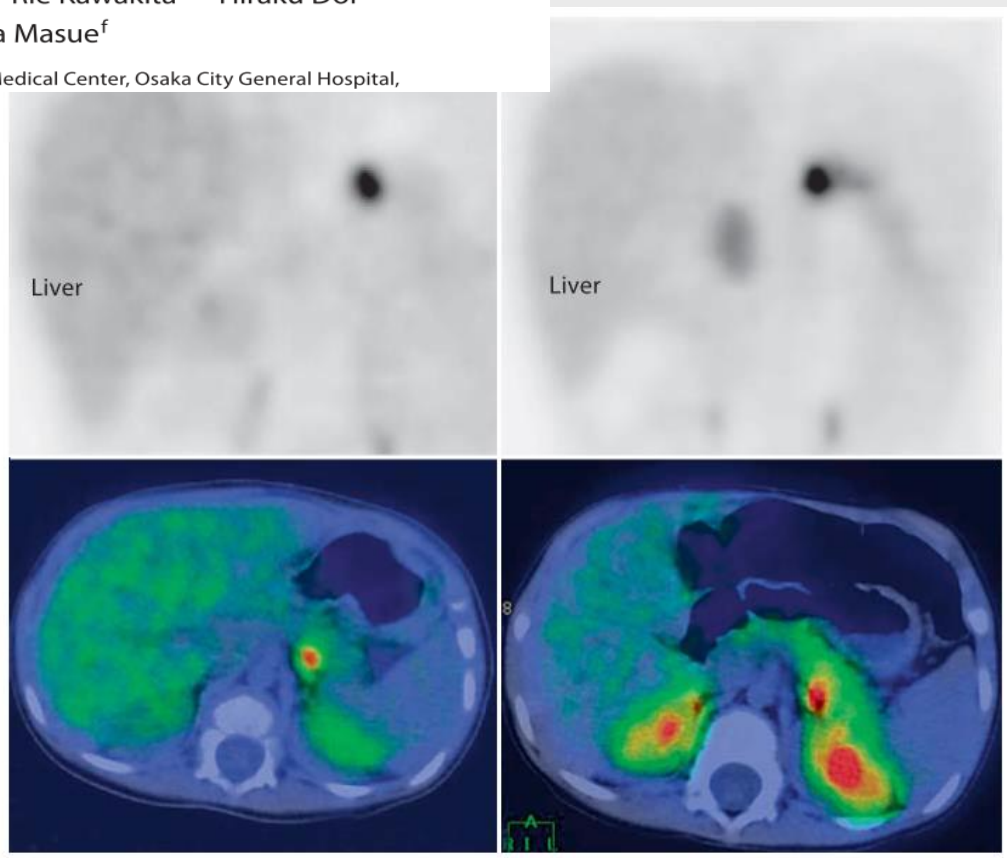
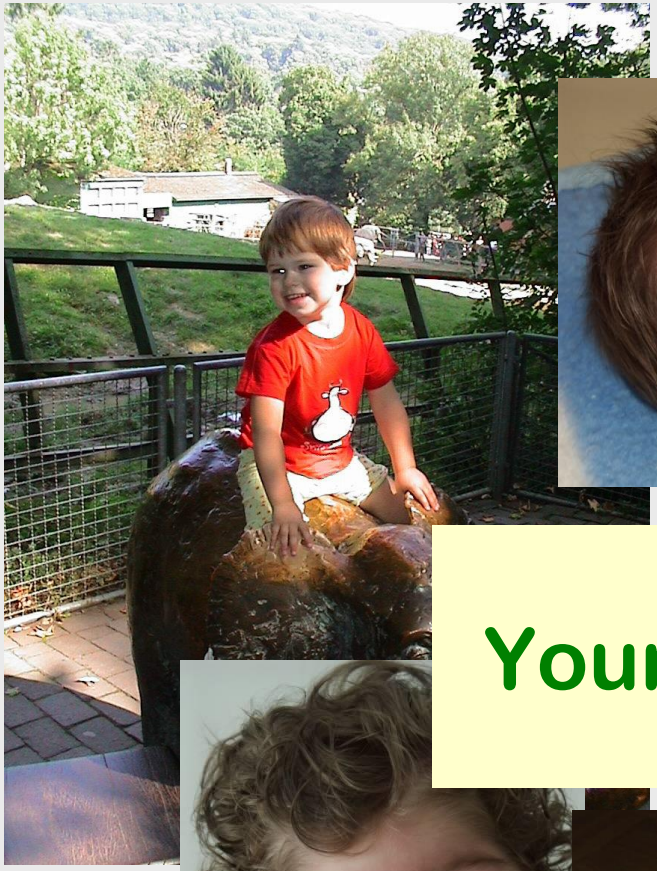


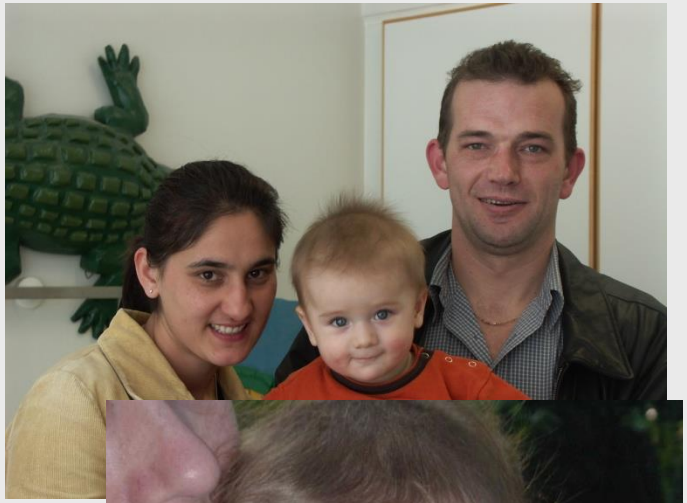
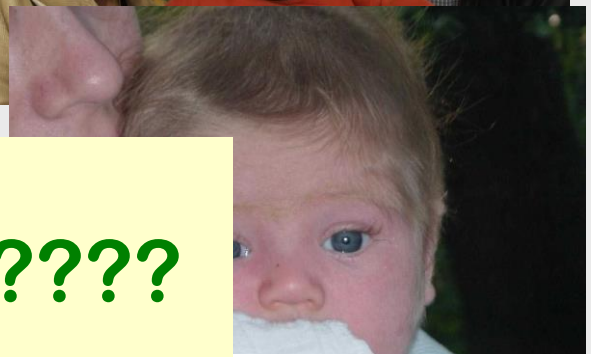
Fig. 1. ^{18}F-DOPA PET scans taken at age 8 months (left) and again at 1 year and 10 months (right). Upper panels show coronal images of abdominal PET scans and lower panels show fused axial PET/CT images. The maximal standardized uptake values for these lesions were 5.0 (left) and 6.8 (right), respectively.

Conclusion(s) ^{18}F-DOPA-PET/CT

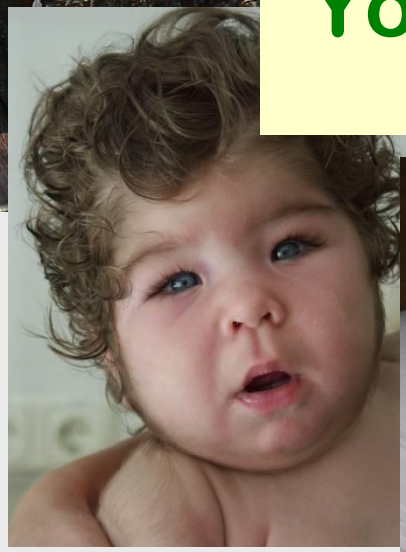
- Very good specifity (95 – 98%),
- Good sensitivity (67 – 96%)
  - more false-negative than false-positive results
- Specific problems of ^{18}F-DOPA-PET/CT:
  - Tracer uptake differences
  - Imaging of tracer uptake without clinical relevance
  - "Missing" of giant foci
- Risk of over-interpretation by the examiners.
  - Age pattern, digital alteration of images

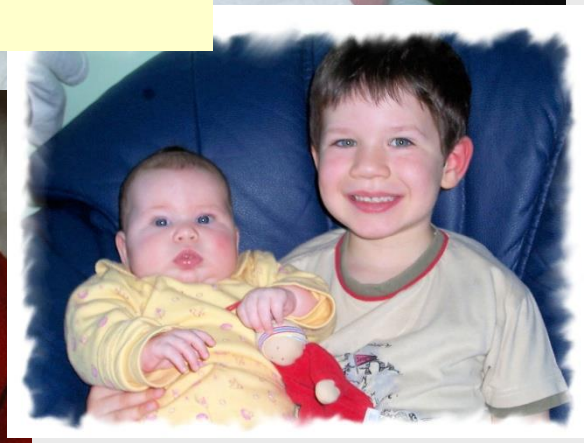
^{18}F-DOPA-PET/CT is not perfect – but it is the best we have



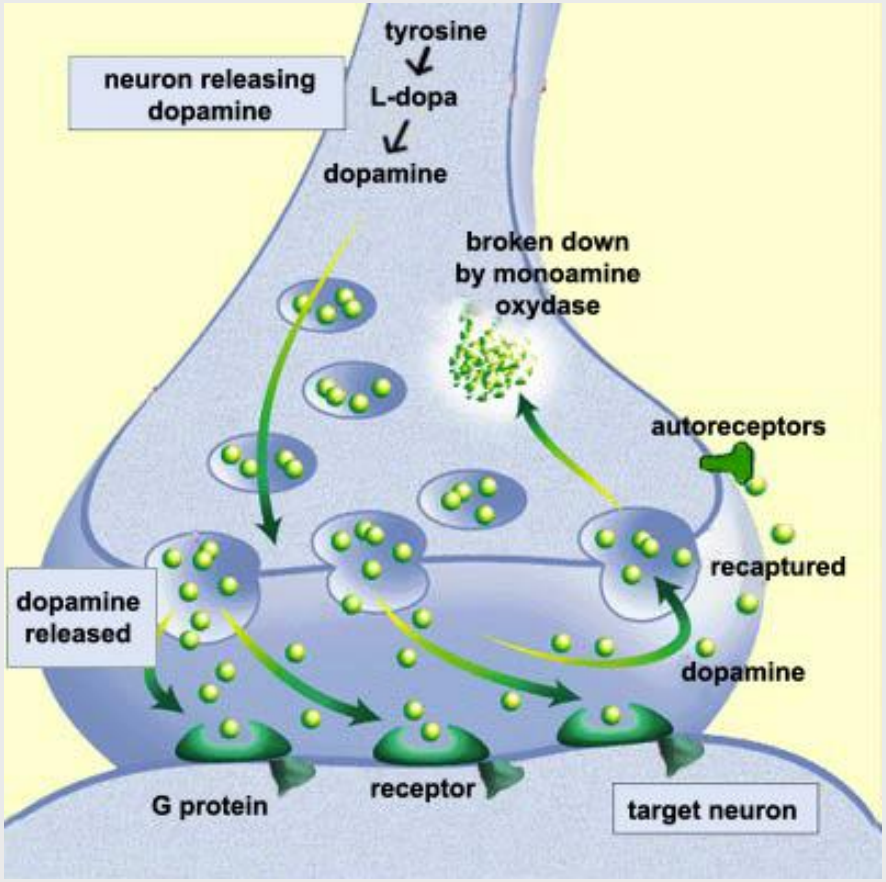



Your questions… ????



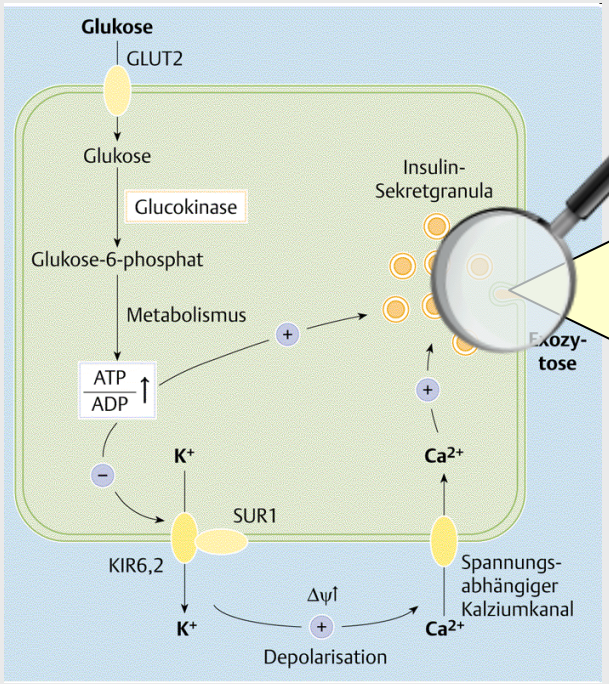


Dopamine in nerve-cells



- Dopamine is a known neuro-transmitter
- 80% of dopamine is inside vesicles
- Dopamine-receptors on cells to transmit signals
- Free dopamine is fast degraded

Auto-/Paracrine regulation durch Dopamin



▲ = Insuline

■ = Dopamine

Secretory vesicle

VMAT 2 = Dopamine transporter

Dopamin-receptor (D2)

Reduces insuline secretion

so much left to do…