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Nuclear Medicine in the Diabetic Foot

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Outline

A. **Imaging modalities – brief technical overview**
B. **Nuclear medicine in the diabetic foot**
C. **Cases**

A. Imaging modalities

A. Imaging modalities

Modalities	Tracers	Principle
SPECT/CT	DPD (bone turnover)	Adsorption to bone
	MoAB (infection)	Granulocyte antibody
PET/CT	FDG (infection, inflammation, tumor…)	Glucose analogon

The Spectrum of Radiological Imaging

Method	Spatial resolution	Sensitivity
Ultrasound	50 µm	10^{-3} mol
CT	50 µm	10^{-3} mol
MR	100 µm	10^{-5} mol
PET + SPECT	**>1mm**	**10^{-9} - 10^{-12} mol**

Molecular Imaging

M.Rudin, R.Weissleder. Molecular imaging in drug discovery and development. Nature Reviews, 2003 Feb;2(2):123-31.

The Principle of Radiological Imaging

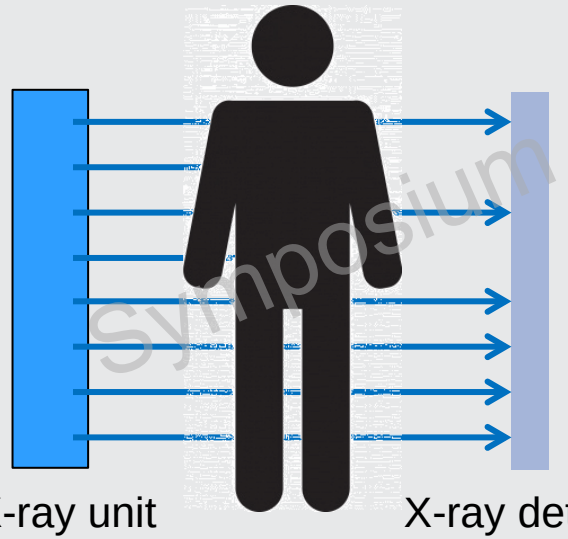
Method	Principle	Dose
CT	f (density)	1 - 15 mSv
MR	f (concentration H+)	-
PET + SPECT	f (organ function)	5 - 8 mSv

Functional Imaging

The Principle of Radiological Imaging

CT

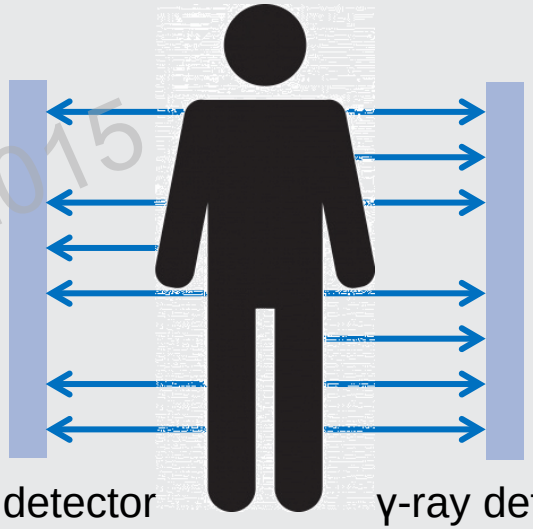
Transmission scan



X-ray unit X-ray detector

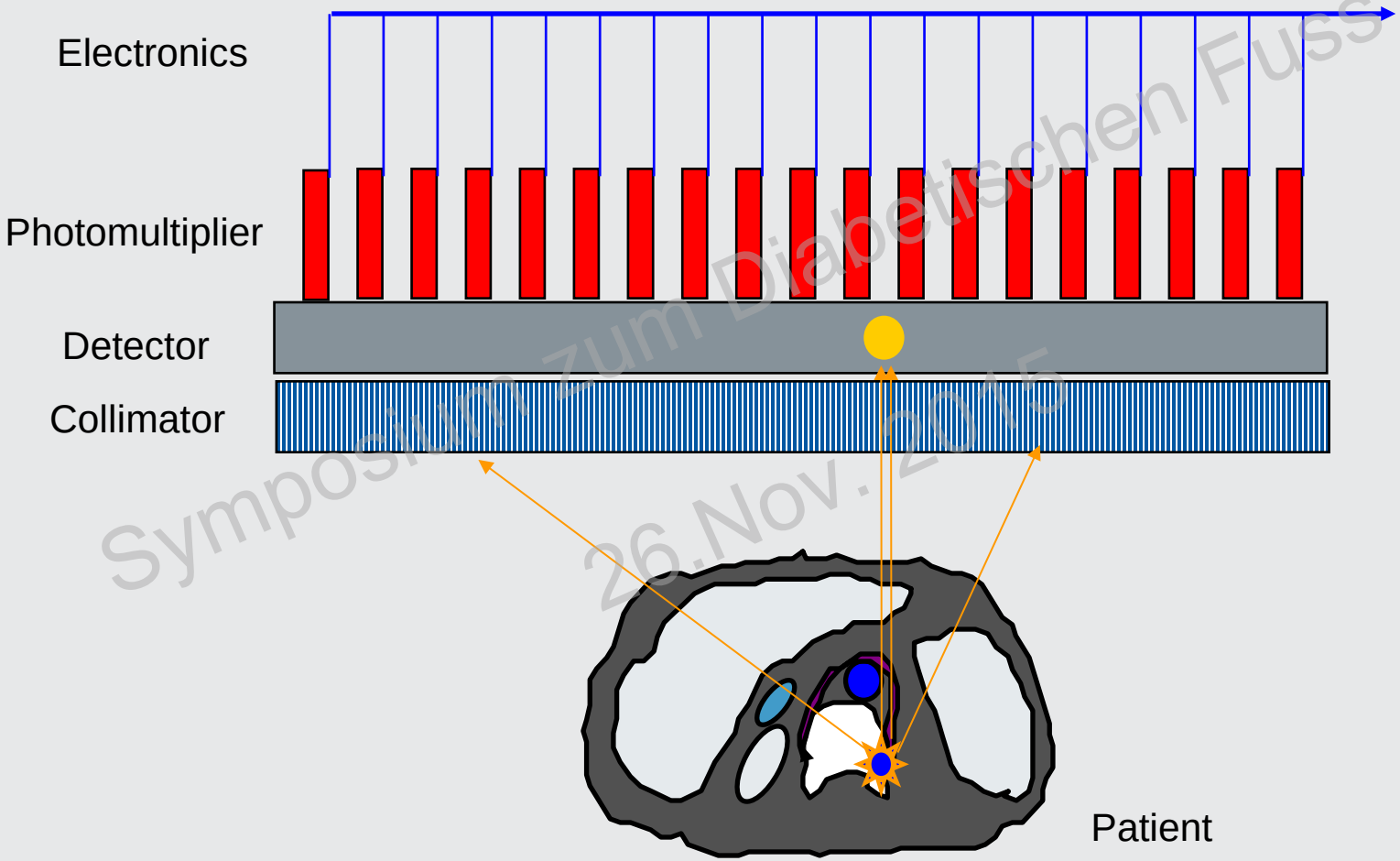
PET, SPECT

Emission scan

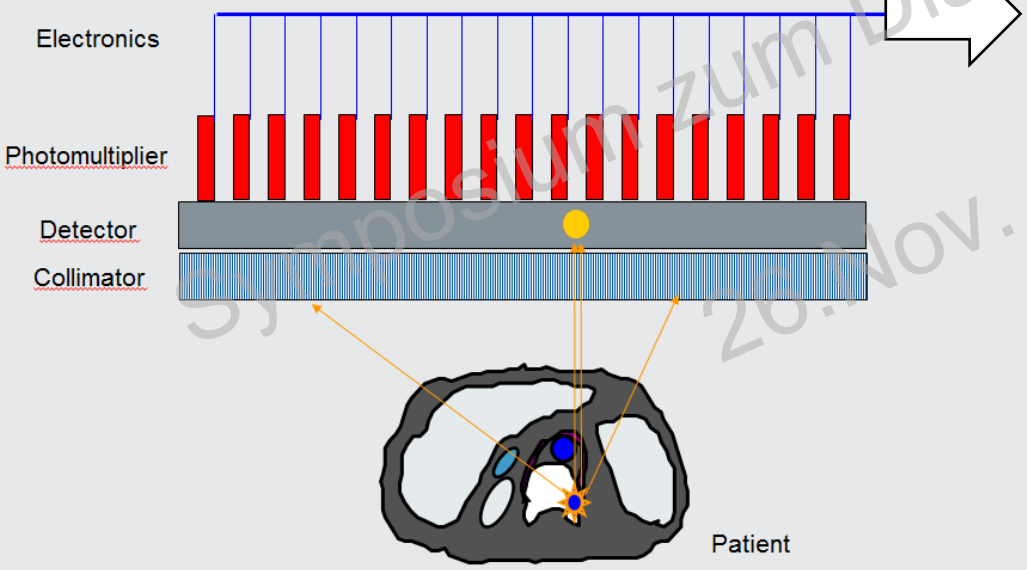


γ-ray detector γ-ray detector

Technology – Planar scintigraphy

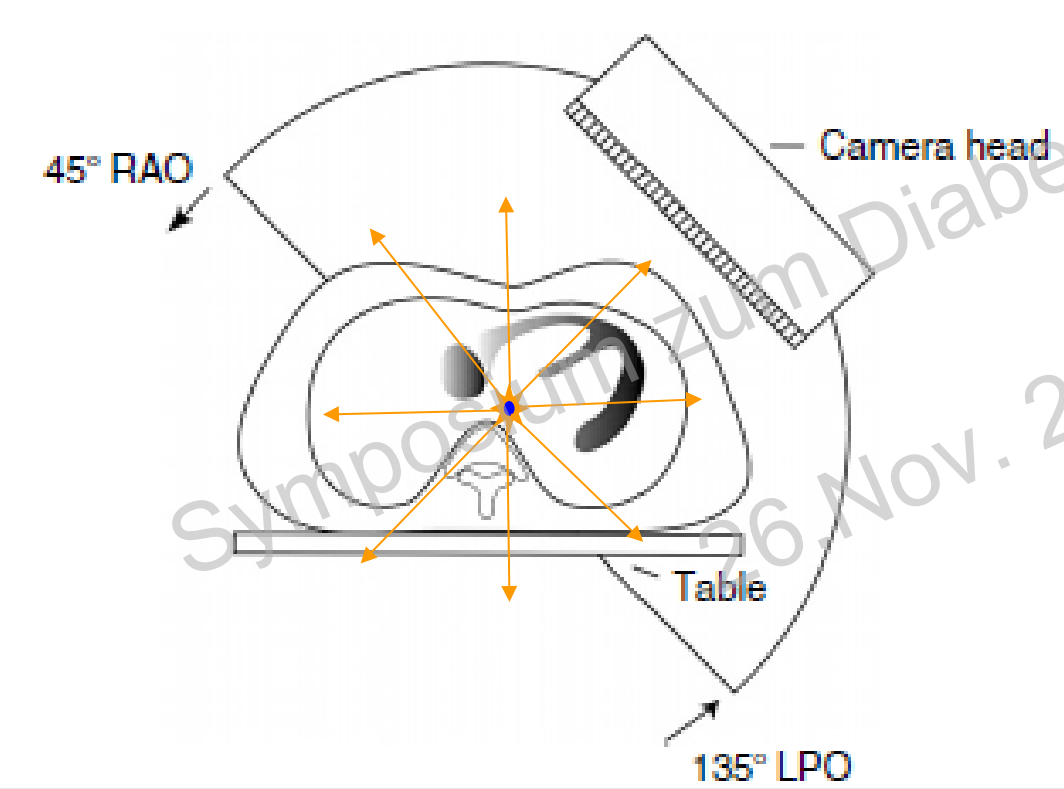


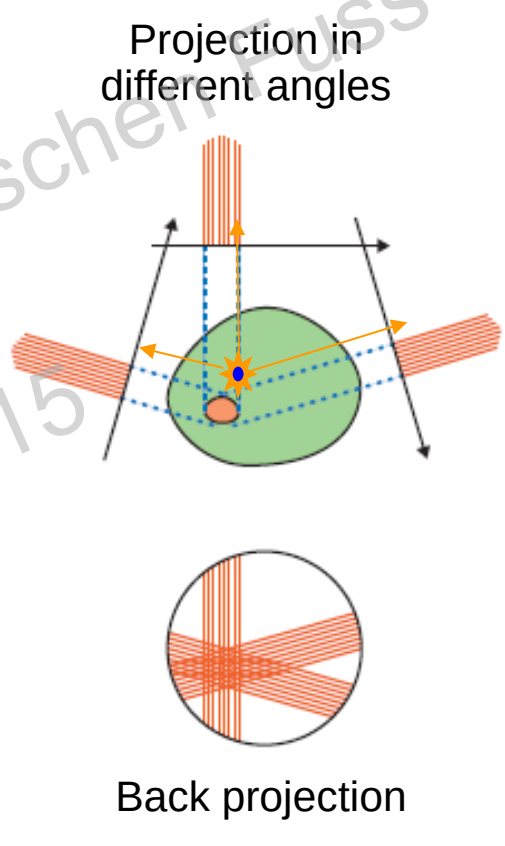
Technology – Planar scintigraphy



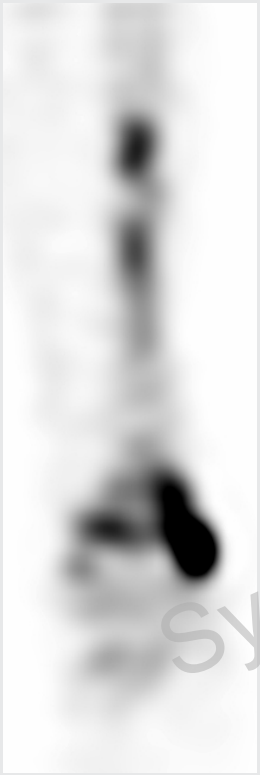
Bone scan

Technology – SPECT (Single photon emission computed tomography)





Technology – SPECT/CT



SPECT

CT

SPECT/CT

SPECT/CT (3D VR)

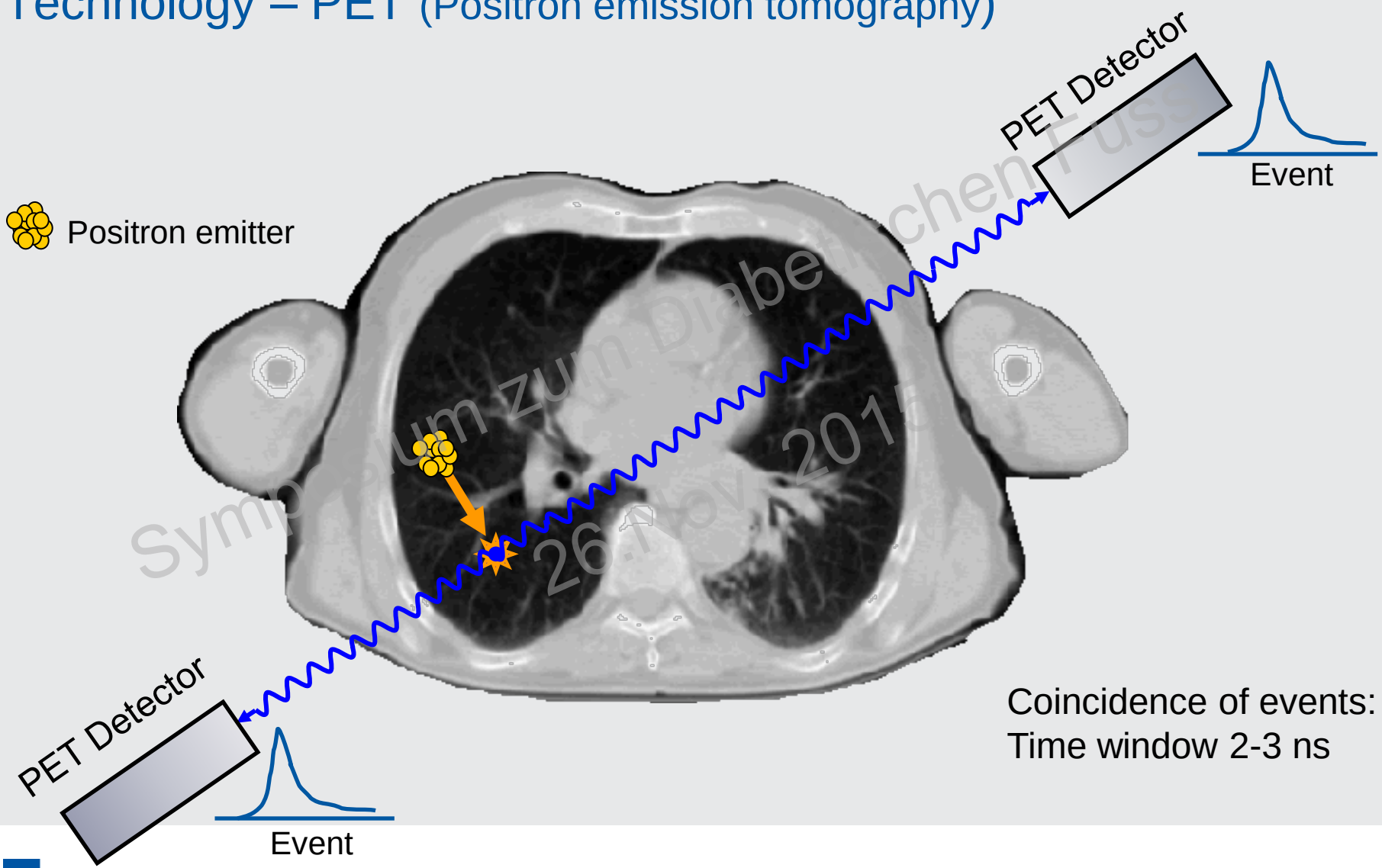
Technology – SPECT/CT

Examination protocol / patient schedule

- Injection of radiotracer
- Uptake time (**0 – 24h**)
- Imaging (planar images, SPECT, SPECT/CT)

Total radiation dose: 5 – 12 mSv

Technology – PET (Positron emission tomography)



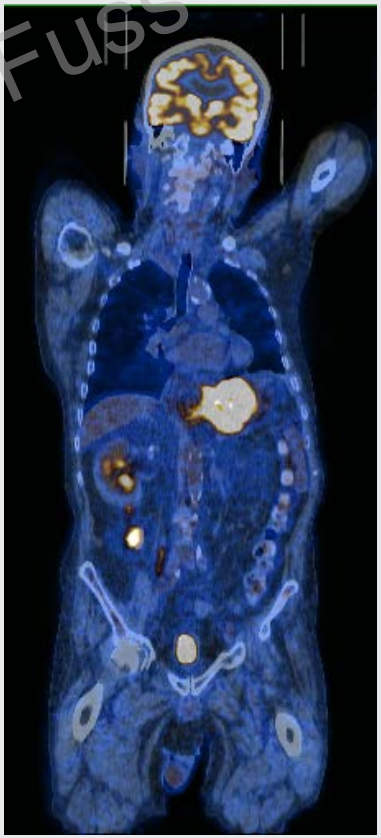
Technology – PET/CT

PET
7x 2 min

+

«low dose» CT
10 sec

=



PET/CT

Technology – PET/CT

Examination protocol / patient schedule

- NPO 4h prior to exam (only ^{18}F-FDG)
- Blood glucose test (only ^{18}F-FDG)
- Injection of radiotracer (~340 MBq ^{18}F-FDG, 200 MBq ^{18}F-Fluoride)
- Uptake time (**0 – 1h**), in dark and quiet ambience
- Voiding
- Imaging (PET/CT)

Total radiation dose: 8 – 12 mSv

Technology

Advantages of hybrid imaging

- Combination of morphological and functional data
- Higher spatial accuracy
- Higher diagnostic accuracy

Technology

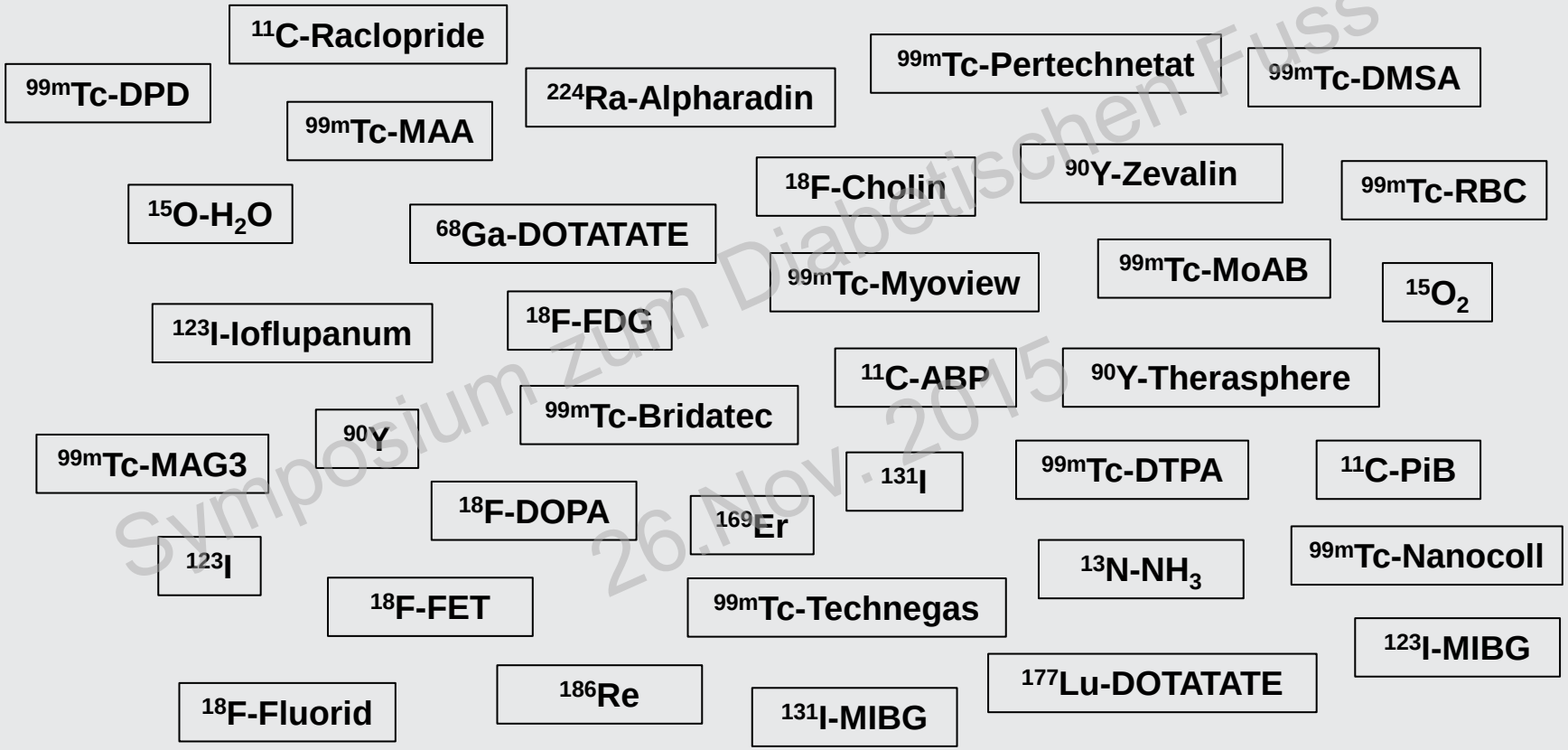
Advantages of hybrid imaging

- Combination of morphological and functional data
- Higher spatial accuracy
- Higher diagnostic accuracy

Bone scan ^{99m}Tc-DPD SPECT ^{18}F-Fluoride PET

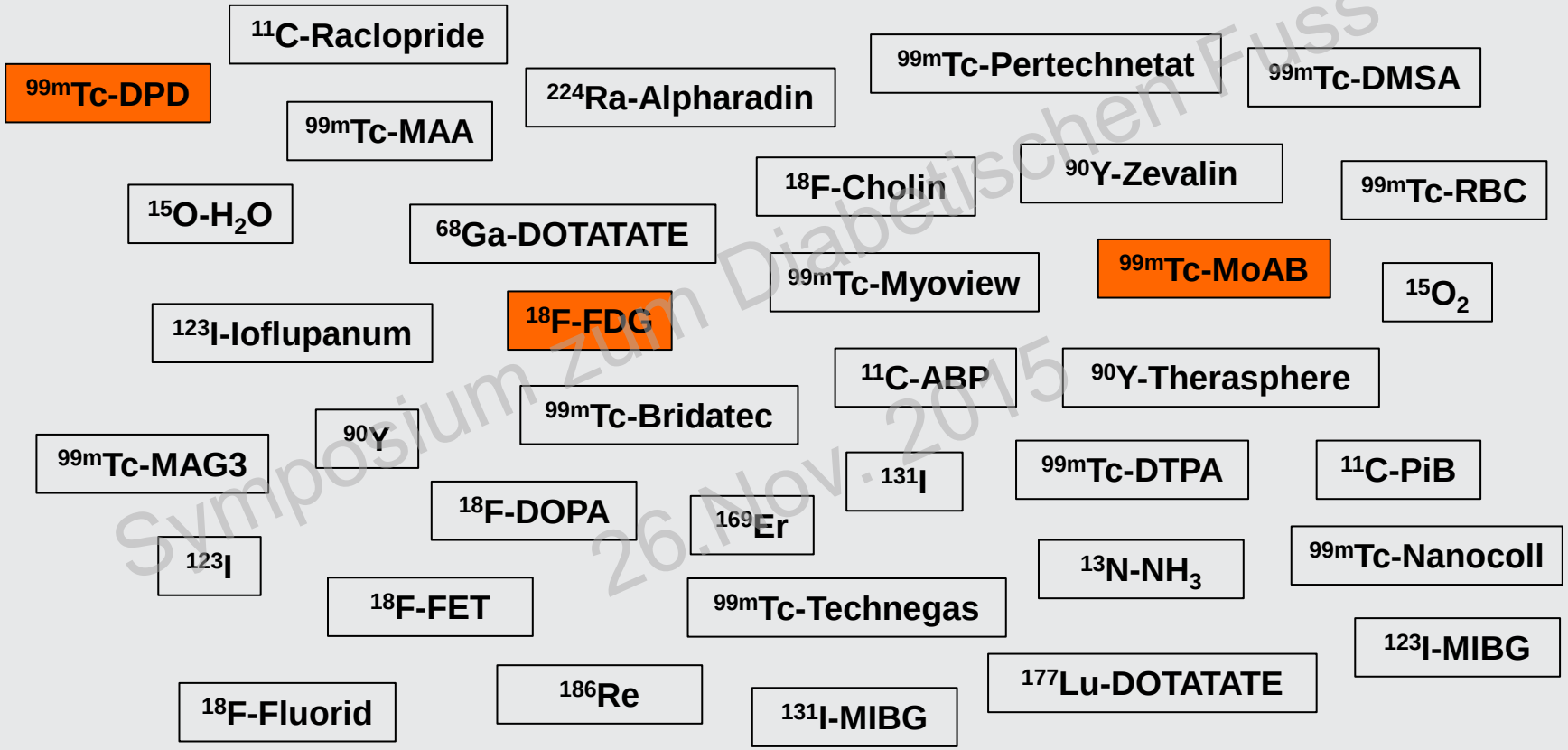
67yo male, prostate cancer with bone metastases

The Tracers Make a Difference!



More than 200 different radiotracers available in clinical and experimental setups.

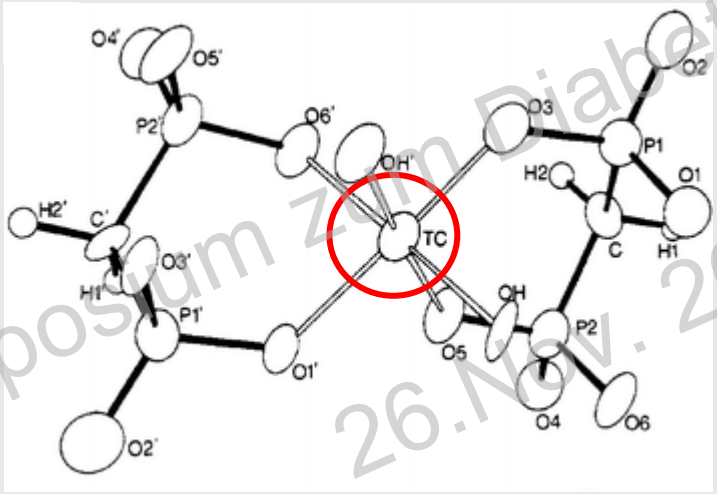
The Tracers Make a Difference!



Relevant diagnostic radiotracers in **diabetic foot imaging**

The Tracers Make a Difference!

Radionuclide (+ Carrier) = **Radiopharmaceutical** («Radiotracer»)



Technetium-DPD

$^{99m}Tc_{56} \rightarrow {}^{99}Tc_{56} + \gamma \quad (t_{/2}: 6h)$

Radiotracers for Diabetic Foot Imaging

Relevant diagnostic radiotracers in **diabetic foot imaging**

Radiotracer	Target	Cell	ED (70kg patient)
^{99m}Tc-DPD	Hydroxyapatite crystal	Osteoblasts	4.4 mSv
^{99m}Tc-MoAB	NCA-95 antigen	Granulocytes + precursors	6-8 mSv
^{18}F-FDG	Hexokinase	Glucose consuming cells	6-8 mSv

Erba PA, Israel O. SPECT/CT in infection and inflammation. Clin Translat Med, 2014 Dec;2(2):92-9.

Radiotracers for Diabetic Foot Imaging

Relevant diagnostic radiotracers in **diabetic foot imaging**

Tool	Radiotracer	Cell	Process imaged	
SPECT/CT	**^{99m}Tc-DPD**	Osteoblasts	Bone turnover	***non-specific***
	^{99m}Tc-MoAB	Granulocytes + precursors	Infection	***specific***
PET/CT	**^{18}F-FDG**	Glucose consuming cells	Tumor, infection, inflammation…	***non-specific***

Erba PA, Israel O. SPECT/CT in infection and inflammation. Clin Translat Med, 2014 Dec;2(2):92-9.

Radiotracers for Diabetic Foot Imaging – Normal Distribution

^{18}F-FDG

Glucose consumption
(and excretion)

^{99m}Tc-DPD

Bone turnover
(and excretion)

^{99m}Tc-MoAB

Granulocytes
(and precursors)

The Tracers Make a Difference!

Same patient, exams are two days apart

Conclusion?

Radiotracers for Diabetic Foot Imaging

Question:

FDG-PET/CT: How much radioactive sugar (**FDG**) do patients get per scan?

A) 1 g

B) 1 mg

C) 1 µg

D) 1 ng

Radiotracers for Diabetic Foot Imaging

Question:

FDG-PET/CT: How much radioactive sugar (**FDG**) do patients get per scan?

A) 1 g

B) 1 mg

C) 1 µg

D) **1 ng**

Radiotracers for Diabetic Foot Imaging

Can I scan patients with…

- ✔ Allergy to contrast medium?
- ✔ Renal insufficiency?
- ✔ Pacemaker?
- ✔ Hyperthyroidism?
- ? Claustrophobia?

Radiotracers for Diabetic Foot Imaging

CT

MR

PET/MR

PET/CT

SPECT/CT

B. Nuclear Medicine in the Diabetic Foot

B. Nuclear Medicine in the Diabetic Foot

Diabetic Foot Ulceration

→ Major complication of diabetes mellitus

- Incidence: 2% per year
- Major cause of **hospitalization** of diabetic patients
- Consequences: **Loss of quality of life, healthcare costs**
- **High mortality**: Life expectancy reduced by 14 years (!) in a diabetic patient with neuropathic ulcer without infection or ischemia (compared to non-diabetic patient)

Lipsky BA et al. Executive summary: 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012 Jun;54(12):1679-84.

B. Nuclear Medicine in the Diabetic Foot

Diabetic Foot Ulceration with Infection

- **>50%** of diabetic ulcers are infected at presentation
- Most important reason for **amputation**
- Independent risk factor for **death**

→ *Early diagnosis of infection is key!*

Lipsky BA et al. Executive summary: 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012 Jun;54(12):1679-84.

Prompers L et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. Diabetologia. 2007 Jan;50(1):18-25.

Diabetic Foot: Diagnosing an Infection

Problem: Differentiation of osteomyelitis, soft tissue infection, inflammation and osteoarthropathy is difficult.

1. All open wounds: Colonized with microorganisms. → *Clinical problem*

2. Neuropathy and vascular disease: May diminish or mimic inflammation. → *Clinical + imaging problem*

Lipsky BA et al. Executive summary: 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012 Jun;54(12):1679-84.

Prompers L et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. Diabetologia. 2007 Jan;50(1):18-25.

Diabetic Foot: Imaging of Infections

X-ray, MRI, Bone scan (DPD), Leucocyte scan (MoAB), or PET/CT (FDG)?

- No evidence of one single superior imaging modality
- Only few small studies so far
- Several societies are currently collaborating on guidelines (EANM, EBJIS, EASD)

	X-ray	MRI	DPD-SPECT/CT	MoAB-SPECT/CT	FDG-PET/CT
Sensitivity	60%	90%	90%	72-100%	29-100%
Specificity	80%	80%	50%	67-100%	67-93%
Cost (CHF)	120	600	1400	2500	2100

Glaudemans AW et al. Challenges in diagnosing infection in the diabetic foot. Diabet Med. 2015 Jun;32(6):748-59.

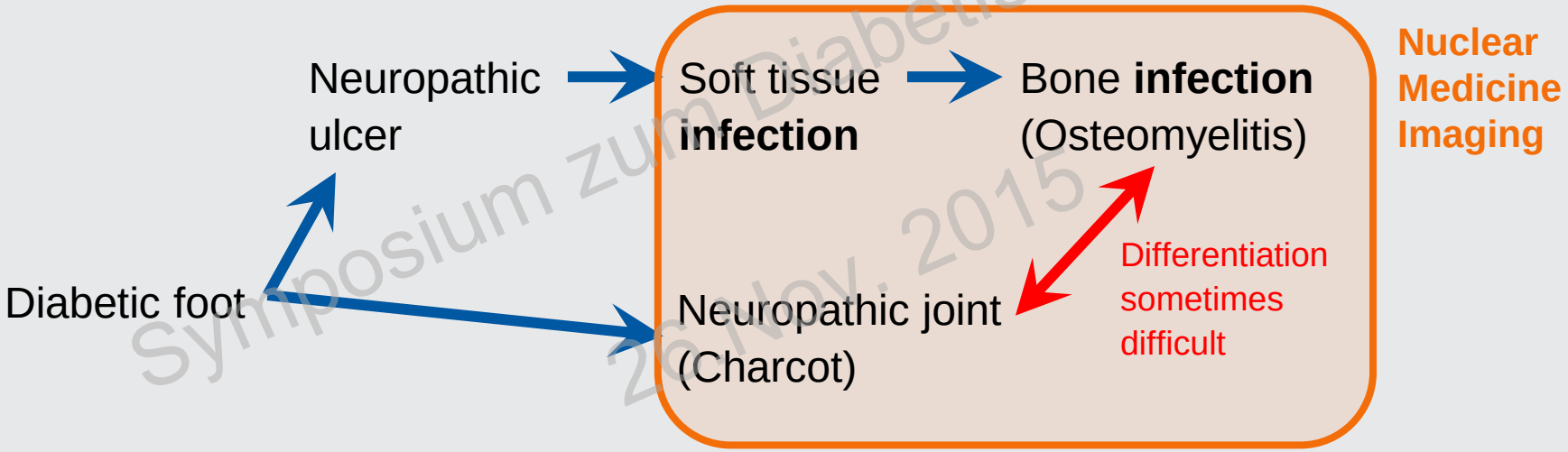
Diabetic Foot: Imaging of Infections

Modality	Advantages	Disadvantages
DPD-SPECT/CT	• Availability • Long experience	• Low specificity: Uptake in any lesion with increased bone turnover
MoAB-SPECT/CT	• Specific for granulocytes • Not affected by antibiotics • Detects acute + chronic infection	• Sterile laboratory required • Long acquisition time (patient returns after 24h)
FDG-PET/CT	• Long experience • Short acquisition time (2h)	• Often unspecific: Uptake in infection, inflammation, osteoarthropathy, tumor…

Glaudemans AW et al. Challenges in diagnosing infection in the diabetic foot. Diabet Med. 2015 Jun;32(6):748-59.

Diabetic Foot: Imaging of Infections

The Course of Disease – And when to Image with Nuclear Medicine



Diabetic Foot: Imaging of Infections

Which modality is most helpful?

DPD-SPECT/CT

MoAB-SPECT/CT

FDG-PET/CT

Diabetic Foot: Imaging of Infections

Which modality is most helpful?

DPD-SPECT/CT

MoAB-SPECT/CT

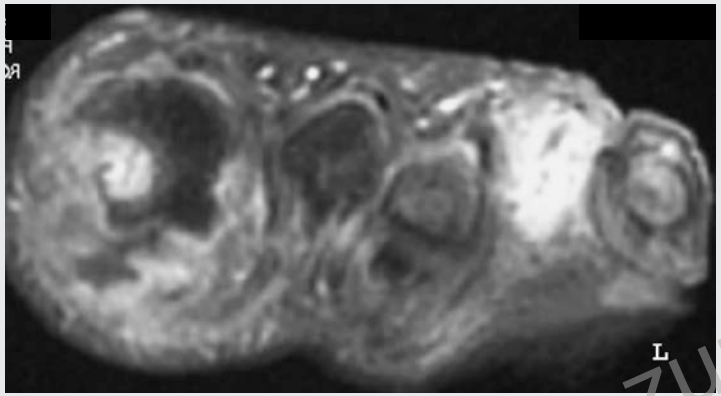
FDG-PET/CT

C. Cases

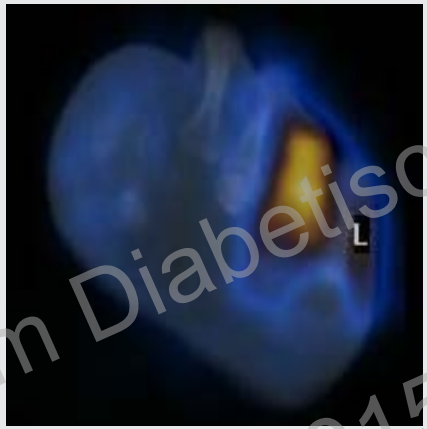
Diabetic Foot

Radiotracer:
^{18}F-FDG

Radiotracer:
^{99m}Tc-MoAB



T1w Gado



PET/CT

PET

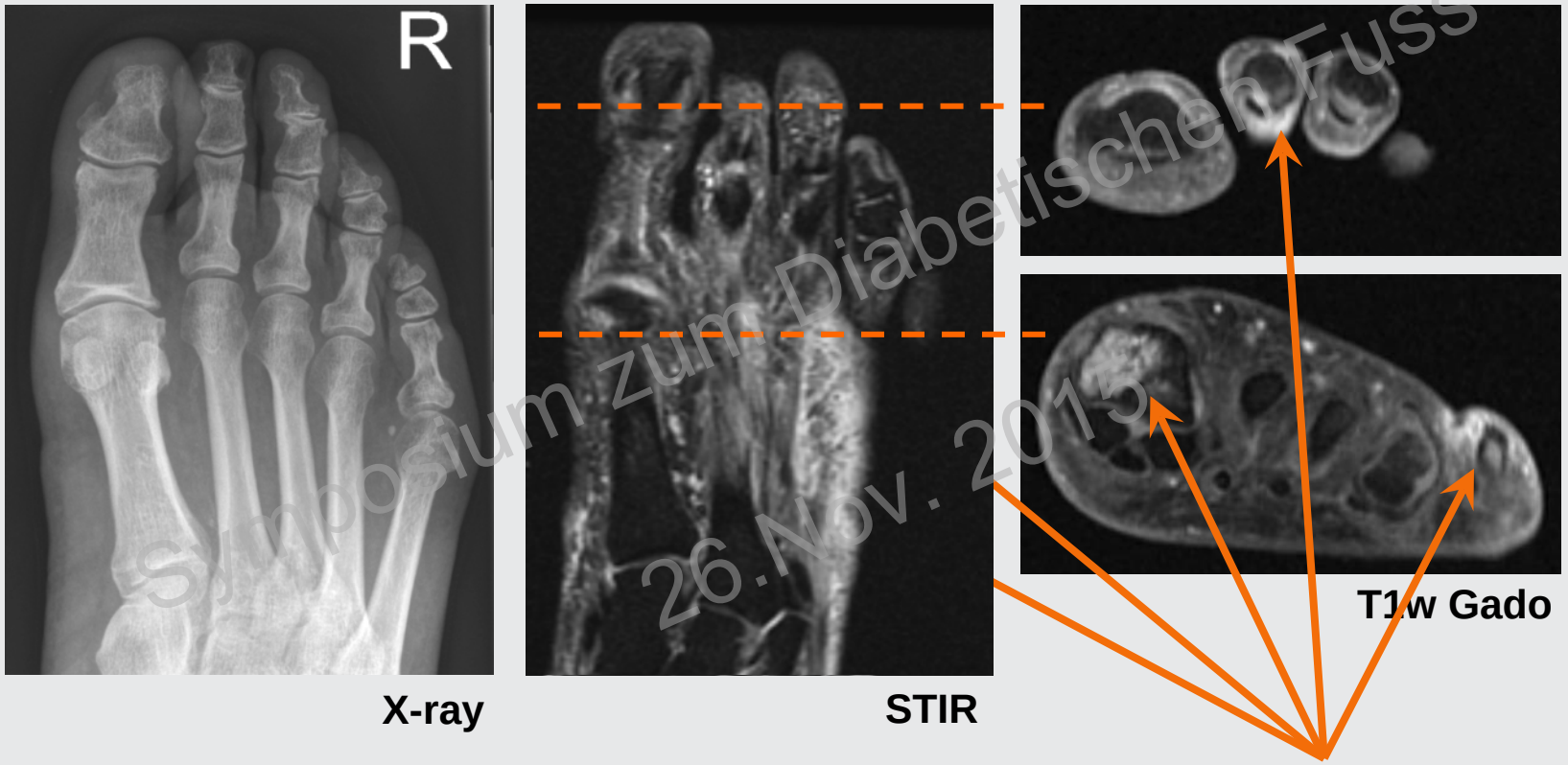
SPECT

70 yo male, infected wound Dig. IV.

Question: Osteomyelitis?

Answer: Yes.

Diabetic Foot



73 yo male, skin necrosis of toes.

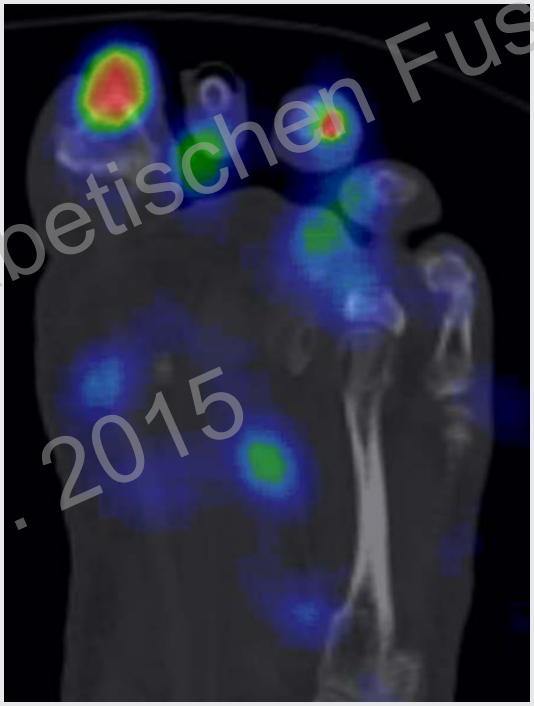
Question: Osteomyelitis? (Or: Which toes will be amputated?)

Diabetic Foot

Radiotracer:
^{99m}Tc-MoAB

STIR

^{99m}Tc-MoAB



SPECT/CT

73 yo male, skin necrosis of toes.

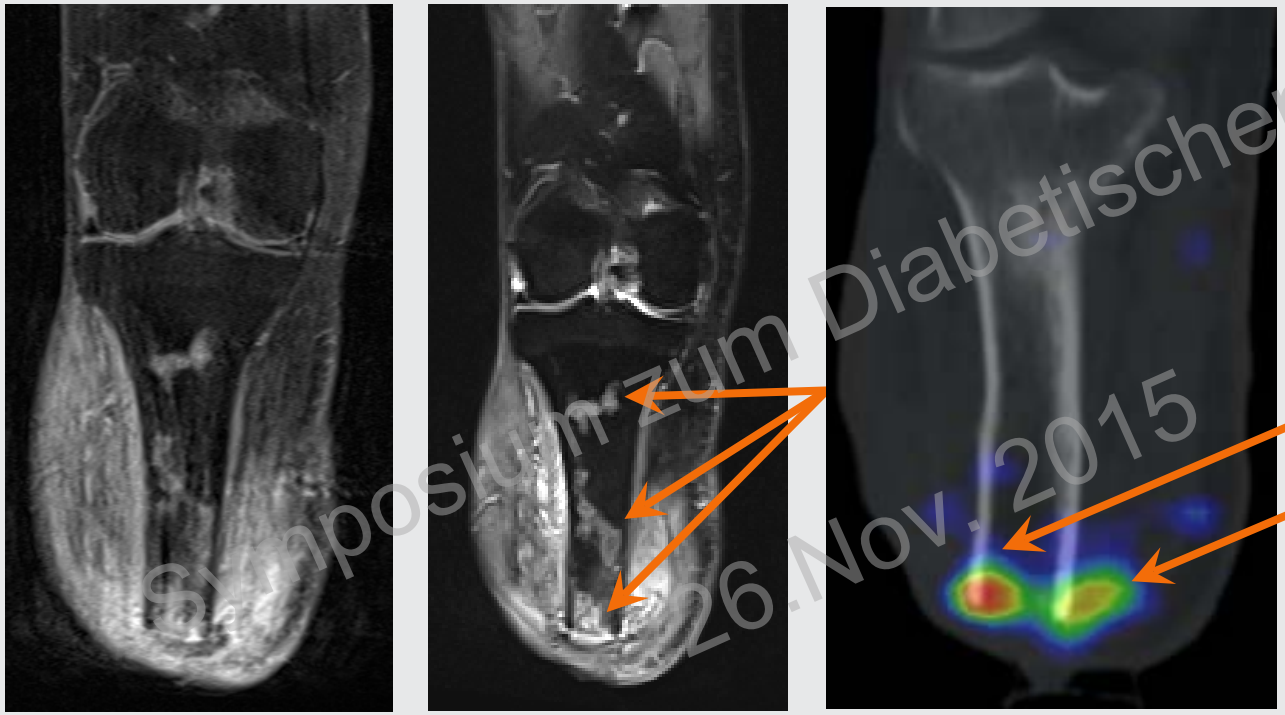
Question: Osteomyelitis? (Or: Which toes will be amputated?) **Answer:** Yes: Dig. I + III.

Osteomyelitis

Radiotracer:
^{99m}Tc-MoAB

Diabetic Foot

Radiotracer:
^{99m}Tc-MoAB



T1w Gd | STIR | SPECT/CT

Answer:

Osteomyelitis +

Soft tissue infection

70 yo male, clinical infection of amputation stump.

Question: Osteomyelitis?

Diabetic Foot

Radiotracer:
^{99m}Tc-MoAB

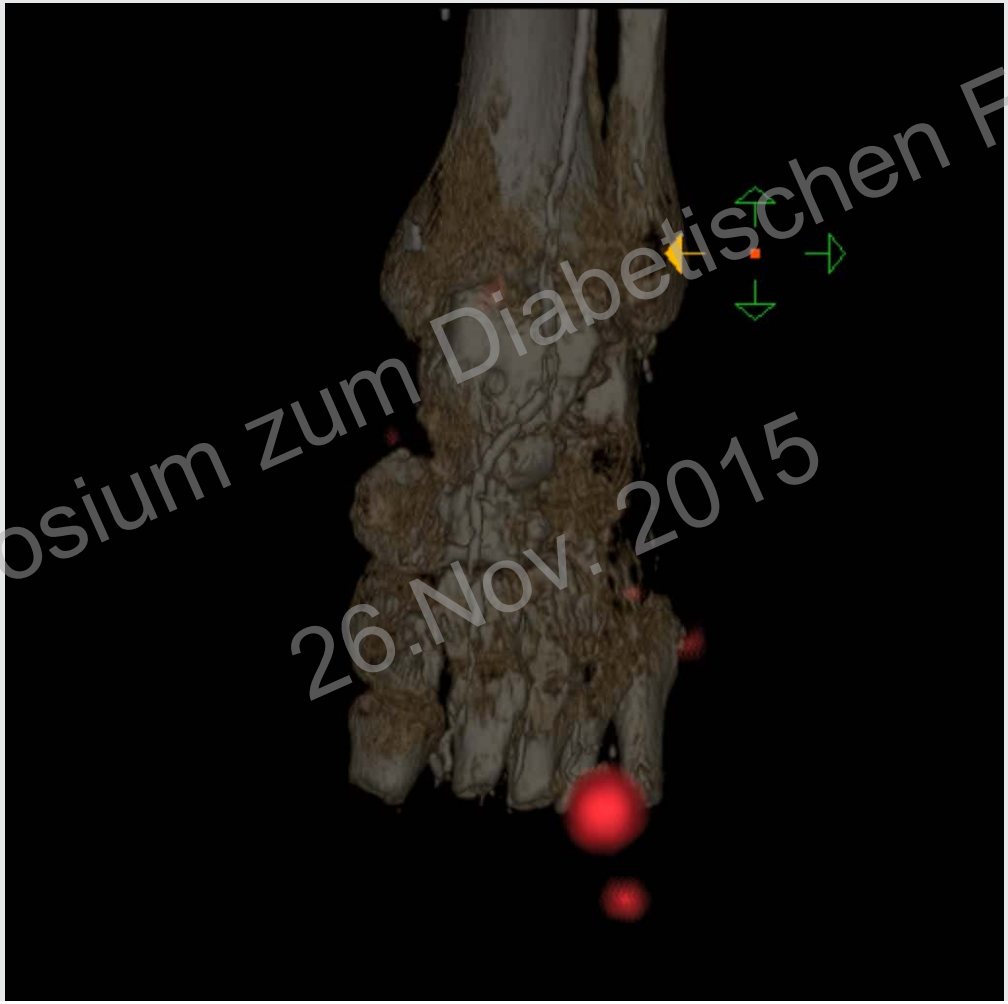
MoAB (5h) **MoAB (24h)** **MoAB-SPECT/CT**

75 yo female, h/o forefoot amputation. **Now:** Skin ulcers.

Question: Infection? Osteomyelitis?

Radiotracer:
^{99m}Tc-MoAB

Soft tissue infection + fistula



Conclusion

The Value of Nuclear Medicine in the Diabetic Foot

- **First line:** MRI, X-ray
- **Second line:** Nuclear medicine → *If questions remain after MRI*
  → *If patient cannot undergo MRI*


Symposium zum Diabetischen Fuss
26.Nov.2015
Questions ?