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

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<th>Tracers</th>
<th>Principle</th>
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<td>SPECT/CT</td>
<td>DPD (bone turnover)</td>
<td>Adsorption to bone</td>
</tr>
<tr>
<td></td>
<td>MoAB (infection)</td>
<td>Granulocyte antibody</td>
</tr>
<tr>
<td>PET/CT</td>
<td>FDG (infection, inflammation, tumor...)</td>
<td>Glucose analogon</td>
</tr>
</tbody>
</table>
# The Spectrum of Radiological Imaging

<table>
<thead>
<tr>
<th>Method</th>
<th>Spatial resolution</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
<td>50 µm</td>
<td>$10^{-3}$ mol</td>
</tr>
<tr>
<td>CT</td>
<td>50 µm</td>
<td>$10^{-3}$ mol</td>
</tr>
<tr>
<td>MR</td>
<td>100 µm</td>
<td>$10^{-5}$ mol</td>
</tr>
<tr>
<td>PET + SPECT</td>
<td>&gt;1mm</td>
<td>$10^{-9}$ - $10^{-12}$ mol</td>
</tr>
</tbody>
</table>

### The Principle of Radiological Imaging

<table>
<thead>
<tr>
<th>Method</th>
<th>Principle</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>$f$ (density)</td>
<td>1 - 15 mSv</td>
</tr>
<tr>
<td>MR</td>
<td>$f$ (concentration $\text{H}^+$)</td>
<td>-</td>
</tr>
<tr>
<td>PET + SPECT</td>
<td>$f$ (organ function)</td>
<td>5 - 8 mSv</td>
</tr>
</tbody>
</table>
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

Electronics

Photomultiplier

Detector

Collimator

Patient
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)

Coincidence of events: Time window 2-3 ns
Technology – PET/CT

PET
7x 2 min

«low dose» CT
10 sec

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

67yo male, prostate cancer with bone metastases

\[ ^{99m} \text{Tc-DPD SPECT} \]

\[ ^{18}\text{F-Fluoride PET} \]
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

- $^{99m}$Tc-MAA
- $^{99m}$Tc-DPD
- $^{15}$O-H$_2$O
- $^{123}$I-Ioflupanum
- $^{123}$I-MAG3
- $^{123}$I-
- $^{18}$F-FDG
- $^{18}$F-DOPA
- $^{18}$F-Fluorid
- $^{18}$F-FET
- $^{186}$Re
- $^{68}$Ga-DOTATATE
- $^{131}$I
- $^{131}$I-MIBG
- $^{124}$Ra-Alpharadin
- $^{224}$Ra-Alpharadin
- $^{18}$F-Cholin
- $^{11}$C-ABP
- $^{18}$F-Fluorid
- $^{99m}$Tc-MoAB
- $^{99m}$Tc-Myoview
- $^{99m}$Tc-Myoview
- $^{99m}$Tc-MoAB
- $^{99m}$Tc-Bridatec
- $^{99m}$Tc-DTPA
- $^{99m}$Tc-Technegas
- $^{11}$C-PiB
- $^{99m}$Tc-Nanocoll
- $^{13}$N-NH$_3$
- $^{177}$Lu-DOTATATE
- $^{99m}$Tc-DMSA
- $^{90}$Y-Zevalin
- $^{90}$Y-Therasphere
- $^{90}$Y-Zevalin
- $^{90}$Y-Therasphere
- $^{90}$Y-Zevalin
- $^{90}$Y-Therasphere
- $^{15}$O$_2$
The Tracers Make a Difference!

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

Technetium-DPD

\[ ^{99m}Tc_{56} \rightarrow ^{99}Tc_{56} + \gamma (t/2: 6\text{h}) \]
Radiotracers for Diabetic Foot Imaging

Relevant diagnostic radiotracers in diabetic foot imaging

| Radiotracer | Target                | Cell                        | ED  
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}\text{Tc-DPD}$</td>
<td>Hydroxyapatite crystal</td>
<td>Osteoblasts</td>
<td>4.4 mSv</td>
</tr>
<tr>
<td>$^{99m}\text{Tc-MoAB}$</td>
<td>NCA-95 antigen</td>
<td>Granulocytes + precursors</td>
<td>6-8 mSv</td>
</tr>
<tr>
<td>$^{18}\text{F-FDG}$</td>
<td>Hexokinase</td>
<td>Glucose consuming cells</td>
<td>6-8 mSv</td>
</tr>
</tbody>
</table>

Radiotracers for Diabetic Foot Imaging

Relevant diagnostic radiotracers in diabetic foot imaging

<table>
<thead>
<tr>
<th>Tool</th>
<th>Radiotracer</th>
<th>Cell</th>
<th>Process imaged</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPECT/CT</td>
<td>$^{99m}$Tc-DPD</td>
<td>Osteoblasts</td>
<td>Bone turnover</td>
</tr>
<tr>
<td></td>
<td>$^{99m}$Tc-MoAB</td>
<td>Granulocytes + precursors</td>
<td>Infection</td>
</tr>
<tr>
<td>PET/CT</td>
<td>$^{18}$F-FDG</td>
<td>Glucose consuming cells</td>
<td>Tumor, infection, inflammation...</td>
</tr>
</tbody>
</table>
Radiotracers for Diabetic Foot Imaging – Normal Distribution

$^{18}$F-FDG  $^{99m}$Tc-DPD  $^{99m}$Tc-MoAB

Glucose consumption (and excretion)
Bone turnover (and excretion)
Granulocytes (and precursors)
The Tracers Make a Difference!

**Lateral wedge:**
Normal uptake after HTO

**Medial wedge:**
Infection of osteotomy gap

Conclusion?

Same patient, exams are two days apart

99mTc-DPD SPECT/CT

99mTc-MoAB SPECT/CT
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
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)

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!


**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**


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)

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

## Diabetic Foot: Imaging of Infections

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

Diabetic Foot: Imaging of Infections

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

- Neuropathic ulcer
- Soft tissue infection
- Bone infection (Osteomyelitis)
- Neuropathic joint (Charcot)

Nuclear Medicine Imaging

Diabetic foot

Differentiation sometimes difficult
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

70 yo male, infected wound Dig. IV.

**Question:** Osteomyelitis?  
**Answer:** Yes.
73 yo male, skin necrosis of toes.

**Question:** Osteomyelitis? (Or: Which toes will be amputated?)
73 yo male, skin necrosis of toes.

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

**Answer:** Yes: Dig. I + III.
Osteomyelitis

Radiotracer: 99mTc-MoAB

Symposium zum Diabetischen Fuss
26.Nov. 2015
70 yo male, clinical infection of amputation stump.

**Question:** Osteomyelitis?
Diabetic Foot

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

**Question:** Infection? Osteomyelitis?
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*