xSPECT – Advances in Nuclear Medicine

27. Ulusal Nükleer Tıp Kongresi
01. – 05. Nisan 2015, Adana, Turkey

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Nuclear medicine

From Wikipedia, the free encyclopedia

Nuclear medicine is a medical specialty involving the application of radioactive substances in the diagnosis and treatment of disease.
What is „theranostics“?

- Combination of therapy and diagnostic
- Therapeutic procedure or product followed by diagnostic procedure (e.g. drug efficacy for patients with specific diseases)
- Diagnostic procedure followed by therapeutic procedure (e.g. imaging procedure for therapy indication)
- Tumor characterization by specific radiopharmaceuticals
Personalized medicine
Theranostics example

- Diagnostic Ga-68 DOTA TATE PET for patient evaluation for Peptide-Receptor-Radionuclide-Therapy with Lu-177 DOTA TATE

\[ \text{\textsuperscript{68}Ga-DOTATATE} \]

\[ \text{\textsuperscript{90}Y-DOTATATE} \]

\[ \text{\textsuperscript{177}Lu-DOTATATE} \]
PET Radiopharmaceuticals 2005 and 2013

2005

- FDG 93.40%
- Cholin 2.03%
- FET 4.58%
- Ga-TATE 4.43%
- FEC 12.57%
- FDOPA 1.08%
- DMFP 0.67%
- FP 0.11%
- Ga-PSMA 0.13%
- F-18 AlzComp 1.31%

Total: 2666

2013

- FDG 70.57%
- FET 9.13%
- Ga-TATE 12.57%
- FEC 4.43%
- FDOPA 0.67%
- DMFP 0.11%
- FP 0.11%
- Ga-PSMA 0.13%
- F-18 AlzComp 1.31%

Total: 6389

2490 FDG
122 FET
54 Choline
2666 total

4509 FDG
803 Ga-TATE
583 FET
282 FEC
84 Alzheimercomp.
69 FDOPA
50 DMFP/FP
8 Ga-PSMA
6389 total
Do we need scintigraphy in this situation?

- Increasing demand for SPECT

Number of scintigraphic investigations at the Department of Nuclear Medicine, LMU Munich 2006 - 2013

- Scintigraphies
- Percentage Of SPECT and/or SPECT / CT
Relevance of Molecular Imaging and SPECT

EANM 2007 Statistics Survey: $\Sigma 7.5 \times 10^6$ per year

Installed cameras:
- PET and PET/CT: 503
- SPECT Cameras: 4250

In-Vivo Diagnostic Procedures in the USA

Delbeke and Segall; J Nucl Med 2011
Status of and trends in Nuclear Medicine in the United States:

- Total: $17 \times 10^6$ per year
- PET/CT and PET: $1.5 \times 10^6$ per year
Relevance of SPECT

Summary
The medical use of radiopharmaceuticals up to 2025
An exploration of the future medical use of high flux reactor isotopes

www.eanm.org – Technopolis report summary
Relevance of SPECT

Figure 1 Relative use of modalities in 2008, 2015 and 2025 (n=23)

www.eanm.org – Technopolis report summary
Relevance of SPECT

Figure 3. Substitution effects of SPECT by multi-modalities

Source: survey Technopolis Group. n=23

www.eanm.org – Technopolis report summary
Advantages of SPECT imaging

- Installed camera basis
- Logistics
  (Availability of kits, radiopharmaceutical production and distribution)
- Development of new camera types / reconstruction algorithms
PET vs. SPECT in clinical oncology

- Inferiority of SPECT in terms of spatial resolution and quantification
- However, due to availability, costs, logistics SPECT might be the better choice

- Mandatory requirements for the future:
  - adequate radiopharmaceuticals
  - development in camera systems and reconstruction methods

- Siemens Symbia Intevo
  - the world’s first xSPECT system
  - „see the unseen“
  - „quantify the difference“
  - „adapt the lowest dose“
  - „double the throughput“
PET vs. SPECT in clinical oncology

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Radiopharmaceuticals for theranostic approaches

- I-131
- I-131 MIBG
- Ga-68 / Lu-177 somatostatine receptor ligands
- Ga-68 / Lu-177 PSMA
- Y-90 Ibritumomab
- Y-90 Microspheres
- Ra-223 Dicholride
- Sm-153 EDTMP
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Somatostatine-receptor ligands for therapy and diagnostics

$^{68}$Ga-DOTATATE

$^{90}$Y-DOTATATE

$^{177}$Lu-DOTATATE
Neuroendocrine Tumors

DOTATATE-PET

Conventional Octreotide-scintigraphy
Relevance of quantification and dosimetry

$^{111}$In-Octreoscan® scintigraphy 24 h p.i.

$^{111}$In-DOTA-BASS scintigraphy 24 h p.i.

$^{111}$In-DOTA-JR11 scintigraphy 24 h p.i.

**Agonist**
affinity profile ($IC_{50}$)
22 ± 3.6 nM

**Antagonist**
affinity profile ($IC_{50}$)
9.4 ± 0.4 nM

**Antagonist**
affinity profile ($IC_{50}$)
3.8 ± 0.7 nM

Courtesy Juri Ruf; Dept. of Nuclear Medicine, Univ. Freiburg
Neuroendocrine Tumors

60yr patient, NET of the pancreas with lymphnode and hepatic filiae
Ga-68 DOTATATE PET/CT prior to therapy and after 2 cycles

2 x therapy
with 7400 MBq
$^{177}$Lu-DOTATATE
RESULTS – $^{177}$LU-DOTATATE

- 310 patients$^1$
- CR 2%, PR 28%, MR 16%
- SD 35%
- PD 20%
- Median TTP 40 months
- Median survival 46 months
- Significant improvement of QoL in 50 patients$^2$

$^1$ Kwekkeboom et al., JCO 2008
$^2$ Teunissen et al., JCO 2004
DOTA-TATE therapies / year

therapies

year

PRRT THERAPY AND THERAPY MONITORING

- Diagnostic PET/CT
- Therapy
- 1h p.i.
- 24h p.i.
- 48h p.i.
- 72h p.i.

**177Lu-DOTATATE PRRT**

- Planar dynamic scintigraphy
- Planar + SPECT
- Blood samples
- Urine
- Planar + SPECT
- Blood samples
- Planar + SPECT
- Blood samples
- Planar + SPECT
- Blood samples

CT, PET, MIP Display of PET, Planar Scintigraphy, SPECT, MIP Display of SPECT

Activity [Bq]

- Bi–exponential fit
- Planar dynamic scans (12 frames a 5 min.)
- Planar whole–body scan (16 min.)

Department of Nuclear Medicine
LMU Munich

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Neuroendocrine Tumors

38yr female patient, NET of the ileum with liver and spleen metastases
Currently undergoing 3rd cycle of Lu-177-DOTATATE treatment
Lu-177-DOTATATE SPECT/CT: xSPECT Reconstruction

upper energy window (both available)
currently no quantitation available (at our site)
Lu-177-DOTATATE SPECT/CT: LMU-Reconstruction

DOSE ESTIMATIONS

„manual“ method

![Spleen met.](SPECT/CT day 0)
![Spleen met.](SPECT/CT day 3)

![Liver met.](SPECT/CT day 0)
![Liver met.](SPECT/CT day 3)
## DOSE ESTIMATIONS

<table>
<thead>
<tr>
<th>Organ</th>
<th>Dose [Gy]</th>
<th>$T_{1/2}$ [h]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor (spleen)</td>
<td>15.2</td>
<td>77.7</td>
</tr>
<tr>
<td>Tumor (liver)</td>
<td>10.5</td>
<td>65.7</td>
</tr>
<tr>
<td>Kidney (left)</td>
<td>4.2</td>
<td>72.2</td>
</tr>
<tr>
<td>Kidney (right)</td>
<td>4.5</td>
<td>61.5</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>0.04</td>
<td>9.1 (0.5 fast)</td>
</tr>
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Radiopharmaceuticals for theranostic approaches

- I-131
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- Ga-68 / Lu-177 PSMA
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- Y-90 Microspheres
- Ra-223 Dichloride
- Sm-153 EDTMP
Radiopharmaceuticals for theranostic approaches

“I go home today. They cured me using this new miracle drug. I’m afraid it’ll be years before it’s approved for humans.”
**68Ga-PSMA in clinical routine**

Glu-NH-CO-NH-Lys-(Ahx)-[68Ga(HBED CC)]

„bench to bedside“

**6/2012**
**first patient data from Afshar-Oromieh, et al. in Heidelberg:**
[68Ga]Gallium-labelled PSMA ligand as superior PET tracer for the diagnosis of prostate cancer: comparison with 18F-FECH

**since 12/2013**
**clinical routine at our institution**
CLINICAL TRANSLATION

Preclinical: LNCaP Xenografts

Patient: recurrent prostate cancer

Background

% ID / g

Tumor

Background

Tumor

[68Ga]HBED-CC-conjugate

[68Ga] Reference

time after injection [min]

Courtesy Uwe Haberkorn, Dept. of Nuclear Medicine
University Hospital Heidelberg
Tracer-Uptake in human studies

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>SUV&lt;sub&gt;max&lt;/sub&gt; in tumor suspicious lesions</th>
<th>average SUV&lt;sub&gt;max&lt;/sub&gt; (± SD) of Choline</th>
<th>average SUV&lt;sub&gt;max&lt;/sub&gt; (± SD) of PSMA</th>
</tr>
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<tbody>
<tr>
<td>Lymph node metastases (n=40)</td>
<td></td>
<td>2.8 ± 2.0</td>
<td>16.2 ± 18.9</td>
</tr>
<tr>
<td>Bone metastases (n=23)</td>
<td></td>
<td>6.1 ± 2.6</td>
<td>9.2 ± 3.8</td>
</tr>
<tr>
<td>Local relapses (n=10)</td>
<td></td>
<td>4.3 ± 1.2</td>
<td>5.4 ± 2.9</td>
</tr>
<tr>
<td>Soft tissue metastases (n=5)</td>
<td></td>
<td>5.2 ± 3.2</td>
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<tr>
<td>Lymph node metastases (n=40)</td>
<td>2.6 ± 1.9</td>
<td>31.5 ± 33.3</td>
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<tr>
<td>Bone metastases (n=23)</td>
<td>3.3 ± 2.1</td>
<td>13.6 ± 11.7</td>
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<tr>
<td>Local relapses (n=10)</td>
<td>4.1 ± 1.6</td>
<td>11.5 ± 7.5</td>
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<tr>
<td>Soft tissue metastases (n=5)</td>
<td>3.5 ± 2.4</td>
<td>8.8 ± 11.3</td>
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Ga-68 PSMA PET / CT in metastatic prostate cancer

- high uptake in bone and soft tissue metastases
- therapy option with Lu-177 labelled ligands
Ga-68 PSMA PET / CT and Lu-177-PSMA therapy

Male, 54 y, 84 kg, prostate-CA, 1 x $^{223}$Ra, 1st cycle of $^{177}$Lu-PSMA (3.7 GBq)
Lu-177-PSMA wholebody planar images

$^{68}$Ga-PSMA PET/CT

$^{177}$Lu-PSMA WB planar
Lu-177-PSMA quantitative SPECT/CT: LMU-reconstruction

PET/CT

LMU-Recon of SPECT & SPECT/CT (Siemens Symbia T1)

(⁶⁸Ga-PSMA)

Day 0

Day 1

Day 2

Day 3

PET GkAc

Min: SUVmax 0.00 — 0 Bq/cc
Max: SUVmax 0.145 — 70228 Bq/cc
Current: SUVmax 2.88 — 28291 Bq/cc

spect-day0-ac1-sc1-bc1

Min: 0 Bq/cc
Max: 710228 Bq/cc
Current: 971189 Bq/cc

spect-day1-ac1-sc1-bc1

Min: 0 Bq/cc
Max: 1210017 Bq/cc
Current: 970099 Bq/cc

spect-day2-ac1-sc1-bc1

Min: 0 Bq/cc
Max: 121628 Bq/cc
Current: 928723 Bq/cc

spect-day3-ac1-sc1-bc1

Min: 0 Bq/cc
Max: 1210017 Bq/cc
Current: 970099 Bq/cc

PET/CT

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Department of Nuclear Medicine
LMU Munich
Lu-177-PSMA quantitative SPECT/CT: LMU-reconstruction

DOSE ESTIMATION

„manual“ method
## Lu-177-PSMA quantitative SPECT/CT: LMU-reconstruction

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<tr>
<td>Tumor (rib)</td>
<td>7.6</td>
<td>93.6</td>
</tr>
<tr>
<td>Tumor (spine)</td>
<td>5.7</td>
<td>67.8</td>
</tr>
<tr>
<td>Kidney (left)</td>
<td>2.3</td>
<td>30.4</td>
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Relevance of quantification / dosimetry

- Patient selection
- Selection of radionuclide
- Therapy monitoring and response
- Correlation with clinical outcome

- Current issues:
  - calibration
  - time and labour
  - manually co-registration
  - segmentation of relevant organ structures
Relevance of Absolute Quantification

e.g. Samarium-153 EDTMP
Therapy response following Ra-223 therapy in metastatic prostate cancer

12.12.2013 (pretherapy)

PSA (ng/ml):
Pre-therapy: 239
After 6 cycles: 16,6
Follow-up 3 months after 6th cycle: 9,98

30.04.2014 (after 6 cycles Ra-223)
Differentiation of benign and malignant lesions

- 62 year old female
- Breast cancer 1998
- s/p ablatio mammae
- s/p radiotherapy
- s/p pulmonary metastasis and lung resection
- CT scan in outside clinic with suspected metastasis of the R. inferior ossis pubis and the sacroiliac joint
Focal activity in the ischial tuberosity without explicit CT-correlate

benign? malignant?
Patient example – pelvis – MRI scan

- Tendinitis of the flexor muscle insertion in the ischial tuberosity
- No signs for malignancy
Patient example – pelvis – xSPECT

- distinct focal activity; differential diagnosis, however, remains difficult
- less overestimation as compared to Flash 3D
Patient example – pelvis – xSPECT

- Absolute quantification of uptake as a reference standard?
Animal models – further research

- Siemens Intevo
- 170 MBq Tc-99m-DPD
- SPECT parameters
  - xSPECT bone recon
  - 256 matrix, 64 views, 30 sec
- CT parameters
  - 16 slices
  - 0,75 mm
THANK YOU VERY MUCH FOR YOUR ATTENTION!

Special thanks to:
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Technichal staff LMU Munich
Hans Vija, Siemens Medical
Juri Ruf, Univ. Freiburg
Uwe Haberkorn, Univ. Heidelberg

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Team of the Dept of Nuclear Medicine, December 2013
Patient 9

- 63 year old male
- suspected stress shielding
- total hip prosthesis left 2009
- s/p tibia fracture left
- s/p foot ankle fracture right

- tracer accumulation around prosthesis stem
- sign for loosening
Patient 9 – xSPECT vs. Flash 3D

- tracer accumulation as a sign for prosthesis loosening
- Flash 3D seems „diffuse“, whereas xSPECT is clearly located around the prosthesis stem
Patient 7

- 65 year old male
- prostate cancer
- s/p thoracic spine osteosynthesis
- s/p prosthesis right hip
- severe pain in lumbal spine

- tracer accumulation in lumbal spine
- malignant? inflammation? fracture?
Patient 7 – lumbal spine – Flash 3D

- upper and lower end plate deformity in lumbal vertebra
- s/p fracture (osteoporotic)
- diagnose only in awareness of CT
Patient 7 – lumbal spine – xSPECT

- confirmation of diagnose
- all relevant information included in xSPECT