Gallium-68 Information Session

Michael Graham, PhD, MD
University of Iowa
Co-Chair SNMMI Clinical Trials Network

SNMMI Annual Meeting June 9, 2014
CTN Mission: Facilitate the use of molecular imaging radiopharmaceuticals in clinical trials

- Ensure quality imaging is conducted in drug development clinical trials
- Facilitate access to investigational radiopharmaceuticals, including PET and SPECT agents
- Provide education and training for molecular imaging professionals performing clinical research
- Develop partnerships to enhance use of new radiopharmaceuticals
SNMMI/CTN Ga68-related Activity

- Bi-annual meetings to raise awareness
- Initial focus on identifying best agent
- More recently:
  - Common end-product specifications
  - Standardized protocols
  - Helping new sites
    - (IND template, consent forms, data forms)
  - Obtained orphan drug designation for DOTATOC
  - Assisting commercialization
Orphan Drugs

The FDA Orphan Drug Designation program provides orphan status to drugs and biologics which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in USA (not more than 5 in 10,000 in EU)

- Fewer subjects needed in pivotal trial
- Application fees are waived
- Eligible for FDA grant funding

- Designation does not mean approved for clinical use
- Designated indication: management of patients with known disease

*
SNMMI/CTN Plan for Ga68 DOTATOC

- NDA approval of DOTATOC
- Waive exclusivity
- Help sites obtain aNDA

Implications

- Other sites can obtain DOTATOC aNDA

Compounding Model

- Companies can develop kits and seek NDA for kits
- Pharmacies will be able to compound and distribute
Current North American Activity

• DOTATOC
  – Iowa, UCSF, JHU (MGH, Wash U, Mt. Sinai, U Penn …)

• DOTATATE
  – Vanderbilt, UCLA, NIH, RadioMedix, Stanford
    (MD Anderson, LSU …)

• DOTANOC
  – Indiana, Edmonton
Cost Recovery

• FDA believes that in most cases the cost of an investigational drug in a clinical trial intended to support a marketing application is an ordinary cost of doing business.

• The purpose of permitting charging for an investigational drug in a clinical trial is to permit a sponsor to recover the costs of making certain drugs when clinical trials could not be conducted without charging because the cost of the drug.

• A sponsor authorized to charge for its drug in a clinical trial can only recover its direct costs.

Charging for imaging is outside the purview of FDA.*
Players

- INVICRO – DOTATOC
- AAA – DOTATATE

Sales
- AAA, ABX, ITG, Biomedica

Manufacturing
- Bachem (Switz)
- BioMedica (Greece)

IP Situation

<table>
<thead>
<tr>
<th></th>
<th>IP Europe</th>
<th>IP US</th>
<th>IP Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOTATOC</td>
<td>2015</td>
<td>2014</td>
<td>2014</td>
</tr>
<tr>
<td>DOTATATE</td>
<td>2014</td>
<td>2015</td>
<td>2015</td>
</tr>
<tr>
<td>DOTANOC</td>
<td>Off Patent</td>
<td>2022</td>
<td>Off Patent</td>
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</table>

Other potential players:
- US DOE
- Mallinckrodt
- iThemba
- Cyclotron Co., Obninsk

Other Considerations: Distribution (Cardinal, IBA, PETNET), Patients, NET oncologists

Pressing issues Requiring Resolution

- Manufacturing or Pharmacy?
- IP and Cost
- GMP or not GMP, Cost
- Can we make enough?
- Long parent half-life is a dual edged sword.

Generators
- Eckert-Ziegler – GMP status?
- ITG – GMP status?
- IDB Holland
- Cyclotron Co. Ltd - Obninsk

Ge-68 Production

The Big Picture

Unknown Primary with Metastatic NET to Liver and Bones, Negative Octreoscan and CT for Primary
Scan Results (N=127)

Diagnosis of NET
  • Ga-68 DOTATOC positive in only 3/27 patients presenting with symptoms / labs suggestive of elevated serotonin without diagnosis of NET (2 false positive, 1 unconfirmed)

Unknown Primary
  • Ga-68 DOTATOC identified primary tumor in 16/25 pts with metastatic disease, 11 true positive. 2 false positive 3 unconfirmed. 9 false negative.

Initial staging & Restaging (75)

Funding is provided via a Cost-Recovery IND
Presentations from Industry and Academia

1. Ronald Walker, Vanderbilt University, Nashville, TN
2. Andre Iagaru, Stanford, Palo Alto, Ca
3. Sherly Mosessian, UCLA, Los Angeles, Ca
4. Jim Fletcher, Indiana University, Indianapolis
5. Harshad Kulkarni, Zentralklinik, Bad Berka, Germany
6. Ebrahim Delpassand, Excel Diagnostics, Houston, Tx
7. Dirk Becker, Eckert & Ziegler, Germany
8. Izabela Tworowska, Radiomedix, Houston, Tx
9. Maurizio Mariani, Advanced Accelerator Applications, France
$^{68}$Ga-DOTATATE PET/CT

Vanderbilt Experience

Ronald C Walker MD, Jeff Clanton RPh BCNP, Eric Liu MD, Dominique Delbeke, MD PhD

Nashville, TN
Table 1: Neuroendocrine tumor types (n=97):

<table>
<thead>
<tr>
<th>Primary Tumor Type</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>7</td>
</tr>
<tr>
<td>Stomach/prox duodenum/pancreas</td>
<td>22</td>
</tr>
<tr>
<td>Mid-gut</td>
<td>44</td>
</tr>
<tr>
<td>Hindgut/rectal</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
</tr>
<tr>
<td>Metastatic disease from unknown primary</td>
<td>16</td>
</tr>
</tbody>
</table>
68Ga-DOTATATE PET/CT - Vanderbilt

- Safety, efficacy and non-inferiority study
- Toxicity (serial EKG, CMP, vital signs) before and after scans – no significant toxicity observed
- Compared to conventional imaging (CT, MRI, ¹¹¹In-Octreotide) for impact on care
- Independent readings for reproducibility
- Impact: none, minor (e.g. change in existing treatment plan) or major (e.g. change to new treatment plan)
Impact on Care vs. all CI:

- No impact: 55 (56.7%)
- Impact: 42 (43.3%)
- Minor impact: 10 (10.3%) – most commonly a change in surgical plan
- Major impact: 32 (33.0%) – most commonly to refer patients to PRRT or to convert patients to a surgical plan.

Number of patients referred to PRRT as a result of $^{68}$GaDOTATATE: 15 (15.5%)

Number of patients where PRRT referral was cancelled (due to poor uptake): 2 (2.1%)

Number of patients referred for PRRT with positive $^{68}$GaDOTATATE and negative $^{111}$InOctreotide: 5 (5.2%)
68Ga DOTA TATE PET: Current Status at Stanford

- 33 patients enrolled to-date since Jan 2014
- IND approved as EAP for 200 participants
- Cost recovery mechanism in place
- Cannot bill patients directly per local IRB
- Cannot bill MediCare/MediCal
- Professional fee waived
- Did not see a decrease in the price of precursor yet
- Almost completely replaced 111In Octreoscan®
- Roughly ¾ of claims reimbursed by insurance
- Changes in management in 15 of the 20 patients who had $^{111}$In-Octreoscan®
- Will apply for funding to do $^{68}$Ga DOTA TATE PET/MRI
UCLA– $^{68}$Ga–DOTATATE PET/CT studies

Clinical
- Johannes Czernin M.D.
- Martin Auerbach M.D.
- Ken Herrmann M.D.

Manufacturing
- Sam Sadeghi Ph.D
  (Director of cyclotron and radiochemistry facility)

Regulatory
- Sherly Mosessian Ph.D
- Shaojun Zhu M.S.
Regulatory summary

1. **UCLA IND (Reference to Vanderbilt IND)**
   - 12/18/12: IND was approved with cost recovery.
   - By March, 2014, 100 patients were imaged.
   - FDA did not grant request to increase number of patients beyond 100 as part of a Phase 1 IND

2. **UCLA Expanded Access IND (Content similar to Stanford Expanded Access IND)**
   - 05/01/14: UCLA Expanded Access IND was approved with cost recovery to enroll 300 patients.
   - Currently in the process of finalizing IRB amendment approval and enrolling human subjects.
Study Aim/Design

- NOPR like design to determine the impact of $^{68}$Ga-DOTATATE PET/CT on the management of patients with NETs

<table>
<thead>
<tr>
<th>Pre Scan Questionnaire</th>
<th>Post Scan Questionnaire</th>
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<tbody>
<tr>
<td>Staging/Restaging</td>
<td>Post Scan M1 Suspicion</td>
</tr>
<tr>
<td>Prior Therapy</td>
<td>Change of M1 Suspicion</td>
</tr>
<tr>
<td>Tumor Location/Grade/Stage</td>
<td>New Metastases?</td>
</tr>
<tr>
<td>M1 Suspicion</td>
<td>Intended Treatment</td>
</tr>
<tr>
<td>Intended Treatment</td>
<td>Treatment Changes?</td>
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</tbody>
</table>
Management changes

- Major management changes: 28%

<table>
<thead>
<tr>
<th>Major change type</th>
<th>N   (% change)</th>
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</thead>
<tbody>
<tr>
<td>Away from surgery</td>
<td>7/61 (11.5 %)</td>
</tr>
<tr>
<td>To surgery</td>
<td>8/61 (13.1%)</td>
</tr>
<tr>
<td>From treatment to no treatment</td>
<td>1/61</td>
</tr>
<tr>
<td>From no treatment to treatment</td>
<td>1/61</td>
</tr>
</tbody>
</table>

- Overall management changes: 31/61 (51%)
First year Experience with $^{68}$Ga DOTA-NOC

James W. Fletcher, Mark Green, Mark Tann, Mary Maluccio, Carla Mathias, Gary Hutchins

Department of Radiology and Imaging Sciences
Indiana University School of Medicine
Indiana/Purdue University in Indianapolis
\( ^{68}\text{Ga} \) DOTA-NOC

- Expanded Access IND # 117,255
- Source of \( ^{68}\text{Ga} \) has been Eckert-Ziegler generator
- Initial estimate of 30 patients per year over 4-years
- Actual enrollment Year 1 → 39 patients
Preparation

- All doses met specified release criteria
- Doses averaged 4.7 ± 0.6 mCi
- Production time: elution → dose release: 46 ± 5 minutes
  (usually 44 minutes, but three doses delayed by need to re-filter or to repeat endotoxin test because device issue)
- Radiochemical purity: 98.2 ± 0.7%
- Virtually no $^{68}$Ge breakthrough $3 \times 10^{-7}$ %
Indications:

1. Patients with neuroendocrine cancers who are potentially candidates for treatment by multivisceral transplant.

2. Patients in whom a liver mass has been upon biopsy found to be a neuroendocrine tumor (presumably metastatic), and whose treatment requires detection of the unknown primary tumor and/or definition of the extent of disease.

3. Patients in whom prior, clinically indicated, $^{111}$In-Octreoscan SPECT has failed to address the clinical diagnostic need, and for whom the superior resolution and target/background contrast of a $^{68}$Ga-DOTA-NOC PET/CT study is clinically judged to be in the patient’s best interest for advancing decisions about their medical care.
Use of $^{68}$Ga-DOTA-NOC PET/CT to locate a primary lesion in patients with liver metastases and an unknown primary $\rightarrow$ 5 patients

- 2 had disease in liver but no evidence of primary site
  - Lack of occult primary led to change in surgical management in 1
- 3 had previously unknown occult primaries located by study (2 pancreas, 1 small bowel)
  - Both PNET patients went on to get systemic treatment which was a change in management
Patient INdications

- Use of $^{68}$Ga-DOTA-NOC PET/CT to determine eligibility for multivisceral transplant → 10 patients
  - Six (6) patients had evidence of previously unknown disease outside the abdomen, making them ineligible for multivisceral transplant under our current eligibility criteria.
    - Two (2) patients had occult asymptomatic bone metastases
    - Four (4) patients had disease in the lungs or extra-abdominal lymph node basins (i.e. mediastinum)
Patient Indications

- Thirteen (13) patients underwent $^{68}$Ga-DOTA-NOC PET/CT to evaluate extent of disease for one of several reasons.
- Five (5) patients had considerably greater disease burden than expected.
- Three (3) patients had disease burden as predicted, or less than predicted.
- Two (2) patients had recurrent disease detected by $^{68}$Ga-DOTA-NOC PET/CT, and a change in management based on that result.
- Three (3) patients had negative $^{68}$Ga-DOTA-NOC PET/CT scans, prompting a change in management and evaluation of other causes of presenting symptoms.
Summary

• No adverse reactions with exception of transient 2-5 minute nausea in ~50% of patients

• No adverse events

• No drop outs

• High quality images that provided information that exceeded what was available from conventional imaging (\(^{111}\text{In-Octreotide, contrast enhanced CT}\))
Sample Images

- Images obtained approximately 1-hour after injection on Siemens mCT device. Typically with contrast enhancement of CT (Isoview 370).
- 3-minutes per bed position.
Update on $^{68}$Ga-DOTATATE (GalioMedix™) and $^{68}$Ge/$^{68}$Ga generators (ITG GmbH)

- RadioMedix Inc. – Phase I/II IND application (IND 117289)  
  *(Compounding, radiolabeling, QC validation, IND submission)*

- Prepared ~ 110 doses

- 1-2 doses of $^{68}$Ga –DOTATATE per day  
  *(PET/CT imaging: 1-3 patients)*

- $^{68}$Ge/$^{68}$Ga generator ITG GmbH (30 mCi); 50mCi

- Consistent and reliable elution profiles;  
  Elution yield >80% on calibration date and during shelf life of generators

**ITG GmbH $^{68}$Ge/$^{68}$Ga generators:**

Novel GMP-grade generators with shelf life of 12 months or 250 elutions  
DMF authorization – final stage
Simplified protocol for the dose preparation using ITG $^{68}$Ge/$^{68}$Ga generators

- No need for pre-purification /pre-concentration of $^{68}$Ga using ion exchange resin
- No need for purification of the final dose

<table>
<thead>
<tr>
<th>Required specification</th>
<th>Observed parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose: 4 – 16 mCi</td>
<td>$7.34 \pm 3.4\text{mCi}$</td>
</tr>
<tr>
<td>RCP &gt; 95% as determined by iTLC</td>
<td>$98.998 \pm 1.1%^*$</td>
</tr>
<tr>
<td>Ge-68 content &lt;0.01%</td>
<td>$0.00265 \pm 2.05E-03%$</td>
</tr>
</tbody>
</table>
RadioMedix Inc. - Distribution and compounding services

RadioMedix Inc. - ITG GmbH (Germany) Business Partnership

• US Exclusive distribution rights for the ITG GmbH products:
  - $^{68}$Ge/$^{68}$Ga generators
  - IQS $^{68}$Ga Fluidic labeling module
  - DOTATOC
    - Ac$^{225}$/Bi$^{213}$ generators
    - and W$^{188}$/Re$^{188}$ generators
• $^{68}$Ga program using ITG GmbH generators has been initiated in US clinical centers and networks of radiopharmacies
• Offer leasing plan for $^{68}$Ge/$^{68}$Ga generators (6, 12, 18 months)

RadioMedix Inc.

• Provide support and on-site training
• Compound and distribute the DOTATOC kits

Izabela Tworowska  itworowska@radiomedix.com

Wednesday, June 11th - Radiopharmacy, Abstract 612
Kit for the preparation of $^{68}$Ga-labeling of sst analog peptides
A sterile, lyophilised, easy-to-use kit approach for the preparation of $^{68}$Ga-labeling of sst analog peptides

- One of the barriers to more widespread use of Ga-68 PET is the absence of sterile, lyophilised easy-to-use kits for the direct preparation of $^{68}$Ga drugs.
- Currently the preparation of $^{68}$Ga-radiopharmaceuticals implies articulate synthesis procedure and/or the use of synthesis modules which need fully-equipped cGMP radiopharmacy.
- **Extensive quality controls** of a product resulting from an extemporaneous production process are also required.
- Both the synthesis set-up and the relevant quality controls are currently under the responsibility of the individual clinical centres.
- Conversely, kit-type production allows a simple $^{68}$Ga-labeling procedure based on **direct reconstitution** of a pre-formulated GMP kit, **not requiring** cGMP manufacturing processing of the eluate or additional filtration or purification steps.
- Kit-type production of $^{68}$Ga-radiopharmaceutical **would definitively make** $^{68}$Ga the PET analogue of $^{99mTc}$. 
No need for cGMP, radiochemistry modules and extensive QC

**Kit approach:** production of $^{68}$Ga-DOTATATE or $^{68}$Ga-DOTATOC injectable solution by reconstitution of a pre-formulated GMP kit adding directly the eluate from a $^{68}$Ge/$^{68}$Ga generator without the need of any automatic module (only an heating block is required).

- **Not standardized procedure**
- **Onerous equipment costs** (module and analytical instruments) in cGMP environment
- **Need for expert staff**
- **Extensive QC**

**Straightforward and standardized reconstitution procedure**

**Test** | **Specifications**
---|---
**pH** | 3.2 – 3.8
**Radiochemical Purity (ITLC)** | % peak with Rf 0-0.1 ≤ 3%

**Standardized pharmaceutical product** with controlled quality and wide availability for PET localization of primary and/or metastatic lesions of GEP-NETs.
68Ga kits are now freely available for clinical trials

- The kit-based approach developed by AAA for the preparation of 68Ga-Dotatate and 68Ga-Dotatoc satisfies the necessity of a standardized pharmaceutical product with controlled quality and wide availability.

- AAA is actively pursuing development of the kits in both USA and Europe for the diagnosis and the management of GEP-NETs.

- The 68Ga-Dotatate kit is the ideal companion diagnostic agent of AAA Lutathera®, currently in Phase III (Netter I study) for the treatment of mid-gut carcinoid, with which it shares the same chemical features.

- The pharmaceutical development of both kits is completed.

- Following the activation of the relevant INDs, the kit can be made available for free for Investigator Driven Studies of relevant interest.
THERANOSTICS OF NEUROENDOCRINE NEOPLASMS: EXPERIENCE IN OVER 9,000 Ga-68 SOMATOSTATIN RECEPTOR RECEPTOR PET/CT STUDIES

Richard P. Baum, Harshad Kulkarni

THERANOSTICS Center for Molecular Radiotherapy & Molecular Imaging (PET/CT)
ENETS Center of Excellence, Zentralklinik Bad Berka, Germany

SNMMI Annual Meeting, June 9, 2014, St. Louis
In-111 OctreoScan. The (g)old standard...

Resection of pancreatic NET and splenectomy 04/2006.
Resection of a single liver metastasis 09/2007. Increasing CgA.
NUCLEAR = UNCLEAR

From „unclear“ medicine to „new clear“ medicine
<table>
<thead>
<tr>
<th>Compound</th>
<th>sst1</th>
<th>sst2</th>
<th>sst3</th>
<th>sst4</th>
<th>sst5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatostatin-28a</td>
<td>5.2 ± 0.3</td>
<td>2.7 ± 0.3</td>
<td>7.7 ± 0.9</td>
<td>5.6 ± 0.4</td>
<td>4.0 ± 0.3</td>
</tr>
<tr>
<td>OC</td>
<td>&gt;10.000</td>
<td>2.0 ± 0.7</td>
<td>187 ± 55</td>
<td>&gt;1000</td>
<td>22 ± 6</td>
</tr>
<tr>
<td>I-TOC</td>
<td>&gt;10.000</td>
<td>1.3 ± 0.3</td>
<td>128 ± 22</td>
<td>867 ± 33</td>
<td>50 ± 12</td>
</tr>
<tr>
<td>I-TATE</td>
<td>&gt;1.000</td>
<td>0.5 ± 0.2</td>
<td>187 ± 38</td>
<td>337 ± 57</td>
<td>50 ± 5.8</td>
</tr>
<tr>
<td>Ga-DOTA-OC</td>
<td>&gt;10.000</td>
<td>7.3 ± 1.9</td>
<td>120 ± 45</td>
<td>&gt;1.000</td>
<td>60 ± 14</td>
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<td>Ga-DOTA-TOC</td>
<td>&gt;10.000</td>
<td>2.5 ± 0.5</td>
<td>613 ± 140</td>
<td>&gt;1.000</td>
<td>73 ± 21</td>
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<tr>
<td>Ga-DOTA-TATE</td>
<td>&gt;10.000</td>
<td>0.20 ± 0.04</td>
<td>&gt;1.000</td>
<td>300 ± 140</td>
<td>377 ± 18</td>
</tr>
<tr>
<td>Y-DOTA-OC</td>
<td>&gt;10.000</td>
<td>20 ± 2</td>
<td>27 ± 8</td>
<td>&gt;10.000</td>
<td>57 ± 22</td>
</tr>
<tr>
<td>Y-DOTA-TOC</td>
<td>&gt;10.000</td>
<td>11.0 ± 1.7</td>
<td>389 ± 135</td>
<td>&gt;10.000</td>
<td>114 ± 29</td>
</tr>
<tr>
<td>Y-DOTA-TATE</td>
<td>&gt;10.000</td>
<td>1.6 ± 0.4</td>
<td>&gt;1.000</td>
<td>523 ± 239</td>
<td>187 ± 50</td>
</tr>
</tbody>
</table>
Molecular Imaging of NET by SMS-Receptor-PET/CT

- Whole-body diagnosis („one-stop shop“)
- Detection of unknown primary tumors (CUP)
- Evaluation of receptor status before and after PRRT
Whole-body diagnosis („one stop shop“)

Receptor-PET/CT using Ga-68 DOTA-NOC
Primary tumor (ileum), liver, lymph node & bone metastases
Detection of unknown primary neuroendocrine tumours (CUP-NET) using $^{68}$Ga-DOTA-NOC receptor PET/CT

Vikas Prasad · Valentina Ambrosini · Merten Hommann · Dieter Hoersch · Stefano Fanti · Richard P. Baum

**Results** In 35 of 59 patients (59%), $^{68}$Ga-DOTA-NOC PET/CT localised the site of the primary: ileum/jejunum (14),

**Conclusion** Our data indicate that $^{68}$Ga-DOTA-NOC PET/CT is highly superior to $^{111}$In-OctreoScan (39% detection rate for CUP according to the literature) and can play a major role in the management of patients with CUP-NET.
Primary tumor (ileum) and synchronous liver metastasis
Treatment decisions based on Ga-68 SMS receptor PET/CT: Bad Berka scoring system is based on SUVs – not on visual analogue scales as previously derived from OctreоScans.
Molecular imaging with $^{68}$Ga-SSTR PET/CT and correlation to immunohistochemistry of somatostatin receptors in neuroendocrine tumours

Daniel Kaemmerer • Luisa Peter • Amelie Lupp • Stefan Schulz • Jörg Sänger • Vikas Prasad • Harshad Kulkarni • Sven-Petter Haugvik • Merten Hommann • Richard Paul Baum
The correlation coefficients for SUV max, SUVmean, and MTV ranged from 0.83 to 0.99 (p<0.005).

The tumor SUVmax showed a significant correlation with immunohistopathology scores.

A correlation was also found between SSTR1-5 staining and the corresponding pathology grading.

**Results**

Somatostatin receptor imaging using Ga-68 DOTA-NOC PET/CT results in accurate estimation of the receptor density.

<table>
<thead>
<tr>
<th>Image Analysis Results</th>
<th>Correlation</th>
<th>Liver Mets SUVmax PET/CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSTR-2</td>
<td>Correlation Coefficient</td>
<td>-0.733</td>
</tr>
<tr>
<td></td>
<td>P Value</td>
<td>0.02</td>
</tr>
<tr>
<td>N1</td>
<td>Correlation Coefficient</td>
<td>-0.750</td>
</tr>
<tr>
<td></td>
<td>P Value</td>
<td>0.0158</td>
</tr>
</tbody>
</table>

**Ga-68 DOTA-SSTR PET/CT provides *in vivo* histopathology!**
Digitalized Histopathology Combined with Somatostatin Receptor PET/CT

From Tissue to Molecular Imaging to Therapy

- Tissue Sampling
- Tissue Staining

Definiens XD Image Analysis

Histopathological Grading

- SMS-R density on tumor cells
- Proliferation rate (Ki-67 / MIB1)
- Chromogranin A / Synaptophysin

- Prognosis
- Selection of most appropriate peptide (DOTATOC, DOTATATE, DOTANOC, SOMscan etc. for SMS-R PET/CT)
- Therapy guidance – peptide receptor radionuclide therapy (PRRNT) vs chemotherapy vs localised therapy vs molecular therapy etc.

Management Strategy

On the Way to Personalized Medicine
43 year old female, admission for intestinal bleeding
Use of Intraoperative Probes for Tumor Localization
Jejunum NEN (diameter 8 mm)
Cardiac metastases not detected on CT scan

Pericardial metastases well appreciated on CT
Surgical Resection of Perimyocardial NET-Metastasis
Responder – 42% reduction in SUV$_{\text{max}}$

*Dose to tumor* – 371 Gy

Non-responder – 125% increase in SUV$_{\text{max}}$

*Dose to tumor* – 25 Gy

This study confirmed - for the first time - that there is a relationship between the radiation dose delivered to liver metastases and the molecular response post PRRNT as measured by somatostatin receptor PET/CT.
$^{68}$Ga DOTA-TOC

Meningeoma - PET/CT 2012
Intra-arterial PRRT of Meninigeoma using 5 GBq of Y-90 DOTATOC
Translational Research: Crossing the Valley of Death

National Institutes of Health (NIH):  
- “Clinical and basic scientists don't really communicate”  
- Excellent basic research, but lack of translation  
- Where do we go from here?

Thank you  