

^{68}Ga Gallium Information Session

Michael Graham, PhD, MD
Dominique Delbeke, MD, PhD
David Dick, PhD
John Sunderland, PhD

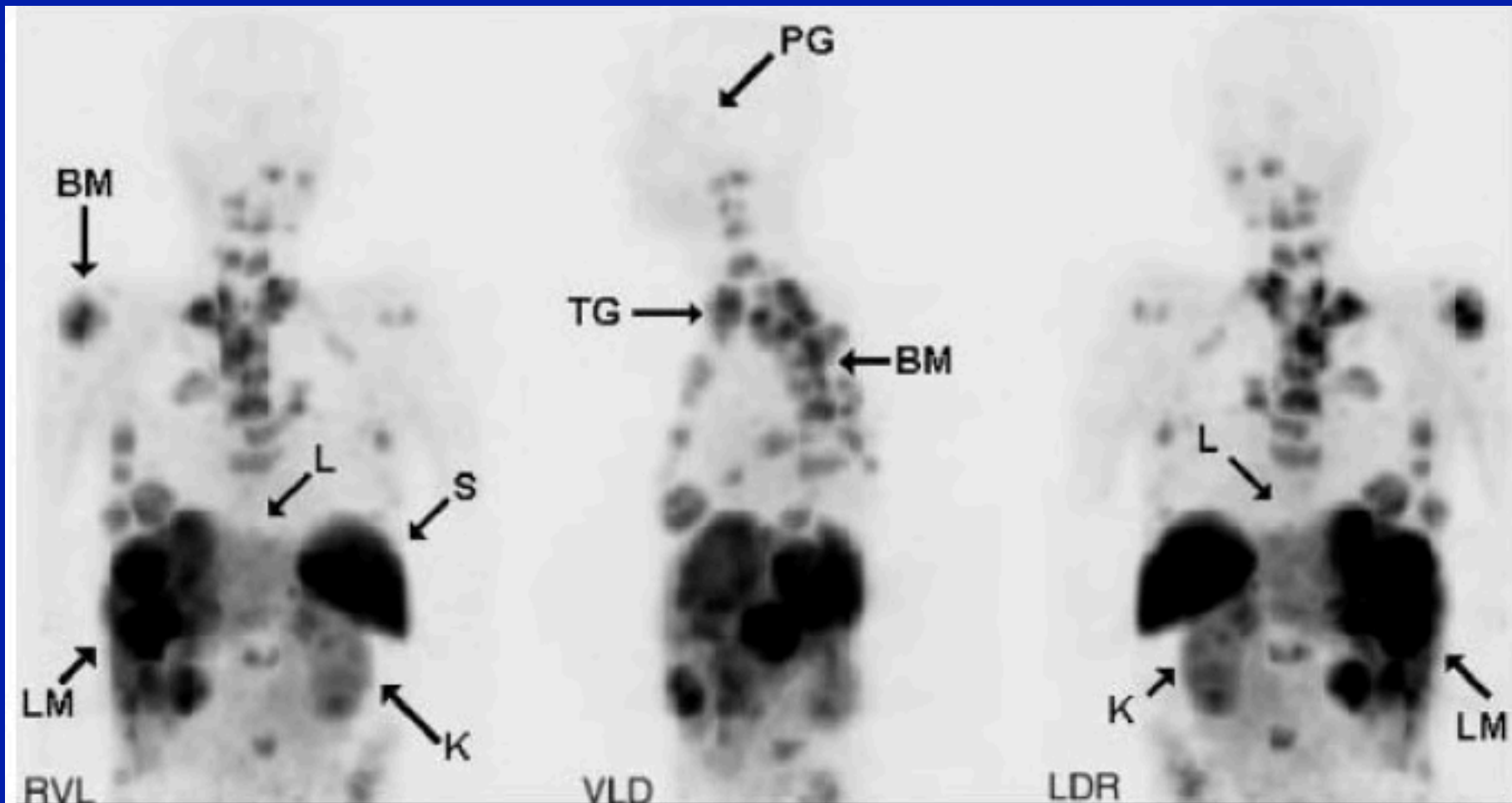
Welcome and Meeting Overview

Imaging with ^{68}Ga -DOTA-XXX

Michael M. Graham, PhD, MD
University of Iowa

Dominique Delbeke, MD, PhD
Vanderbilt University

Hofmann M, et al. Biokinetics and imaging with the somatostatin receptor PET radioligand ^{68}Ga -DOTATOC: preliminary data. Eur J Nucl Med. 2001 Dec;28(12):1751-7.

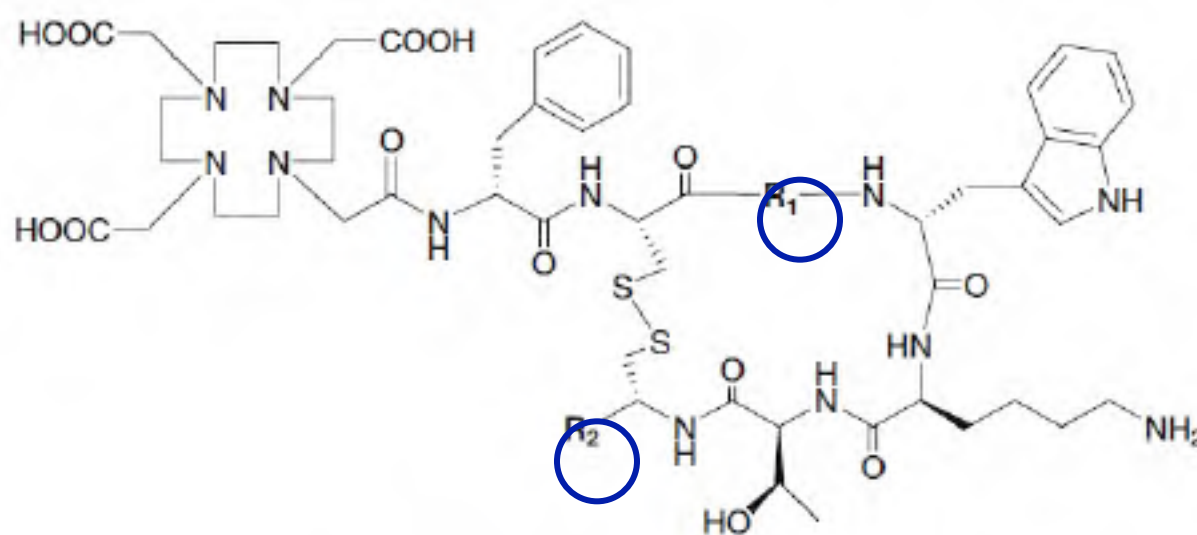


Images done at 90 min.

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Germany

Antunes P, et al. Are radiogallium-labelled DOTA-conjugated somatostatin analogues superior to those labelled with other radiometals? Eur J Nucl Med Mol Imaging. 2007 Jul;34:982-93.



<i>Compound</i>	R_1	R_2
DOTA-OC	Phe	Thr(ol)
DOTA-TOC	Tyr	Thr(ol)
DOTA-TATE	Tyr	Thr
DOTA-NOC	Nal-1	Thr(ol)
DOTA-NOC-ATE	Nal-1	Thr
DOTA-BOC	BzThi	Thr(ol)
DOTA-BOC-ATE	BzThi	Thr



How to Choose which one

- Accuracy
- Simplicity of Synthesis
- Patent Status
- Precursor availability

Antunes P, et al. Are radiogallium-labelled DOTA-conjugated somatostatin analogues superior to those labelled with other radiometals? Eur J Nucl Med Mol Imaging. 2007 Jul;34:982-93.

Table 1 Affinity profiles of DOTA-octapeptides (IC₅₀) for hsst1-5 receptors IC₅₀ values are in nmol/l (mean±SEM)

Compound	hsst1	hsst2	hsst3	hsst4	hsst5
Somatostatin-28	3.8±0.3 (10)	2.5±0.3 (11)	5.7±0.6 (10)	4.2±0.3 (11)	3.7±0.4 (11)
<u>Ga-DOTA-NOC</u>	>10,000 (3)	1.9±0.4 (3)	40.0±5.8 (3)	260±74 (3)	7.2±1.6 (3)
In-DOTA-NOC	>10,000 (3)	2.9±0.1 (3) ^a	8.0±2.0 (3) ^b	227±18 (3)	11.2±3.5 (3)
Lu-DOTA-NOC	>10,000 (3)	3.4±0.4 (3) ^b	12.0±3.3 (3) ^b	747±47 (3) ^b	14.0±3.5 (3) ^b
In-DOTA-BOC	>1,000 (2)	4.4±0.4 (3) ^b	6.8±0.3 (3) ^b	ND	10.5±1.5 (3) ^b
Lu-DOTA-BOC	>1,000 (2)	4.0±0.4 (3) ^b	6.3±0.2 (3) ^b	591±88 (2)	6.5±0.1 (3) ^b
Ga-DOTA-BOC	700±300 (2)	1.7±0.2(3)	10.5±0.5 (3)	ND	4.4±1.2 (3)
Y-DOTA-NOC-ATE	>1,000 (2)	4.2±2.0 (3)	47±1 (3)	ND	12±1 (3) ^b
Lu-DOTA-NOC-ATE	>1,000 (2)	3.6±0.3 (3) ^b	30±2 (3)	ND	15±1 (3) ^b
Ga-DOTA-NOC-ATE	>1,000 (2)	2.6±0.3 (3)	113±80 (2)	53±30 (2)	25±4 (3)
Y-DOTA-BOC-ATE	>1,000 (2)	2.9±0.3 (3) ^b	23±1 (3)	ND	7.8±2.0 (3)
Ga-DOTA-BOC-ATE	>1,000 (2)	2.0±0.2 (3)	33±23 (2)	35±24 (2)	19.5±13.0 (2)
Somatostatin-28 ^a	5.2±0.3 (19)	2.7±0.3 (19)	7.7±0.9 (15)	5.6±0.4 (19)	4.0±0.3 (19)
<u>Ga-DOTA-TOC^a</u>	>10,000	2.5±0.5	613±140	>1,000	73±21
Y-DOTA-TOC ^a	>10,000	11.0±1.7 ^b	389±135	>10,000	114±29
Ga-DOTA-OC ^a	>10,000	7.3±1.9	120±45	>1,000	60±14
Y-DOTA-OC ^a	>10,000	20±2 ^b	27±8 ^b	>10,000	57±22
<u>Ga-DOTA-TATE^a</u>	>10,000	0.20±0.04	>1,000	300±140	377±18
Y-DOTA-TATE ^a	>10,000	1.6±0.4 ^b	>1,000	523±239	187±50 ^b

Poeppel TD, et al. ^{68}Ga -DOTATOC versus ^{68}Ga -DOTATATE PET/CT in functional imaging of neuroendocrine tumors. J Nucl Med. 2011 52:1864

- 78 sites were found positive with ^{68}Ga -DOTATATE versus 79 regions with ^{68}Ga -DOTATOC
- Within the defined regions, 254 lesions were detected with ^{68}Ga -DOTATATE versus 262 lesions with ^{68}Ga -DOTATOC (P =0.012).
- On average, 8.2 lesions were found per patient with ^{68}Ga - DOTATATE versus 8.5 lesions with ^{68}Ga -DOTATOC.

Current North American Activity

- DOTA-TOC
 - Iowa (MGH)
- DOTA-TATE
 - Vanderbilt, UCLA, Excel Therapeutics (NIH, Stanford, MD Anderson)
- DOTA-NOC
 - Indiana, Edmonton

University of Iowa Experience

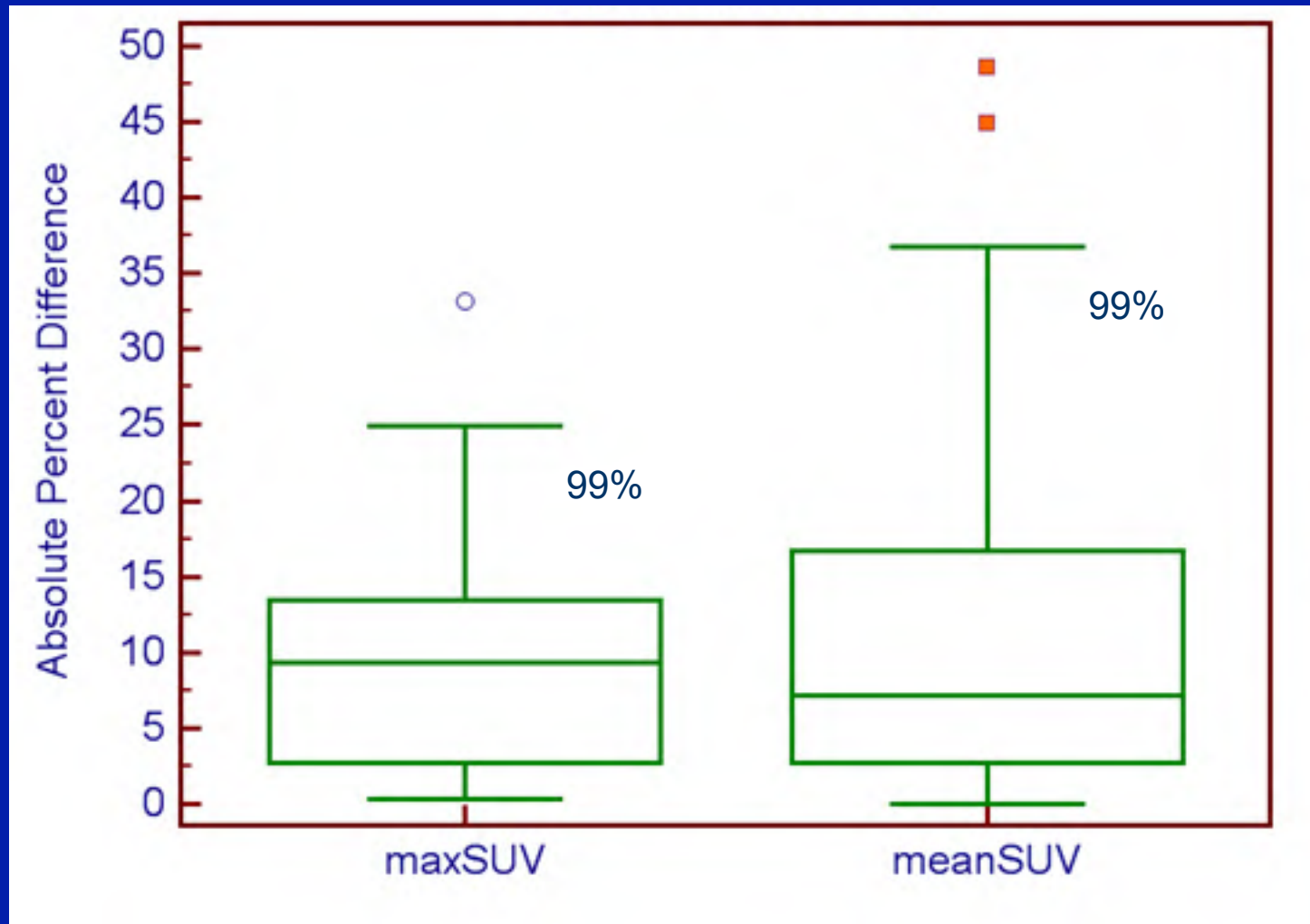
Ga-68 DOTA-TOC

RDRC: N=5

IND: N =120

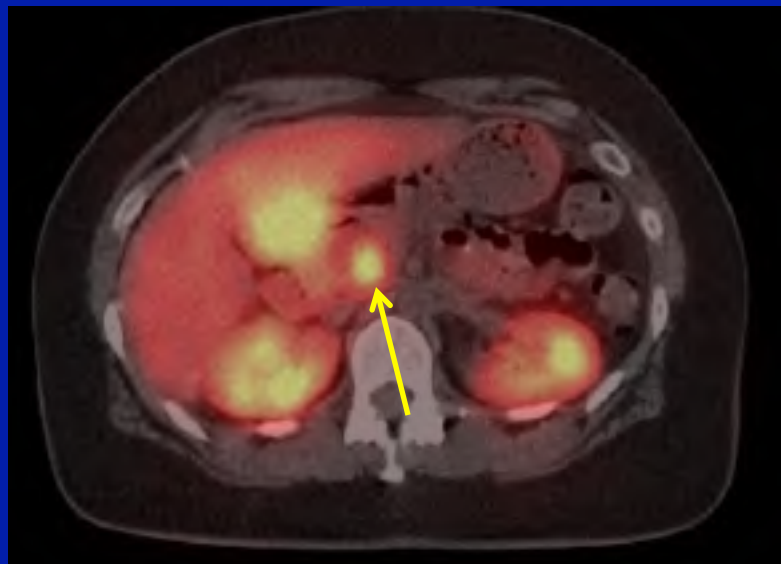
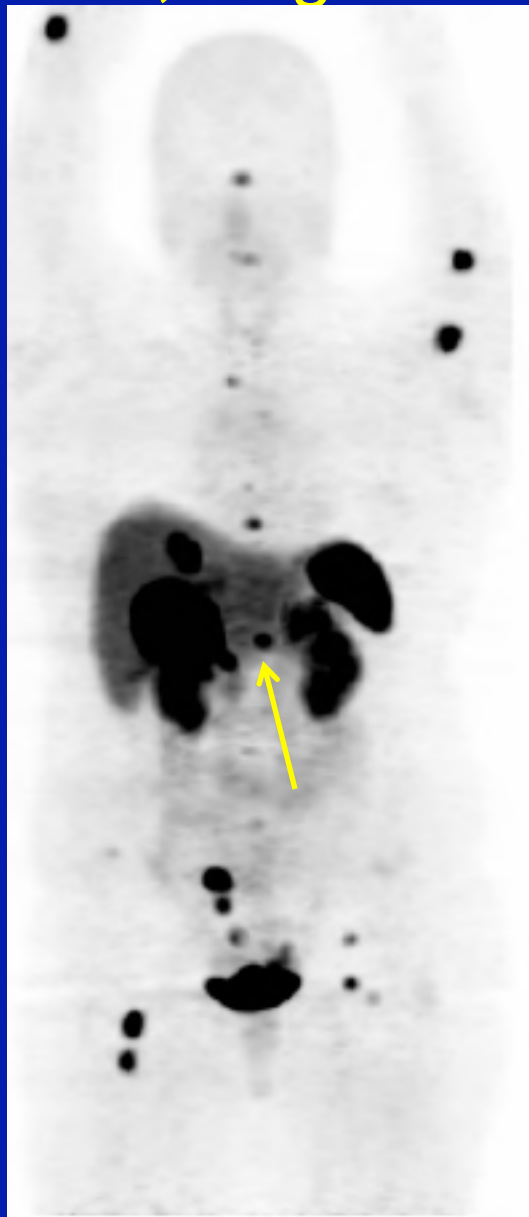
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Y Menda, LL Boles Ponto, M Schultz, GKD Zamba, GL Watkins, DL Bushnell,
MT Madsen, JJ Sunderland, MM Graham, TM O'Dorisio, MS O'Dorisio.
Repeatability of Ga-68 DOTATOC PET Imaging in Neuroendocrine Tumors.
Pancreas (2013) in press



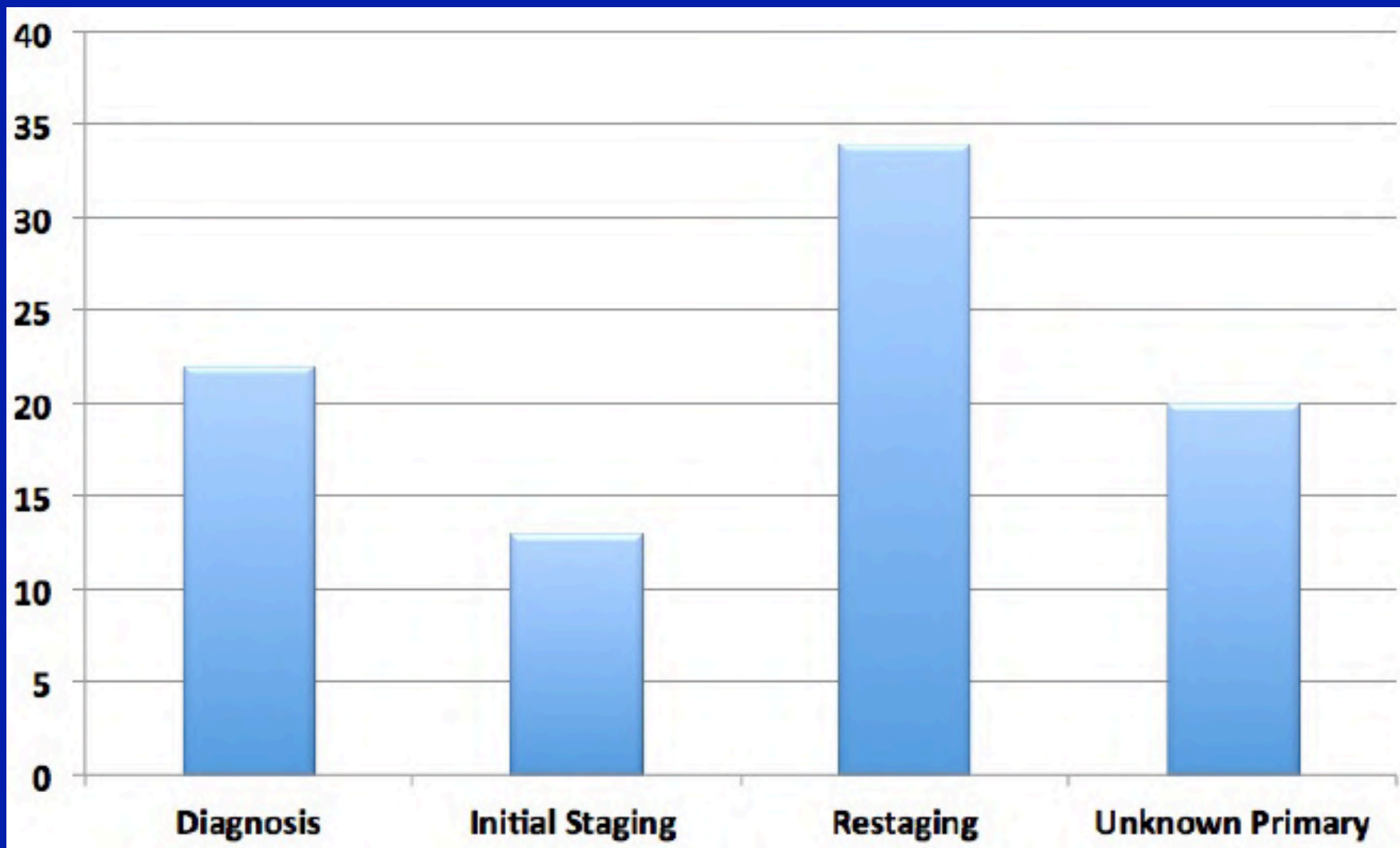
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Unknown Primary with Metastatic NET to Liver and Bones, Negative Octreoscan and CT for Primary



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Indications for Ga-68 DOTATOC (N=89) [Cost-recovery IND study at Iowa]



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Scan Results (Needs to be updated)

Diagnosis of NET

- Ga-68 DOTATOC positive in only 1/22 patients presenting with symptoms / labs suggestive of elevated serotonin without diagnosis of NET (false positive)

Unknown Primary

- Ga-68 DOTATOC identified primary tumor in 14/20 pts with metastatic disease, 7 have gone to surgery to remove primary. 2 others confirmed by biopsy. Conventional imaging found 3.

Initial staging (13)

Restaging (34)

Capurso G, et al. Systematic review of resection of primary midgut carcinoid tumour in patients with un-resectable liver metastases. Br J Surg 2012; 99: 1480-1486

First author	Number	Median OS	5y survival	Number	Median OS	5y survival
	Resected	(months)		Unresected	(months)	
Givi	66	108	81%	18	50	21%
Strosberg	100	110		35	88	
Ahmed	209	119	74%	76	57	46%
Søreide	53	139		12	69	
Norlen	493		75%	86		28%
Van der Horst-Schrivers	27	75	57%	49	52	44%
	948	110.2	72%	276	63.2	35%
	total	average	average	total	average	average

Available data suggest a possible benefit of resection of the primary lesion in patients with un-resectable liver metastases, but the studies have several limitations and the results should therefore be considered with caution.000

^{68}Ga -DOTATATE: The Vanderbilt Experience

Dominique Delbeke, MD, PhD

Ron Walker, MD (Imaging)

Eric Liu, MD (surgery)

Jeff Clanton, RD (Radiopharmacy)



^{68}Ga Consortium meeting, SNMMI Annual meeting
June 11, 2013, Vancouver, Canada

Clinical Trial at Vanderbilt/VAMC

^{68}Ga -DOTATATE Manufacturing

- Equipment needed: Radiochemistry laboratory
 - $^{68}\text{Ge}/^{68}\text{Ga}$ generator:
 - Eckert & Ziegler (Berlin, Germany)
 - Precursor: DOTATATE from ABX (Advanced Biochemical Compounds, Radelberg, Germany)
 - Quality control equipment

Clinical Trial at Vanderbilt/VAMC

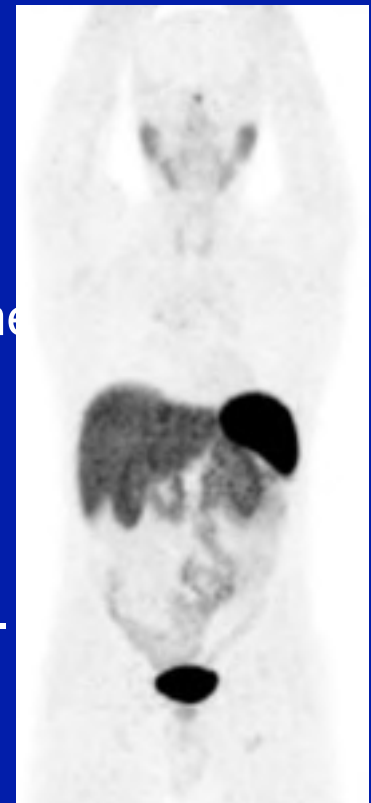
^{68}Ga -DOTATATE PET/CT Imaging Protocol

- Administered activity:
 - 50 microg or less of the peptide
 - Average activity: 196 MBq (5.3 mCi)
 - Range: 159-222 MBq (4.3-6.0 mCi)
- PET/CT protocol for image acquisition: same as ^{18}F -FDG
 - Field of view: from vertex to mid-thighs
 - Uptake time: 60 +/- 10 min (dynamic for dosimetry)
 - CT: Low-mAs helical CT without contrast
 - PET: 3D 4 min/bed

Clinical Trial at the TN Valley VA Healthcare System: ^{68}Ga -DOTATATE PET/CT Imaging in Lung Nodule (Funded by a VA Merit Grant)

Human dosimetry analysis under RDRC approval for biodistribution investigation:

- Have been completed in 6 patients.
- No observed adverse events in the immediate or delayed time frames, with follow-up of one year.
- Critical organ: Spleen followed by the bladder, kidneys, liver.
- Whole body dosimetry:
 - ◆ Similar to the closely related ^{68}Ga -DOTATOC and NOC.
 - ◆ Less than ^{111}In -DTPA-octreotide or ^{18}F -FDG



	^{68}Ga - DOTATATE	^{68}Ga - DOTATOC	^{68}Ga - DOTANOC	^{111}In - Octreotide	^{18}F -FDG
Effective Dose per scan	4.8 mSv	4.3 mSv	3.1 mSv	5.9 mSv	7 mSv

Clinical Trial at Vanderbilt: ^{68}Ga -DOTATATE PET/CT Imaging in Neuroendocrine Cancer

- VUMC has an IND (Investigational New Drug application) from the US FDA (#111972) for the use of ^{68}Ga -DOTATATE in evaluation patients with advanced NET
- The study is investigator-initiated
- Funding:
 - Investigational procedures are not reimbursed by Medicare
 - FDA grants permission to charge insurances and patients for the experimental drug (^{68}Ga -DOTATATE): Application to the US FDA for “cost-recovery”
 - Imaging procedure is also charged.

Clinical Trial at Vanderbilt: ^{68}Ga -DOTATATE PET/CT Imaging in Neuroendocrine Cancer

- ◆ www.clinicaltrials.gov: NCT01396382
- **Study purpose:** To determine the safety and efficacy of ^{68}Ga -DOTATATE in patient with neuroendocrine cancer.
- **Patient Population:** From 5/2011 to 5/2013, 80 adult patients who had suspected or known NET
 - Need of diagnosis 11% (9/80)
 - Need of staging 1% (1/80)
 - **Need of restaging 88% (70/80)**
 - **Small bowel 56% (45/80)**
 - Pancreas 16% (13/80)
 - Bronchial 9% (7/80)
 - Rectum 3% (2/80)
 - UP 4% (3/80)

Clinical Trial at Vanderbilt: ^{68}Ga -DOTATATE PET/CT Imaging in Neuroendocrine Cancer

- **Safety evaluation (NCI criteria):**
 - **Patient observation and vital signs:** before ^{68}Ga -DOTATATE administration and 3 hours after administration
 - blood pressure and heart rate
 - body temperature
 - pulse oximetry on room air
 - **12 leads EKG:** pre-injection and 3 hours post administration
 - **Laboratory tests:** pre-injection and 1 week post administration:
 - Tumor markers
 - Complete blood counts with differential
 - Electrolytes
 - Comprehensive metabolic panel: renal and liver function

Clinical Trial at Vanderbilt: ^{68}Ga -DOTATATE PET/CT Imaging in Neuroendocrine Cancer

- Summary of adverse experiences: None
- Interpretation of the ^{68}Ga -DOTATATE images:
 - High degree of inter-observer (n=3) agreement
 - Discordant findings between observers would have lead to a change in management in 1 of 80 patients

Clinical Trial at Vanderbilt: ^{68}Ga -DOTATATE PET/CT Imaging in Neuroendocrine Cancer

- **Clinical efficacy analysis:** Change of patient's management
 - No impact: 48% of patients
 - **Inter-modality change: 42% (33/80)**
 - Candidates for surgery: 15% (12/80), 2/3 UP
 - Not candidates for surgery: 4% (3/80), 1/9 diagnosis
 - Candidates for PRRT: 20% (16/80)
 - Not candidates for PRRT: 3% (2/80)
 - **Intra-modality change: 10% (8/80)**
 - Change in surgical plans: 3.5% (3/80)
 - Additional PRRT: 3.5% (3/80)
 - Refer to endoscopic ultrasound: 3% (2/80)
- **Conclusions: change in patient's management**
 - Restaging NET: 57% (40/70)
 - Diagnosis: 11% (1/9)

The pathway towards approval



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Ga-68 DOTA-TOC and DOTA-TATE

The Plan

- 1st step: Orphan drug designation
- CTN template documents
 - IND template for DOTA-XXX
 - Basic clinical and imaging protocol
 - Data collections forms
- FDA meeting for Confirmatory trial
 - Population: pts with known disease
 - Change in management, biopsy results
 - Support w expanded access, cost-recovery IND

Important FDA Concepts

- Cost Recovery
- Expanded Access
- Orphan drug status

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.

Expanded Access IND

- The primary purpose is to diagnose, monitor, or treat a patient's disease or condition, rather than characterize the safety and/or effectiveness of the investigational drug.
- The aim of expanded access is to facilitate the availability of the investigational new drug to patients with serious diseases or conditions when there is no comparable or satisfactory alternative therapy to diagnose, monitor or treat the patient's disease or condition.

General Criteria for Expanded Access

- The patient has a serious or immediately life threatening disease or condition.
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.
- The potential patient benefit justifies the potential risks
- Providing the investigational drug for the requested use will not interfere with the clinical investigations that could support marketing approval

For expanded access, all of the following conditions exist:

- Use of the PET drug by the institution producing the PET drug is limited to use within that institution.
- The isotope properties (e.g., very short half-life) and nature of use (e.g., use is limited to a small niche population) of the PET drug preclude commercialization.
- There is no commercially available formulation of the PET drug.

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

Summary

- Ga-68 DOTA-XXX provides an accurate way to image neuroendocrine tumors
- Used clinically in Europe for > 10 years
- Requires:
 - Ge-68 / Ga-68 generator, Precursor supply
 - Synthesis unit, Cost recovery IND
 - Radiochemist (or equivalent)
 - Referral source of neuroendocrine tumor patients
- NDA approval is likely with 5 years

^{68}Ga Generator Issues and Update Precursor Availability Status

David Dick, PhD
University of Iowa

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Ga-68 Generators

- Cyclotron Company Ltd
 - Obninsk, Russia
- Eckert & Ziegler
 - Berlin, Germany
- iThemba Labs
 - Cape Town, South Africa
- ITG GmbH
 - Munich, Germany

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Patent Expiration

- DOTATATE
 - US/Canada: Expires in 2015
 - Europe: Expires in 2014
- DOTATOC
 - US/Canada: Expires in 2014
 - Europe: Expires in 2015
- DOTANOC
 - US: Expires in 2022 (BioSynthema)
 - Everywhere else: expired

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Precursor suppliers

- DOTATATE
 - ABX, Bachem
- DOTATOC
 - Bachem, IBD
- DOTANOC
 - ABX, piCHEM

Major QC Equipment for Ga-68 DOTATATE/TOC/NOC

- Gas Chromatograph
- HPLC with radiation detector
- radioTLC reader
- NaI Well Counter with MultiChannel Analyzer (MCA)

Cost Recovery IND Procedures

John Sunderland, PhD
University of Iowa

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[Code of Federal Regulations]
[Title 21, Volume 5]
[Revised as of April 1, 2012][CITE: 21CFR312.8]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER D--DRUGS FOR HUMAN USE

PART 312 -- INVESTIGATIONAL NEW DRUG APPLICATION

Subpart A--General Provisions

Sec. 312.8 Charging for investigational drugs under an IND.

This is only about 2 pages of text, and relative to other CFR documents, this is quite understandable.

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.8>

Or do Google search of "IND Cost Recovery"

Cost Recovery for a Standard IND

APPLIES ONLY TO COST RECOVERY OF MANUFACTURE OF DRUG – NOT IMAGING

- a) *General criteria for charging.*
 - 1) You have to follow the rules in b-d, and get written permission from FDA. Applies to IND and Expanded Access IND.
- b) *Charging in a **clinical trial***
 - 1) *Clinical benefit over and above available drugs.*
 - 2) *Data will be useful in obtaining FDA approval.*
 - 3) *Demonstrate that you NEED to charge because of extraordinary costs.*
- d) *Costs recoverable when charging for an investigational drug*
 - 1) *ONLY Direct Costs (labor, supplies equipment)*
 - 2) *NOT Indirect Costs*
 - 3) *must provide supporting documentation of expenses (Receipts, quotes...).*
The documentation must be accompanied by a statement that an independent certified public accountant has reviewed and approved the calculations.

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Cost Recovery for an Expanded Access IND

APPLIES ONLY TO COST RECOVERY OF MANUFACTURE OF DRUG AND **CERTAIN IND ADMINISTRATIVE COSTS**– NOT IMAGING

- (c) *Charging for expanded access to investigational drug for treatment use*
 - (i) *Evidence of sufficient enrollment to complete trial*
 - (ii) *Evidence of adequate progress in the development of the drug for marketing approval; and*
 - (iii) *Information submitted under the general investigational plan (312.23(a)(3)(iv)) specifying the drug development milestones the sponsor plans to meet in the next year.*

E-Mail from Lucie Yang, M.D., Ph.D. CDER, FDA 2/14/12

Your question:

Can the sponsor of a traditional (clinical trial) IND or expanded access IND for a PET drug recover the costs not only of the drug (direct costs) but also the costs of image acquisition and image interpretation?

Our answer:

FDA authorizes cost recovery only for the drug. Seeking cost recovery for monitoring or supportive aspects (e.g. radiographic procedures) is beyond the FDA purview. Conceivably, these investigational costs may be charged to the patient, contingent upon the local IRB expectations.

Let me know if you need further clarification.

Thank you,
-lucie

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Allowed Direct Costs

- Capital Expenses Depreciated:
 - Hot Cell, Synthesis Module (5 year depreciation or whatever you want. Break this cost down to \$/patient based upon projected volume)
- Ge-68/Ga-68 Generator (\$40K/6 months – Break this cost down to \$/patient based upon projected volume)
- Synthesis Costs
 - Cassettes, Reagents, GMP Peptide, Vials... (\$350)
- Personnel Costs
 - Radiochemists time (about 5 man hours/synthesis) (\$300)
- QC Costs (\$50)

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Independent CPA three Page Letter

Conclusion

Based upon the results of our testing and conversations with management, we can conclude that all costs included in the client calculation tie to invoices supplied without deviation. Furthermore, all formulae prepared by client have been recalculated and are correctly applied to the cost calculation.

With regard to the application of costs associated with this IND we can conclude that the calculation is consistent with the requirements of paragraphs (d)(1) of *Code of Federal Regulations, Title 21, Volume 5, Part 312, Section 312.8*.

Sincerely,

DRAFT

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Financial Modeling

Modular Lab Depreciation Schedule:					
Type	Linear				
Duration	5 years				
Cost	\$85,906				
	Year				
Schedule	1	2	3	4	5
	\$17,181	\$17,181	\$17,181	\$17,181	\$17,181

Hot Cell Depreciation					
Type	Linear				
Duration	5 years				
Cost	\$40,000				
	Year				
Schedule	1	2	3	4	5
	\$8,000	\$8,000	\$8,000	\$8,000	\$8,000

Total Depreciation Costs/Year
 \$25,181
 Subjects Imaged/Year
 70 Patients per year

Depreciated Costs per Patient
 \$360

GA GENERATOR \$34,648
 Generator Replacement 150 Days
 Subjects/year 70
 Generators/year 2.43
 Generators/Subject 0.035
 Generator Cost/Subject \$1,204

Generator Cost Prorated

Accounting Synthesis/Year Expense	ACCOUNTING NET INCOME DOTATOC MODEL n patient per synthesis with Scan Cost															
	Cost Recovery per Patient															
	\$200	\$400	\$600	\$800	\$1,000	\$1,200	\$1,400	\$1,600	\$1,800	\$2,000	\$2,200	\$2,400	\$2,600	\$2,800	\$3,000	
50	-\$144,206	(\$191,206)	(\$173,206)	(\$155,206)	(\$137,206)	(\$119,206)	(\$101,206)	(\$83,206)	(\$65,206)	(\$47,206)	(\$29,206)	(\$11,206)	\$6,794	\$24,794	\$42,794	\$60,794
60	-\$151,148	(\$207,548)	(\$189,548)	(\$171,548)	(\$153,548)	(\$135,548)	(\$117,548)	(\$99,548)	(\$81,548)	(\$63,548)	(\$45,548)	(\$27,548)	\$8,452	\$30,052	\$51,652	\$73,252
70	-\$158,091	(\$223,891)	(\$205,891)	(\$187,891)	(\$169,891)	(\$151,891)	(\$133,891)	(\$115,891)	(\$97,891)	(\$79,891)	(\$61,891)	(\$43,891)	\$2,909	\$28,109	\$53,309	\$78,509
80	-\$165,034	(\$240,234)	(\$222,234)	(\$204,234)	(\$186,234)	(\$168,234)	(\$150,234)	(\$132,234)	(\$114,234)	(\$96,234)	(\$78,234)	(\$60,234)	\$18,966	\$47,766	\$76,566	\$105,366
90	-\$171,977	(\$256,577)	(\$238,577)	(\$220,577)	(\$202,577)	(\$184,577)	(\$166,577)	(\$148,577)	(\$130,577)	(\$112,577)	(\$94,577)	(\$76,577)	\$2,623	\$35,023	\$67,423	\$99,823
100	-\$178,920	(\$272,920)	(\$254,920)	(\$236,920)	(\$218,920)	(\$200,920)	(\$182,920)	(\$164,920)	(\$146,920)	(\$128,920)	(\$110,920)	(\$92,920)	\$15,080	\$51,080	\$87,080	\$123,080
110	-\$185,863	(\$289,263)	(\$271,263)	(\$253,263)	(\$235,263)	(\$217,263)	(\$199,263)	(\$181,263)	(\$163,263)	(\$145,263)	(\$127,263)	(\$109,263)	\$27,537	\$67,137	\$106,737	\$146,337
120	-\$192,806	(\$305,606)	(\$287,606)	(\$269,606)	(\$251,606)	(\$233,606)	(\$215,606)	(\$197,606)	(\$179,606)	(\$161,606)	(\$143,606)	(\$125,606)	\$39,995	\$83,195	\$126,395	\$169,595
130	-\$199,749	(\$321,949)	(\$303,949)	(\$285,949)	(\$267,949)	(\$249,949)	(\$231,949)	(\$213,949)	(\$195,949)	(\$177,949)	(\$159,949)	(\$141,949)	\$52,452	\$99,252	\$146,052	\$192,852
140	-\$206,692	(\$338,292)	(\$320,292)	(\$302,292)	(\$284,292)	(\$266,292)	(\$248,292)	(\$230,292)	(\$212,292)	(\$194,292)	(\$176,292)	(\$158,292)	\$64,909	\$115,309	\$166,709	\$217,509
150	-\$213,635	(\$354,635)	(\$336,635)	(\$318,635)	(\$300,635)	(\$282,635)	(\$264,635)	(\$246,635)	(\$228,635)	(\$210,635)	(\$192,635)	(\$174,635)	\$77,366	\$131,366	\$185,366	\$239,366
160	-\$220,578	(\$370,978)	(\$352,978)	(\$334,978)	(\$316,978)	(\$298,978)	(\$280,978)	(\$262,978)	(\$244,978)	(\$226,978)	(\$208,978)	(\$190,978)	\$89,823	\$147,423	\$205,023	\$262,623
170	-\$227,521	(\$387,321)	(\$369,321)	(\$351,321)	(\$333,321)	(\$315,321)	(\$297,321)	(\$279,321)	(\$261,321)	(\$243,321)	(\$225,321)	(\$207,321)	\$101,880	\$160,480	\$218,080	\$276,680
180	-\$234,464	(\$403,664)	(\$385,664)	(\$367,664)	(\$349,664)	(\$331,664)	(\$313,664)	(\$295,664)	(\$277,664)	(\$259,664)	(\$241,664)	(\$223,664)	\$113,837	\$174,437	\$232,037	\$290,637
190	-\$241,407	(\$420,007)	(\$402,007)	(\$384,007)	(\$366,007)	(\$348,007)	(\$330,007)	(\$312,007)	(\$294,007)	(\$276,007)	(\$258,007)	(\$240,007)	\$125,794	\$187,394	\$245,594	\$304,194
200	-\$248,350	(\$436,350)	(\$418,350)	(\$400,350)	(\$382,350)	(\$364,350)	(\$346,350)	(\$328,350)	(\$310,350)	(\$292,350)	(\$274,350)	(\$256,350)	\$137,751	\$199,351	\$259,551	\$318,151

Synthesis Costs	
CASSETTES/Synthesis	\$250
Reagents/synthesis	\$20
GMP DOTATOC/synthesis	\$65
GMP VIALS	\$8
Total Synthesis	\$343

Based upon 2501 cost. Assume 10 cassettes per purchase?
 Estimate, including reagents syringes
 based upon \$6500 in 2009 - assuming enough for 100 syntheses, but no quantity given
 Estimate.

Personnel Costs	
Radiochemist 4 hours/synthesis	\$245
2nd Chemist Oversight @ 1 hr	\$61
Total Personnel	\$306

Radiochemist \$99,500 2080hrs/year \$48\$/hour
 Benefit Rate 28%
 Benefits \$27,860
 Total \$127,360 \$61\$/hr

QC Costs	
LAL Cartridge	\$35
syringes, vials...	\$10
Total QC	\$45

Total Production Cost/Scan \$1,899

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Questions and Answers

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