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ACMUI Activities: Overview

Christopher J. Palestro, M.D.
ACMUI Chairman
April 4, 2019


Overview of the ACMUI

- Role
- Membership
- Topics
- Future

ACMUI's Role

- Provide advice on policy and technical issues that arise in regulating medical use of radioactive material for diagnosis and therapy
- Comment on changes to NRC regulations and guidance
- Evaluate certain non-routine uses of radioactive material
- Provide technical assistance
- Bring key issues to the attention of the Commission for appropriate action.

ACMUI Membership (13 members)

- Healthcare administrator (Dr. Arthur Schleipman)
- Nuclear medicine physician (Dr. Christopher Palestro)
- 2 Radiation oncologists (Dr. Ronald Ennis & Dr. Harvey Wolkov*)
- Nuclear cardiologist (Dr. Vasken Dilsizian)
- Diagnostic radiologist (Dr. Darlene Metter)

*pending clearance

ACMUI Membership (13 members)

- 2 Medical physicists
  Nuclear medicine (Ms. Melissa Martin)
  Radiation therapy (Mr. Zoubir Ouhib)
- Nuclear pharmacist (Mr. Richard Green)
- Radiation safety officer (Mr. Michael Sheetz)
- Patients' rights advocate (Ms. Laura Weil)
- FDA representative (Dr. Michael O'Hara)
- Agreement states representative (Ms. Megan Shober)

ACMUI Topics (2018-2019)

- Analysis of medical events
- ABS medical event case study program
- Non-medical events
- Training & experience for all modalities
- Draft revision of Leksell Gamma Knife® Perfexion & Icon
- Compounding sterile/non-sterile radiopharmaceuticals

ACMUI Topics (2018-2019)

- Nursing mothers' guidelines
- ACMUI Bylaws
- Appropriateness of medical event reporting
- Yttrium-90 Microspheres Brachytherapy Licensing
- ACMUI external communications

ACMUI Topics (2018-2019) Staff Presentations

- T & E stakeholder outreach plan
- ACMUI Reporting Structure
- Medical Related Events
- Summary of Changes to 10 CFR Part 35
- Yttrium-90 Microspheres Brachytherapy Licensing Guidance
- Medical Team Highlights
- How ACMUI, Subcommittees, NRC Staff & Management work together under FACA

Future

- ACMUI will continue to
  - Provide advice and technical assistance
  - Comment on NRC regulations and guidance
  - Evaluate uses of radioactive material
  - Bring key issues to the attention of the Commission

Rest of Today's Agenda

- Darlene F. Metter, M.D. (ACMUI Vice Chair)
  -Comments on the Guidelines to Nursing Mothers for Exposure from the Medical Administration of Radioactive Materials
  -Comments on T & E Requirements for All Modalities (35.300 Uses)
- Ronald D. Ennis, M.D. (ACMUI Radiation Oncologist Brachytherapy)
  -Review and Analysis of Reported Medical Events for FY's 2014-2017

Rest of Today's Agenda (cont'd)

- Laura Weil (ACMUI Patients' Rights Advocate)

  -Perspective on:

  Nursing Mother Guidelines

  T & E Requirements for All Modalities (35.300 Uses)

  Medical Event Reporting

Acronyms

- ABS: American Brachytherapy Society
- ACMUI: Advisory Committee on Medical Uses of Isotopes
- FDA: Food and Drug Administration
- FY: Fiscal Year
- T&E: Training and Experience

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Comments on the Guidelines to Nursing Mothers for Exposure from the Medical Administration of Radioactive Materials

Darlene F. Metter, M.D.
ACMUI Vice Chairman
April 4, 2019


Subcommittee Members

- Vasken Dilsizian, M.D.
- Darlene Metter, M.D. (Chair)
- Christopher Palestro, M.D.
- Pat Zanzonico, Ph.D. (previous member)

Nursing Mother Guidelines

Charge: “Review the radiation exposure from diagnostic and therapeutic radiopharmaceuticals, including brachytherapy, to the nursing mother and child.”

Patient Release

- Patient release (nursing mother): Total EDE to the nursing child is < 5 mSv.
- If exposure could exceed 1 mSv to the nursing child, written instructions of adverse consequences must be given if nursing is not stopped & guidance on the discontinuation of breast feeding. (10 CFR 35.75)

Radiopharmaceuticals (RP) in Breast Milk

- Most nursing mothers administered RP require a temporary cessation of breast feeding.

- A few nursing mothers administered RP may require complete cessation of breast feeding.

Radiopharmaceuticals (RP) in Breast Milk

- **Exception**: (to decrease the breast dose)
- ^{131}I-NaI dose to the lactating breast
  - ^{131}I-NaI 150 mCi = 200 R (breast)
- To decrease the breast dose, lactation must cease. Thus, breastfeeding must stop 6 weeks prior to RP administration and for that child. May breastfeed for future children.

Radiation Exposure During Nursing

- Mother: Internal
- Child: External & Internal

Radiation Exposure: Nursing Child - External

- Mother is a significant radiation source, especially during routine child care.

- ALARA:
- Time: increased
- Distance: decreased

Radiation Exposure: Nursing Child - Internal

- Ingested radioactive breast milk
- Depends on the RP (~0.3-5% in milk)
- ^{131}I-NaI: Cease breast feeding 6 weeks before administration and for the current child.
- May breast feed for future children.

Nursing Mother Recommendations

Nursing interruption	Radiopharmaceutical
Stop	^{131}I-NaI*, ^{124} I-NaI, all alpha, ^{177}Lu dotatate diagnostic or therapeutic
None	^{15}O, ^{82}Rb, ^{68}Ga
1 hour	^{11}C, ^{13}N
4 hours	^{18}F

* Stop breast feeding 6 weeks prior to therapy

Nursing Mother Recommendations (Continued)

Nursing interruption	Radiopharmaceutical
24 hours	^{99m}Tc
3 days	^{123}I-NaI,
4 days	^{201}Tl-chloride
6 days	^{111}In-WBC, - pentetreotide
28 days	^{67}Ga, ^{89}Zr

Sealed Sources

- Y-90 Microspheres: No interruption

- Breast & sentinel lymph node sources: No interruption as long as source(s) is(are) not in the nursing mother

Nuclear Medicine Department Signage

- Inform nursing mothers or mothers planning to nurse in the near future who are scheduled for a NM procedure, that certain RP may require radiation safety precautions.

- Such patients are advised to notify the NM staff or physician prior to their procedure.

Subcommittee Report

- February 1, 2018 public teleconference

  ACMUI unanimously approved the submitted report with some caveats (e.g., calculations, modifications to tables).

- September 20, 2018 ACMUI Fall Meeting

  ACMUI unanimously approved the revised report with additional language regarding FDA-approved RP and the need to evaluate RPs not encompassed in the report.

Acronyms

- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- ALARA – As Low As(Is) Reasonably Achievable
- CFR – *Code of Federal Regulations*
- EDE – Effective Dose Equivalent
- NRC – Nuclear Regulatory Commission
- R – Rad
- RP – Radiopharmaceuticals

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Comments on Training & Experience Requirements for All Modalities (35.300 Uses)

Darlene F. Metter, M.D.
ACMUI Vice Chairman
April 4, 2019


Subcommittee Members

- Ronald Ennis, M.D.
- Darlene Metter, M.D. (*Chair*)
- A. Robert Schleipman, Ph.D.
- Michael Sheetz, M.S.
- Megan Shober, M.S.
- Laura Weil, M.S.

March 2018 Subcommittee Recommendation

- No current AU shortage.
- Reconsider an alternate AU pathway under 10 CFR 35.390
- Rationale: 2 recent events
  - 1/2018 FDA approved ^{177}Lu dotatate with a potential for greater use
  - Decrease in number of 1st time candidates sitting for the American Board of Nuclear Medicine exam

Potential AU Shortage

10 CFR 35.390 AU Pathways

- Pathway 1: Board Certification*
  - Nuclear Medicine (NM)
  - Radiation Oncology (RO)

- American Boards of Nuclear Medicine, Radiology & Osteopathic Radiology

10 CFR 35.390 AU Pathways

- Pathway 2: Alternate Pathway
- 700 hours of T&E includes 200 lab hours in basic radionuclide handling techniques in the medical uses of unsealed byproduct material requiring a WD
- Diag Radiology, redesigned* (rDR)
- Nuclear Radiology (NR)

*16 months NM in a 48 month Diagnostic Radiology program

2018-2019 for Pathways 1 & 2

- In-Training
  - NM: 79
  - NR: 11
  - rDR: 56
  - RO: 775

  Total: 921

- ~Graduates/year
  - NM: 50
  - NR: 11
  - rDR: 14
  - RO: 194

  Total: 269

AU Shortage?

- 2018-19 AU 35.390 pipeline: 921*
- 2019 Graduates: 269*
- 2018 ABNM: 3,591 practicing AU

- 2019: **No AU shortage**

* Graduate totals include Pathway 1 & 2

Limited-Scope AU

Radionuclide Therapy

- Radionuclide(RN) therapy: highest risk & highest impact of all NM procedures.
- To protect public health & safety, AUs must have a basic level of T&E.
- Limited-scope & full AUs **must** have equivalent level of procedural competency.

Limited- Scope AU

- Basic knowledge topics: § 35.390
- Due to complexity & overlap of these topics, any category would include nearly all of § 35.390
- Conclusion: Subcommittee **does not recommend** a limited-scope AU pathway

Final ACMUI Recommendations

Final Recommendations

- The Committee **strongly supports** the current AU pathways for § 35.390, which protects the public's health & safety.

- There is no objective data to support an AU shortage.

Final Recommendations

- The Committee **does not recommend** a limited-scope AU pathway for unsealed byproduct material for which a written directive is required.

Final Recommendations

- The Committee **unanimously agrees** that if the NRC pursues a limited-scope AU pathway, the AU candidate **must** attest to the acquisition of § 35.390 knowledge topics & skills by successfully completing a formal competency assessment with continued formal periodic competency reassessment to maintain his/her limited-scope AU status.

Subcommittee Report

- February 26, 2019
- ACMUI approved the report and its recommendations (11Y/1N) with one revision to add the language below:
  - Subcommittee will work with the NRC staff to develop an AU curriculum of knowledge topics.

Acronyms

- ABNM – American Board of Nuclear Medicine
- ABR – American Board of Radiology
- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- AU - Authorized User
- CFR – *Code of Federal Regulations*
- FDA – U. S. Food and Drug Administration
- ^{177}Lu – ^{177} Lutetium
- NM – Nuclear Medicine

Acronyms

- NR – Nuclear Radiology
- NRC – Nuclear Regulatory Commission
- R – Rad
- RN - Radionuclide
- RO – Radiation Oncology
- RP – Radiopharmaceutical
- rDR- redesigned Diagnostic Radiology pathway
- T&E – Training and Experience
- WD – Written Directive

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ACMUI's Review and Analysis of Reported Medical Events from FYs 2014-2017

Ronald D. Ennis, M.D.
ACMUI Radiation Oncologist

April 4, 2019

Subcommittee Members

- Ronald D. Ennis, M.D. (Chair)
- Richard Green
- Darlene Metter, M.D.
- Michael O'Hara, Ph.D.
- John Suh, M.D. *former member*
- Michael Sheetz

Subcommittee Objective

- To discern common themes within each section of 10 CFR Part 35 and across the sections, to inform a discussion of possible ways to decrease MEs.

- The subcommittee reviewed the last three reports of this subcommittee (FYs 2014-16) as well as the staff's spring report for FY 2017.

Probable ME Themes

- Two overarching themes emerged
  - Performance of a time out immediately prior to administration of radioactive byproduct material, as is done in surgery and other settings, could have prevented some MEs
  - Lack of recent or frequent performance of the specific administration appears to be a contributing factor in a number of cases

35.200 Use of Unsealed Byproduct Material for Imaging and Localization

Medical Events Summary

	2014	2015	2016	2017	Total
Cause					
Wrong drug*	0	3	3	0	6
Wrong dosage	5	0	3	3	11
Wrong patient	1	1	2	0	4
Total	6	4	8	3	21

* In most cases wrong drug was also wrong dosage

21 events over 4 years

35.200 Use of Unsealed Byproduct Material for Imaging and Localization

How Can These Events Be Prevented?

- Wrong drug: Time out - confirm the order, compare to the prescription
- Wrong dosage: If a dose calibrator is available – measure the activity
- Wrong patient: Time out - Verify patients by two means of identification
- 10/21 preventable if time out had been used

35.400 Manual Brachytherapy

Medical Event Summary

	2014	2015	2016	2017	Total
Applicator issue (e.g. movement during implant	1	1	1	0	3
Wrong site implanted (e.g. penile bulb)	3	1	1	1	6
Activity/prescription error (e.g. air kerma vs mCi)	1	2	0	1	4
Prostate Dose	0	4	18	5	27

35.400 Manual Brachytherapy

Medical Event Summary

	2014	2015	2016	2017	Total
Total ME	5	8	20	7	40
“Time out” may have prevented	1	2	0	1	4 (10%)
Lack of experience may have played a role	3	1	1	1	6 (15%)

35.400 Manual Brachytherapy

- Many MEs in this category are no longer categorized as MEs due to change from dose- to activity-based definition.
- Lack of experience possibly plays a role in the true MEs of this type, but hard to assess to what degree in each case.
- In approximately 25% of cases, a “time out” or enhanced retraining prior to performance of an uncommon procedure might have prevented the ME.

35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

Medical Event Summary

	2014	2015	2016	2017
Cause				
Wrong position	3	6	1	2
Wrong reference length	2	3	0	2
Wrong plan	1	3	1	0
Wrong dose/source strength	2	0	0	0
Machine malfunction	2	2	3	2
Software failure	0	0	0	2 (9 pts)
Total [37 events over 4 years]	10	14	5	8 (14 pts)

35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

Medical Event Summary

	2014	2015	2016	2017
Location				
Breast	1	1	0	0
Gynecological	5	9	2	7 (14 pts)
Skin	2	1	1	0
Bronchus	1	2	0	0
Prostate	0	0	2	0
Brain	1	1	0	1
Total	10	14	5	8 (14 pts)

GYN tumors most common site of ME

35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

MEs that may have been prevented by “timeout” (wrong plans or dose)

- 2014 3/10 events
- 2015 3/14 events
- 2016 1/5 events
- 2017 0/8 events

Total 6/37 (16.2%)

35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

MEs caused by "infrequent user"

This is difficult to determine based on information on NMED. If assumption is made about wrong position as surrogate for "infrequent" user

- 2014 3/10 events
- 2015 6/14 events
- 2016 1/5 events
- 2017 2/8 events
- Total 12/37 (32.4%)

35.1000 Radioactive Seed Localization

Medical Event Summary

	2014	2015	2016	2017
Total Medical Events	1	1	0	2
Cause:				
Delayed seed removal (patient intervention)	1	1		
Lost seed				1
Wrong implant site				1

35.1000 Leksell Gamma Knife® Perfexion ™ and Leksell Gamma Knife® Icon ™

Medical Event Summary

	2014	2015	2016	2017
Total Medical Events	1	8	3	0
Cause:				
Patient positioning system misalignment by vendor (same site)		8		
Patient setup error			2	
Patient movement			1	
Wrong site (treatment plan)	1			

35.1000 Y-90 Theraspheres

Medical Event Summary

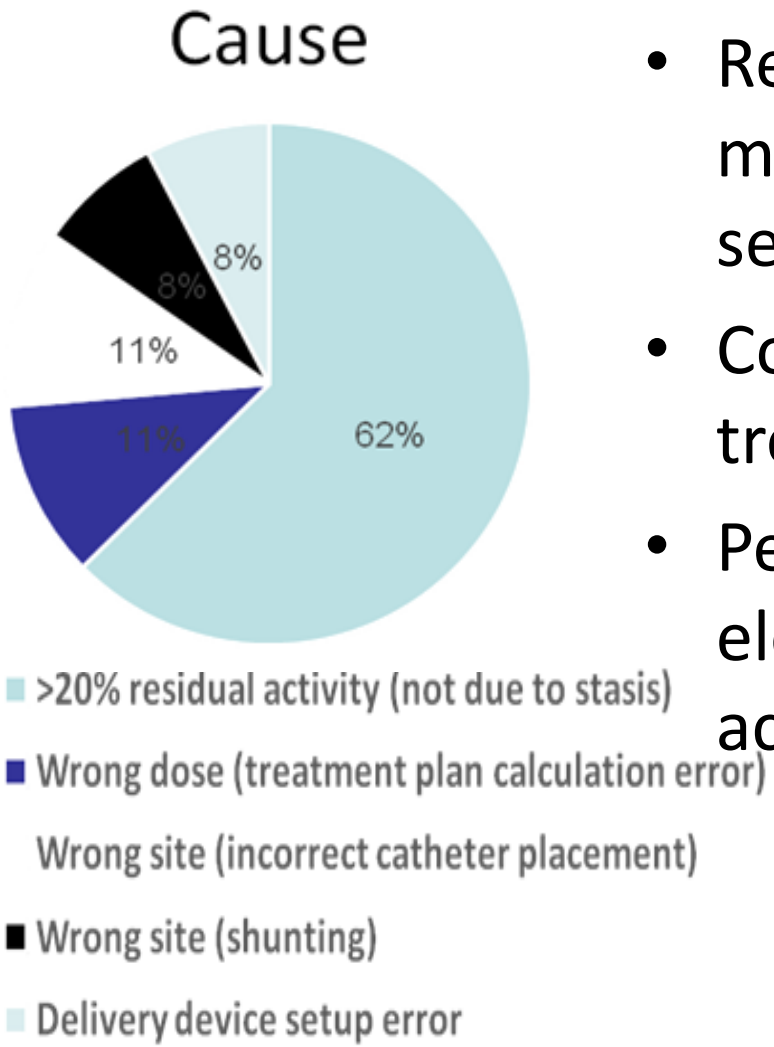
	2014	2015	2016	2017
Total Medical Events	9	8	13	15
Cause:				
> 20% residual activity remaining in delivery device	6	7	9	7
Delivery device setup error			1	2
Wrong dose (treatment plan calculation error)	1		1	4
Wrong site (catheter placement error)	1	1	2	2
Wrong site (shunting)	1			

35.1000 Y-90 SirSpheres

Medical Event Summary

	2014	2015	2016	2017
Total Medical Events	15	10	13	8
Cause:				
> 20% residual activity remaining in delivery device not due to stasis	10	2	9	7
Wrong site (shunting)	2	4		
Delivery device setup error	1	3		
Wrong dose (treatment plan calculation error)	1	1	2	
Wrong site (catheter placement error)	1		2	1

Actions to Prevent 35.1000 Y-90 Microsphere MEs



- Review mechanics of Y-90 microsphere delivery device and setup procedures
- Confirm all data and calculations in treatment plan
- Perform “Time Out” to assure all elements of treatment are in accordance with Written Directive

35.1000 MEs That May Have Been Prevented by "Time Out"

	RSL	Perfexion/Icon	Y-90 Microspheres
2014	1/2	1/1	3/24
2015	0/1	0/8	2/18
2016	0/1	2/3	3/26
2017	0	0	3/23
Total	1/4 (25%)	3/12 (25%)	11/91 (12%)

35.1000 MEs That May Have Been Attributed to Lack of Experience or Infrequent User

	RSL	Perfexion/Icon	Y-90 Microspheres
2014	0/2	0/1	1/24
2015	0/1	0/8	3/18
2016	0/1	2/3	1/26
2017	0	0	2/23
Total	0/4 (0%)	2/12 (17%)	7/91 (8%)

Possible Elements of a “Time Out”

- Identity of patient via two identifiers (e.g. name and DOB)
- Procedure to be performed
- Isotope
- Activity
- Dosage

- Others as applicable
  - units of activity (LDR prostate)
  - anatomic location
  - patient name on treatment plan
  - treatment plan independent second check has been performed
  - reference length (HDR)
  - Implant site location (RSL)

Possible Elements of Refresher for Infrequent Procedure

- Take review course from professional society
- Read review articles
- Speak to colleague with experience
- Do dry run of procedure with the team
- Review mechanics of device set up and procedure

Recommendation for Action

At the September 2018 ACMUI Meeting, the ACMUI recommended the NRC issue an Information Notice alerting AUs to the themes identified herein.

The NRC staff accepted this recommendation, pending resource availability

Acronyms

- 10 CFR – Title 10 of the *Code of Federal Regulations*
- ABS – American Brachytherapy Society
- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- AUs – authorized users
- DOB – date of birth
- FDA: Food and Drug Administration
- FY – Fiscal Year
- Gy – Gray

Acronyms

- gyn – gynecological
- HDR – high dose-rate
- LDR – low dose rate
- mCi – milliCurie
- ME – Medical Event
- RSL – radioactive seed localization
- T&E – training and experience
- Y – Yttrium

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Patients' Rights Advocates' Perspectives

Laura M. Weil
ACMUI Patients' Rights Advocate
April 4, 2019


Topics

- Nursing Mother Guidelines
- The Training and Experience Requirements for All Modalities

  [Title 10 *Code of Federal Regulation* 35.300 Uses]
- Medical Event Reporting