Overview: 2021 ACMUI Activities

Darlene Metter, M.D.
ACMUI Chair/Diagnostic Radiologist
October 5, 2021
Today’s Agenda

• Darlene Metter, MD (ACMUI Chair)
  – Overview of ACMUI Activities

• Ronald Ennis, MD (ACMUI Radiation Oncologist)
  – Review and Analysis of Reported Medical Events from Fiscal Year 2020
  – Abnormal Occurrence Criteria
Today’s Agenda cont’d

• Hossein Jadvar, MD PhD (ACMUI Nuclear Medicine Physician)
  – Emerging Radiopharmaceutical Knowledge Requirements in Theranostics

• Josh Mailman (ACMUI Patient Advocate)
  – Perspectives on the Role of the Patient Advocate
Overview of the ACMUI

• ACMUI Role
• Membership
• 2020-2021 Topics
• Current Subcommittees
• Future
Role of the ACMUI

• Advise the U.S. Nuclear Regulatory Commission (NRC) staff on policy & technical issues that arise in the regulation of the medical use of radioactive material in diagnosis & therapy.

• Comment on changes to NRC regulations & guidance.

• Evaluate certain non-routine uses of radioactive material.
Role of the ACMUI (cont’d)

- Provide technical assistance in licensing, inspection & enforcement cases.
- Bring key issues to the attention of the Commission for appropriate action.
ACMUI Membership (13 members)

- Nuclear Medicine Physician (Dr. Hossein Jadvar)
- 2 Radiation Oncologists (Drs. Ronald Ennis & Harvey Wolkov)
- Nuclear Cardiologist (Dr. Vasken Dilsizian)
- Diagnostic Radiologist (Dr. Darlene Metter)
- Nuclear Pharmacist (Mr. Richard Green)
- FDA Representative (Dr. Michael O’Hara)
ACMUI Membership (13 members)

- 2 Medical Physicists (Ms. Melissa Martin & Mr. Zoubir Ouhib)
- Patients’ Rights Advocate (Mr. Josh Mailman)
- Agreement State Representative (Ms. Megan Shober)
- Healthcare Administrator (Ms. Rebecca Allen)
- Radiation Safety Officer (vacant position)
ACMUI Topics Addressed in 2021

- Extravasations in Nuclear Medicine (J van der Pol, MD Maastricht University Medical Centre, Netherlands)
- Calibration Procedures for Brachtherapy Sources (L DeWerd, PhD University of Wisconsin)
- Revised Abnormal Occurrence Criteria
- Extravasations and Medical Event Reporting
ACMUI Topics Addressed in 2021

• Emerging Radiopharmaceutical Knowledge Requirements in Theranostics
• Radionuclide Generator Knowledge and Practice Requirements
• Production Challenges for Therapeutic Radiopharmaceuticals
• Future of Personalized Dosimetry
Staff Presentations to the ACMUI (2021)

- Patient Release Evaluation of Emerging Brachytherapy Sources
- ACMUI Reporting Structure
- Medical Related Events
- INFOSEC, Ethics and Allegations Training
Current ACMUI Subcommittees

- T&E for All Modalities
- Medical Events (ME)
- Infiltrations/Extravasations and ME Reporting
- Abnormal Occurrence
Current ACMUI Subcommittees

- Emerging Radiopharmaceutical Knowledge Requirements in Theranostics
- Radionuclide Generator Knowledge and Practice Requirements
- Diffusing Alpha-emitters Radiation Therapy (DART) Manual Brachytherapy Sources Licensing Guidance
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
Acronyms

• ACMUI - Advisory Committee on Medical Uses of Isotopes
• CFR - Code of Federal Regulations
• FDA - U.S. Food & Drug Administration
• INFOSEC - Information Security
• ME - Medical Event
• NMED - Nuclear Material Events Database
Acronyms (cont’d)

• NRC - U.S. Nuclear Regulatory Commission
• T&E - training and experience
Agenda

• Subcommittee Members
• Key Messages
• Medical Event Review and Analysis
Subcommittee Members

- Ronald D. Ennis, M.D. (Chair)
- Richard Green
- Darlene Metter, M.D.
- Zoubir Ouhib, M.S.
- Michael O’Hara, Ph.D.
- Michael Sheetz (former)
- Harvey Wolkov, M.D.
Key Messages

• Two overarching themes remain
  – Performance of a time out/use of a checklist immediately prior to administration of radioactive byproduct material, as is done in surgery and other settings, could have prevented some MEs
Key Messages

• Two overarching themes remain (cont’d)
  – Lack of recent or frequent performance of the specific administration or inattention during performance of the procedure/treatment appear to be contributing factor(s) in a number of cases

• NRC issued an Information Notice alerting the users to these issues in 2019.
  https://www.nrc.gov/docs/ML1924/ML19240A450.pdf
Key Messages

• Specific issues
  – Increase complexity of unsealed source administrations of newer agents may lead to more equipment related MEs in future
Key Messages

• Specific issues (cont’d)
  – MEs involving Y90 administration continue to be the most common MEs. The ACMUI proposed the creation of a subcommittee to evaluate this issue in more depth and, in conjunction with the vendors, propose solutions to decrease the frequency of Y90 MEs
Medical Events Summary: §35.200 Use of Unsealed Byproduct Material for Imaging and Localization

<table>
<thead>
<tr>
<th>Cause</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong drug</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wrong dosage</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Wrong patient</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Extravasation</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Human error</td>
<td>0</td>
<td>0</td>
<td>1 (8 patients)</td>
<td>0</td>
<td>1 (8 patients)</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

3/5 possibly preventable by time out
### Medical Events Summary:

**§35.300  Use of Unsealed Byproduct Material, Written Directive Required**

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>WD not done or incorrectly</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Error in delivery (#capsules)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Equipment</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Human Error</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Wrong patient</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4</td>
<td>2</td>
<td>9</td>
<td>2</td>
<td>17</td>
</tr>
</tbody>
</table>
# Medical Events Summary: §35.400 Manual Brachytherapy

<table>
<thead>
<tr>
<th>Problem Description</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applicator issue (e.g. jam, eye plaque dislodged)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Wrong site implanted (e.g. penile bulb, bladder)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Activity/prescription error (e.g. air kerma vs mCi, enter wrong activity in planning software)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Prostate Dose</td>
<td>5</td>
<td>11</td>
<td>3</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>New device</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Wrong source</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Patient health (?patient intervention)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
### Medical Events Summary: §35.400 Manual Brachytherapy

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ME</td>
<td>7</td>
<td>13</td>
<td>5</td>
<td>6</td>
<td>31</td>
</tr>
<tr>
<td>“Time out” may have prevented</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Lack of experience/inattention may have played a role</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

In approximately 15% of cases, a “time out/checklist”, enhanced retraining prior to performance of an uncommon procedure or increase attention during the procedure might have prevented the ME.
Medical Events Summary: § 35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

<table>
<thead>
<tr>
<th>Medical Event Summary</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong position</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Wrong reference length</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Wrong plan</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Wrong dose/source strength</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Machin/applicator malfunction</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Software/hardware failure</td>
<td>2 (9 pts)</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Treatment planning</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>8 (14 pts)</td>
<td>10</td>
<td>10</td>
<td>13</td>
<td>41</td>
</tr>
</tbody>
</table>
Medical Events Summary: § 35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

<table>
<thead>
<tr>
<th>Location</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Gynecological</td>
<td>7 (14 pts)</td>
<td>7</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Skin/neck</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Bronchus</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Prostate</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Brain</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>8 (14 pts)</td>
<td>10</td>
<td>10</td>
<td>13</td>
</tr>
</tbody>
</table>

GYN tumors most common site of ME
Medical Events Summary: § 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 plan or dose)

• 2017 0/8 events
• 2018 3/10 events
• 2019 3/10 events
• 2020 10/13 events

Total 16/41 (39%)
Medical Events Summary: § 35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

MEs caused by “infrequent user/inattention”

This is difficult to determine based on information in NMED. For this assessment, assumed wrong position is a surrogate for “infrequent” user/inattention

2017 2/8 events
• 2018 1/10 events
• 2019 1/10 events
• 2020 9/13 events

Total 13/41 (32%)
# Medical Events Summary: §35.1000 Radioactive Seed Localization

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Medical Events</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cause:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed seed removal (patient intervention)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lost seed</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wrong implant site</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Seed migration</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
### Medical Events Summary: §35.1000 Intravenous Cardiac Brachytherapy

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not follow proper procedure</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Tortuous vessel anatomy</td>
<td>0</td>
<td>1</td>
<td>1*</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Catheter issue</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

*AU felt this is “patient intervention”

No time out issues

Difficult to assess the unfamiliarity issue, but possibly played a role in some
Medical Events Summary:
§ 35.1000  Gamma Knife® Perfexion™ and Icon™

<table>
<thead>
<tr>
<th>Cause:</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Medical Events</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Cause:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back-up battery power source failure</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient setup error</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Patient movement</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Wrong site (treatment plan)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pt motion management system failure</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
# Medical Events Summary: § 35.1000 Y-90 Theraspheres

<table>
<thead>
<tr>
<th>Cause:</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 20% residual activity remaining in delivery device</td>
<td>7</td>
<td>11</td>
<td>9</td>
<td>12</td>
<td>39</td>
</tr>
<tr>
<td>Delivery device setup error</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Wrong dose (treatment plan calculation error)</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Wrong site (catheter placement error)</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Wrong dose vial selected</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

For 2020: Time out 3/15 (20%), Infrequent/inattention 12/15 (80%)
# Medical Events Summary: § 35.1000 Y-90 SirSpheres

<table>
<thead>
<tr>
<th>Cause</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Medical Events</td>
<td>8</td>
<td>7</td>
<td>11</td>
<td>8</td>
<td>34</td>
</tr>
<tr>
<td>Cause</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 20% residual activity remaining in delivery device not due to stasis</td>
<td>7</td>
<td>2</td>
<td>8</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>Wrong dose (treatment plan calculation error)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Wrong site (catheter placement error)</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Wrong site (WD error)</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

2020: Time out: 0
Infrequent/inattention: 8/8 (100%)
Actions to Prevent §35.1000 Y-90 Microsphere Medical Events

- 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
Acronyms

• 10 CFR – Title 10 of the *Code of Federal Regulations*
• AUs – authorized users
• FY – Fiscal Year
• gyn – gynecological
• HDR – high dose-rate
• LDR – low dose rate
• mCi – milliCurie
• ME – Medical Event
• RSL – radioactive seed localization
• Y – Yttrium
Abnormal Occurrence
Subcommittee Report

Ronald Ennis, MD
ACMUI Radiation Oncologist

October 5, 2021
Agenda

• ACMUI Subcommittee Membership
• ACMUI Subcommittee Charge
• Current Medical AO Criteria
• NRC Proposed Changes to Medical Event AO Criteria
• Analysis of Number of Medical AOs Reported by Criteria
• ACMUI Recommendations
• Dissenting Opinion
Subcommittee Members

- Ronald Ennis, MD
- Hossein Jadvar, MD, PhD
- Zoubir Ouhib
- Michael Sheetz (Former)
- Megan Shober
- NRC Staff Resource: Donna-Beth Howe, PhD
Subcommittee Charge

- Define patient harm in medical AO
- Reassess the current medical AO criteria
- Define goals of AO criteria and reporting
- Evaluate whether the current medical AO criteria are appropriate regarding public health and safety
- Comment on NRC staff proposed AO changes
Current Medical AO Criteria (2017)

• Medical Event must meet both a dose threshold and incident criteria

• Dose Threshold
  – Equal or greater than
    • 1 Gy to bone marrow or lens of the eye
    • 2.5 Gy to the gonads, or
  – Exceeds, by 10 Gy, the expected dose to any other tissue
Current Medical AO Criteria (2017)

• Incident Criteria
  – Dose that is at least 50% greater than prescribed
  – Wrong radiopharmaceutical, route of administration, or treatment mode
  – Leaking source
  – Wrong patient or research subject
Evaluation of Current Medical AO Criteria

• Overly conservative and capture events that are not significant from the standpoint of public health or safety
• AOs should have a high reporting threshold that require patient harm
• Goal of AO reporting is to elevate significant events to the level of Congressional and Public attention
NRC Proposed Changes to Medical Event AO Criteria

• Retains current dose threshold criteria
• Addition of a medical-consequence criterion to the dose-based criteria
  – Unintended radiation induced injury causing permanent impairment of bodily function or permanent damage to a body structure
  – Or surgical intervention is needed to preclude permanent impairment
Analysis of Number of Medical AOs Reported by Criteria

• Average of 12 medical AOs reported to Congress each year (2010-2020)
• No significant difference in number reported based on pre or post 2017 criteria
• Proposed AO criteria would reduce number to 3 or 4 medical AOs reported to Congress each year
Analysis of Number of Medical AOs Reported by Criteria (cont’d)

• New medical AO criteria will better identify those events that are significant from a public health or safety perspective, and eliminate reporting of events with little or no adverse health
ACMUI Recommendations

- Fully supports the NRC proposed changes to the Medical AO criteria
- Recommends that communication be prepared for distribution to all NRC and Agreement State medical licensees to inform of best practices in preparing a medical event report so that complete and accurate information is provided in describing the event, root cause analysis on why the event occurred, and the medical effect on the individual
AO Subcommittee Member
Dissenting Opinion (M. Sheetz)

• Disagrees on embryo/fetal events reported under 10 CFR 35.3047 being included in AO criteria I.A.2. with a dose threshold of 50 mSv

• Supports previous ACMUI AO subcommittees’ position that medical-related events reported under 35.3047 be screened under same AO criteria for medical use of radioactive material
AO Subcommittee Member
Dissenting Opinion (M. Sheetz)

- Supports events reported under 35.3047 be included under AO criteria III.C. which will result in unintended radiation induced injury causing permanent impairment or damage
Acronyms

• ACMUI – Advisory Committee on the Medical Uses of Isotopes
• AO – Abnormal Occurrence
• Gy – Gray
• mSv – millisievert
• NRC – Nuclear Regulatory Commission
Emerging Radiopharmaceutical Therapy Knowledge Requirements in Theranostics

Hossein Jadvar, MD, PhD, MPH, MBA
Advisory Committee on the Medical Uses of Isotopes
October 5, 2021
Agenda

• ACMUI Subcommittee Membership
• ACMUI Subcommittee Charge
• Theranostics (Background)
• Theranostics (Emerging Agents)
• Theranostics (Challenges)
• Knowledge Requirements
• Theranostics Room Setup
Emerging RPT Knowledge Requirements in Theranostics - ACMUI Subcommittee Membership

• Hossein Jadvar, MD, PhD (Nuclear Medicine Physician; Chair)
• Vasken Dilsizian, MD (Nuclear Cardiologist)
• Ronald Ennis, MD ( Radiation Oncologist)
• Michael O’Hara, PhD (FDA Representative)
• Zoubir Ouhib (Therapy Medical Physicist)
• Josh Mailman (Patients Rights Advocate)
• Maryann Ayoade (NRC Staff Resource)
ACMUI Subcommittee Charge

• To outline the knowledge and specific or specialized practice or policy requirements needed for the safe use and handling of emerging radiopharmaceuticals in theranostics.

• Provide considerations and recommendations to staff.
• **Definition:** Systemic integration of diagnostic tools (e.g., nuclear imaging) and therapeutic agents (e.g., radiopharmaceuticals) related to the same (or similar*) biomolecular target (or parameter*) →
  • Precision / Personalized Medicine

• **History:** 1941 with treatment of a hyperthyroid patient with radiiodine by Saul Hertz, MD, at Massachusetts General Hospital
Background (contd.)

• Current oncologic theranostic agents
  • $^{123}\text{I}/^{131}\text{I}$ (NaI symporter; thyroid)
  • $^{111}\text{In}/^{90}\text{Y}$-ibritumomab (anti-CD20; lymphoma)
  • $^{18}\text{F}$-NaF/$^{99m}\text{Tc}$-MDP; $^{223}\text{RaCl}_2$ (osteoblastic mets; mCRPC)*
  • $^{99m}\text{Tc}$-MAA; $^{90}\text{Y}$-microspheres (hyperperfusion; liver tumors)*
  • $^{123}\text{I}/^{131}\text{I}$-MIBG (norepinephrine transporter; pheochromocytoma, paraganglioma)
  • $^{68}\text{Ga}/^{64}\text{Cu}$-DOTATATE, $^{68}\text{Ga}$-DOTATOC; $^{177}\text{Lu}$-DOTATATE (SSTR+ neuroendocrine tumors)
Theranostics (Emerging Agents)

- **Within near future**
  - $^{68}$Ga*/$^{18}$F-PSMA*; $^{177}$Lu-PSMA** (mCRPC)
    (*FDA approved; ** FDA approval anticipated)

- **In the horizon**
  - $^{225}$Ac/$^{227}$Th-PSMA (alpha RLT; mCRPC)
  - $^{68}$Ga-pentixafor/$^{177}$Lu-, $^{90}$Y-pentixather (chemokine receptor 4; multiple myeloma)
  - $^{68}$Ga/$^{177}$Lu-NeoB (GRPR; solid tumors)
  - $^{68}$Ga/$^{177}$Lu-FAPI (fibroblast activation protein; multiple cancers)
Theranostics (Emerging Agents) (contd.)

• In the horizon (contd.)
  • $^{89}$Zr/$^{177}$Lu-girentuximab (carbonic anhydrase IX; clear cell RCC)
  • $^{68}$Ga/$^{177}$Lu-FF58 (integrin $\alpha_3\beta_5$; GBM)
  • $^{18}$F/$^{131}$I-PARPi (DNA repair enzyme Poly-(ADP ribose) polymerase 1; multiple cancers)
Theranostics (Challenges)

• Technical
  • Interdisciplinary teams
  • Standardized protocols
  • Radionuclide pipeline / supply chain

• Economic
  • Comparative cost; cost-utility
  • Reimbursement
  • R&D funding
Theranostics (Challenges) (contd.)

• Biomedical
  • Basic science, pre-clinical, first-in-human, and large prospective clinical trials
  • Single, tandem, combination therapies
  • New applications
Emerging RPT Knowledge Requirements in Theranostics

• Make up of the healthcare team at the time of administration
  
  • Depending upon the therapy, the team administering the dose may consist of – AU with appropriate training in theranostics, CNMT, RSO, Registered Nurse, and Medical Physicist (if available/applicable)

• AU must be present at the time of dose administration
Emerging RPT Knowledge Requirements in Theranostics (contd.)

• Therapy should be done in a dedicated and regulatory-approved room appropriate for radioisotope administrations.

• Non-radiation workers (e.g., oncology nurse) participating in the procedure may need to wear a radiation badge as determined by the RSO.
Emerging RPT Knowledge Requirements in Theranostics (contd.)

- Extravasation; patient release criteria (addressed by other ACMUI subcommittees)
- Radioactive waste management (refer to the facility established guidelines and regulations)
- The AU is responsible for patient concerns related to RPT, including radiation induced injuries
- Ensure that emerging theranostics are within the regulatory guidelines
Emerging RPT Knowledge Requirements in Theranostics (contd.)

• AU is encouraged to avail themselves of all the newest training information for each new theranostics as they emerge

• Patient specific dosimetry may play an important role; as relevant data becomes mature, AUs should stay abreast of developments

• Outreach to promote accurate information about safety and efficacy of theranostics
Acronyms

- ACMUI: Advisory Committee on the Medical Uses of Isotopes
- AU: Authorized User
- CNMT: Certified Nuclear Medicine Technologist
- FDA: Food and Drug Administration
- R&D: Research and Development
- RPT: Radiopharmaceutical Therapy
- RSO: Radiation Safety Officer
Patient Advocacy
Bringing about Change for Patients

Josh Mailman
ACMUI Patients’ Rights Advocate
October 5, 2021
Agenda

• Perspectives on the role of the patient advocate
We are patients first…

In 2009 - I asked my oncologist how can I help?
How did I get involved in Nuclear Medicine Advocacy
What Exactly is Patient Advocacy?

Patient advocacy is an area of specialization in health care concerned with advocacy for patients, survivors, and caregivers.
The patient advocate may be an individual or an organization, often, though not always, concerned with one specific group of disorders.

The terms patient advocate and patient advocacy can refer both to individual advocates providing services that organizations also provide, and to organizations whose functions extend to individual patients.

Some patient advocates work for the institutions that are directly responsible for the patient's care, others for non profits associated with their disease while others can be independent.
Typical Advocacy Activities

- Patient rights
- Matters of privacy
- Informed consent, patient representation
- Awareness building
- Support and education of patients, survivors and their caregivers
Patient Advocates give a voice to Patients, Survivors and their Carers

Healthcare-related (public) topics, informing the public, the political and regulatory world, health-care providers (hospitals, insurers, pharmaceutical companies etc.), organizations of health-care professionals, the educational world, and the medical and pharmaceutical research communities.
The Worlds of Patient Advocacy
Resources that help expand or focus on the research and policy aspect of advocacy.

- National Cancer Institute has been working with advocates for over 30 years
  - Patient Advocacy Steering Committee
  - Task Force and Steering Committees
  - The Language of trials (online dictionary)
  - Onboarding
  - Role and responsibility
- Many of the Cooperative Group and Large Advocacy organization now conduct trainings
In Clinical Trial Design

“I better appreciate how patient advocates should be involved very early on in protocol development, and it should be a continuous, fluid discussion. Not a one-time check-in after the protocol is already completed.”

“I think I have often previously focused on scientific data that I’ve read or had access to, rather than fully thinking about things from the vantage point of our patients. While I’ve been inspired and motivated to develop this trial for our patients (and I feel so privileged to take care of patients), I hadn’t previously really taken the time to put myself in our patients’ shoes and think about how this trial/therapy would sound and feel from their perspective.”
Where do I spend my time?

*How do I keep up to date?*
Support/ Awareness/ Fundraising

• President, NorCal CarciNET Community
• Society of Nuclear Medicine and Molecular Imaging - Inaugural Chair Patient Advocacy, Member of Ga68 Working Group
• Board Member, Neuroendocrine Tumor Research Foundation
• Board Member, Education and Research Foundation for Nuclear Medicine and Molecular Imaging
• World Association of Radiopharmaceutical and Molecular Therapy
Research

- National Cancer Institutes - Steering Committee on Patient Advocacy / Steering Committee on GI Cancer
- ASCO Scientific Research Committee
- Faculty ASCO/AACR, Methods in Clinical Research Workshop
- Research Committee Member NETRF, Healing NET and Education Research Foundation for Nuclear Medicine and Molecular Imaging
- Patient Representative - NET SPORE
- Patient PI - PCORI CER-NET Study
- Guideline Committee – Somatostatin Positive PET Imaging for NETs / PRRT for NETS
Regulatory

- FDA Patient Representative
- Nuclear Regulatory Commission's Advisory Committee on the Medical Uses of Isotopes
Mostly I Listen to Fellow Patients Journeys and Challenges
Thank You

Josh@norcalcarcinet.org
Acronyms

- SC – Steering Committee
- NETS – Neuroendocrine Tumors
- Ga-68 – gallium-68
- GI – Gastrointestinal
- ASCO – American Society of Clinical Oncology
- AACR – American Association for Cancer Research
- PI – Primary Investigator
- CER-NET – Comparative Effectiveness Research for Neuroendocrine Tumors
- PCORI – Patient-Centered Outcomes Research Institute
- PRRT – Peptide Receptor Radionuclide Therapy