Developing an Institutional
$^{131}$I MIBG Therapy Program

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Boston Children’s Hospital

- Pediatric Tertiary Care Center
- 400 Beds
- 25,000 admissions/yr
- 230 clinical programs
- US News & World Report
  - Top 3 in all pediatric specialties
  - #1 in cardiology, neurology, oncology, urology and nephrology
Planning of a $^{131}$I MIBG Therapy Program

- Initial planning
- Treatment room site selection
- Treatment room design/shielding
- Operational planning
- Training and education
- Radiation exposure (workers & caregivers)
- Radioactivity containment and disposal
- Patient discharge
Initial Planning of a $^{131}$I MIBG Therapy Program

• Needs Assessment
  – Clinical demand
    • State of disease
    • Potential patients
    • Geographical proximity to other programs

• Institutional Resources
  – Available expertise
  – Available related programs
  – Financial
Initial Planning of a $^{131}$I MIBG Therapy Program

• Goals
  – Effective and safe treatment of the patient
  – Radiation Protection for all
    • Healthcare Professionals
    • Non-Professionals

• Careful planning by all is necessary for an effective and safe program
Neuroblastoma

- Most common extracranial solid tumor
  - 600 new cases per year in US
- Tumor of early childhood
  - Most common tumor of infancy
  - 2/3 of cases occur in children < 5 years
- Tumor of the sympathetic nervous system
  - Adrenal gland is most common location
- Symptoms vary depending on location
Prognostic Features Determine Risk Group

- **Low-Risk (30%)**
  - Local disease
  - Observation or surgery only

- **Intermediate-Risk (15%)**
  - Regional disease or metastatic in very young patient
  - Outpatient chemotherapy

- **High-Risk (55%)**
  - Metastatic disease
  - Locally invasive or unfavorable prognostic factor
    - Intense, multimodal therapy
High-risk neuroblastoma remains a major challenge for pediatric oncologists

- Less than half of children are cured
- 15% of childhood cancer deaths
- Treatment and cure result in significant long-term side effects
- Relapse even more difficult to treat
MIBG - $^{131}$I-Metaiodobenzylguanidine

- Developed as an anti-hypertensive
- Concentrated in nervous tissue, including the majority of neuroblastomas
- Can be labeled with radioactive iodine and used for imaging ($^{123}$I-MIBG) and treatment ($^{131}$I-MIBG)
- Taken up by surface receptors on NB cells and directly delivers radiation to the cells
- Orphan drug status in US
**131I MIBG Therapy Business Plan Summary**

- **Proposal:** Establish a new program for treatment of NB using MIBG.
  - Add lead shielding to one room to permit treatment
  - Add 2.0 FTEs in nursing, radiation safety, and nuclear medicine to coordinate program and manage radiopharmaceuticals

- **Clinical Benefits:** Very effective agent for relapsed neuroblastoma.

- **Strategic Benefits:** BCH would be one of a small number of institutions offering this treatment, and could become a leader in its development.

- **Capital Request:** $309,000 renovation & startup equipment

- **Volumes:** Projected 15-20 cases per year.

- **Financial Impact:** $192k net loss per year over 5 years

- **Outside Funding:** St. Baldrick’s infrastructure grant, Team Brent
Planning of a $^{131}$I MIBG Therapy Program

- Multi-disciplinary project
  - Oncology
  - Nuclear Medicine
  - Nursing
  - Radiation Protection
Radiation Protection of $^{131}$I MIBG Therapy

- Healthcare Professionals
  - NM Technologists
  - Nurses
  - Physicians

- Non-professionals
  - Caregivers
  - Family members
  - Other patients
Treatment Room Site Selection

• Clinical Criteria
  – Oncological Nursing and Clinical Support
  – Clinical apparatus
  – Child Life/Engagement Apparatus

• Radiation Safety Criteria
  – Dedicated bathroom and sink
  – Limited Patients/Others in Neighboring Areas
  – Corner or Isolated Room
  – Nearby Area for Caregivers
BCH Example

- Oncology Unit
- One outside wall
- Stair case
- Mechanical space below
- Common area above
- Private bath
- Anteroom for caregivers
Treatment Room Design and Shielding

- Private room, own bath, caregiver area
- Shielding considerations
  - Amount of radioactivity used (e.g. up to 1 Ci)
  - Estimated workload (e.g. 1 patient per week)
  - Length of stay (4 days, 50% clearance by Day 2)
  - Control levels (CL; <1 mSv in 1 yr*; <20μSv in 1 wk)
  - Occupancy in adjacent areas
  - Construction materials (concrete in walls)
Shielding Design

• Occupancy
  – 1.0 in working areas
  – 1/16 in hallways/stairwells
  – 1/4 in patient room

• Patient considered an unattenuated pt source

• Exposure Rate
  – \( DR = \Gamma \times A/d^2 \)
  – \( \Gamma = 7.64 \times 10^{-5} \text{ mSv MBq per m}^2 \text{ h} \)

• \( Pb = \text{HVL}/\ln(2) \times \ln(CL/20) \)

• 10 cm of concrete \( \approx 0.6 \text{ cm of Pb} \)
**BCH Example Recommended Shielding**

<table>
<thead>
<tr>
<th>Dose Point</th>
<th>Design Lead Thickness (inches)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wall A</td>
<td>1.0 (1”)</td>
</tr>
<tr>
<td>Wall B*</td>
<td>0.25 (1/4”)</td>
</tr>
<tr>
<td>Wall C</td>
<td>0.5 (1/2”)</td>
</tr>
<tr>
<td>Ceiling Above*</td>
<td>0.625 (5/8”)</td>
</tr>
<tr>
<td>Floor Below*</td>
<td>0.125 (1/8”)</td>
</tr>
</tbody>
</table>
Wall A – 1” of Lead
Operational Plan

• Commercial provider of $^{131}$I MIBG
  – When and how often available?
  – Delivery logistics

• $^{131}$I MIBG Therapy considered experimental
  – IRB and Rad Safety Committee approval

• Radiation Safety Officer involvement
  – Liaison to state and federal regulatory authorities
  – License amendment of high activity of $^{131}$I
  – Construction authorization
  – Caregiver exposure approval
Treatment Workflow

- Patient selected for therapy
- Dose decided between Oncology and NM
- Patient Arrives (family education)
- Dose arrives, prepared and administered by NM
- Patient care from familial caregivers and nurses
- Patient discharges after 4-5 days
- Imaging on last day by NM
Patient Room Preparation

- Large mobile lead shields surround the bed.
- A lead box at the foot of the bed shields the urine collection bag.
- Most surfaces of the room (floors, bedrails, etc) will be covered with plastic.
- Equipment will also be covered with plastic.
- Several large containers are used for waste.
**131I MIBG Administration**

- Frozen $^{131}$I MIBG thawed; placed in 30 cc syringe
- Shielded infusion pump
- Brought to treatment room
- Patency of IV confirmed
- Administered over 90-120 min (in our case by NM)
- Once complete, infusion apparatus disconnected and returned to NM
Managing Patient Radiation Exposure

• Protect thyroid gland
  - Determine % free iodine of product
  - Potassium iodide (SSKI): 1 mg/kg q 4hrs x 7days; then 1 mg/kg QD x 5 weeks

• Protect bladder - Foley catheter

• Brisk hydration to facilitate excretion

• Protect soft tissues from extravasation
  - Slow infusion into CVL or long angiocatheter
Clinical Policies and Procedures

- Foley placement and care (who, where, how)
- Nursing responsibilities – vitals q shift, limit meds and complexity of care, facilitate monitoring from outside room
- Blood Draws – limit as much as possible
- Fever plan
- Anxiolysis – IV Versed
- Emergencies - make plan with code team and ICU
Training and Education

• Development and refining of NM, medical and nursing guidelines

• Radiation safety training of staff
  – Oncology had little training in RA therapy
  – All had no experience with these levels of RA
  – Visits to other sites

• Initial classes, annual online updates and face-to-face when necessary

• Caregiver education
Managing Radiation Exposure to Staff

- Protective clothing
- Personnel monitoring
  - Real-time monitoring
  - TLD badges
- G-M Meter
Managing Radiation Exposure to Familial Caregivers

• Approval from Commonwealth of Massachusetts for caregivers to receive 20 mSv
• Request there be 2 caregivers
• Specific radiation safety training
  – Use of protective clothing
  – Handling and disposal of body fluids (manage spills)
  – Time/Distance/Shielding
  – Use of dosimeter and G-M meter
• Sign contract outlining requirements/responsibilities
Caregiver Exposure vs Administered Activity

Ranges

Admin Act
7.4-23.3 mSv

Caregiver Dose
0.7-3.8 mSv

Administered Activity
Caregiver and Nurse Dose vs Age

<table>
<thead>
<tr>
<th></th>
<th>All ages (n = 14)</th>
<th>&lt; 7 y (n = 6)</th>
<th>&gt; 7 y (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administered activity (GBq)</td>
<td>13.65</td>
<td>8.76</td>
<td>17.32</td>
</tr>
<tr>
<td>Caregiver exposure (mSv)</td>
<td>1.79</td>
<td>1.94</td>
<td>1.69</td>
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<tr>
<td>Nursing exposure (mSv)</td>
<td>0.44</td>
<td>0.50</td>
<td>0.40</td>
</tr>
<tr>
<td>Name</td>
<td>Tues</td>
<td>Wed</td>
<td>Thu</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td></td>
<td>2/17/2009 (1330 hrs)</td>
<td>18-Feb</td>
<td>19-Feb</td>
</tr>
<tr>
<td>Mom</td>
<td></td>
<td></td>
<td>213 (@ 11 a.m.)</td>
</tr>
<tr>
<td>Uncle</td>
<td></td>
<td>8.0 mrem</td>
<td></td>
</tr>
<tr>
<td>Steve (NM)</td>
<td>11 mrem</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kelly (Nursing)</td>
<td>15 mrem (1310-1900 hrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Megan (Nursing)</td>
<td>8 mrem (1900-0700 hrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Michelle (Nursing)</td>
<td>6 mrem (0700-1900 hrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Megan G. (Nursing)</td>
<td>1 mrem 1900-0700 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denise (Nursing)</td>
<td></td>
<td></td>
<td>5 mrem (1900-0700 hrs)</td>
</tr>
<tr>
<td>Byrnn (Nursing)</td>
<td></td>
<td></td>
<td>9 mrem (0700-1600 hrs)</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td>Daily Totals</td>
<td>34 mrem</td>
<td>14 mrem</td>
<td>1 mrem</td>
</tr>
</tbody>
</table>

CareGiver Total = 263 mrem
Nursing Total = 44 mrem
Nuc Med Total = 11 mrem
Staff Total = 55 mrem
Average Exposure Distribution to Nurses & Caregivers

- Infusion at ~2 pm on day 1
- Discharge in afternoon of day 4
MIBG I-131 Patient Exposure Rate at ~1 Meter
Patient Dose, 520 mCi

\[ y = 36.212e^{-0.9609x} \]
\[ R^2 = 0.9402 \]
Patient Release and Waste Management

- Dictated by medical needs
- Follows license requirements - NRC Regulatory Guide 8.39
  - Exposures less than 500 mrem to others
    - Based on calculated or measured values
  - Parent (caregiver) provided instructions
- Contaminated items held in storage for decay (30-40 ft³ per therapy)
Post-Therapy Imaging

5-year-old boy with neuroblastoma

Diagnostic Scan  5-days post Therapy

$^{123}\text{I}$ 2.6 mCi  $^{131}\text{I}$ 337.8 mCi
BCH Experience with $^{131}$I MIBG Therapy

- Two-years from initial planning to 1st patient
- First patient treated February 2009
- 32 patients treated, 8 treated twice as of 5/10/13
- Response noted in 26 patients (5 pending)
  - Complete Response: 5 (19%)
  - Partial Response: 6 (23%)
  - Stable Disease: 8 (31%)
  - Progressive Disease: 7 (27%)
BCH Experience with $^{131}$I MIBG Therapy

$^{131}$I MIBG Pre-Rx

$^{123}$I MIBG Pre-Rx

$^{131}$I MIBG 4 days Post-Rx

13 YO

639 mCi

$^{123}$I MIBG Post-Rx
Questions?