Implementation Experience with Y-90 Microsphere Brachytherapy Licensing Guidance

Ashley Cockerham
Founder & Principal Consultant

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Disclosures

Medical Consultant
Boston Scientific – Peripheral Interventions
Ashley.Cockerham@bsci.com
c. (703) 945-5959
Topics for Discussion

● Overview of NRC Guidance changes from 2016-2021
  ● Minor changes
  ● Major changes - AU to AU training & proctoring; attestation

● Other state-specific requirements or license commitments
  ● Attestations for board certified individuals
  ● Physical presence
  ● Semi-annual physical inventories
  ● Nuclear medicine technician accreditation
  ● Possession licensing language
  ● Authorized use licensing language
Review of NRC Guidance Changes

- 2016 Revision 9
- 2019 Revision 10
- 2020 Revision 10.1
- 2021 Revision 10.2
Review of NRC Guidance Changes - Minor

- Deleted per vial limits and 2 Ci total limit suggestion
  - Now listed as ‘X’ Ci total only
- Added license commitment for therapeutic use as approved in the SSDR, including max activity per vial limit
- Revised requirement for semi-annual physical inventory due to short half life of Y-90 and other requirements for accountability
Review of NRC Guidance Changes - Major

- Authorized Individuals
  - Existing AUs for Y-90 recognized
  - Certain parts of old "A-G" training must be supervised by an existing AU instead of the manufacturer
  - Time limits regarding proctored cases (initiate within 6 months; 12 months to complete; documentation in 60 days)
  - Recentness of training requirements now applicable
  - AU to AU proctoring required effective May 6, 2020
  - Written attestation required
Review of NRC Guidance Changes

- Authorized Individuals
  - Existing AUs for Y-90 recognized
  - Certain parts of old "A-G" training must be supervised by an existing AU instead of the manufacturer
  - Time limits regarding proctored cases (initiate within 6 months; 12 months to complete; paperwork in 60 days)
  - Recentness of training requirements now applicable

- **AU to AU proctoring required effective November 8, 2021**
  - Written attestation required
Review of NRC Guidance Changes

• TheraSphere™ receives FDA Pre-Market Approval March 21, 2021

• Guidance revised to remove references to Humanitarian Device Exemption and Institutional Review Boards
Agreement State Survey

• Does your state allow manufacturer representatives to proctor?

• If so, will you continue to allow it after Nov 8, 2021?

• Any other requirements (e.g., physical presence)?

• Do you publish your own Y-90 microsphere guidance?

Take the survey!
### Agreement State Implementation

<table>
<thead>
<tr>
<th>Yes</th>
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- **40% response rate**
- **Red = different from NRC regulations or guidance**
Agreement State Implementation

- **73%** allow manufacturer representatives to proctor
- **36%** may continue to allow manufacturer representatives to proctor or are undecided
- **32%** require preceptor attestations for board certified physicians
- **32%** require semi-annual physical inventories for Y-90 microspheres
- **11%** list specific tumor types or clinical indications on the license
Agreement State Implementation

- **58%** allow licensees to request ability to provide notification for an existing AU at a new site.

- **53%** allow licensees to request ability to make rad safety program changes without an amendment.

- **21%** require accreditation for nuclear medicine technologist.

- **21%** require physical presence of AU or AMP or RSO.

- **11%** require Institutional Review Board in license.
Most Difficult to Implement - Training and Attestations

• AU to AU proctoring
  • New NRC Guidance “Part B”

• Attestations for Y-go microsphere brachytherapy training and experience and ability to fulfill radiation safety-related duties as an AU
  • New NRC Guidance “Part C”

• Parts of “A-G” training must now be supervised by an AU
  • Preparing and administering patient dosage
  • Using administrative controls to prevent medical event
  • Evaluation of patient to determine if medical event occurred

• Attestations for diagnostic radiology training and experience
  • Even for board certified individuals
2 states issue their own guidance or checklists for Y-90 licensing

2 states are in full alignment with NRC now and going forward

Agreement State Implementation Summary
Licensing Examples - Possession

- SSDR per vial limit for SIR-Spheres 189 mCi
- SSDR per vial limit for TheraSphere 540 mCi

<table>
<thead>
<tr>
<th>Radionuclides</th>
<th>TheraSphere®</th>
<th>SIR-Spheres®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yttrium-90</td>
<td>Yttrium-90</td>
<td>Yttrium-90</td>
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Chemical/Physical Form
- Glass microsphere (current manufacturer as listed in the Sealed Source and Device Registry [e.g., BWXT Medical Ltd. Model TheraSphere®])
- Resin microsphere (current manufacturer as listed in the Sealed Source and Device Registry [e.g., Sirtex Model SIR-Spheres®])

Maximum Possession Limit
<table>
<thead>
<tr>
<th>D. Yttrium 90</th>
<th>D. Microsphere</th>
<th>D. 200 millicuries</th>
</tr>
</thead>
</table>

Purpose of Use
- TheraSphere® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry
- SIR-Spheres® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry

Form sometimes listed as
- radiopharmaceutical
- liquid
- solution

* Based on the maximum amount the applicant anticipates having at one time (i.e., 3 Ci)
Licensing Examples – Authorized Use

F. To be used in MDS Nordion model TheraSpheres® Mark III Administration Set brachytherapy afterloader for treatment of malignant hepatic tumors. **NOTE:** As of this amendment, there are no AUR for this material.

H. Medical use with the MDS Nordion TheraSphere delivery system and the Sirtex SIR-Sphere delivery system.

R. For use in a Sirtex brachytherapy afterloader for the treatment of non-resectable liver cell tumors.

GG. For use in a Radioembolization with a Microsphere Brachytherapy Device (RMBD) for the treatment of liver malignancies in humans.

L. For use of SIRTEX Medical Model SIR- Spheres® for treatment of unresectable hepatocellular carcinoma.
## Licensing Examples – Authorized Use

### Treatment of Hepatic, Kidney and Adrenal Tumors

<table>
<thead>
<tr>
<th>Purpose of Use</th>
<th>TherataSphere® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry</th>
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</table>

| Y 90 | Total 1 Ci | Microspheres* | MDS Nordion Model Theraspheres | Treatment of Metastatic Kidney Tumors |

### D. No single vial of solution to exceed 189 millicuries
Total: 500 millicuries

### D. Interstitial treatment of cancer as indicated in [state manual brachytherapy regs]

| HH. Y-90 | HH. Sealed source (microspheres in solution) | HH. No single source to exceed 540 mCi Total: 1.4 Ci | HH. Interstitial treatment of cancer as indicated in [state manual brachytherapy regs] |
Authorized Users

• Should license indicate an AU still needs to complete proctored cases?
  ● NRC and most Agreement States are issuing one amendment
  ● Licensee must provide follow-up documentation
  ● Can be verified during inspection

• At least one state is opting to amend license twice to add/remove conditional authorization

[Physician Name] TheraSphere Y-90 microspheres use permitted by [state regs for manual brachytherapy] (This authorization is limited to proctored cases and expires on June 4, 2022)
Questions

• What are biggest challenges for understanding or implementing latest NRC guidance?
• How to best communicate state-specific requirements and license commitments to licensees?
Acronyms & References

AU – Authorized User
AMP – Authorized Medical Physicist
IRB – Institutional Review Board
RSO – Radiation Safety Officer
SSDR – Sealed Source and Device Registry

NRCY-90 Microsphere Licensing Guidance – Revision 9 (Feb 2016) ML15350A099
NRCY-90 Microsphere Licensing Guidance – Revision 10 (November 2019) ML19338E099
NRCY-90 Microsphere Licensing Guidance – Revision 10.1 (March 2020) ML20080J208
NRCY-90 Microsphere Licensing Guidance – Revision 10.2 (April 2021) ML21089A364