REGULATORY ISSUES AND PRACTICE VARIABILITY WITH Y-90 MICROSPHERE TREATMENTS

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Disclaimer

- No conflicts of interest
- This talk will discuss the two specific Y-90 microsphere products on the market, SIR-spheres and TheraSphere
- Not an endorsement of either product

Outline

- Regulatory updates
  - Regulatory framework
  - NRC Licensing Guidance update
  - NRC Regulatory Guide 8.39 update
- Y-90 State of Practice Survey Results
  - Academic vs. Community hospitals
  - Medical physicist involvement
  - Therapy, diagnostic, and nuclear differences

Virtual Library Presentations

- Cheenu Kappadath, Y90 Imaging and Dosimetry (2020 SCM)

https://www.aapm.org/education/vl/vl.asp?id=14049

- Vanessa Gates, Treatment Efficacy and Dose Response (2017 AM)

https://www.aapm.org/education/VL/vl.asp?id=12296

- Matt Vanderhoek, Emerging Trends and Future Directions (2017 AM)

https://www.aapm.org/education/VL/vl.asp?id=12297

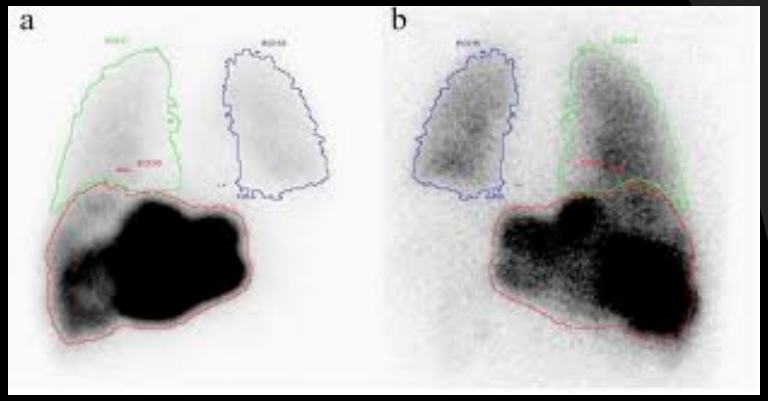
- Right after this!

2:00 PM TH-CD-TRACK 2-3	Mathematical Models to Improve Prediction of Absorbed Dose from 90Y Microspheres E.Roncali*

Treatment Summary

- Pre-treatment mapping study
  - Tc-99m MAA, lung shunt calculation
  - Dose calculations
- Dose verification or assay
- Delivery device (box) setup
- Microcatheter placement
- Dose infusion
- Post-treatment imaging

Physics involvement



Pretreatment

- Mapping imaging
  - Planar, SPECT
- Lung shunt ROIs / calculation from mapping study
- Liver contouring for dosimetry
- Dosimetry calculations (BSA, partition, voxel-based, etc)

Physics involvement

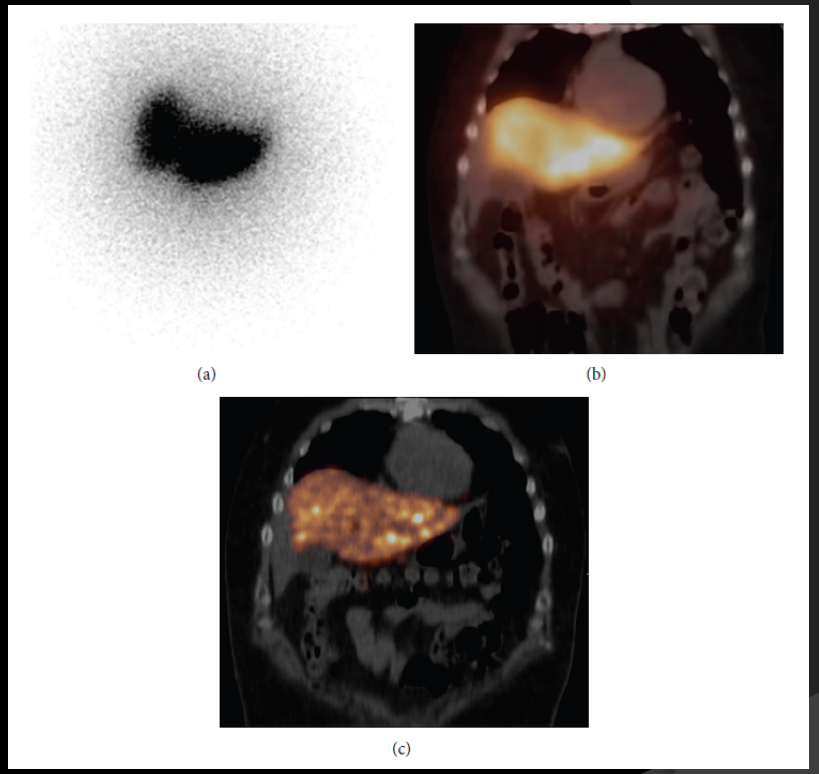
Day of treatment

- Discharge instruction consultation
- Dose draw or verification
- Exposure rate measurements, pre- and post-treatment
- IR room prep
- Delivery device prep
- Post procedure staff and room surveys
- Dose/activity delivered calculations

Physics involvement

Post-treatment

- Post-treatment imaging
  - SPECT, PET
- RAM waste management
- Post-treatment voxel-based dosimetry



Planar, SPECT/CT, and PET/CT post treatment imaging. Wright et. Al. 2015.

NRC Licensing Guidance

Yttrium-90 Microsphere Brachytherapy Sources and Devices

TheraSphere® and SIR-Spheres® Licensing Guidance

November 8, 2019, Revision 10

- Still under 10 CFR 35.1000 – Other medical uses of byproduct material
- Rev 10 updates include
  - Training and experience criteria
  - Medical event reporting
  - Inventory requirements
  - Waste disposal
- Original 2017 draft proposed elimination of “alternate pathway” of 3 proctored cases for Interventional Radiologists

NRC Licensing Guidance

Yttrium-90 Microsphere Brachytherapy Sources and Devices

TheraSphere® and SIR-Spheres® Licensing Guidance

November 8, 2019, Revision 10

Criteria for Authorized User status

- AU for byproduct material for which a written directive is required
- AU for manual brachytherapy

Or the alternate pathway

- Experience in IR and DR, e.g. IR/DR boarded
- Microsphere manufacturer sign-off on training
- Attestation from existing AU
- Three cases done with proctor
- One year time limit for case experience (new)

NRC Licensing Guidance

Medical event reporting requirements

- Total dose (rad or Gy) or activity (mCi or GBq) differs from the prescribed dose by 20 percent or more
- Except when stasis or emergent patient conditions (arterial spasm, blood pressure drop) are documented
- *Kinking or clogging of the catheter is not considered stasis* (new in Rev 10)

NRC Licensing Guidance

RSO

- No discrete approval for different microsphere uses
- RSO should be familiar will all devices

Training

- Required for anyone preparing, measuring, performing dosimetry calibrations, or administering
- Depending on level of physics involvement, this could include NM and IR staff

NRC Licensing Guidance

- *Semi-annual inventory (10 CFR 35.67 and 35.2406) not required (new in Rev 10)*
- Source accountability (35.406), receipt (20.1906), labeling (20.1904 and 35.69), storage (20.1801 and 35.92), and disposal are required
- Label with device name (i.e. SIR-sphere or TheraSphere)

NRC Reg Guide 8.39

April 1997 Rev 0

Table 1. Activities and Dose Rates for Auth

	COLUMN 1 ACTIVITY AT OR BELOW WHICH PATIENTS MAY BE RELEASED	
RADIONUCLIDE	(GBq)	(mCi)
Ag-111	19	520
Au-198	3.5	93
Cr-51	4.8	130
Cu-64	8.4	230
Cu-67	14	390
Ga-67	8.7	240
I-123	6.0	160
I-125	0.25	7
I-125 implant	0.33	9
I-131	1.2	33
In-111	2.4	64
Ir-192 implant	0.074	2
P-32	(c)	(c)
Pd-103 implant	1.5	40
Re-186	28	770
Re-188	29	790
Sc-47	11	310
Se-75	0.089	2
Sm-153	26	700
Sn-117m	1.1	29
Sr-89	(c)	(c)
Tc-99m	28	760
Tl-201	16	430
Y-90	(c)	(c)
Yb-169	0.37	10

c. Activity and dose rate limits are not applicable in this case because of the minimal exposures to members of the public resulting from activities normally administered for diagnostic or therapeutic purposes.

April 2020 Rev 1

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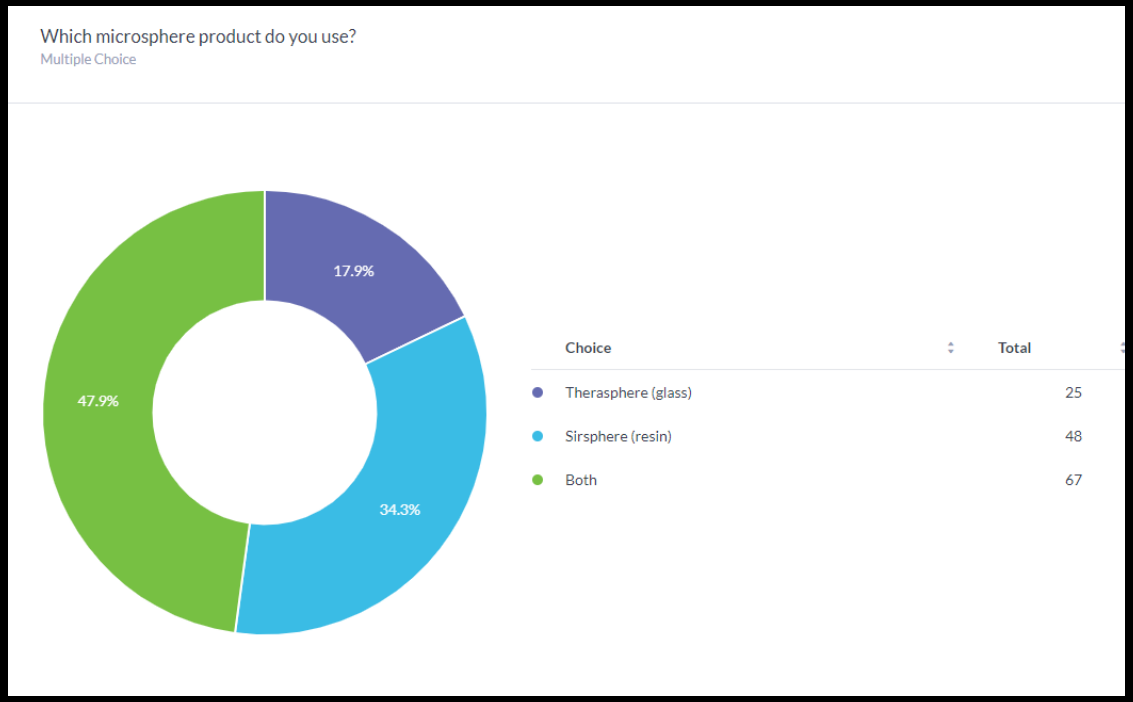
State of Practice Survey Results

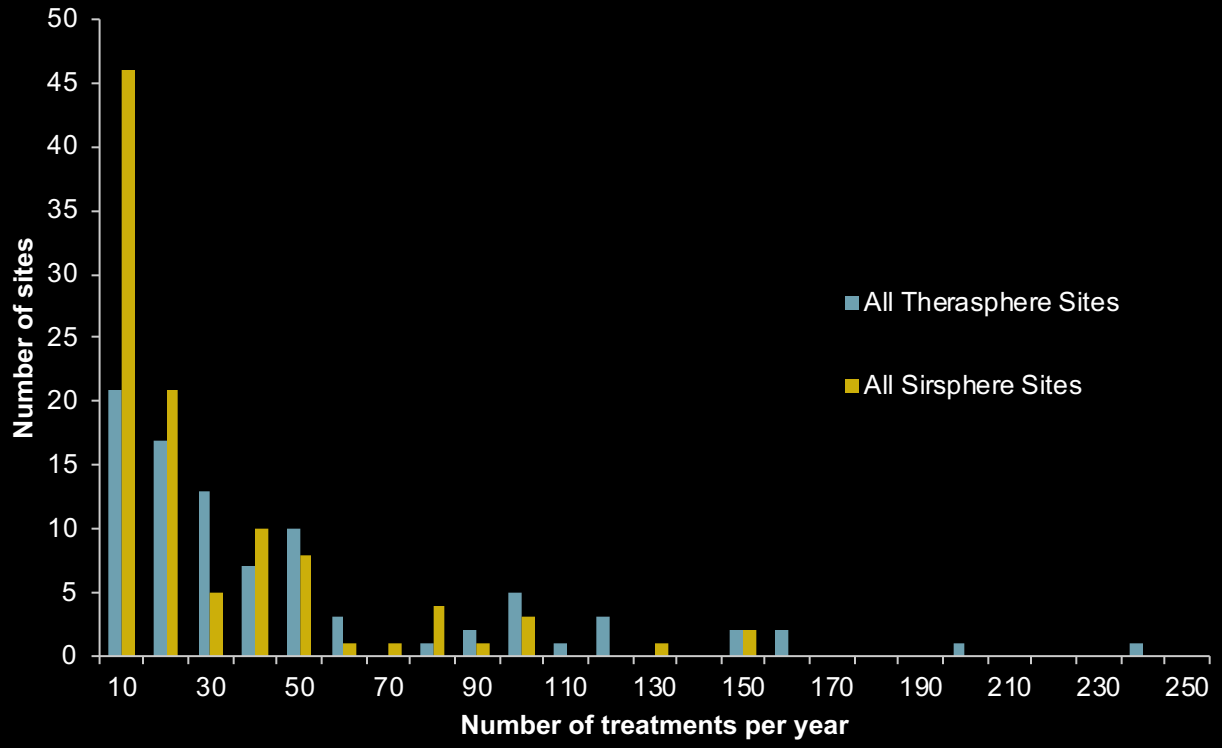
- Survey posted to MEDPHYSUSA, DXIMGMEDPHYS, and AMRSO list servers in May 2020 – 136 responses received
- Hypotheses: MP involvement and level of supervision varies with product, facility size, and jurisdiction
- Others welcome to examine data – posted online: https://cutt.ly/5yBbXRX

Microsphere Type



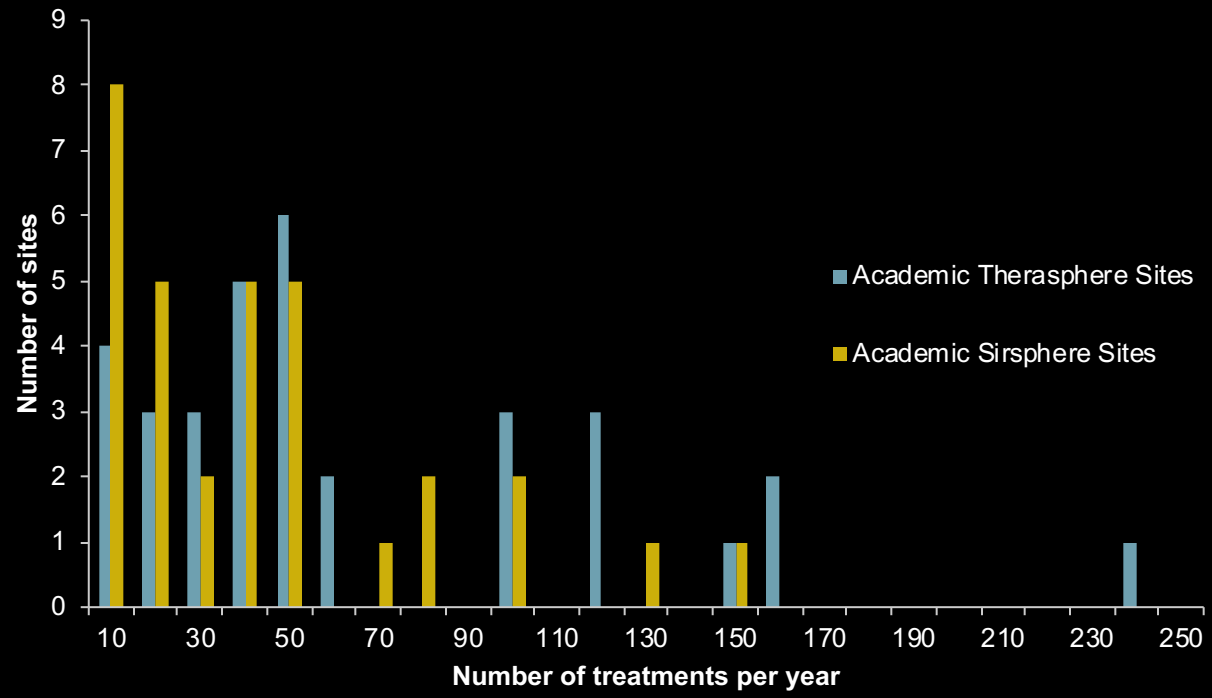
- About half of all sites use both products
- 34% use only Sirsphere

Microsphere Type



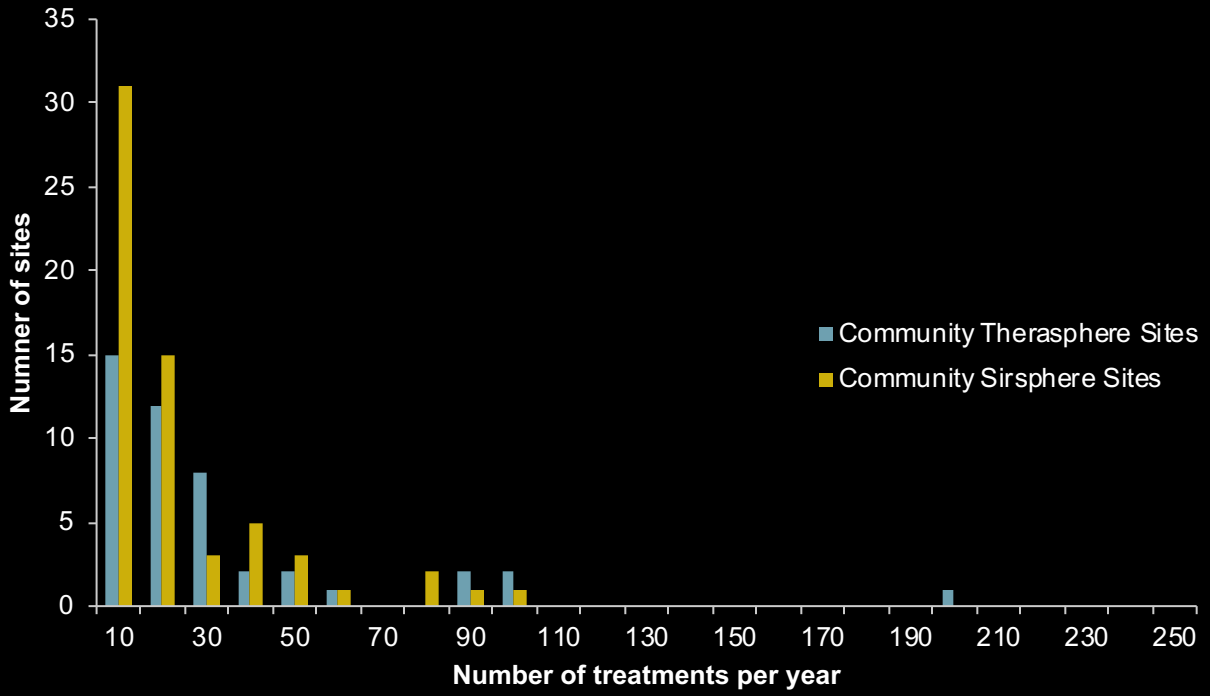
- 65% use Therasphere (avg 44 / facility, median 25)
- 76% use Sirsphere (avg 27 / facility, median 15)

Microsphere Type (Academic)



- Academic centers doing at least 40 treatments a year represent the bulk of Therasphere usage
- Distribution for Sirspheres more varied, although none with the same volume as Therasphere

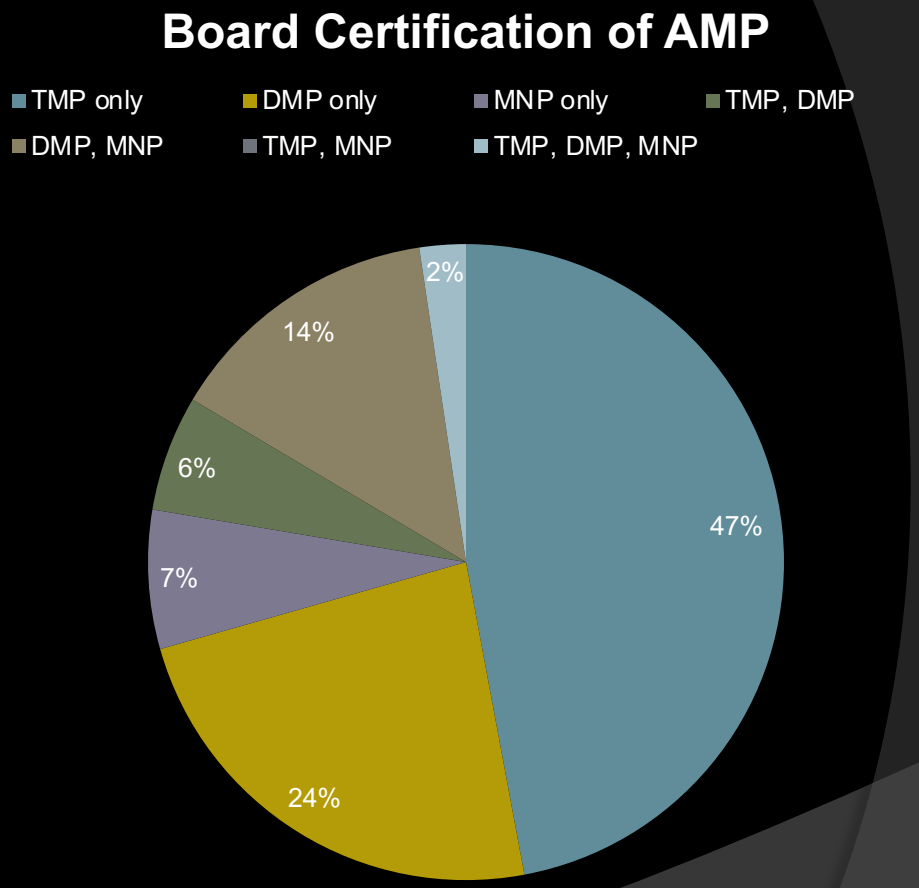
Microsphere Type (Community)



- Fewer Community hospital Therasphere sites relative to Sirsphere, although still more than academic in total number
- Large number of Sirsphere sites doing small number of cases

Authorized Medical Physicists

- 66% of respondents said an Authorized Medical Physicist (AMP) is involved in the case
- Requirements for AMP originate from some states, not found in NRC guidance
- Survey limitation: did not ask about DABSNM, HP/CHP, NM, or other radiation safety professionals supporting the procedure



TMP = Therapeutic Medical Physics

DMP = Diagnostic Medical Physi

MNP = Medical Nuclear Physics

AMP Supervision of procedure

Which portions of the treatment does the AMP personally (in room) supervise?

- Draw draw / verification assay 79%
- Delivery device (box) setup 51%
- IR procedure before dose administration 27%
- IR procedure during dose administration 68%
- Post procedure IR staff and room surveys 80%

- Percentages are of 66% that said AMP was involved

Which portions of the treatment does the AMP personally (in room) supervision

	TMP	DMP	MNP
Draw draw / verification assay	60%	74%	40%
Delivery device (box) setup	45%	51%	15%
IR procedure before dose administration	26%	28%	15%
IR procedure during dose administration	60%	67%	25%
Post procedure IR staff and room surveys	64%	79%	30%

- Percentages are of 47 respondents who listed TMP as AMP, 39 for DMP, and 20 for MNP

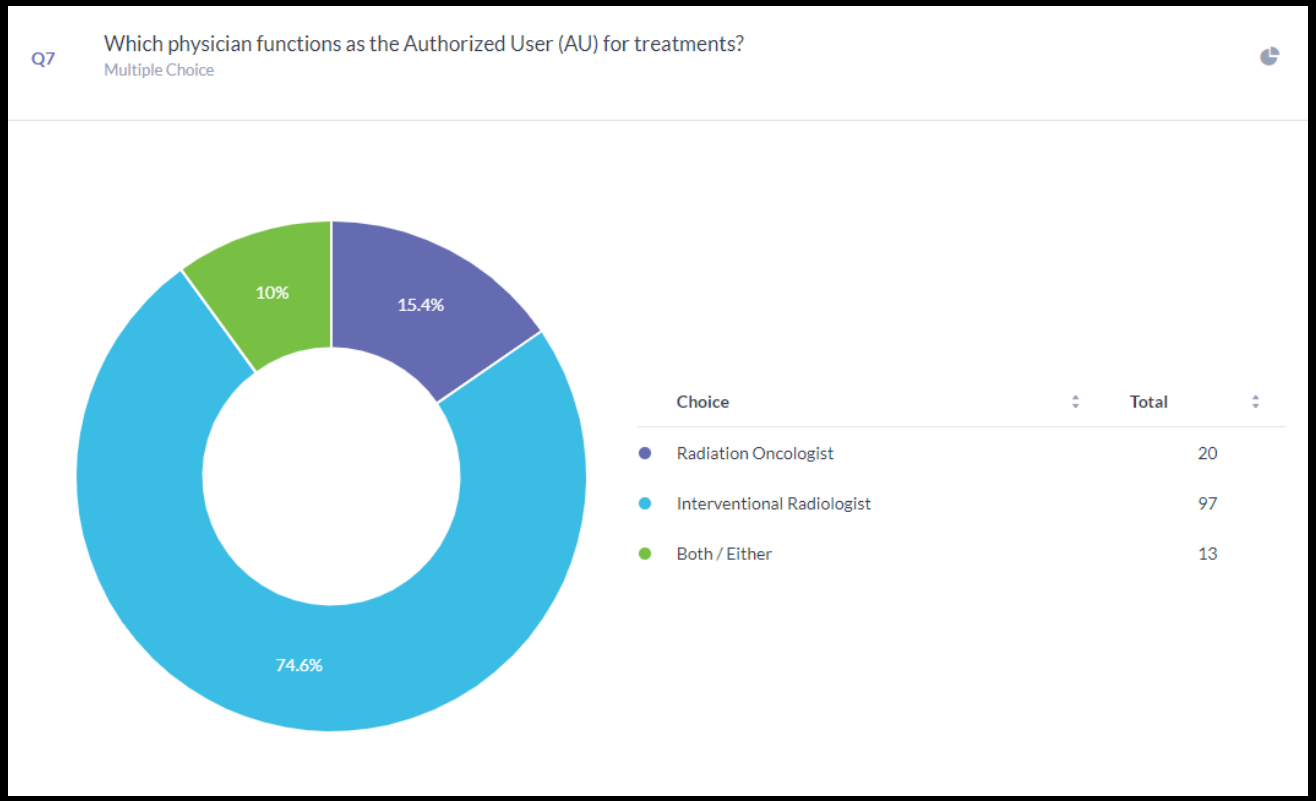
AMP Supervision by Product

Which portions of the treatment does the AMP personally (in room) supervision

	Both	Sirs	Thera
Draw draw / verification assay	39%	58%	56%
Delivery device (box) setup	24%	36%	44%
IR procedure before dose administration	18%	13%	20%
IR procedure during dose administration	42%	36%	52%
Post procedure IR staff and room surveys	44%	56%	52%

- Percentages are of 66 respondents who use both, 45 who use Sirspheres, and 25 who use Theraspheres

Who serves as AU?



- Clearly preserving the IR AU pathway is critical
- Five respondents noted NM physicians as AU
- Two said NM AU push syringe after IR places microcatheter

Other Survey Comments

- “The AU focus is delivering the Y-90 to the correct place; I support to make sure that happens.”
- “We need to change our practice to have more Radiation Oncology input into all stages of patient care and treatment. I am trying to do this more as the AMP.”
- “TMP set up program, but handed everything off to Nuc Med and IR.”
- “AMP from Rad On performs pre-infusion and post-infusion dose calc, but does not attend infusion. AMP from Diag or Health Physicist (non-boarded) attends infusion - delivers dose, and performs all surveys.”
- “Significant vendor support. Vendor tech rep in attendance at 90% of cases, assists physicians during procedure. Also assists at dose draw.”
- “Physicist needs to be involved in these "new" therapies such as Y90 and Lutathera, and soon-to-be PSMA. In part because these are not done often enough for others to keep up their skills at doing it.”

Conclusions and Recommendations

- Practice volume and physics support differ substantially
- Physics involvement – independent of AMP requirements – should be tied to
  - Volume of cases: <10/yr more oversight
  - Availability of other HP/RSO expertise
  - Experience of AU
- We bring continuity and process-oriented ideas to the team

AAPM Updates

- New WG being formed by William (Andy) Dezarn
- Most likely to lead to MPPG in near term
- TG report later

References

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Thanks!

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