# Physics Requirements for Implementing a Radiopharmaceutical Therapy (RPT) Program: The Clinician's Perspective

AAPM Virtual Annual Meeting

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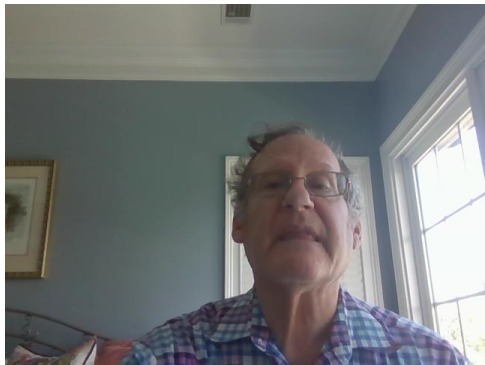
July 15, 2020

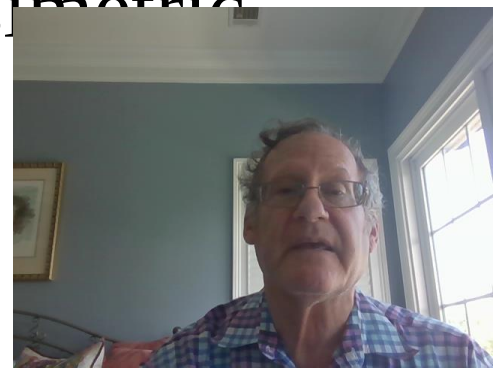


# RPT Program - Clinician’s Perspective

- Disclosures - None

# RPT Program - Clinician's Perspective

- Objectives of this session –
- To prepare the medical physicist to introduce RPT programs and provide tools to support these RPT programs.
- To educate medical physicists in the basics of radiopharmaceutical therapy and how it differs from "radiation therapy" (external beam therapy and brachytherapy) and diagnostic nuclear medicine
- How to introduce dosimetry and discuss different dosimetric methodologies



# Clinician's Perspective – General Considerations

- Radiopharmaceutical therapy (RPT) –is also known as *Targeted Radiotherapy*, *Radioligand Therapy*, *Therapeutic Nuclear Medicine*, *Molecular-Targeted Radiopharmaceutical Therapy (MTRT*), *Targeted Alpha Therapy (TAT)*, or *Theranostics* (from **thera**py and diag**nostics**). Also *Radiotheranostics.*
- Peptide Receptor Radionuclide Therapy (PRRT), a subset of RPT, defines the targeting moiety as a peptide, and targets a defined receptor. Example – targeting somatostatin receptors on tumor cells – utilizing Lu-177 Dotatate for neuroendocrine tumors

# Clinician's Perspective – General Considerations

- Therapeutic radiopharmaceuticals and their administration can be complex.
- Industry predicts huge growth in this area – 13% of NM currently, predicted to reach 30% in 2030.
- NCI estimates 50% of all radiation therapy will include RPT in 10 yrs.
- RPT is unlike external beam therapy, chemotherapy, or "oversized" diagnostic radiopharmaceuticals.
- RPT has unique benefits and risks and requires unique experti

# Clinician's Perspective

- **Definition of RPT –**
- **The systemic administration of a targeted radiopharmaceutical utilizing beta and/or alpha particles to achieve a clinically important outcome for a patient, usually with a primary or metastatic cancer.**
- External beam therapy and brachytherapy are generally given to a localized area.
- Diagnostic nuclear medicine studies generally detect disease processes or evaluate various organs to diagnose, determine staging/re-staging, evaluate response to therapy, and may provide a prognosis.

# RPT Program - Clinician's Perspective

- Current FDA-approved RP therapies:
- I-131 – differentiated thyroid cancer, hyperthyroidism
- Sm-153 EDTMP or Sr-89 chloride - approved 1980's for bone pain palliation
- Ra-223 dichloride - approved 5/15/2013 for bone metastases due to advanced prostate cancer
- Lu-177 Dotatate - approved 1/26/2018 for gastroenteropancreatic neuroendocrine tumors (GEP-NETS)
- I-131 iobenguane (metaiodobenzylguanidine [mIBG]) - appro
  7/30/2018 – for pheochromocytoma, paraganglioma, GEP-NE

# Clinician's Perspective – Current Radionuclides for Radiopharmaceutical Therapy in Clinical Use in the US

| RN | T1/2 | Emission | Max E (keV) | Max range (mm) |
|---|---|---|---|---|
| I-131 | 8 d | beta | 610 | 2 |
| Y-90 | 64 hr | beta | 2280 | 12 |
| Lu-177 | 6.7 d | beta | 496 | 2 |
| Sm-153 | 46.3 hr | beta | 805 | 3 |
| Ra-223 | 11.4 d | alpha(s) 5 | 7500 | <0.1 |
| | | beta(s) 3 | 427 | 2 |

# Clinician's Perspective – What Is Involved

- Medical decision making
- Regulations
- Patient evaluation – appropriateness of treatment, informed consent, especially including discussion of risks and benefits
- Ordering the radiopharmaceutical (RP), determination of administered activity, administration of the RP (by a physician or a technologist)
- Concomitant or adjunctive medications
- Evaluation of status or response to therapy – *the image is the biomarker*
- Evaluation of toxicity/adverse reactions, treatment if necessar

# Clinician’s Perspective - Components

- Clinical Implementation of RPTs
  - RPT availability
  - Preparing logistics – evaluation of workflow, patient flow management
  - Determination of administered activity
  - RPT ordering
  - Preparing facilities
  - Injection/infusion methods
  - Understand biology and radiobiology
  - Evaluate dosimetry
  - Patient Discharge

# Clinician’s Perspective

- Administration of radiopharmaceutical
- Establish iv line
- ancillary – amino acids, antiemetics
- Infusion timeline different with each type of radiopharmaceutical
- Treatment location
- Regulatory and radiation safety issues
- Room preparation

# Clinician's Perspective

- Infusion of Radiopharmaceutical
- Varies with each individual radiopharmaceutical
- Sm-153 EDTMP – iv 1 mCi/kg
- Ra-223 dichloride – iv 1.49 uCi/kg (55kBq/kg) – 4 cycles
- Lu-177 Dotatate – iv 200 mCi (7.4 MBq) every 8 wks – 4 cycles. Provide antiemetic. Give amino acids iv for renal protection.

# Clinician's Perspective – Duties of the Authorized User

- Prescribe administered activity (dosage)
  **Dosage = administered activity; dose = radiation exposure.**
- Supervision by Authorized User requires:
- Patient care preparation, including radiation safety precautions (will vary depending on which radiopharmaceutical is used)
- Calculation of dosage (medical physicist – dose calibrator settings)
- Administration
- Record keeping
- Reporting the administration in the medical record, including indication effects/ toxicities

# Clinician’s Perspective – Minimum Requirements

- Patient consultation space
- Document medical decision making
- Radiopharmaceutical preparation room (“hot lab”)
- Administration space
- Follow up consultation room
- Active involvement in tumor boards
- Multidisciplinary care

# Theranostics Clinic – Personnel Involved

- Nuclear Med physician [“Nuclear Oncologist”]/ Radiation Oncologist
- Nurse navigator
- Infusion Nurse
- NM technologists
- Therapeutic Nuclear Medicine Advanced Associate (NMAA) – mid-level providers with MS degree
- **Medical Physicist**
- RSO
- Other physicians – medical oncologists, radiologists, endocrinologists, u pathologists, endocrine surgeons, other surgeons, etc.

# Regulatory and Radiation Safety Requirements

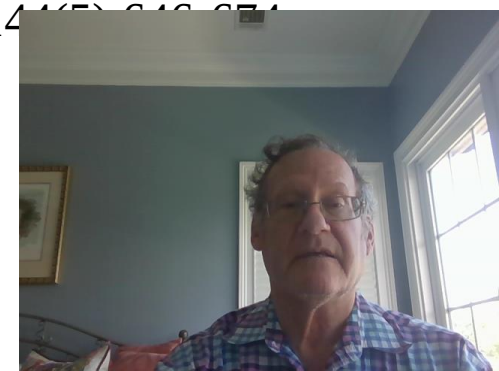
- Regulatory requirements
- Regulatory agencies (NRC, etc.) - regulations
- AU training and experience requirements
- Radiopharmaceuticals – FDA approval or under IND protocol
- Written Directive
- Patient instructions, including patient release criteria
- Radiation area surveys
- Medical event criteria

# Clinician's Perspective

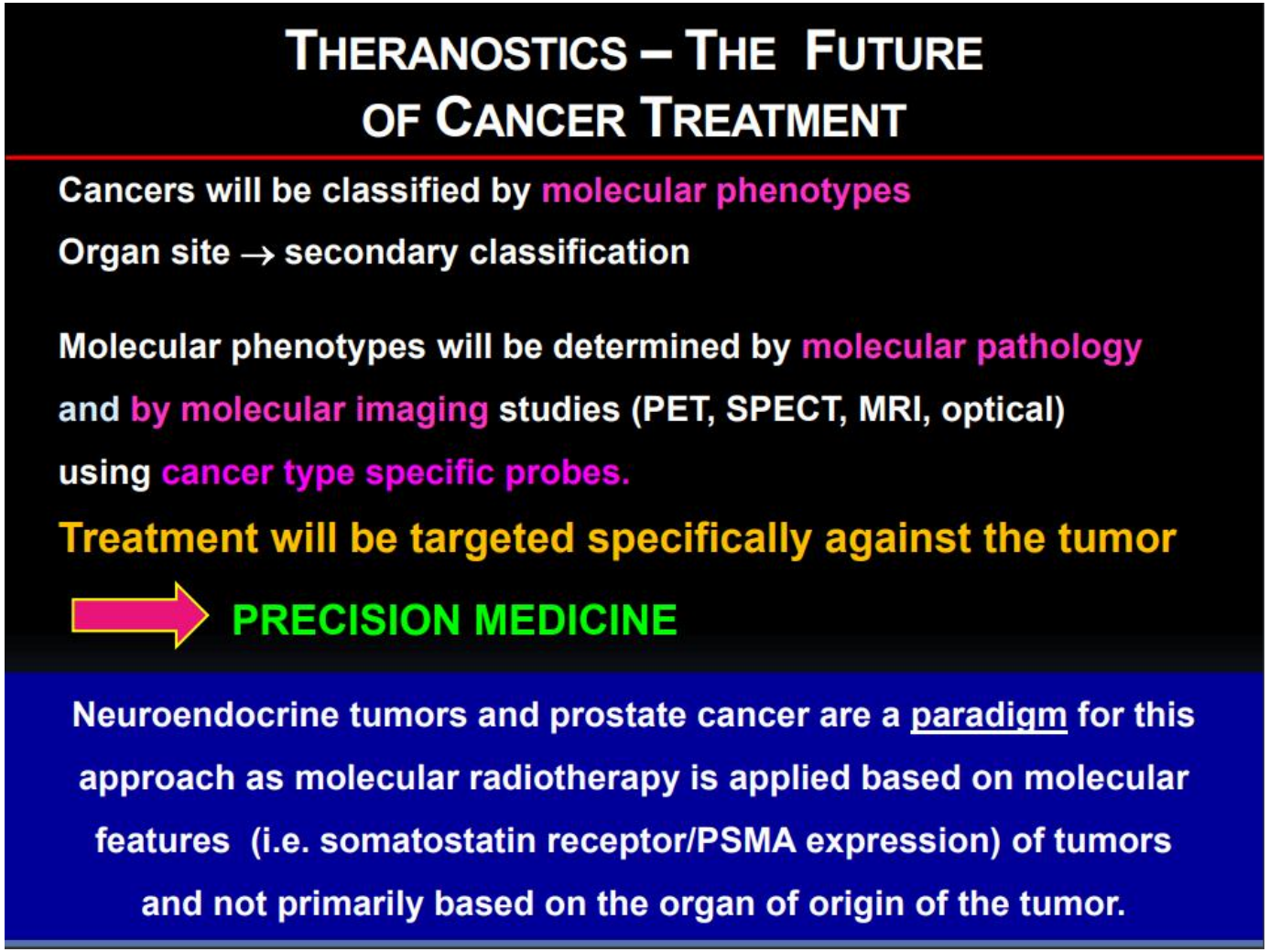
- Regulations and Radiation Safety
- Contact Radiation Safety Office
- Responsibilities of the RSO:
- Pre-therapy room preparation
- Supervise/Provide Radiation Safety training
- Radioactive materials license
- Radioactive waste storage and disposal

# 8 Hallmarks of Cancer – Hanahan and Weinberg

- Self-sufficiency in growth signals
- Evading growth suppressors
- Evading apoptosis
- Enabling replicative immortality
- Induced/Sustained angiogenesis
- Tissue invasion and metastasis
- Reprogramming of energy metabolism
- Evading immune destruction
- Ref: Hanahan and Weinberg, Cell, 2011; 14
- Also: Tumor-promoting inflammation/Tumor microenvironment
- Genome instability and mutation

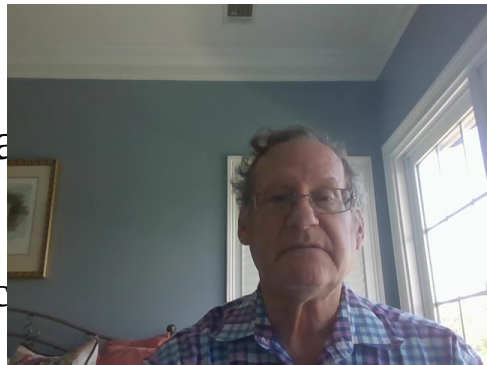


# Clinician's Perspective - Future

- 


Also thyroid ca

Courtesy of: Ric



# Clinician’s Perspective - Dosimetry

- Different methodologies
- Currently, the majority of radiopharmaceutical therapies are weight-based or with fixed activity (no dosimetry).
- I believe that detailed dosimetry will become important for future therapies, including determination of dosimetry of the whole body and multiple organs, bone marrow and especially lesional dosimetry. This will be discussed in greater detail later in the session.