Radionuclide Therapy Events: What we can learn and what to do

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Disclosure

The picture can't be displayed.

- Professor Emeritus of Medical Physics at the University of Wisconsin.
- The President of the Center for the Assessment of Radiological Sciences, a 501(c)(3) non-profit Patient Safety Organization listed with the Agency for Heathcare Research and Quality, dedicated to improving quality and patient safety in radiotherapy and radiology. ***I receive no remuneration from CARS***.

Learning Objectives

1. Understand the nature of radionuclide therapy events that have been reported.
2. Learn some practical steps to prevent events.

Radionuclide Therapy

- Also called radiopharmaceutical therapy
- The goal is to have some carrier (chemical or molecule) deliver a radioactive atom to a disease cell.
- This approach delivers a high dose to the target cell while, in theory, giving other cells a much lower dose.
- The big challenge is having a carrier that goes more to the target than other cells.

Some Useful Treatments

- $Na^{131}I$ to treat thyroid cancer or hyperthyroidism (dating to just after WWII)
- A secession of treatments for metastatic bone pain – $^{87}SrCl_2$, ^{153}Sm lexidronam, $^{223}RaCl_2$
- ^{131}I-MIBG for neuroblastoma

Not Discussed

This presentation will not discuss microsphere treatments because it is very different from radiopharmaceutical therapy and in many ways is more like brachytherapy, and is a form of microbrachytherapy.

We just do not have time to cover both.

The Radionuclide Engine I

- Beta emitters
  - Range of several millimeters
  - Betas effective if in, or on the surface of, a cell, and can also effect neighboring cells.
  - Radiation covers hundreds of cells but few interactions per cell (low LET) with an RBE of 1
- Alpha emitters
  - Range on order of 30 μm – about the diameter of a cell
  - Great if taken into the cell; little effect on neighboring cells.
  - Radiation densely ionizing (high LET) with hoards of hits per cell, highly deadly with RBE ~ 20.

The Radionuclide Engine II

- Auger-electron Emitters
  - Energy < 0.5 keV and range of < 25 nm (Note: cell nucleus ~ 6 μm)
  - No effect on other cells.
  - Effective if taken into the nucleus and attached to DNA
  - Intermediate LET between α and β, with RBE about 5.
- Gammas
  - Delivers dose locally and to distant cells, but not very efficiently
  - Not good for therapy – Can use for imaging

Actions Underlying Radionuclide Therapy

Mechanism	Example
Proximity	^{32}P Synovectomy
Chemical	^{223}Ra or ^{89}Sr for bone pain
Physiological	^{131}I for thyroid disease, ^{131}I-MIBG for neuroblastoma or radio-immune therapy

Rise and Fall and Rise of Radionuclide Therapy

- There have been several radionuclide therapy treatments that have come and gone (almost always because of improved chemotherapy), such as:
  - ^{32}P colloid for perineal effusion (and ^{198}Au before that)
  - ^{32}P for Polycythemia Vera
  - ^{131}I-Bexar and ^{90}Y-Zevalin for non-Hodgkin's lymphoma
- However, radionuclide therapy is on the rise again

Why Renewed Interest?

- Many new studies with new carriers and new radionuclides that have had remarkable effects.
  - ^{177}Lu-DOTATATE, a somatostatin analog for neuroendocrine tumors
  - ^{225}Ac-PSMA for prostate cancer
- We are now at a point where using gamma, or particularly positron, emissions in carrier labels, we can do image-based dosimetry and individually-designed, patient-specific treatments.

Of Concern

- With the increase in the use of radionuclide therapy, particularly with the variety of carriers and radionuclides, comes the danger of increase in medical events with these treatments.
- Which brings us to the topic of this presentation (sorry for the long introduction): prevention of events in radionuclide therapy.

Source of information for this presentation

- Most of the information comes from reports to the US Nuclear Regulatory Commission, and those mostly in the last six years.
- Some information is from other sources.
- All events have involved something undesirable involving the patient; none are close calls.
- Events involving microspheres are not included in this discussion because of the time allotted and major differences between the modalities.

Definition of Radiopharmaceutical Medical Event (U.S. NRC)

- The total dosage delivered differs from the prescribed dosage by 20 percent or more or falls outside the prescribed dosage range; or
- A dose that exceeds 0.05 Sv effective dose equivalent, 0.5 Sv to an organ or tissue or shallow dose equivalent to the skin from any of the following:
  - Wrong activity
  - Wrong radionuclide
  - Wrong pharmaceutical
  - Incomplete administration
  - Wrong patient
  - Wrong route
  - Subcutaneous injection
  - Contamination of the patient, staff or facilities

Report Data for Radionuclide Therapy

- Between 2013 and 2019 (6 years) the NRC received reports on 22 events.
- There are two Patient Safety Organizations (PSO) in the US that could also accept reports of incidents – not just events but anything that does not go as intended.
- Neither PSO had radionuclide therapy events.
- SAFRON only had reports on microsphere events.

Review of the Reported Events

- 22 events are not enough to draw significant conclusions.
- Some of the events fall into groups (some fell into more than one group):
  - 8 were partial delivery of the dosage,
  - 6 were wrong patient,
  - 6 involved technical issues (equipment, injection, EHR),
  - 5 were errors in prescribing or ordering,
  - 2 or 3 were dose to unintended tissues,
  - 2 were documentation errors,
  - 1 was two doses given to one patient (also wrong patient).

Review of the Reported Events II

- 2 cases in 2019 were documentation differed from treatment, although the treatment was what was intended.
- The table on the next slide gives thumbnail descriptions of the events.
- The colors just group events with similarities, but sometimes there are other similarities not noted.
- You can look more closely on the slides if you download them.

Nuclide	Action	Background	Failure
I-131	Wrong syringe used	Order changed	Activity not checked, syringe not measured
I-131	Wrong Pt's Dose	Two Pts	Activity and Script not checked
I-131	One of two capsules taken	Two capsules in vial	One capsule stuck to bottom
I-131	One of two capsules taken	Two capsules in vial	One capsule stuck to bottom
I-131	One of two capsules taken	Two capsules in vial	One capsule stuck to bottom
I-131	Wrong Pt, not for treatment	Not English speaker	Wrong wrist band
I-131	Dx activity given instead of Rx	EHR not used in Rx cases	Error in Rx script process
Ra-223	Wrong Pt's Dose	Two Pts	Activity and Script not checked
Ra-223	Wrong Pt's Dose	Two Pts	Activity and Script not checked
Ra-223	Low dose - but correct	Script 10x to high	Tech measured dose but did not notice discrpancy
Sm-153	High dose - wrong script	RO calculated incorrectly	No checks perfromed
Ra-223	High dose - double injection	Clinic had two doses	Tech used both not checking the script
I-124	Low dose - connector leaked		Report says procedural error
Ra-223	Subcu injection		Procedural error
Tc-99m	Wrong Pt		
F-18	Wrong dose	Refering Dr ordered scan by mistake	Clerical and NM Dr not check
Lu-177	Dose to Kidneys	Did not give blocking amino acids	1. Aminos were secondary bag, saline primary so no alarm; 2, checlist not performed
Lu-177	Dose to skin	Fowley Leak	No explanation
Ra-223	Wrong documented dose	Correct dose prescribed and delivered	1. Either wrong setting on dose calibrator; OR 2. mistaking Pt's mass for activity.
Lu-177	High dose on 4th Tx	3 doses correct, last dose was changed to half. Could not obtain half dose nor cut the dose on site. MD and Physicist agreed to give full dose. Prescrption was not changed.	Given the confusion at the time, forgot to update the prescription
I-131	Low dose - Partial infusion	Clinical Trial with vendor of the delivery system supervising. Stopped after the vendor's specified time.	Device not allow visualization of the vial.
ra-223	Low dose - 1 of 2 syeringed used.	Technologist did not notice that 2 syringes were ordered for Pt until after he left.	Did not check the presciption.
Sm-153	Low dose - tubing or connector leak	Activity leaked during injected.	Maybe tubing "abraded" duing needle insertion.

A little More Detail I

- 8 Partial Dosages
  - 3 were when ^{131}I capsules stuck to the vial and were not taken; No checks performed after having patient take the capsules
  - 1 only one of two syringes was given
  - 4 Technical issues
    - 2 dosage was low because a connector or tube leaked
    - 1 was a delivery-device failure
    - 1 was a subcutaneous injection
- 6 were wrong patient
  - 4 the activity was not checked, prescription was not checked.
  - 1 the clinic had two syringes and used both for the same patient.
  - 1 the patient was not an English speaker and was given the wrong wrist band (or it may have been claiming to be a different person).

A little More Detail II

- 5 Prescription or Ordering Errors
  - 1 physician calculation error
  - 1 prescribed wrong and no checks were made.
  - 1 given Dx dosage because EHR not set up for Rx
  - 1 was prescribed 10x too high, but the right dosage was given; the technologist did not notice the discrepancy when measuring the syringe.
  - 1 referring physician order scan and clericals and MN physician not check

A little More Detail III

- 2 Dose to unintended tissues
  - 1 Fowley catheter leaked ^{177}Lu, perineal skin received dose.
  - 1 dose to kidneys because pretreatment amino acid delivery failed.
  - There were some other leaks but doses to skin was not mentioned.
- 2 Documentation errors (dosage was correct)
  - 1 unknow cause (either wrong setting on dose calibrator or mistaking Pt's mass for activity).
  - 1 dosage on 4th fraction to be half other 3 but could not be done; physician approved full dosage but not change prescription.

A little More Detail IV

- 6 were technical issues (all noted above)
  - The EHR defaulting to imaging instead of therapy dosage
  - 2 Connector leaks
  - Subcutaneous injection
  - Fowley leak
  - Injection device malfunction

Pertinent Fact

In at least 18 of the 22 events, some checks were omitted!

What Fraction of All Treatments have Events?

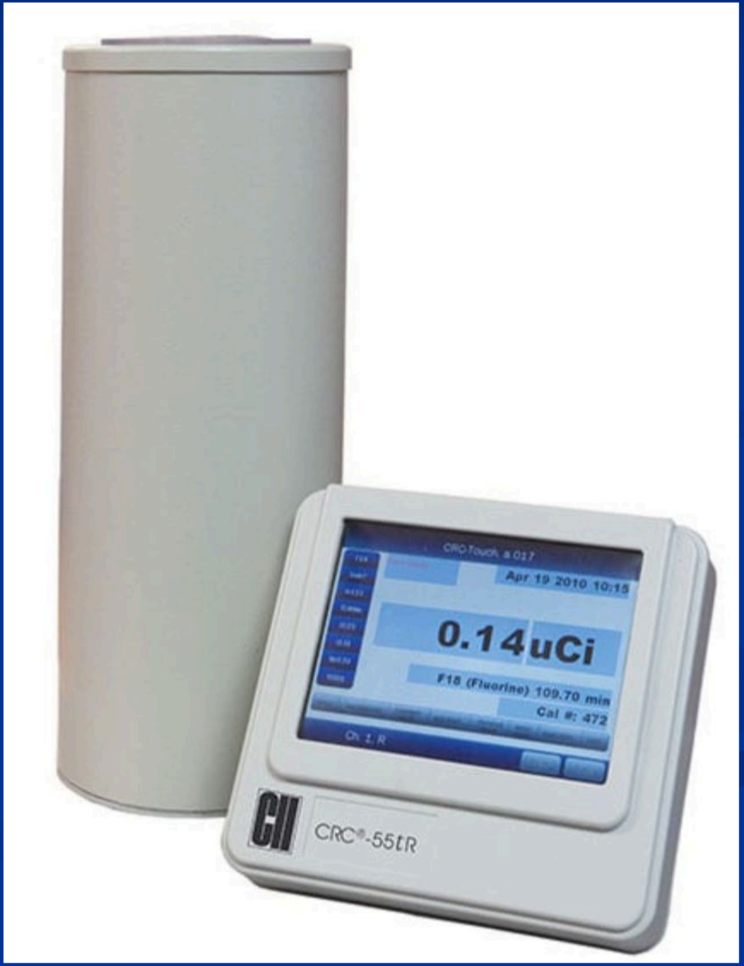
- We do not know the denominator so we do not know the fractional error rate. (See the next slide)
- It may be high.
- Errors are easier than with external-beam radiotherapy or brachytherapy where the more complex treatments have some checks built in.
- Most of these treatments involve no computerization and are done quickly

An Important Aspect of Radionuclide Therapy

- Almost all therapeutic applications in the US come as a unit dose from a commercial radiopharmacy, and are exempt from measurement in the clinic!
- Thus, any incorrect activity or incorrect radionuclide would never be detected, for example:
  - Some of the errors have been from exchange of a diagnostic and therapy dose, only discovered by accident.
  - Some were errors in ordering.
  - There may have been wrong dosages or materials – we just would not know.

What Could be Done to Prevent Events I?

1. All doses should be measured *just before* injection or ingestion. The figure shows a dose calibrator, but other devices could be used. (The figure is just an example – no indorsement is intended.)



What Could be Done to Prevent Events II?

2. All prescriptions and orders need to be checked: are they normal, consistent, correct? Orders should have feedback from the vendor to make sure they got the order right.

What Could be Done to Prevent Events III?

3. Time outs to verify the patient and the dose (by checking the prescription, the dose-calibrator reading and **the chart**) need to be performed with attention.

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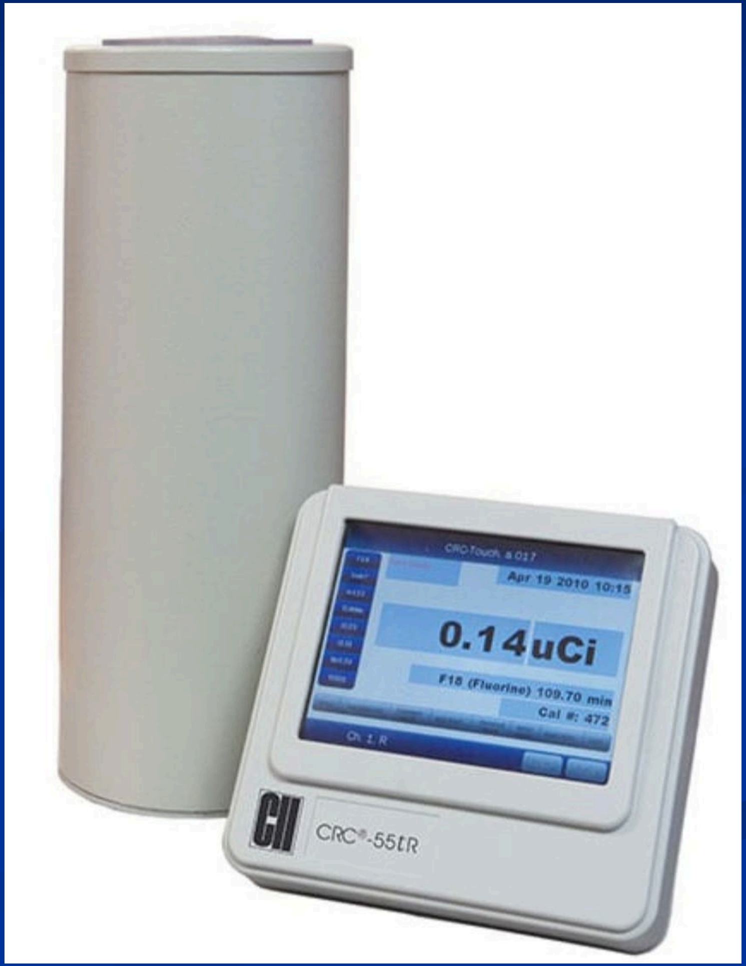
Medical Physics Practice Guideline 4.a: Development, implementation, use and maintenance of safety checklists

Task Group Authors: Luis E. Fong de los Santos, Chair, Suzanne Evans, Eric C. Ford, James E. Gaiser, Sandra E. Hayden, Kristina E. Huffman, Jennifer L. Johnson, James G. Mechalakos, Robin L. Stern, Stephanie Terezakis, Bruce R. Thomadsen, Peter J. Pronovost, Lynne A. Fairobent, AAPM Staff

What Could be Done to Prevent Events IV?

4. Vials and syringes should be assayed *after* administration. This is the only way to know the treatment was completed.



Not on the Detector

- Again, it does not have to be a dose calibrator, although that would be best and easiest.
- Another type of detector could be used as long as:
  - It is sensitive to the radiation and amount,
  - Responds in a predictable way to the radiation (linear response is best but if it is calibrated over the range of activity, that can work,
  - The set-up is completely reproducible.

How to Help Prevent Events

If you have an event, report it to SAFRON so others can learn from it.

Summary

- Events happen even when everyone tries to do a good job.
- Radionuclide therapy is simple compared with external beam and brachytherapy, but still has events happening.
- Events usually happen in a small number of ways.
- Most events probably are never recognized.
- Verify dosages just before delivery with measurement to catch erroneous therapies.