



Radionuclide Therapy

Overview

After reviewing this tutorial, the users should be able to

- list the most important characteristics of the ideal therapeutic radiopharmaceutical and briefly discuss each of these as it relates to current practice in Radionuclide Therapy.
- discuss the various thyroid diseases that are treatable with radioiodine and should know the activities administered for each condition and the radiation dose delivered to the patient.
- describe P-32 therapy for patients with polycythemia vera and malignant effusions
- identify the appropriate radiopharmaceutical for each of these diseases
- describe the procedure, radiation dosimetry, and projected outcome in patients treated with Sr-89 chloride, Sm-153 EDTMP, and Ra-223 chloride for palliation of bone pain secondary to metastases
- describe the treatment of intractable rheumatoid arthritis using radiation synovectomy with radiolabeled ferric hydroxide macroaggregates.

Therapeutic Radiopharmaceuticals in Nuclear Medicine

- **Definition:** A radioactive drug which, when used for therapeutic purposes, typically elicits no physiological response from the patient.
- **Characteristics of the Ideal Therapeutic Radiopharmaceutical**
 - Moderately long t_{eff} (measured in days). For I-131 NaI, t_{eff} in thyroid = 6 d
 - Prefer β - particle emitters (high LET) to maximize tissue dose/mCi injected.
 - Prefer high energy (>1 MeV)
 - Must have high target:non-target ratio to minimize radiation dose to non-target organs
 - Prefer rapid excretion of unbound material.
 - Readily available, inexpensive
 - Minimal radiation exposure to personnel in contact with patient, i.e., pure β -emitters like P-32, Sr-89, Y-90

- **Types of Emissions Used for Therapy**

- alpha particles
- beta- particles
- electrons
- gamma rays
- X-rays

- **Radioisotopes Used for Therapy**

- I-131 for treatment of thyroid diseases and lymphoma
- P-32 for treatment of polycythemia vera
- P-32, Sr-89, 153Sm, 186Re for palliation of pain from bony metastases
- 165Dy, 166Ho for radiation synovectomy
- 90Y for treatment of non-Hodgkin's lymphoma and liver metastases from a variety of primary malignancies

Therapeutic radiopharmaceuticals whose use does not require hospitalization for purposes of radiation safety.

1. I-131 NaI for treatment of hyperthyroidism
2. P-32 as soluble sodium phosphate for treatment of polycythemia vera
3. P-32 as insoluble chromic phosphate colloid for intracavitary treatment of malignant effusions.
4. Sr-89 as soluble SrCl_2 for palliation of pain in patients with metastatic breast or prostate cancer.
5. Any investigational therapeutic radiopharmaceutical not requiring hospitalization for purposes of radiation safety.

Clinical use of I-131 NaI for Hyperthyroidism

Dose Determination for Therapy in Graves Disease

Method 1: Measure % uptake; estimate mass of thyroid (g)

$$\text{Calculated Dose} = 60\text{-}100 \text{ uCi/g} \times \text{mass (g)} \times 100\% \text{ \% uptake}$$

Disadvantage: since 60-100 uCi /g is a wide range, it is difficult to determine the appropriate factor for an individual patient. In addition, determination of thyroid mass is not accurate. Use of this formula often results in incorrect estimate of the required dose, resulting in over-dosing or under-dosing of patient.

Method 2: A standard dose of I-131 NaI is given orally to all patients (8 mCi to females, 10 mCi to males); these doses may be modified based on % RAIU

- Advantage: adequately treats 85% of all Graves disease patients with 1 treatment.
- Disadvantage: the 15% who are refractory require a second administration of I-131

Response of hyperthyroid patients to treatment with I-131 sodium iodide

1. Day of administration no immediate effect
2. 4-6 weeks patient begins to notice beneficial effects
3. 12 weeks maximum beneficial effects observed
4. 6 months few observable changes after this interval

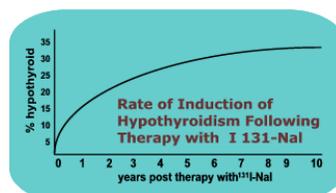
Epidemiology of hyperthyroidism and efficacy of treatment in men and women.

1. Hyperthyroidism is much more common in women than in men. The most often quoted ratio is 80:20.
2. Women are easier to treat than men from the standpoint of how many mCi are required to cure the patient. Typical male dose is ~ 10 mCi; typical female dose is ~ 8 mCi.

Long-term Side Effect

As indicated in the following graph, the rate of hypothyroidism after the first year is 3%/year for all patients treated with I-131 sodium iodide for Graves disease. They are treated with synthroid daily for the rest of their lives.

Rate of Induction of Hypothyroidism Following Therapy with I-131-NaI



Use of Sr-89 strontium chloride

- Therapy for Palliation of Bony Metastases
- Physical Characteristics of Sr-89
 - prepared by Sr-88 (n, γ) Sr-89 reaction
 - $t_{1/2}$ = 50.5 days
 - type of decay: β^-
 - maximum energy: 1.463 MeV, 100%
 - range of β^- in tissue: 8 mm

Advances in Cancer Therapy

- Longer survival in many cancers
- Better pain control medication
- More aggressive radiotherapy
- End result: More people living with bone pain.

Epidemiology of Bony Metastases in Breast and Prostate Cancer

- Prostate cancer: 50% of patients have bone disease at time of diagnosis
- Breast cancer 15% of stage III patients and 50% of Stage IV patients have bone metastases

Therapeutic Approaches to Bone Pain

- NSAIDs
- Chemotherapy
- Hormonal Therapy
- External Beam Radiation
- Narcotic Therapy
- Radiopharmaceutical Therapy

Historical Approach to Radionuclide Therapy

- P-32 Na_3PO_4 in 1940's
- Sr-89 SrCl_2 in late 1980's
- Sm-153 EDTMP in late 1990's

P-32 Na₃PO₄

- long history
- 2. 60-75% response rate in literature
- 3. significant marrow depression- end point is toxicity
- infrequently used

Sr-89 strontium chloride therapy for palliation of bony metastases

- Indications: bone pain caused by any primary malignancy metastatic to bone.
Implication: Must have a bone scan positive for metastases. Most commonly used for breast and prostate cancer
- Palliative, not curative
- Bone localizer; calcium analog with distribution very similar to 99mTc-MDP
- 80% Response rate overall
- Ratio of metastatic lesions to normal bone = 5:1
- Ratio of metastatic lesions to marrow = 10:1
- Retention of Sr-89 in metastases longer than in bone
- No reported adverse reactions
- 30-50% of patients have measurable decrease in WBC and platelets
- Recovery begins at about 6 weeks
- Flare phenomenon often prognostic indicator of successful treatment

Typical Dose: Sr-89 chloride

- 4 mCi given by IV Injection for intractable bone pain from prostate, breast cancer or other primary malignancy

Radiation dosimetry of Sr-89 chloride

organ	rad/mCi
red marrow	80.0
bladder wall	0.5
whole body	6.0

Sr-89 SrCl₂ Therapy: Clinical Outcomes

- 80% response divided into 3 groups:
 - moderate response morphine codeine
 - marked response morphine advil
 - dramatic response morphine no meds

Use of P-32 Compounds

Typical Administered Doses for P-32 Compounds

- polycythemia vera: soluble P-32 Na₃PO₄ 3-5 mCi IV injection
- malignant effusions: colloidal P-32 CrPO₄ 8-12 mCi intracavitary injection

P-32 Na phosphate for treatment of polycythemia vera

- IV injection of 3-4 mCi for initial treatment, which adequately treats 50% of patients.
- Of 50% requiring 2nd injection, 35% are successfully treated. Remainder are refractory to treatment and may require 3rd or 4th dose.
- Median survival time for untreated patients after time of diagnosis is 1.5 yr. After treatment with P-32 Na phosphate, interval is increased to 12 yr.
- 11% incidence of leukemia in successfully treated patients.
- Controversy: Is 11% incidence of leukemia a result of injection of P-32 Na phosphate or is P. Vera a preleukemogenic condition whose natural course is development of leukemia? The increased risk of leukemia is probably partially attributable to both causes.

Radiation dosimetry following IV injection of 4 mCi of P-32 Na phosphate

organ	absorbed dose (rads)
skeleton	240
liver	24
spleen	29
gonads	4
whole body	40

P-32 chromic phosphate colloid for palliation of malignant effusions

- Intracavitary injection: 10 mCi in 250 ml saline
- >90% of patients respond => significantly decreased frequency of "tapping" required to remove fluid.
- Rarely need to retreat patient.
- Palliative, not curative.
- Approved drug, ~\$,1000 per treatment

Therapeutic radiopharmaceuticals that sometimes require hospitalization for purposes of radiation safety.

This has been amended recently because the NRC no longer requires hospitalization. But some agreement states still enforce this and you need to check with the individual state.

Examples

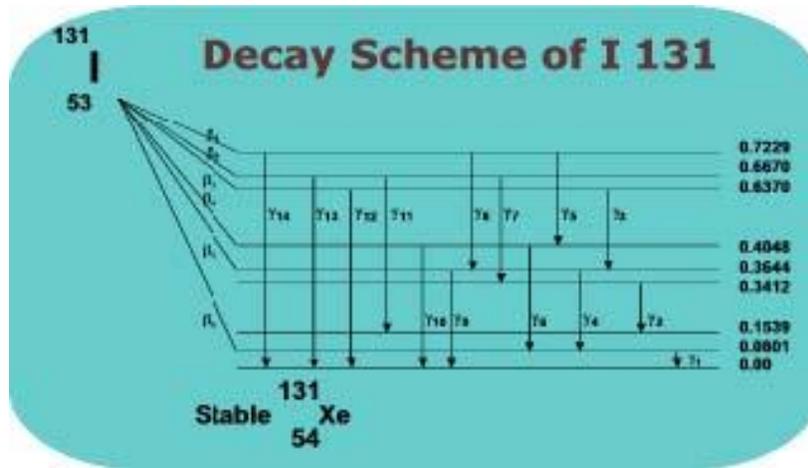
- I-131 NaI for treatment of thyroid Ca
- Y-90 labeled antibody to NHL cell site-e.g., Zevalin
- Au-198 for intracavitary treatment of malignant effusions
- Any investigational therapeutic radiopharmaceutical requiring hospitalization for purposes of radiation safety.

Overview of Thyroid Diseases Treatable With I-131-Nai

- hyperthyroidism (Graves disease)
- toxic nodular goiter (Plummer's disease)
- thyroid carcinoma (ranked in order of likelihood of I-131 uptake)
 1. Follicular
 2. Papillary
- The other two types of thyroid cancer, medullary and anaplastic, are not treatable with I-131

Decay Scheme of I-131

The decay scheme below indicates that there are 14 gammas and 6 betas emitted from I-131. Therefore, **True or False**, 14/20 of the tissue damage is attributable to gammas and 6/20 to betas.



Answer

False for 2 reasons:

- The LET (Linear Transfer Rate) for betas is much higher than for gammas; consequently they confer a much higher radiation dose
- The fractions 14/20 and 6/20 imply that the % abundance of each of these 20 emissions is exactly 5%, which is not possible. In fact the % abundances vary from a fraction of 1% to almost 85%.
- Correct answer is that ~90% of tissue damage is attributable to beta particles.

Typical Administered Doses of I-131 Compounds

procedure	dose (mCi)	route of administration
raiu: normal	0.005	oral
raiu and scan: substernal	0.100	oral
total body mets survey	5-10	oral
hyperthyroidism	5-10	oral
toxic nodular goiter	25	oral
thyroid Ca therapy	75-225	oral

Radiation Dosimetry of I-131- NaI

Following oral administration of I-131-NaI for treatment of hyperthyroidism, 90% of dose to tissue is achieved by β - emissions. For a hyperthyroid patient treated with a 10 mCi dose of I-131:

Tissue	Absorbed Radiation Dose (rads/10 mCi of ¹³¹I)
Thyroid	11,000
Testes	9.2
Ovaries	9.3
Whole Body	16.0

Source: Mallinckrodt package insert

Precautions to be Observed with High-dose I-131 Therapy Patient (>33 mCi)

- Keep your distance to minimize personal radiation dose
- Patient is assigned a private room
- Everyone involved with patient must wear film badge
- Gloves must be used by patient to handle telephone, bed controls
- Housekeeping not allowed in room until room is released by RSO
- No visitors allowed for at least 24 hr
- No bed baths
- Patient must stay in bed unless instructed otherwise
- Absorbent pads taped to floor from toilet to bed
- Patient must use disposable items for food service
- Diagnostic blood samples taken by Nuclear Medicine
- If patient dies, attending physician must be notified immediately
- Room must be surveyed by RSO prior to release for next use.
- Every participant in therapy must have thyroid counted 24 hr post dose

Patient Release Criteria for Hospitalized Patients

- For NRC States*...Reading <7 mR/hr at 1 meter from patient's chest, which is equivalent to a body burden <33 mCi of I-131.
- For Some Agreement States...Reading <5 mR/hr at 1 meter from patient's chest, which is equivalent to a body burden <30 mCi of I-131.
- Note: NRC is no longer requiring hospitalization for I-131 therapy unless medically indicated.

Sealed Sources and devices containing byproduct material that are used for therapeutic applications.

Examples

- Am-241 as a sealed source in a bone mineral analyzer
- Cs-137 encased in needles and applicator cells for topical, interstitial, and intracavitary treatment of cancer
- Co-60 encased in needles and applicator cells for topical, interstitial, and intracavitary treatment of cancer
- Au-198 seeds for interstitial treatment of Ca
- I-125 as a sealed source in a bone mineral analyzer
- Ir-128 as seeds encased in nylon ribbon for interstitial treatment of cancer
- Sr-90 sealed in an applicator for treatment of superficial eye conditions

Recent Advances in Radiotherapy In Nuclear Medicine

Octreotide Therapy

- Potentially useful in neuroendocrine tumors
- Tumor must have somatostatin receptor present
- Both In-111 and Y-90 have been used
- Some successful remissions have occurred with high doses

Zevalin Lymphoma Therapy

- Y-90 labeled antibody to NHL cell site
- Avg. dose 20-32 mCi antibody

Y-90 Microsphere Therapy for treating liver metastases from colon cancer

- Y-90 labeled resin microspheres- SIR-spheres and TheraSpheres
- Requires MAA study and angiogram prior to administration of microspheres
- Injected dose 20-60 mCi depending upon many factors
- lobar vs whole liver
- degree of shunting

Radiation Synovectomy

- Purpose: therapy of rheumatic synovitis in knees of patients with rheumatoid arthritis
- Goal: removal of inflamed joint lining prevention of joint destruction
- Radiopharmaceutical: 270 mCi of Dy-165 FHMA or 10 mCi of Ho-166 FHMA, pure β -emitters
- $t_{\text{phys}} = 2.3$ hour and 27 hour, respectively
- Injected into knee joint, requires overnight hospitalization
- Ideal candidate:
 - patient disabled with chronic knee effusions
 - patient beyond child-bearing years
 - minimal evidence of joint destruction
 - resistance to conventional management > 6 months



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