Use of radionuclides in medicine: ethical issues

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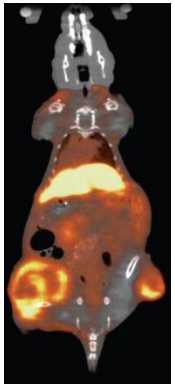
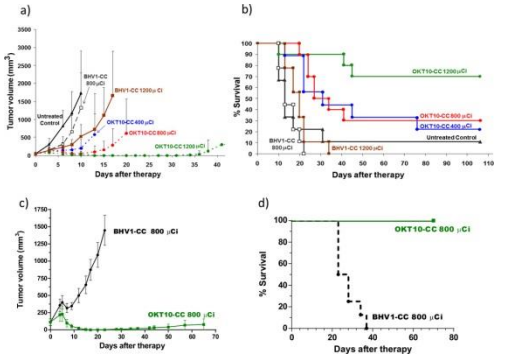
Ethics, animal testing, and use of radionuclides

- Strategy of 3Rs: reduction, refinement and replacement: is it applicable to the use of radionuclides in nuclear medicine (imaging and therapy) ?

Some reduction and refinement could be possible but not replacement





The experiments should be performed by qualified technicians under the control of a qualified veterinarian

Four principles of biomedical ethics

- **Autonomy** (respect for the person, human dignity)
- **Beneficence** (benefit to the research participant)
- **Non-maleficence** (absence of harm to the research participant)
- **Justice** (equal distribution of risks and benefits between communities)

Autonomy (self-governing)

- Information:
  - what is a « radioactive drug »
  - what are the « risks » of irradiation » etc.…
- Counseling:
  - are there any alternative, non irradiating, options ?
  - why the radionuclide use is thought to be the most appropriate for the specific patient ?
- Confidentiality, individuality, independence moral responsibility
- **Informed consent**

Beneficence

- The health care provider must promote the well-being of patients:
  - to avoid irradiation when alternative, non radioactive, option is considered to have at least the same efficacy (Ex: PET vs MRI)
  - when patients refuse radionuclide therapy without alternative treatment (Ex: ^{131}I in thyroid cancer) the harm with no treatment must be weighed and explained
  - the advantages of radionuclide use should be clearly explained (Ex: radioimmunotherapy vs chemotherapy)

Nonmaleficence

- The health care provider must strive not to inflict harm to a patient.
  - to warn patients and third parties about the risks related to irradiation (for patients and relatives)
  - to base injected activity on dosimetric estimates
  - to come to a patient's aid in the event of adverse side effects

Justice

- A distributive justice that guides access to radionuclide therapy or imaging, resource allocation and access to information
  - information to the patient should take into consideration person's literacy skills and education levels
  - economic barriers should be considered

Informed consent and radionuclide use

1- To elicit from the patient what he or she knows about the use of radionuclides in medicine, his or her diagnosis, alternatives available to manage it and prognosis
2- To correct factual errors and incompleteness
3- To explain clinical judgment about the patient's condition and all available management strategies including non radioactive ones
4- To help patient identify relevant values or beliefs influencing decision making (for example deep collective historical fears…)
5- To help the patient to evaluate alternatives in terms of those values or beliefs
6- The patient expresses his or her subjective or deliberative interest-based preferences
7- To make a recommendation based on clinical judgment
8- To reach and implement a mutual decision

Use of radionuclides in medicine

Quantitative Benefit-Risk analysis of medical radiation exposures

Semin Nucl Med 2014; 44:210-214

Quantitative benefit/risk analysis in the use of ^{18}FDG PET/CT in preoperative assessment of suspected NSCLC

	Performed thoracotomies	Futile thoracotomies	Futile Surgical deaths/yr
Without PET	81%	41%	3766
With PET	65%	21%	1547

- Surgery-related mortality: 6.5%
- ER: $5x10^{-4}$ per person per rem
- ED of PET/CT: 14 mSv
- Radiogenic cancer-related death: 122
- **NET BENEFIT: 2219-122= 2097 lives saved per year**

Semin Nucl Med 2014; 44:210-214

Treatment of benign disease with radionuclides: example of ankylosing spondylitis

- Story: 1471 patients treated with repeated injections of ^{224}Ra between 1948 and 1975
- Efficacy: long-lasting benefit with a reduction ++ in the need of antirheumatic and analgesic drugs including opioids
- Long-term study of late effects comparing an exposure group (1006) and a control group (1072)

	Exposure group			**Control group**		
	observed	expected	P-value	observed	expected	P-value
leukaemia	19	6.8	<0.001	12	7.5	<0.08

Rheumatology 2008;47:855-859

Use of radionuclides in healthy individuals: example of use of radionuclides (PET imaging) for assessing brain function

Testing guidelines:

- Measurements (neural transmission using radiolabeled agents binding to specific receptors) which cannot be made through other testing methods.
- « Substantial » benefit to society
- Effective dose on human should be estimated from animal testing

To satisfy to the three fundamental principles of protection

- The principle of **justification**: using a radionuclide for diagnosis or therapy should yield an individual or societal benefit that is higher than the detriment it causes
- The principle of **optimisation of protection:** optimisation involves keeping exposures as low as reasonably achievable taking into account economic and societal factor
- The principle of **limitation of maximum doses**

Potential toxicity of a radiopharmaceutical

- Toxicity of the vector:

  - most often very low due to the small injected quantities

- Toxicity of the radionuclide

  - negligible for the element due to the extremely low quantitiy of this element.

  Ex: possible theranostic use of ^{72}As from a $^{72}Se/^{72}As$ generator

  - mainly related to the emitted radiation

Principles of Ethics of the American College of Radiology

- Render service with full respect for human dignity
- Continual improvement in medical knowledge
- Be aware of limitations and seek appropriate consultations
- Safeguard against those physicians deficient in moral character
- Nuclear medicine physicians may not reveal confidences entrusted to them or deficiencies in character unless to protect welfare of the individual or the community
- Decision to render a service by a nuclear medicine physicianis a matter of the individual physician and patient choice
- Bond between nuclear medicine physicians and radiation oncologists should not be used for personal advantage

Rules of Ethics

- Consultative opinion on scans regardless of origin
- Nuclear medicine physician should be accepted as a member of the staff
- Mutual respect of other members of the health care team. No harassment or discrimination
- Ensure that the system of health care delivery does not unduly influence the selection and performance of appropriate available imaging or therapy procedures
- No care at substandard level. Cost-effective studies
- Fast response to patients' inquiries regarding fees or financial incentive
- No compensation dependent onoutcome
- Research reported with integrity
- No untruthful or misleading advertising

Scenario 1 of ethical case

- Story: A patient referred for a bone scan inadvertenlyis injected with Tc-99m-DTPA. What do you do ?

- Ethical dilemna: The question is: whether or not to inform the patient of such misadministration ?

- Suggested solution:
  - to inform the referring physician ?
  - to inform the patient?
  - what else ?

Scenario 2 of ethical case

- Story: A patient with a colon cancer had an MRI scan interpreted as « classic for hemangioma ». Serial CT and MRI scans showed that the lesion was gettin bigger.
- Ethical dilemna: The radiologist is confident of his interpretation and does not think that a PET scan would be useful.
- Suggested solution:
  - Wait and Watch standpoint ? trusting interpretation's radiologist
  - The referring physician notifies, in a polite and dignified way the radiologist that a PET scan could be useful but the radiologist does not agree
  - The referring physician contacts nuclear medicine department for a PET scan despite radiologist's opinion

Conclusion

- Nuclear medicine has a great future, both in imaging and molecular therapy.
- For this increasing use of radionuclides it is crucial to respect ethical principles and rules and not to stray from the guidelines of ethics.
  - complete information on potential late detrimental effects of irradiation with high activities (therapy)
  - importance of informed consent with its components: disclosure, capacity and competency, and voluntariness