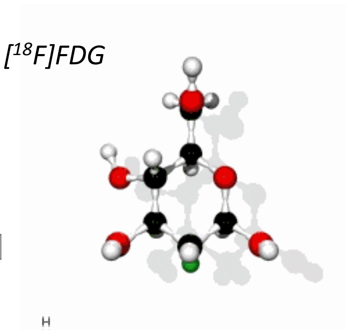
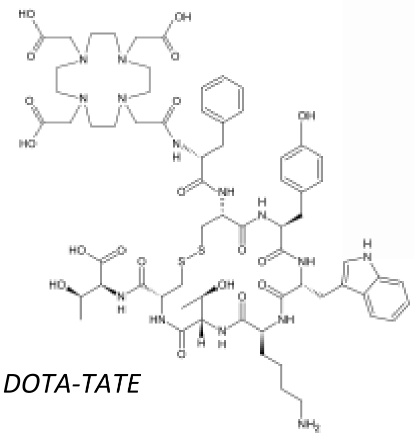
Molecular Imaging Agents (CCRI(II)/13-31)

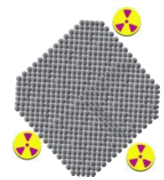
Quantitative Molecular Imaging



[^{18}F]FDG



DOTA-TATE



Nanoparticle-based imaging agents

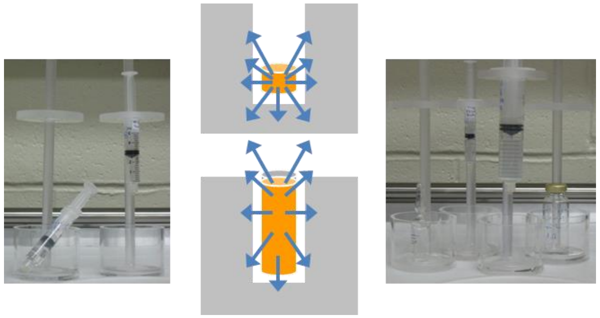
Commercial Radionuclide calibrators

PET-CT scanner

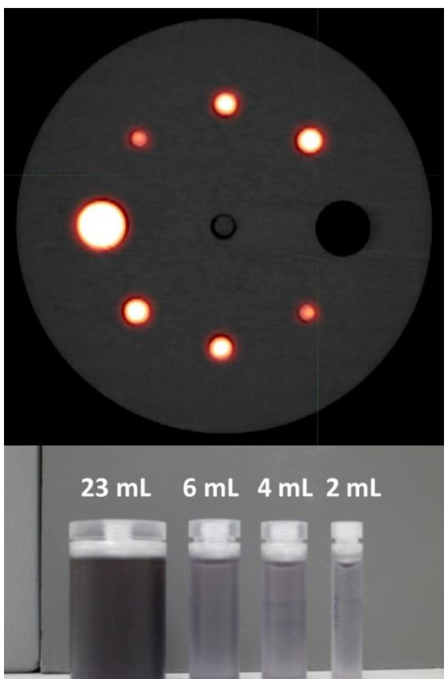
- Primary and national activity standards for molecular-imaging nuclides
- Secondary activity standards for clinical applications
  - Calibration factors: chemical formulation and container geometry
  - Programs to ensure calibrations are traceable to national standards
- Specific applications
  - PET, SPECT
  - *in vitro* quantitation

Meeting the Need

Example from NIST



Radionuclide calibrator sensitivity to chemical and geometrical effects.



NIST -developed calibrated phantom inserts for PET and SPECT imaging platforms.

- Novel chemical formulations affecting response
  - Inclusion of complex biomolecules or nanoparticles
  - Unique calibration factors
  - NIST investigated chemical and geometrical effects in the determination of “dial settings” for commercial radionuclide calibrators
- Implementation in the clinic
  - Fillable, standard geometries
  - Stable (long-lived, chemical) surrogates linked via primary standards to imaging agents
  - NIST worked to develop calibration phantoms for PET and SPECT

Impact

- Crucial for regulatory compliance
  - Medical applications
  - Trade
- Critical to advance technology and applications
  - 10 % accuracy needed for quantitative molecular imaging (requires ≈ 1 % uncertainty on administered activity)
  - Absolute requirement to enable
    - Imaging-based multicenter trials (development of new drugs)
    - Accurate monitoring of disease (from cancer to Alzheimer's) progression is impossible, complicating efficacious intervention

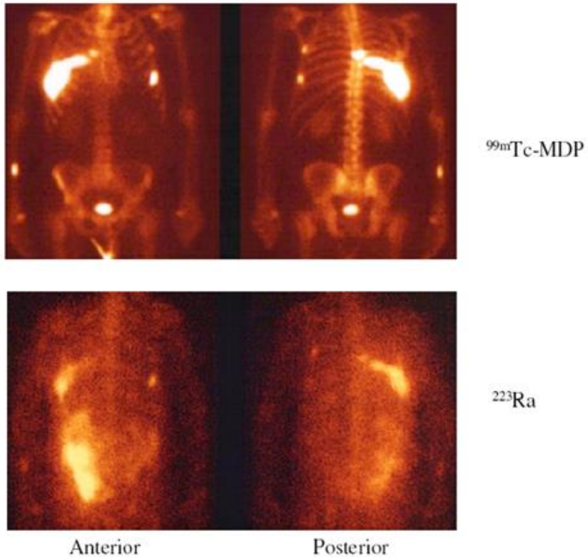
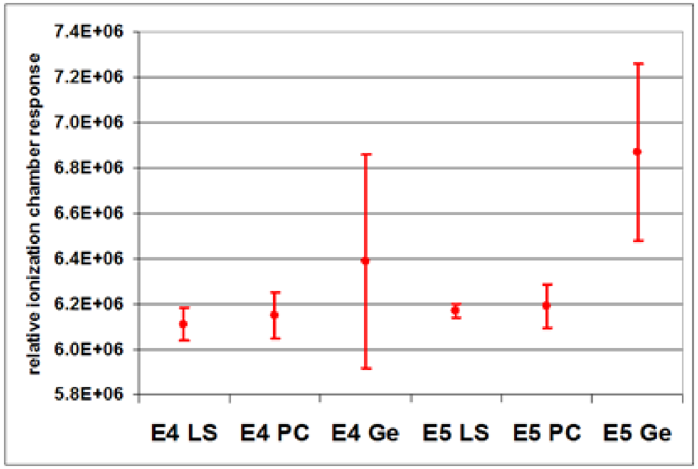


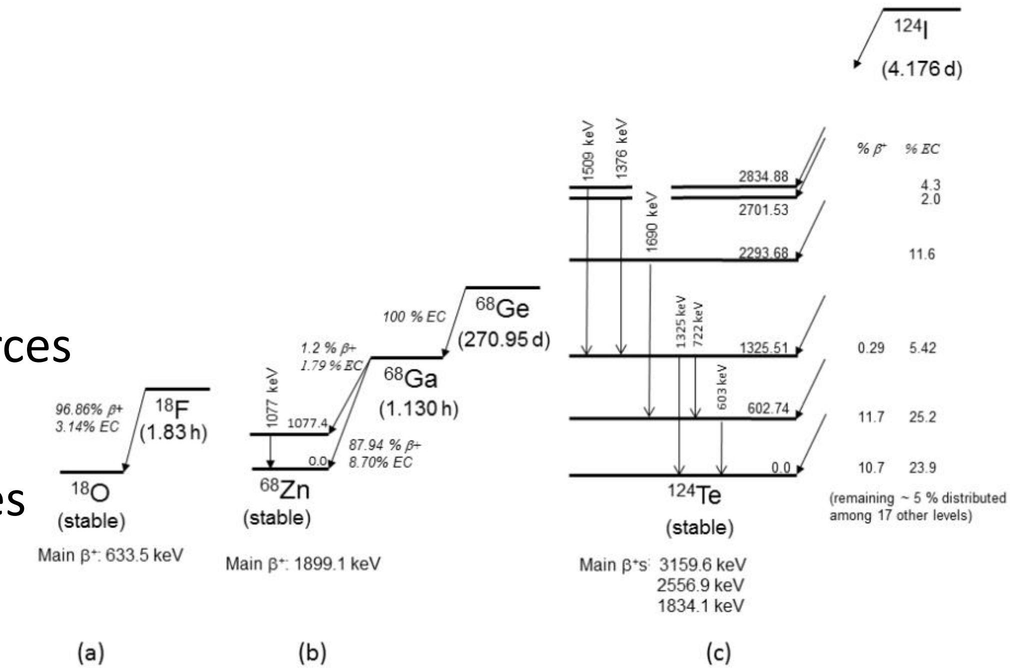
Figure 4. Scintigraphic images demonstrating accumulation of ^{223}Ra in skeletal lesions in accordance with ^{99m}Tc-MDP uptake . Radium image taken 24 hrs post injection, hence radium excreted and in transit in the large bowel is evident in the lower left image. (Image quality is dependent on dose administered: 750 MBq ^{99m}Tc-MDP vs. 12 MBq ^{223}Ra)



Methods for New Radionuclides

New and Improved Standardization

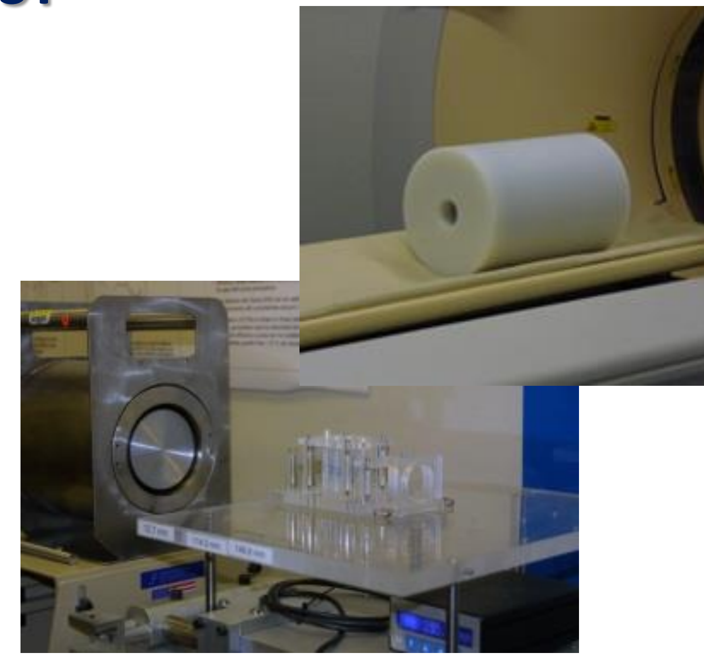
- Evolutions and modifications of current methods
  - Mass spec
  - TDCR
- New/rare nuclides
  - Surrogates for clinical sources
  - Short-lived isotopes
  - Low concentration isotopes
- Improving availability of infrastructure
  - Improved facilities
  - New "real world" facilities
- Need to establish in anticipation of the unknown

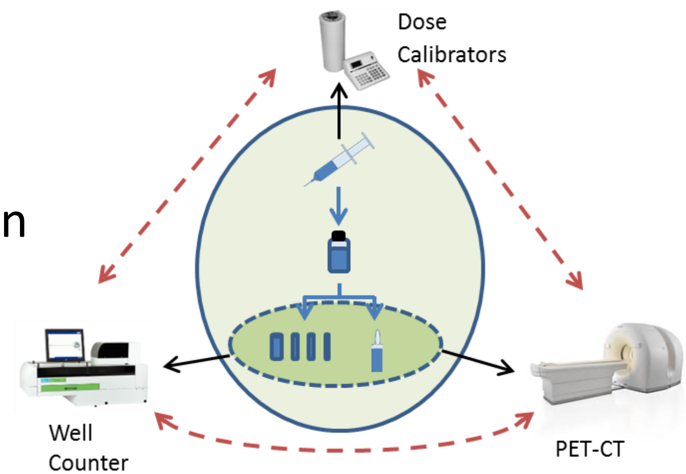


Meeting the Need

Example from NIST

- Input from stakeholders
  - Driven by emerging applications
  - Near Term: ^{64}Cu, $^{82}Sr/^{82}Rb$, ^{124}I (in progress)
  - Medium term: ^{11}C, ^{13}N, ^{15}O
- Increased attention by regulators
  - End user: appropriate secondary standards
  - Collaboration facilitates trade
- NIST activities
  - Primary standards with multiple techniques (usually LTAC, TDCR, CNET)
  - Secondary standards for clinical instrumentation
  - Positron emitters: links between short-lived radionuclides and long-lived surrogates
  - Primary standards for very short lived nuclides (^{11}C, ^{13}N, ^{15}O) needs portability for radiopharmacy





Impact

- Crucial for regulatory compliance
  - Medical applications
  - Environmental cleanup
  - "Repopulation"
  - Policy decision making
- Improvements in accuracy
  - Increased acceptance by regulators
    - Imaging useable as a tool
    - Sound decisions
  - Enhanced safety
    - Higher accuracy leads to better decisions
    - Confidence
  - Lower costs