Radionuclide Dosimetry - 2: Measurement of Radioactivity by 3-D Imaging for Estimating Dose: Use of PET and SPECT

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SPECT and PET

- PET and especially SPECT are low resolution. Therefore, end result of imaging:

1) is macrodose (spatial average over volume of interest, for ex. over a tumor or organ) and
2) is dose distribution on a millimeter scale.
3) is not microdose, i.e , is not cellular or inter-cellular dose.

Absolute or Relative Activity

- Absolute activity is needed to generate un-biased dose estimates.
- Relative activity is sufficient:

1) for a self-contained study of correlation of dose with response.
2) if only a distribution is needed and normalization to dose will be provided.

SPECT versus PET

- PET delivers absolute activity, but appropriate radionuclides with multiple-day half lives are hard to find.
- SPECT probably needs at least attenuation correction. This correction, in turn, probably requires a multi-modality (PSPECT/CT) imager or SPECT-CT registration.

PET Radionuclides for Dosimetry

Radionuclide	Halflife	Comments
I-124	4.2 d	High-energy γ's in cascade with β's. Complication.
Y-86	14.7 h	Surrogate for Y-90. Needs correction.

Possible PET Radionuclides for Dosimetry

Radionuclide	Halflife	Comments
Cu-64	12.7 h	
Zr-89	3.27 d	Under consideration.

PET Radionuclides for Dosimetry (2)

- References for I-124 procedure:
  Pentlow et al. JNM 1996;37:1557-62.
- References for Y-86 correction:
  Pentlow et al. Clin Pos Im 2000;3(3):85-90.
- Reference for Cu-64:
  Philpott et al. JNM 1995;36:1818-24.
- Reference for Zr-89 labeling:
  Verel et al. JNM 2003;44:1271-81.

Common SPECT Radionuclides

Radionuclide	Gamma energy	Comments
I-131	364 keV	
In-111	247 keV, 172 keV	Surrogate for Y-90

Conversion Factor

To obtain absolute activity, one needs a conversion factor from reconstructed counts to activity (MBq/counts per second, for example).

This conversion factor is frequently called the system sensitivity.

PET Conversion Factor

1) Usually uses tomographic imaging of a uniform cylinder of a given activity density.
2) Image reconstruction requires same attenuation compensation and scatter correction as that used for the patient.

SPECT Conversion Factor

Planar imaging of a point source in air may be used.

1) For this, and tomographic imaging of a sphere, spatial location is usually assumed to be unimportant.
2) The correct approach for point-source imaging (or simulation) is not obvious:

SPECT Conversion Factor using a Point Source

Using a point source, it seems obvious that the reconstruction program, after attenuation compensation and scatter correction, needs to distribute one projection image count over the image space so as to yield an increment of a total of one among the reconstructed voxels.

SPECT Conversion Factor using a Point Source (2)

Ljungberg et al, JNM 2002;43:1101-9

1) Were after "narrow-beam" geometry.
2) Simulated a point source in a "scatter- and attenuation-free environment" with septal penetration not allowed.
3) Then used total counts.

SPECT Conversion Factor using a "Point" Source (3)

Gonzales-Trotter et al, IEEE TNS 2001;48:65-73

1) Calculated the geometric sensitivity of the collimator.
2) Given that sensitivity, they measured the crystal efficiency in air using a 1cm x 1cm vial containing I-131.
3) Having both sensitivity and efficiency, they calculated the equivalent of a conversion factor.

SPECT Conversion Factor using a Point Source (4)

Recall that:

The geometric efficiency is the fraction of impinging gamma rays that get through the collimator.

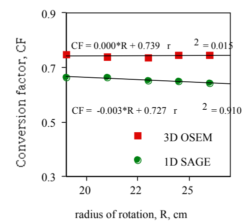
The crystal efficiency equals the probability of a photopeak count, given a normally-incident gamma ray of the appropriate energy.

SPECT Conversion Factor (3)

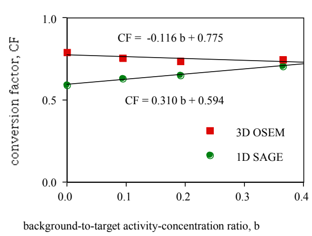
Tomographic imaging of

1) a uniform cylinder, or of
2) a geometry simulating the desired target(s), for example, a sphere inside an elliptical cylinder.
3) Image reconstruction requires same attenuation compensation and scatter correction as that used for the patient.

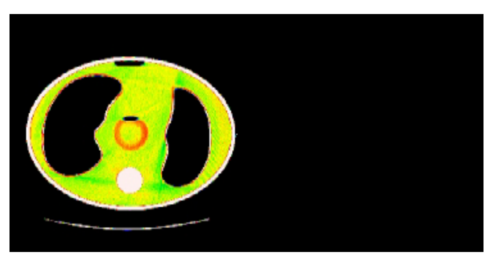
Comparison of CF Dependence on SPECT Radius of Rotation for Two Models



Comparison of CF Dependence on Background Activity Level for Two Models



Test Phantom: 100-cubic-centimeter Sphere Centrally-located below Lungs in Anthropomorphic Phantom. No background activity.



Bias and Noise Comparison for Total Activity in Sphere using High-energy(HE) and Ultra-high-energy (UHE) Collimation

- 3D OSEM

activity bias

UHE: -5.2% ± 8.6%

HE: -7.3% ± 5.7%

- 1D SAGE

activity bias

UHE: -10.7% ± 2.4%

HE: -4.3% ± 7.4%

Macrodose definition

The macrodose is the energy deposited in a volume, divided by the mass of that volume.

Appropriate Volume (1)

For a tumor, appropriate volume may be:

1) Entire volume of tumor as defined on CT
2) Proliferating volume as defined by high uptake with therapeutic radiopharmaceutical, or with proliferation-specific radiopharmaceutical.

Appropriate Volume (2)

However, especially for a bone metastasis, and even for other occult metastasis, the lesion may not be seen on CT, so:

1) it may not be possible to define its volume from CT
2) one may need to define the volume on the SPECT image, and the accuracy may be low.

Appropriate Volume (3)

Also:

1) Tumor volume is usually assumed to be constant during time radiation dose is delivered
2) But, in non-Hodgkin's lymphoma treated with I-131-Lym 1, superficial cancerous lymph nodes decreased in volume during therapy. The dose correction was more than a factor of 2 in >50% (Hartmann-Siantar et al. JNM 2003;44:1322-9).

Appropriate Volume (4)

Proliferation-specific radiopharmaceuticals:

1) Require an additional scan.
2) Often use DNA synthesis as a marker since a high proliferation rate implies a high rate of DNA synthesis {Schwartz et al, JNM2003;44:2027-32}.
3) Examples of DNA synthesis-radiopharmaceuticals are 131-I-iododeoxyuridine (131IdU) and radiolabeled thymidine (TdR).

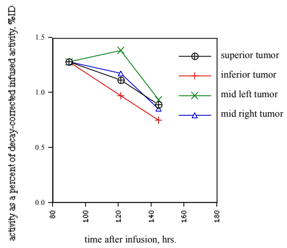
Time Course

1. From a complete series of tomographic images obtained during therapy.
2. From a similar series during evaluation with the assumption kinetics during therapy are same and activity scales by ratio of administered activities.
3. From an evaluation conjugate-view time series with activity-magnitude scaling based on a single intra-therapy SPECT measurement.

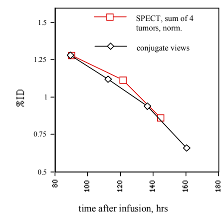
Time Course by Scaling Evaluation-conjugate-view Composite-tumor Time-activity Curve by Intra-therapy SPECT Activity Estimates for Individual Tumors

- Method explained in Koral et al.Cancer Biother&Raiopharm 2000;15(4):347-355.
- Conjugate-view activity is first distributed among component individual tumors corresponding to their volume.
- Scaling factors are used to get final doses.

Time Course for Different Individual Tumors is Similar. Intra-therapy SPECT Evaluation



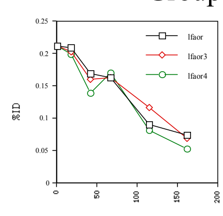
Comparison of Time Course with Intra-therapy SPECT (Sum of 4 Tumors) versus Evaluative Conjugate-Views (Corresponding Composite Tumor)

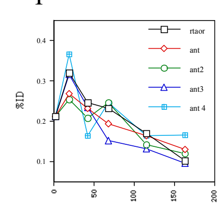


Activity Time Course

- Conclusion is that evaluation activity time course for a composite tumor from conjugate views matches the average time course for individual tumors from intra-therapy SPECT.
- However, in another patient, tracer SPECT indicates activity-time-course variation between individual tumors:

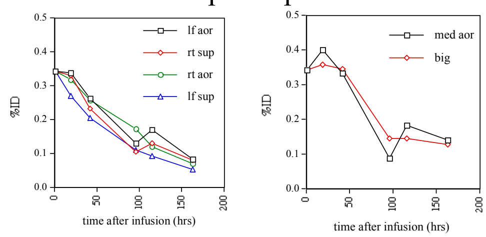
By Tracer SPECT, Tumors Fell into Two Groups for pt 43





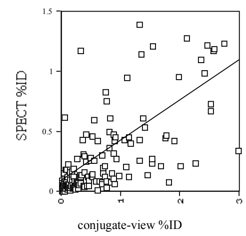
- Time activity shape was different. Within each group, normalization at earliest time point.

By Tracer SPECT, Tumors Fell into Two Groups for pt 64

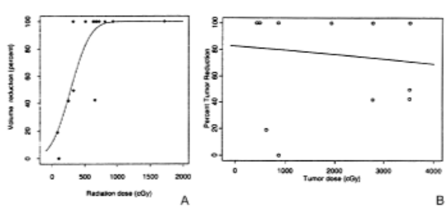


- Time activity shape was different. Within each group, normalization at earliest time point.

Correlation of Radiation Dose from Intra-therapy Hybrid SPECT versus that from Evaluative Conjugate Views. Individual Tumors.



Volume Reduction versus Radiation Dose. Small (<10g) Individual Tumors in PR Patients

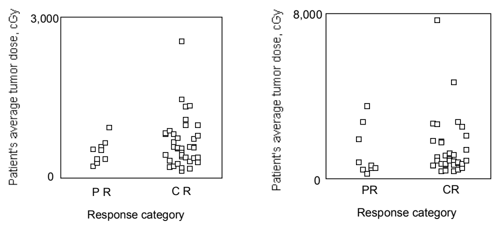


A) With hybrid SPECT. B) With conjugate views.

Volume Reduction versus Radiation Dose. Individual Tumors in PR Patients (2)

- Reference is Koral et al.Cancer 2002;94(4S):1258-63.
- Tentative conclusion is that for this application, the hybrid SPECT method gives better results than conjugate views alone.

Patient's Average Tumor Radiation Dose.
Versus his/her Response (PR or CR)



A) hybrid SPECT
Mean different? p=0.18

B) conjugate views
p=0.25

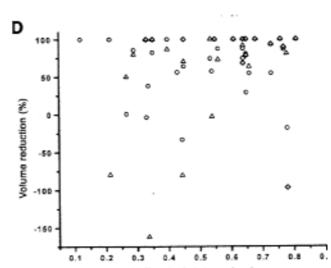
Patient's Average Tumor Radiation Dose. Versus his/her Response (PR or CR) (2)

- Reference is Koral et al.JNM 2003;44:457-64.
- Tentative conclusion is that for this application, the hybrid SPECT method gives only marginally better results than conjugate views alone. (Only a large hybrid average dose is effective for prediction.)

Tumor Dose Uniformity Correlates with Volume Reduction

- Post-therapy volume reduction correlates with tumor uniformity. r = 0.37, p=0.06.
- Reference is Sgouros et al. JNM 2003;44:260-268.
- Uniformity was measured by SPECT and assessed by min/max dose.

Uniformity versus Volume Reduction (2)



3D Patient-specific Dose

- The following slides are courtesy of Dr. Yuni Dewaraja, University of Michigan.
- Abstract reference is Dewaraja et al. JNM 2004;45(5):54P.

Accurate dose estimation in I-131 radionuclide therapy

- I-131 radionuclide therapy studies (RIT, MIBG) have not shown a strong dose-response relationship
  - possibly due to inaccuracies in activity quantification and dose estimation.
- The goal of the present work was to establish that accurate dosimetry is possible.
  - 3D SPECT combined with 3D patient-specific dosimetry
- In the future, the 3D methods will be used to potentially establish a dose-response relationship.

3-D SPECT reconstruction

- 3D OSEM reconstruction included
  - Depth dependant detector response
  - Patient specific attenuation correction
  - Triple energy window scatter compensation
  - Counts to activity conversion based on imaging a known activity hot-sphere in a warm background ellipsoid phantom

3D patient-specific dosimetry

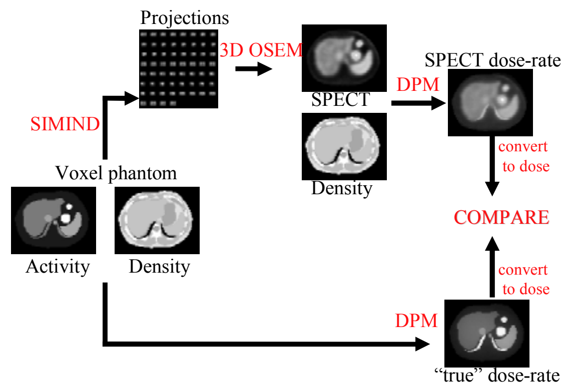
- Monte Carlo dose calculation using the new DPM (Dose Planning Method) code
  - code from external beam therapy adapted here for internal therapy
  - fast, validated
  - inputs are
    - co-registered SPECT image and CT density map.
    - masks defining tumors and organs
  - output is
    - 3D dose-rate distribution
      tumor dose-volume histograms, average dose

Simulation studies: evaluation of quantification and dosimetry

- Voxel phantom with tumors in abdominal region
- Realistic activity map based on RIT patient data
  - relative concentration: tumors, 25; blood, 12; kidney, 20; liver, 7; lung, 7; spleen, 13; rest of body, 1

Two slices of the voxel phantom activity map

Phantom-based evaluations



Phantom based evaluations

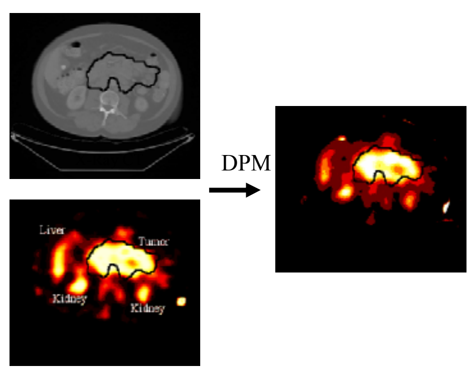
Activity quantification

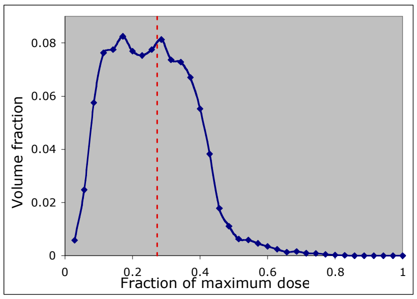
Organ	True activity Mbq	SPECT based mean activity Mbq	Error %	Relative standard deviation %
7 cc tumor	2.9	1.8	38.4	9.4
16 cc tumor	6.4	5.9	7.9	2.2
59 cc tumor	23.0	20.6	10.3	1.2
135 cc tumor	52.8	53.0	-0.5	0.9
liver	205.2	200.9	2.1	0.4
kidney	152.5	138.3	9.3	0.5
spleen	72.5	70.2	3.2	0.7

DPM 3D dosimetry

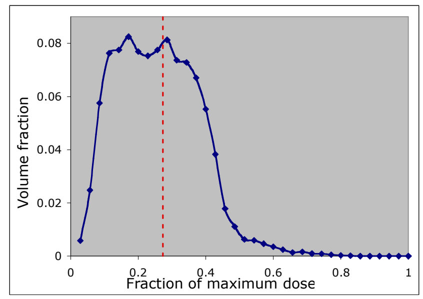
Organ	ÑTrueÓ dose cGy	SPECT based mean dose cGy	Error %	Relative standard deviation %
7 cc tumor	1308.8	897.8	31.4	8.0
16 cc tumor	1344.8	1274.1	5.3	1.9
59 cc tumor	1450.0	1356.7	6.4	1.0
135 cc tumor	1458.3	1493.3	-2.4	0.8
liver	500.2	502.3	-0.4	0.3
kidney	1160.1	1098.6	5.3	0.4
spleen	812.7	812.6	0.0	0.6

3D Dosimetry: RIT Patient Study





Dose Volume Histogram for Patient



Patient study: Conversion of SPECT-based 3D dose-rate to dose

- Only one SPECT time point was available
- Planar imaging time-activity curves used for residence times
  - total body residence time: must account for limited SPECT field of view
  - tumor residence time: accuracy can be improved by combining results of conjugate-view and quantitative SPECT at the single time point

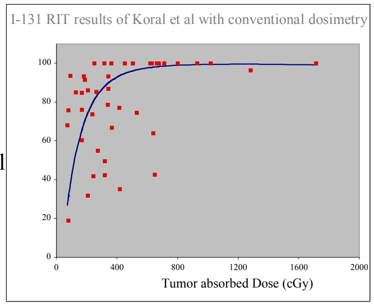
Patient example: comparison of 3D and conventional dosimetry

	Average tumor dose (cGy)	
	3D DPM	***Conventional***
Tumor -->Tumor	485.1(88%)	487.7 (95%)
Rest of body --> Tumor	69.0 (12%)	28.1 (5%)
Total	554.1	515.9

- Compared with DPM, conventional dosimetry significantly underestimates the rest of the body contribution to tumor dose in this patient.
- DPM average tumor dose is 7% higher than conventional

Future Work

- Goal is to carry out 3D SPECT reconstruction followed by patient specific 3D dosimetry for several patients and re-evaluate relationship between dose and volume reduction



Summary

- Phantom studies showed that accurate I-131 dose estimation is possible with 3D methods for SPECT reconstruction and dosimetry.
  - Errors better than 6.5% for tumor/organs down to 16 cc
- When applied to a patient, the average tumor dose was 7% higher with the new calculation compared with conventional MIRD-based calculation.
  - Possibly due to more accurate calculation of the rest of the body photon dose contribution
- New 3D methods will be applied to existing I-131 RIT patient data and dose-volume reduction relationship will be re-evaluated.