Available SRT Dosimetry Methods/Approaches

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Disclosures

Consultant: Bayer, Roche

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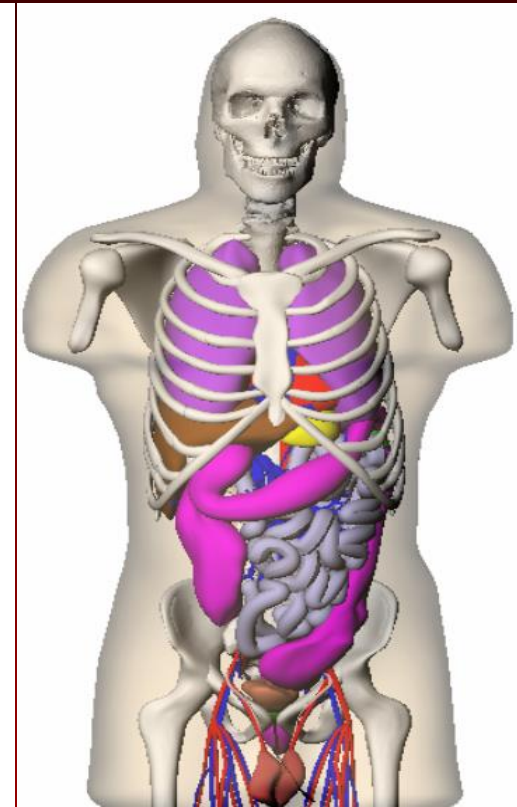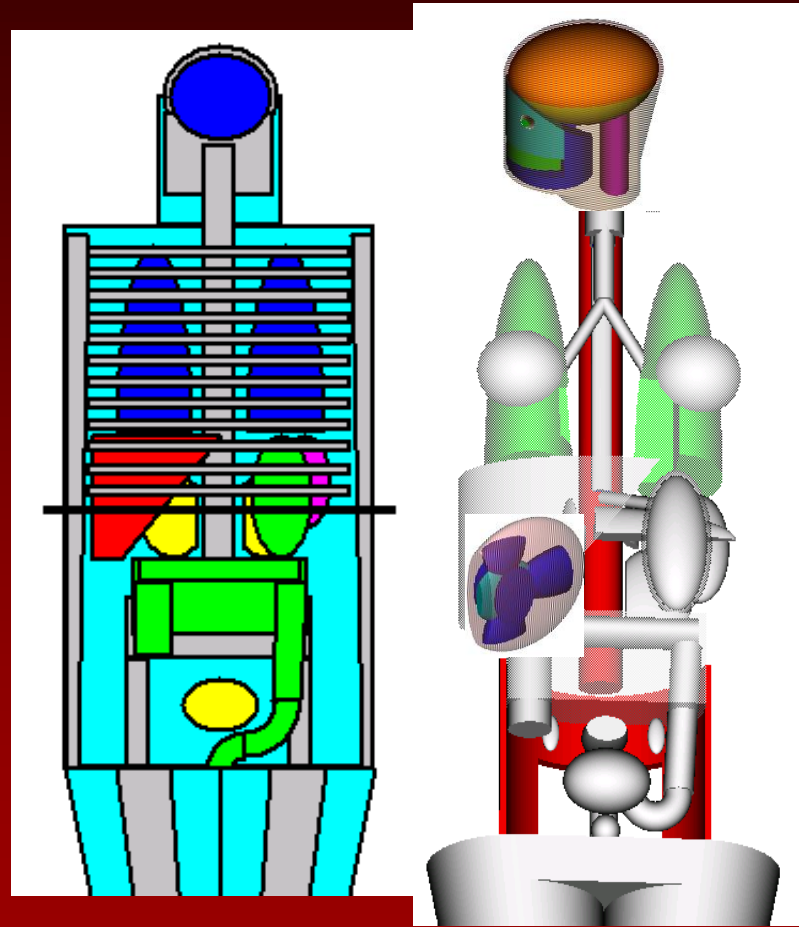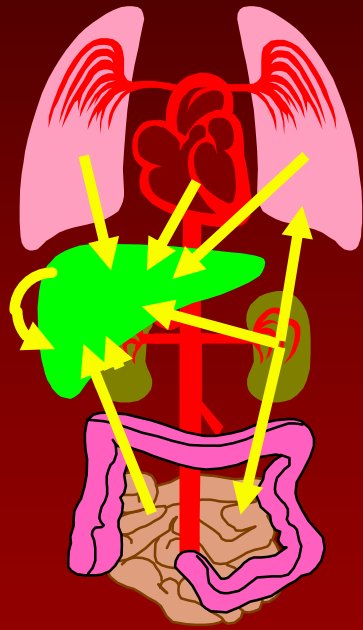Founder: Radiopharmaceutical Imaging and Dosimetry (RAPID), LLC

Biomarkers

- **Select patients most likely to respond**
- **Avoid toxicity**
- **Tumor biopsy**
- **Serum sampling**
- **Genetic and epigenetic marker analysis**
- **Must be rigorously qualified/validated retrospectively or in prospective studies**
- **Standardized**
- **Incorporated in the design of clinical trials**

Dosimetry

- Select patients most likely to respond
- Avoid toxicity
- Quantitative Imaging / Tumor Isotope Imaging
- Blood Sampling / Branch Sampling
- Dose Calculation / Genetic and cytogenetic marker analysis
- Must be rigorously qualified/validated retrospectively or in prospective studies
- Standardized
- Incorporated in the design of clinical trials

Phantoms

Summary of Experience

- RPT dosimetry has used model-based methods appropriate for risk evaluation

- not patient-specific, no accounting for non-uniformity, no accounting for radiobiology

- did not predict toxicity/efficacy

- dosimetry more involved, costly & w/o benefit.

- not essential in RPT planning

- adopt chemo-based dosing.
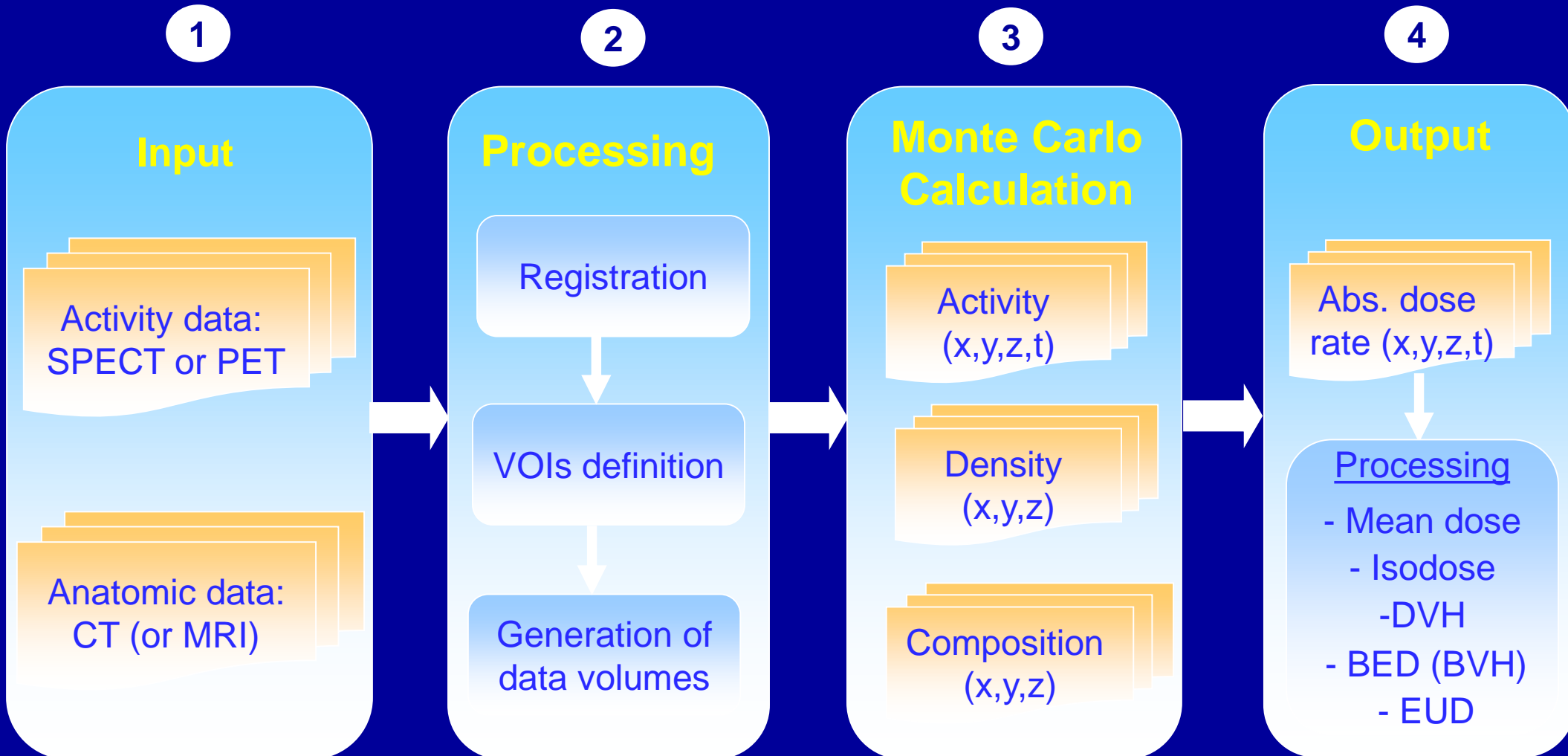
Patient-specific, 3-D dosimetry

3D-Internal Dosimetry (3D-ID)

- Patient specific, using 3-D anatomy and activity data
- Calculates absorbed dose voxel by voxel
- Output dose as mean over chosen volume or DVH

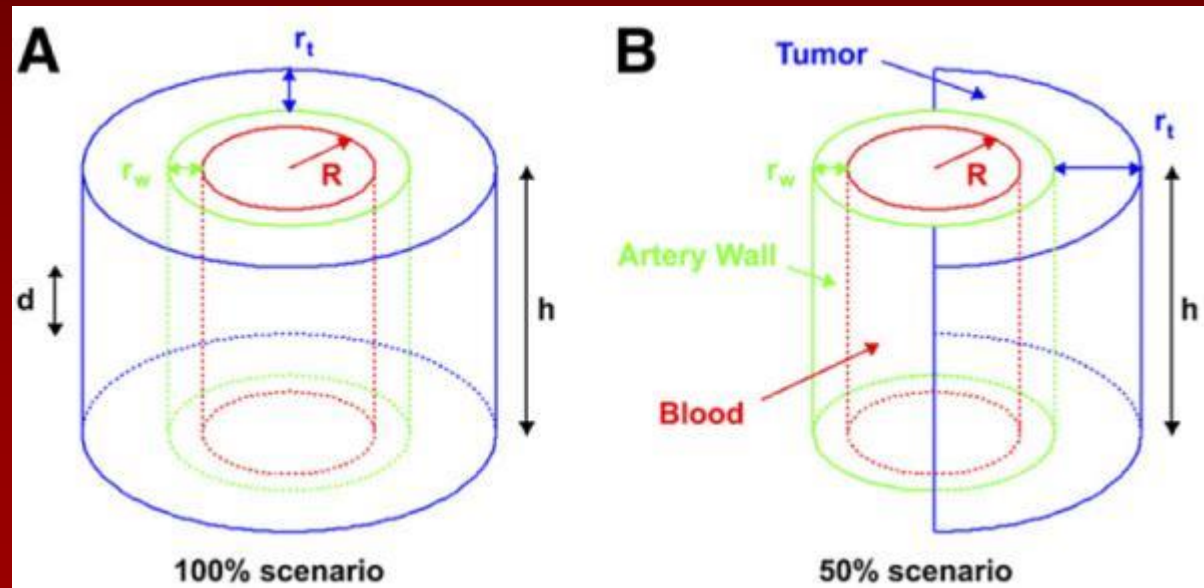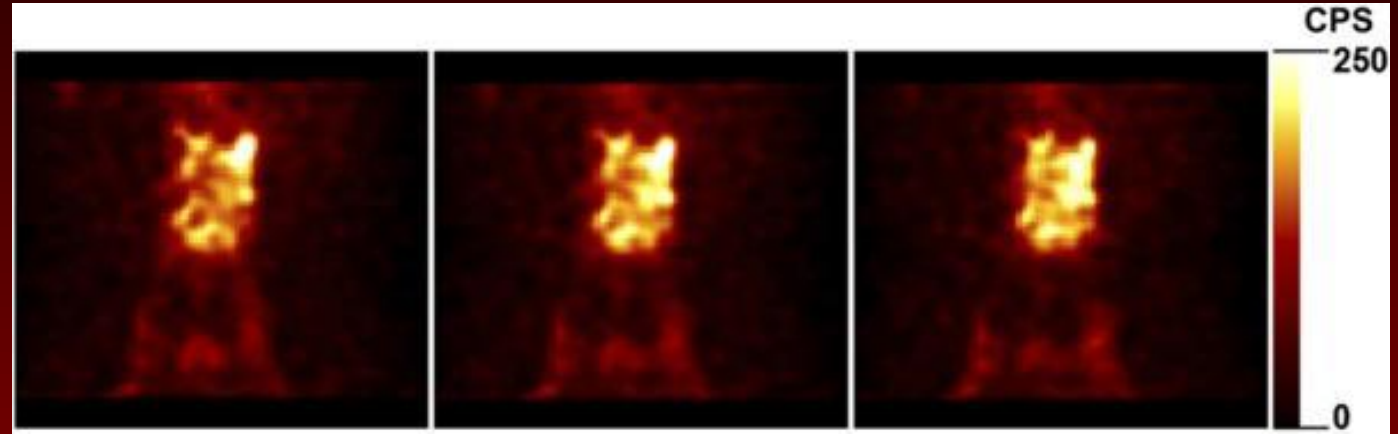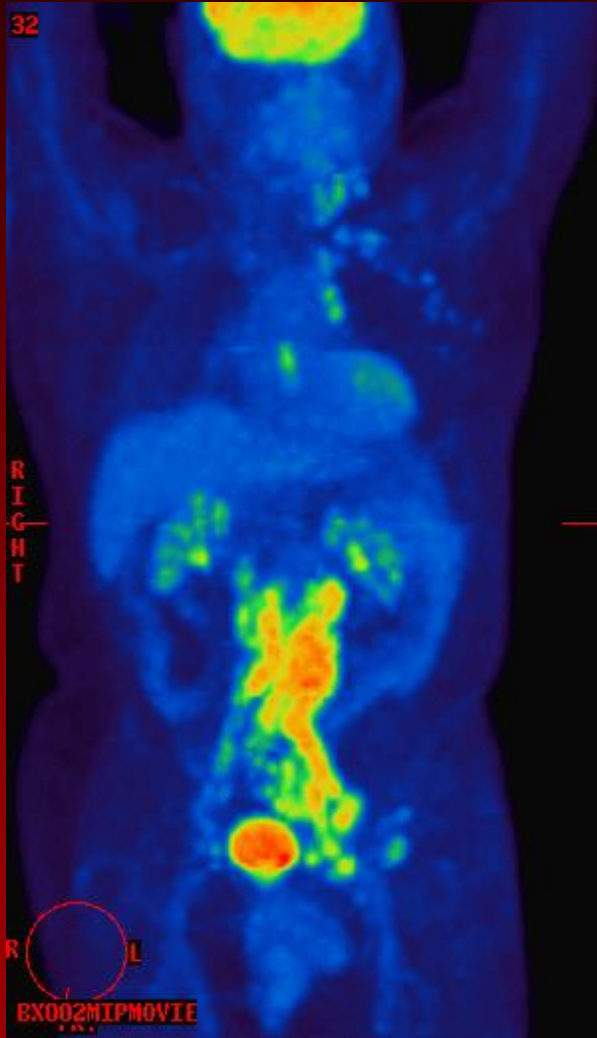## 3D-Radiobiological Dosimetry (3D-RD)

- Integrates Monte Carlo calculation
- Radiobiological modeling: absorbed dose $\rightarrow$ response
- Better predict tumor response and toxicity

Sgouros, et al. JNM '90,
Prideaux, et al. JNM '07
Kolbert, et al. JNM '97

3D-RD Flowchart

1 — **Input**
- Activity data: SPECT or PET
- Anatomic data: CT (or MRI)

2 — **Processing**
- Registration
- VOIs definition
- Generation of data volumes

3 — **Monte Carlo Calculation**
- Activity (x,y,z,t)
- Density (x,y,z)
- Composition (x,y,z)

4 — **Output**
- Abs. dose rate (x,y,z,t)
- Processing
  - Mean dose
  - Isodose
  - DVH
  - BED (BVH)
  - EUD

MIRD Pamphlet 23: Quantitative SPECT for Patient-Specific 3-D Dosimetry in Radionuclide Therapy, JNM 2012

Patient   Simplified model
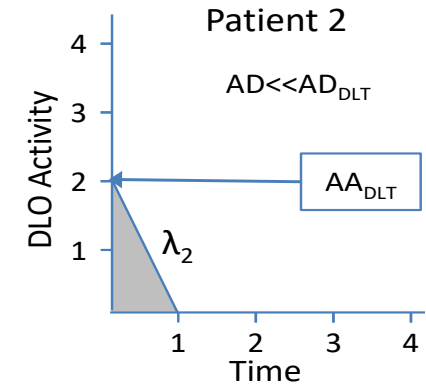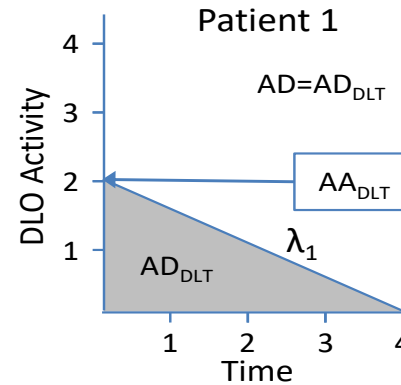

Hobbs, et al. JNM '10

AA vs AD-based Dosing

AA-based dosing

Escalation Study
- AA level 1, 2, etc
- Assess Tox at each AA level
- Identify AA level for Limiting Tox (AA_{DLT})

Patient 1

$AD=AD_{DLT}$

AA_{DLT}

λ_1

AD_{DLT}

DLO Activity vs Time

Patient 2

$AD<<AD_{DLT}$

AA_{DLT}

λ_2

DLO Activity vs Time
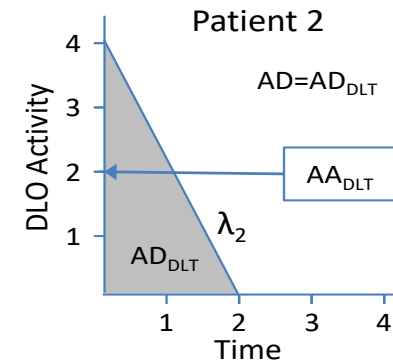
AD-based dosing

Tracer Study (imaging)
- Activity Data SPECT or PET
- Anatomy Data CT (or MRI)
- For each patient
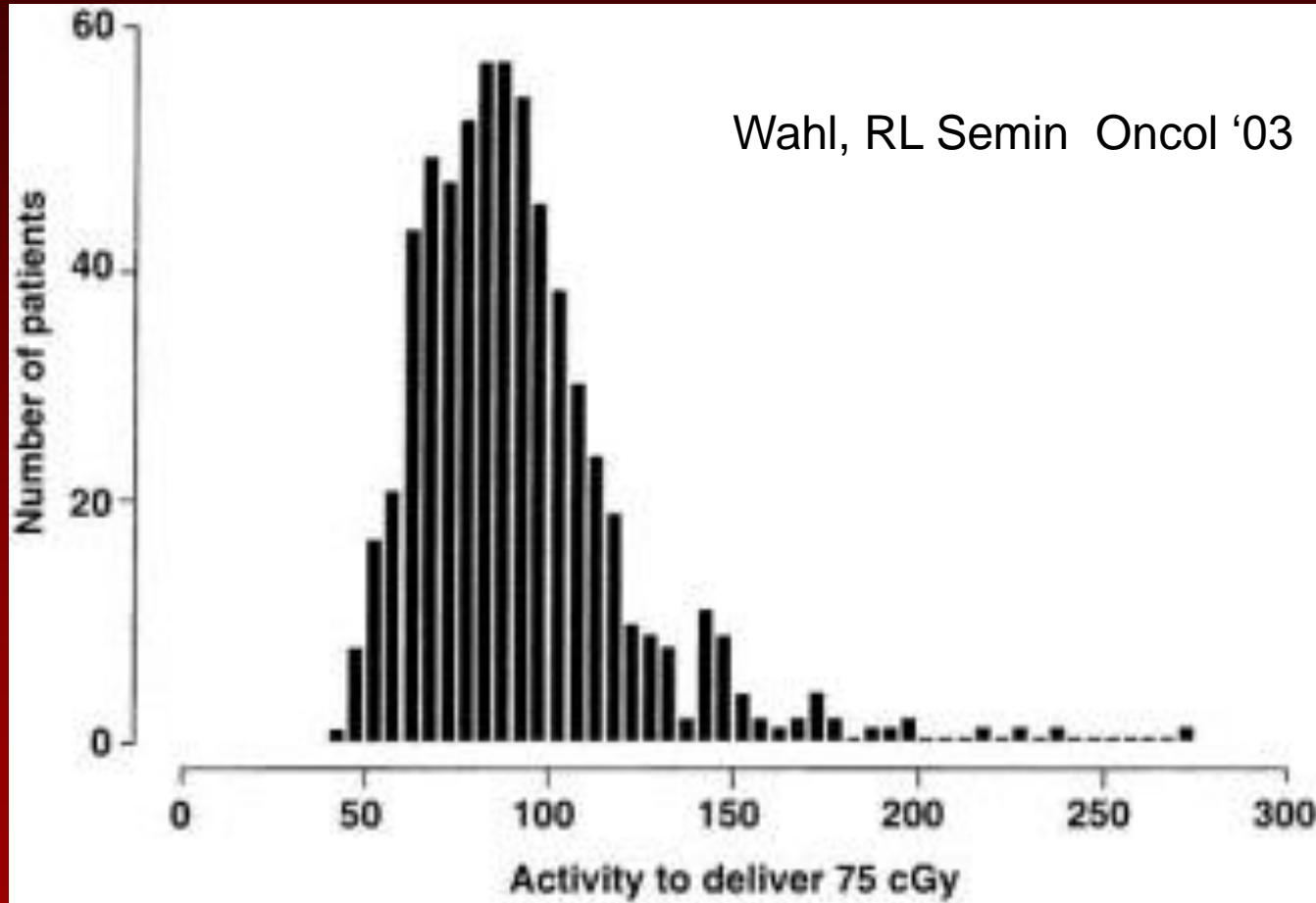
Patient-specific Dosimetry
- Calculate AD
- Determine AA for AD level 1, 2, etc

Escalation Study
- Assess Tox at each AD level
- Identify AD level for Dose Limiting Tox (AD_{DLT})

Patient 2

$AD=AD_{DLT}$

AA_{DLT}

λ_2

AD_{DLT}

DLO Activity vs Time

Admin Activity (AA) vs Abs Dose

Wahl, RL Semin Oncol '03

Treatment Planning Paradigm

Tracer Study imaging

- Activity Data SPECT or PET
- Anatomy Data CT (or MRI)

Other input

- RadioBio Params
- Normal Organ Tolerance (BED)
- from x-beam
- from Phase I study
- M2M model

3DRD

- AD
- BED
- EUD
- AA for AD_{DLT}
- AA for tumor kill

Treat

- To normal organ tolerance
- To tumor kill

PRECISION RPT IMPLEMENTATION

A — **Pre-clinical studies**
Determine the Maximum Tolerated Absorbed Dose (MTAD)
Identify the Dose-Limiting Organ (DLO)

B — **Phase I trial**
Pre-treatment imaging for dosimetry to calculate AA that delivers target AD for each patient

C — **Phase I trial Analysis**
Evalaute AD vs toxicity.
Determine need for treatment planning

D — **Phase II, III trials,**
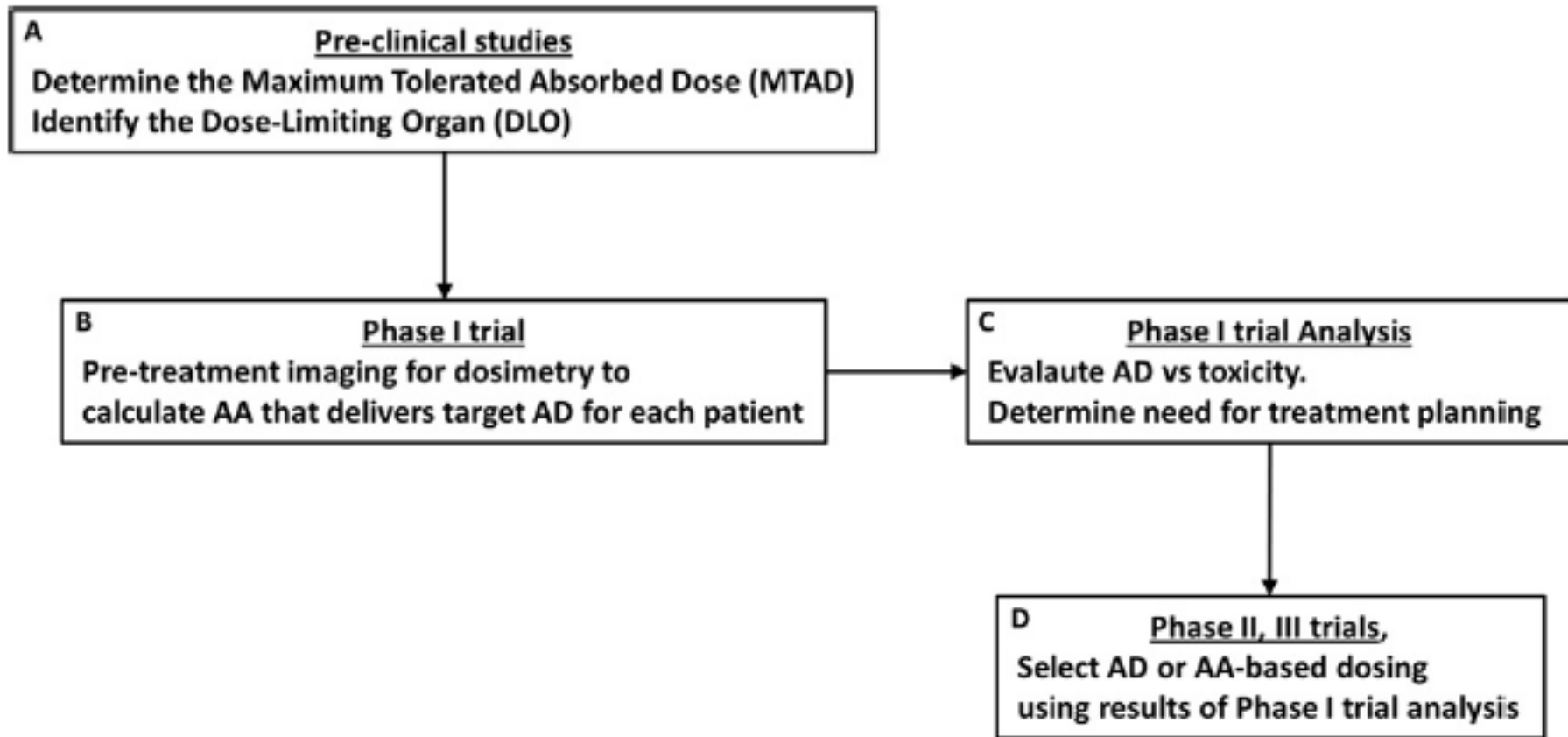Select AD or AA-based dosing using results of Phase I trial analysis

Fig. 1. A simplified approach to precision radiopharmaceutical therapy is illustrated.

Conclusions

- RPT dosimetry is the ideal biomarker
- Mechanism of action is well understood
- Needed measurements are known
- Patient-specific dosimetry tools are available
- Response data from radiotherapy
- Can measure delivery of the therapeutic agent to tumor targets and to normal organs
- Calculate radiation dose to tumors, normal organs and
- Guide escalation protocols and plan treatment

Need to overcome prior history—2nd chance

Implement standardized, validated activity quantification and dosimetry methods in early phase clinical trials to gather rigorous evidence that dosimetry will improve patient care