The MIRDsoft suite, free software for organ-based dosimetry

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EFOMP SMRD2 2025 – Athens, Greece

Introductory perspective

Reaching for the sky – a New Yorker's perspective

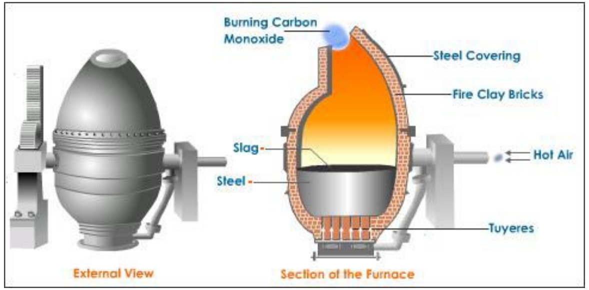
Introductory context

- Building height
  - For much of history, masonry used to support upper floors of building
    - Taller building the thicker the wall, less space to use

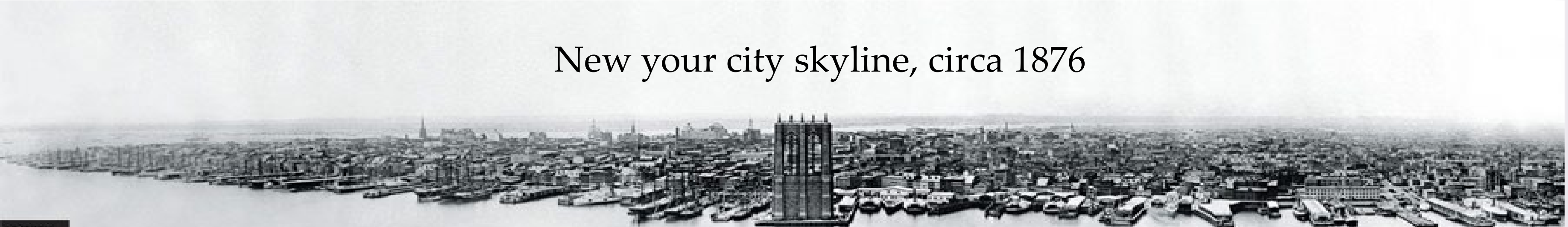
- Wrought iron - introduced mid 1800 wall thickness decreased
  - Material iron had inherent problems, soft and brittle

Introductory context

- 1848 Henry Bessemer process enabled conversion of large amounts of iron to steel
  - Steel great building material: tensile, strong
  - Steel beams can create new building model: "steel skeleton"
    - Taller structure, large windows



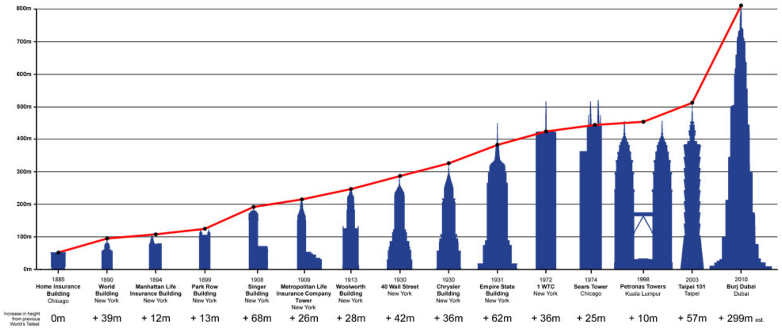
- New age - now building could be built to almost any height
  - **Problem – a lot of stairs!**



New your city skyline, circa 1876

Introductory context

- 1853 – Otis safety elevator unveiled at New York worlds fair
  - 1857 first steam powered elevator installed
  - 1867 Otis Brothers & Co. incorporated
  - 1898 company sold first electric elevators
- After that, the sky's the limit



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MIRD COMMITTEE
MEDICAL INTERNAL RADIATION DOSE
MIRDsoft

MIRDsoft.org collaboration
Adam Kesner, PhD

Introductory context

- 1853 – Otis safety elevator unveiled at New York worlds fair
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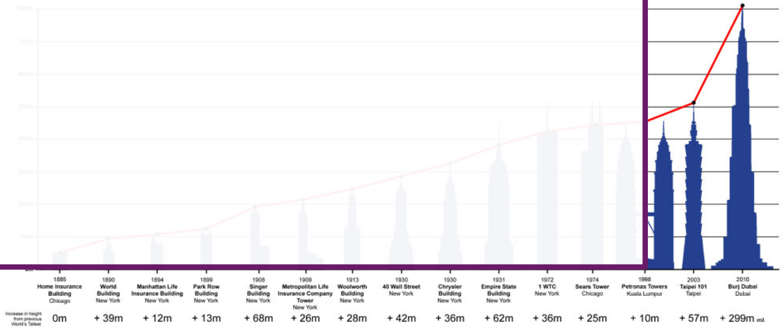
Lesson –
It's easier to reach for the sky when you have a safe, vetted, multifaceted infrastructure to support the aspiration



SNMMI MIRD committee

- New MIRD initiative to advance the state of the art – www.MIRDsoft.org
  - Expand format of community resources

Hardcopy

Dx Dosimetry
- Absorbed dose
- Organ-level

Population-averaged Dosimetry

⟹ +

Software

Tx Dosimetry
- Bioeffect modeling
- Voxel- → Cell-level

Individualized Dosimetry

  - Webspace supports
    - Accessibility, education, translation and standardization
    - Dosimetry community resource

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MIRDsoft.org

- MIRDsoft.org
  - Software distribution
  - Online community
  - Scalable innovation

- Funding support

MIRDcalc is a **NIH/NIBIB U01** (Bolch /Kesner) grant supported project to make free dosimetry tools for the community

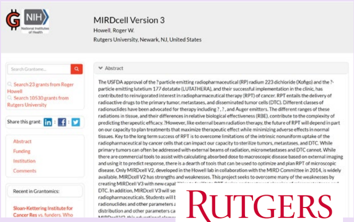
- UF and MSK collaboration
- Funded for 5 years
- NM dosimetry, CT dosimetry, Curvfitting, Monte Carlo
- All **free** for community

UF UNIVERSITY of FLORIDA

Memorial Sloan Kettering Cancer Center

MIRDcell is a **R01** (Howell) grant supported project to build free cellular level dosimetry tool for the community

- Funded for 5 years
- **Free** for community



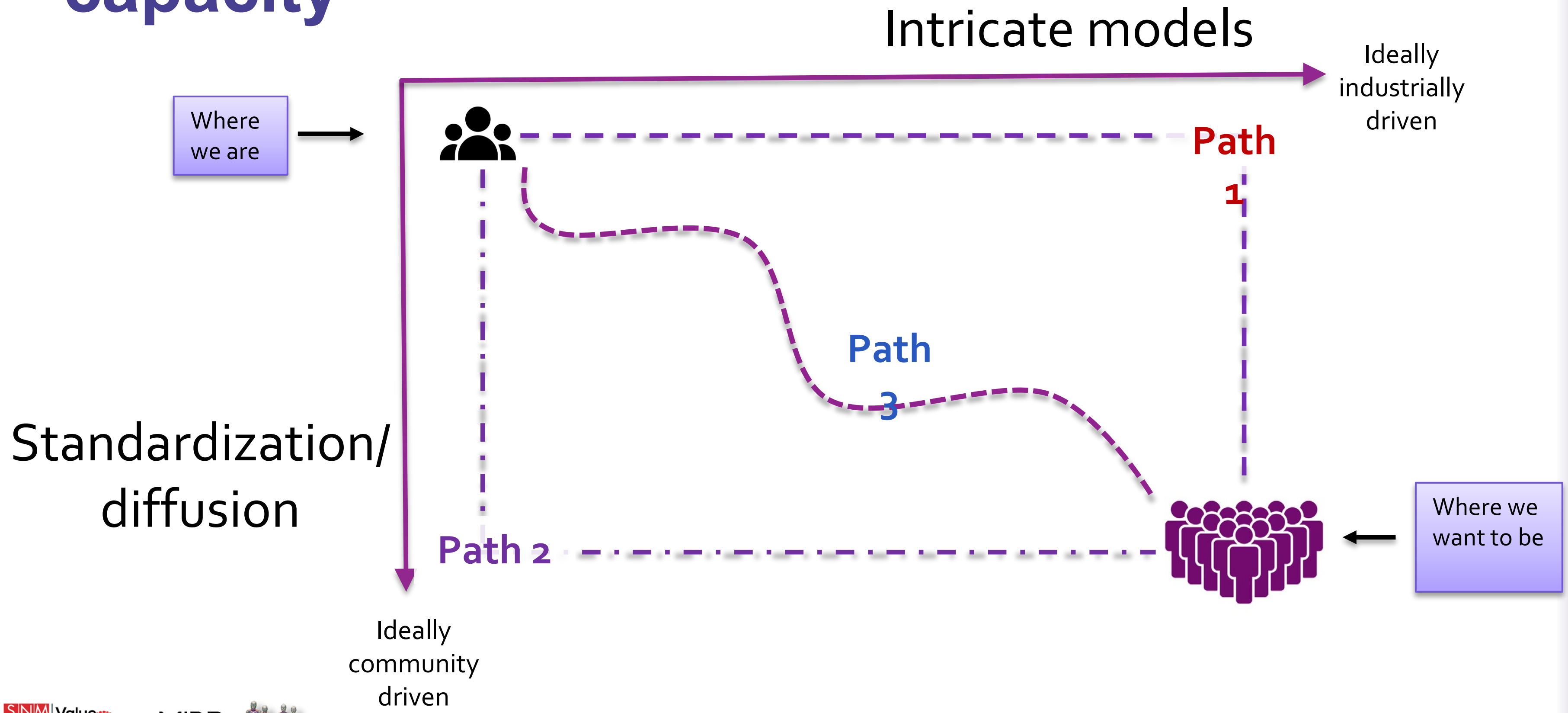
RUTGERS THE STATE UNIVERSITY OF NEW JERSEY

MIRDsoft.org

- Website status: **live**
- Available now
  - **MIRDcalc v1 – organ-level internal dosimetry**
  - **MIRDcell v4 – cell-level dosimetry**
  - **MIRDy90 – microsphere planning worksheet**
  - **MIRDdcm – dosimetry report converter**
  - **MIRDfit – biodistribution fitting/statistical analysis** new
  - **MIRDct – CT dosimetry** new
  - **MIRDspecs – Isotope information database** new
  - **MIRDcalc S value database** new
  - **MIRDpvc – partial volume correction tool** new
- Coming soon
  - MIRDrelease – patient release worksheets
  - Digital phantom libraries – opening to large populations
  - And more…

Note- software not regulatory approved

Current status of personalized dosimetry capacity



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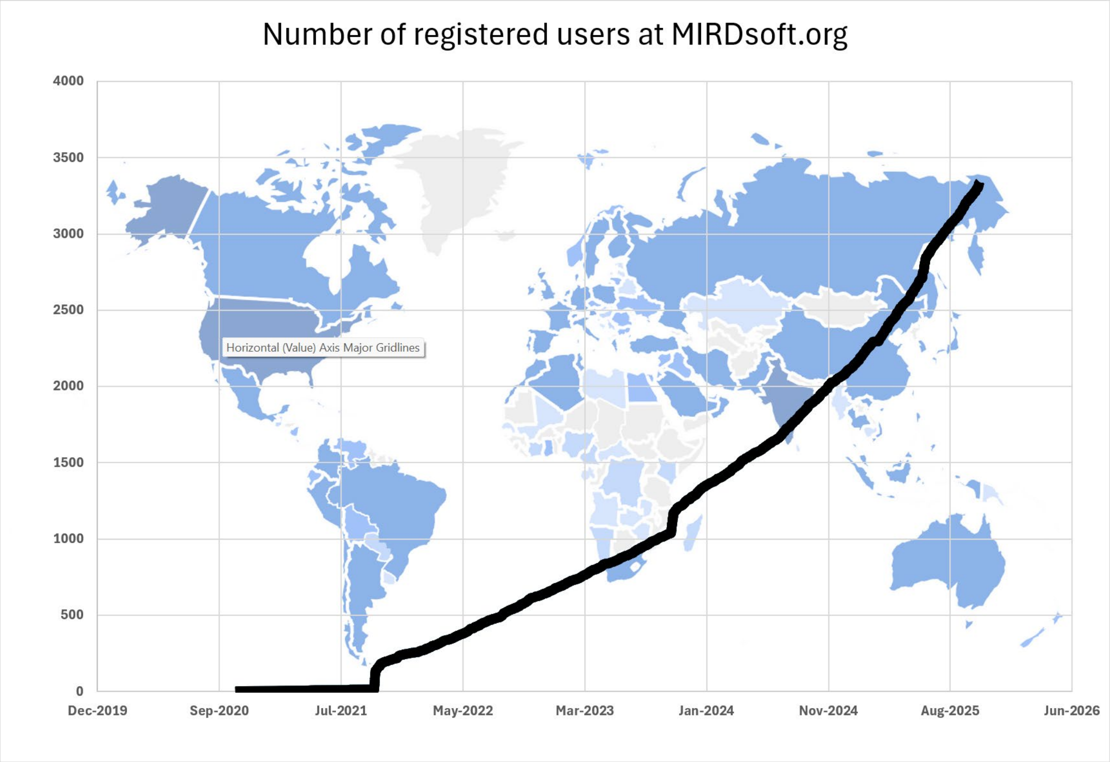


MIRDsoft.org

- We have developed a recipe for creating tools
  - We identify need in the community for tool
  - Most solutions built in Microsoft Excel (with VB code + compiler)
    - Easy to install, navigate
    - Significant capacity for graphics, usability
    - Capable of thorough single screen interfaces
    - All calculations transparent to users
  - UF develops back end (computational phantoms, dose libraries)
  - MSK develops front end (user interface and user interactions)
  - MIRD committee advises and vets
  - Ultimately tools are released freely
    - With aim to help clinicians, physicists, technologists, industry, patients, students, educators

Download

MIRDsoft products

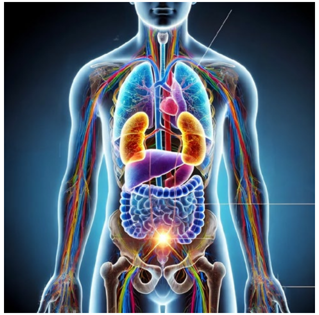
- IDEA: accessible, vetted, easy-to-use software solutions can translate academic ideas and have a large impact on the field.

- SCOPE of MIRDsoft products
  - Complex enough to provide utility in reducing tasks to achieve standardized model processing
  - Simple enough to work as stand-alone solutions

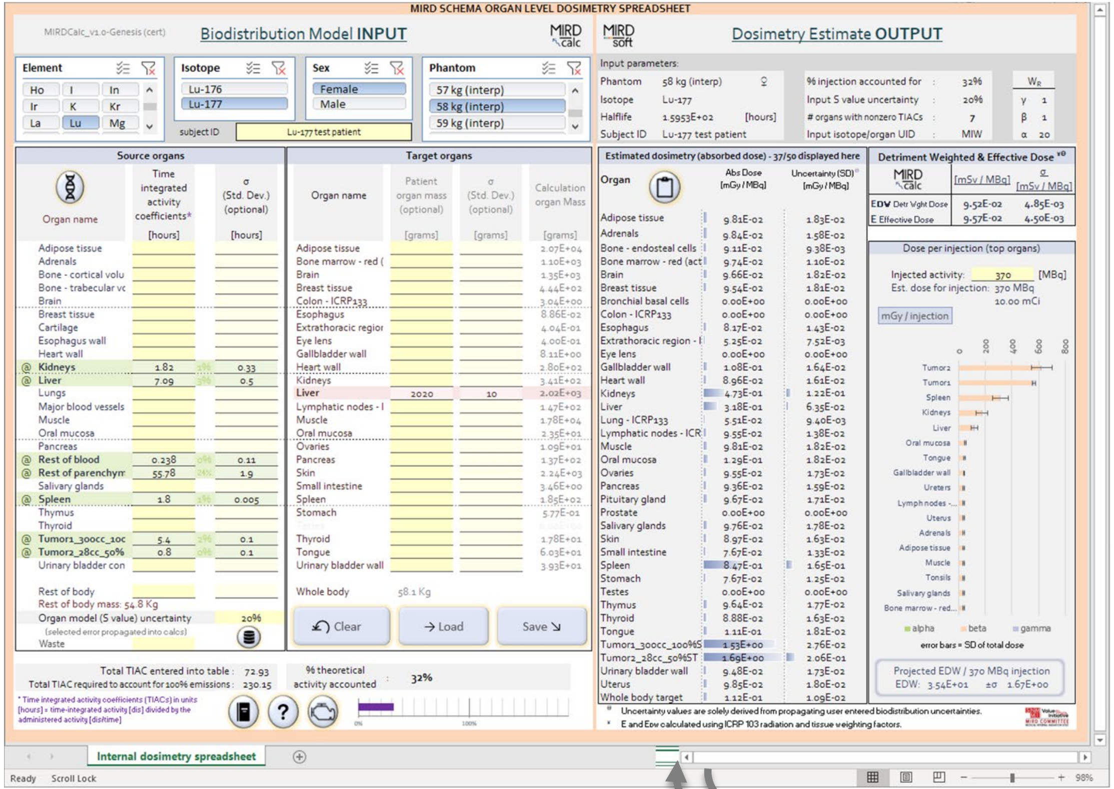
Community software	Commercial software
• Gateway software • Open/Functional/clunky • Can support standardization • Sets bar for commercial software to clear • Can be used to benchmark vendor software	• Develops user experience • Provides user training/support • Regulatory cleared • Can invest in innovation • Can promote use/sales/billing

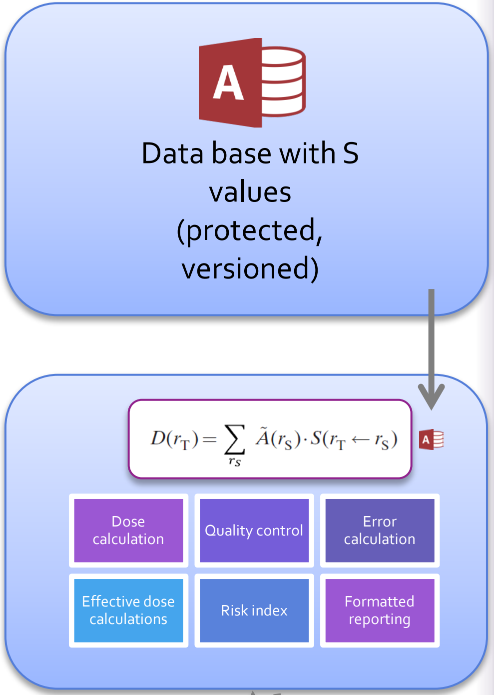
MIRDcalc

- MIRDcalc project
  - Organ-level dosimetry calculation software tool
    - Scope: biodistribution-to-dosimetry
    - Calculations based on MIRD formalism
  - Created to meet needs of community
    - Vetted software
    - Open source
    - Free distribution
  - Looking towards future – a platform to innovate
- MIRDcalc architecture
  - Excel platform
    - Easy to install
    - Intuitive, easy to use
    - Reviewable/open source (supports QC, education, community development)
    - Includes patches with Visual Basic, compiled to .exe



MIRDcalc screenshot





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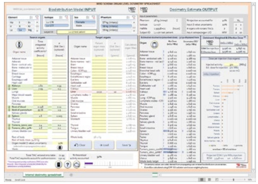
MIRDcalc



- Innovations
  - 81 source regions, 48 target regions, 333 isotopes
  - Single screen user interface
  - Real time processing
  - Graphical quality control checks
  - Modern ICRP digital phantoms
    - Well documented
  - **Spectrum of phantom models (m/f, pediatric to adult, 1 kg steps)**
  - **Dynamic source regions**
    - Rest of body
    - Rest of blood
    - Rest of Parenchyma
  - **(New) blood models**
  - **Uncertainty propagation**
  - **Integrated tumor dosimetry model**
  - Output: Organ dose, effective dose, detriment weighted dose, risk index
  - Thorough case documentation
    - Highly detailed output text files
    - Default screen capture
  - Command line execution
    - Supports batch processing, possibly 3rd party
  - And more…

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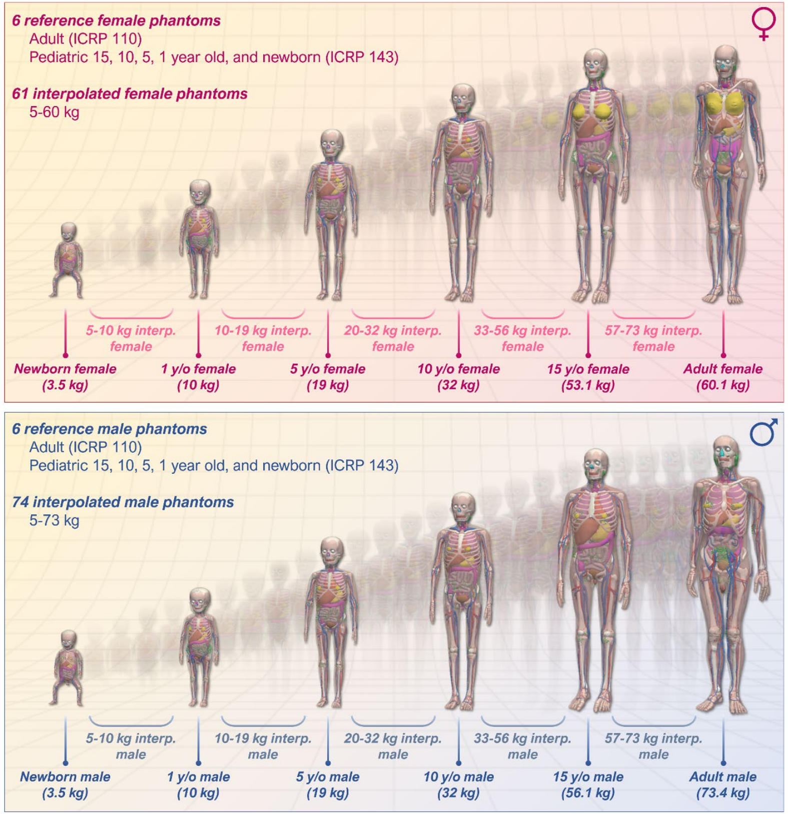
MIRDcalc phantoms

- Phantom models
  - ICRP reference phantoms (reports 110 and 143)
    - Newborn (m/f)
    - 1 year-old (m/f)
    - 5 year-old (m/f)
    - 10-year old (m/f)
    - 15-year old (m/f)
    - Adult (m/f)
  - MIRDcalc interpolation feature
    - Organ masses interpolated linearly relative to whole body mass
    - S values interpolated log-log
  - Additional source regions generated
    - Heart contents
    - Major blood vessels



Visualization of MIRDcalc phantom library

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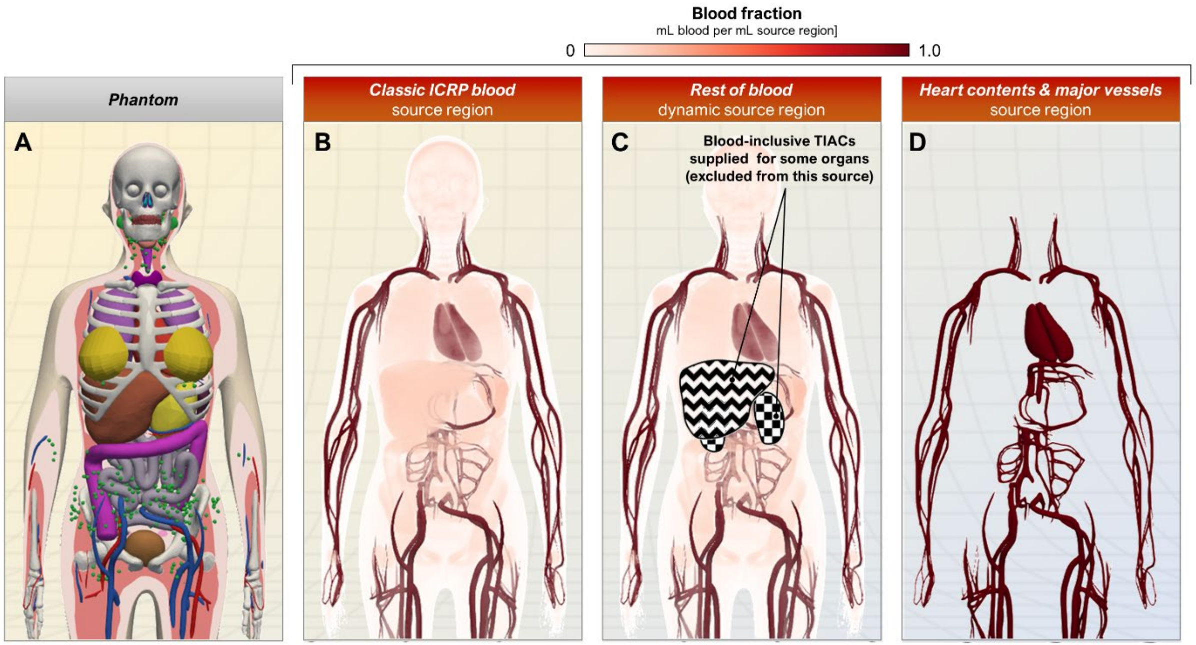
MIRDcalc blood model

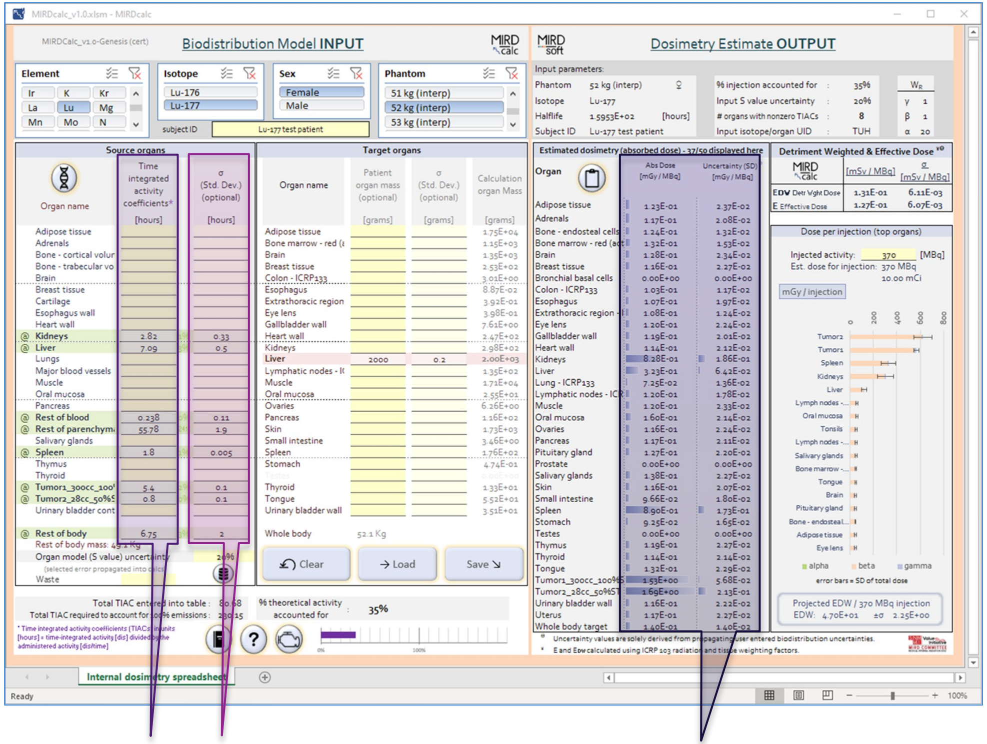
- User has multiple options for modelling blood source activity



MIRDcalc blood source options

MIRDcalc uncertainty propagation

- Significant interest in dosimetric uncertainty estimation
- MIRDcalc can propagate uncertainty in user input into dose estimation
  - TIAC, mass, global S value
- Aligned with
  - EANM guidelines (Gear et al, 2018)
  - GUM guidelines (2008)
- Integrates with MIRDfit, which assists in deriving uncertainty in curve fits



TIACσ$_{TIAC}$

Dose ± σ_{Dose}

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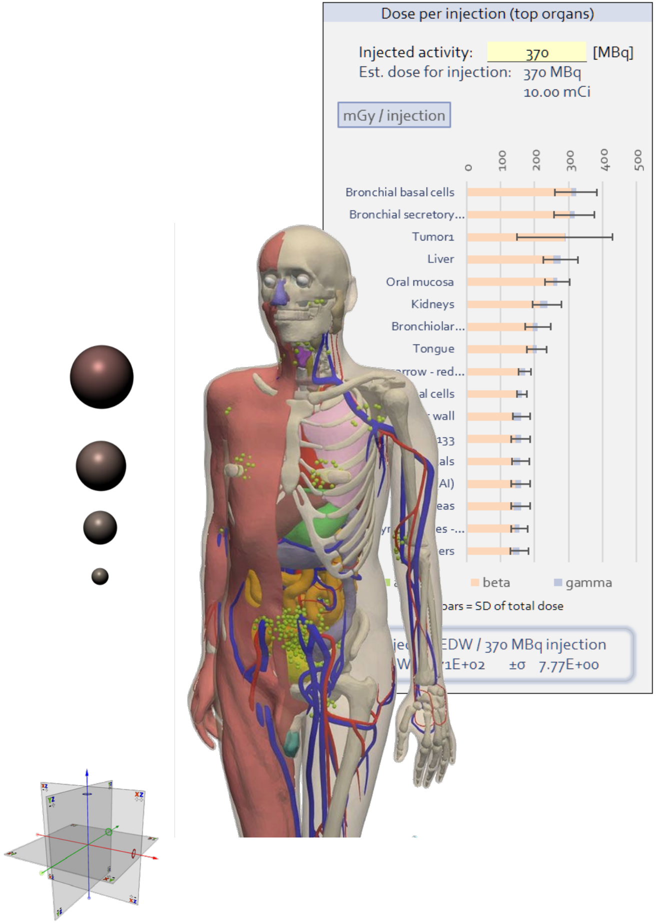
MIRDcalc tumor dosimetry

- MIRDcalc tumor dose model
  - Spherical tumor model
    - Olguin et. al, PMB, 2020
  - Model parameters
    - Sphere volume (optional uncertainty)
    - TIAC (optional uncertainty)
    - Tissue composition (bone/soft tissue)
  - Dosimetry semi-integrated with organ dosimetry
    - Self dose (no cross dose)
    - Integrated TIAC accounting



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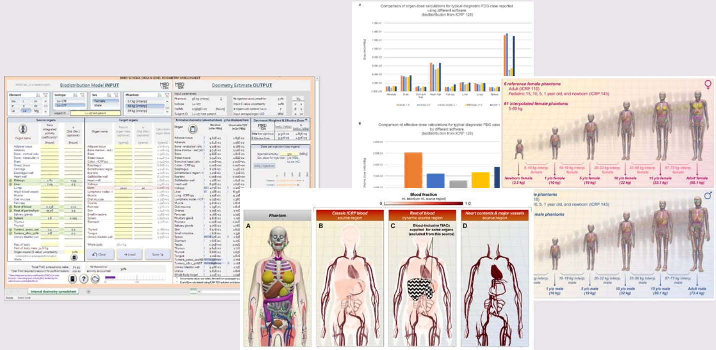
MIRDcalc publications

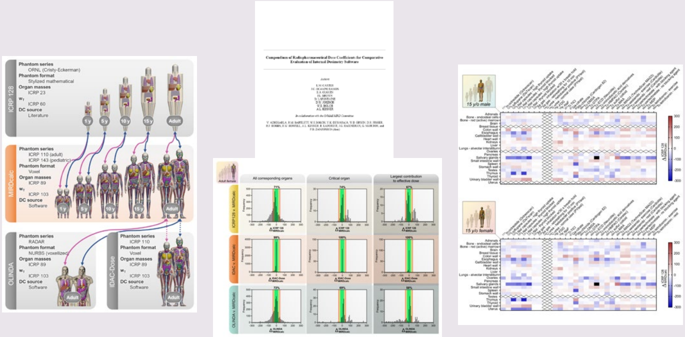
MIRD Pamphlet No. 28, Part 1: MIRDcalc – a software tool for medical internal radiation dosimetry *

- Introduction of software and features
- Supplemental phantom data and practice cases



MIRD Pamphlet No. 28, Part 2: Comparative evaluation of MIRDcalc dosimetry software across a compendium of diagnostic radiopharmaceuticals*

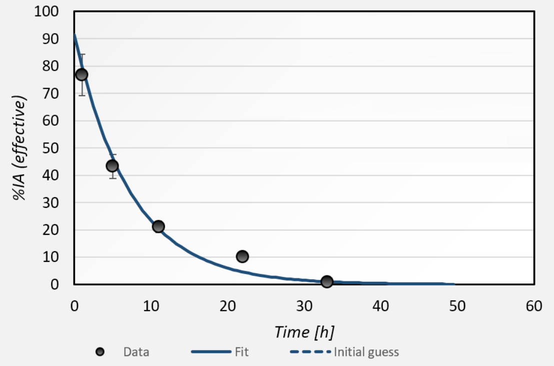
- Benchmark MIRDcalc with existing software
- Dose compendium (120 radiopharmaceuticals)



MIRDfit curve fitting tool

Module driven by
Lukas Carter, PhD
and supported by
UF

- MIRDfit is a biodistribution fitting software
  - Curvefitting fundamental part of the dosimetry workflow
  - Software helps user compute time-integrated activity coefficients (TIACs) (to be used in nuclear medicine dosimetry)
  - Workflow can be readily integrated with MIRDcalc
- Features
  - Single-screen interface
  - Pre-populated ICRP/MIRDcalc organ regions, tumors
    - User regions also possible
  - Uncertainty propagations
  - Supports multi-model comparisons
  - Quality control checks
  - Robustly described output

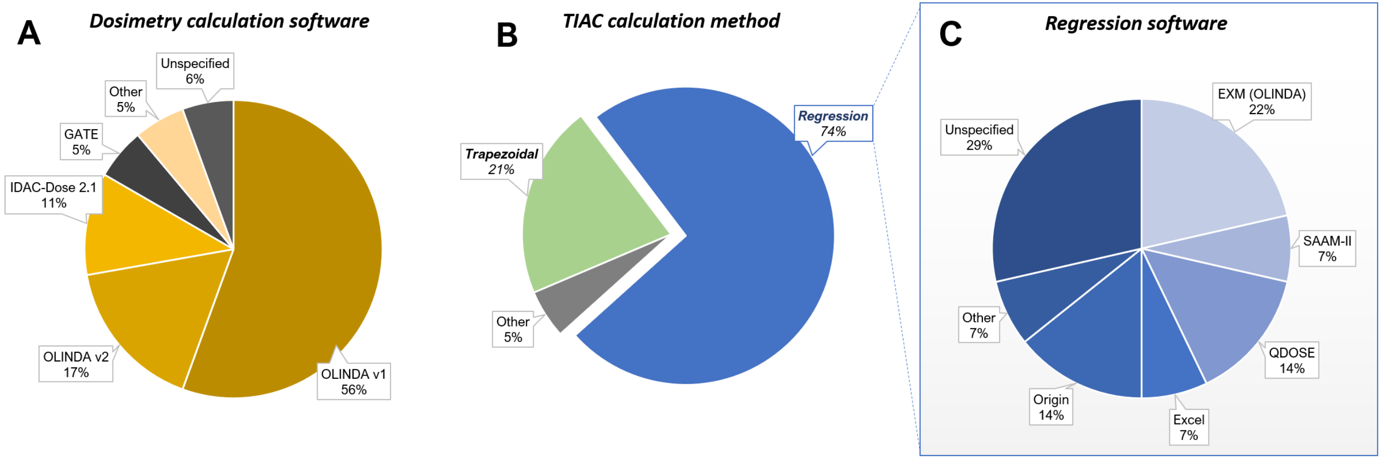


MIRDsoft.org collaboration

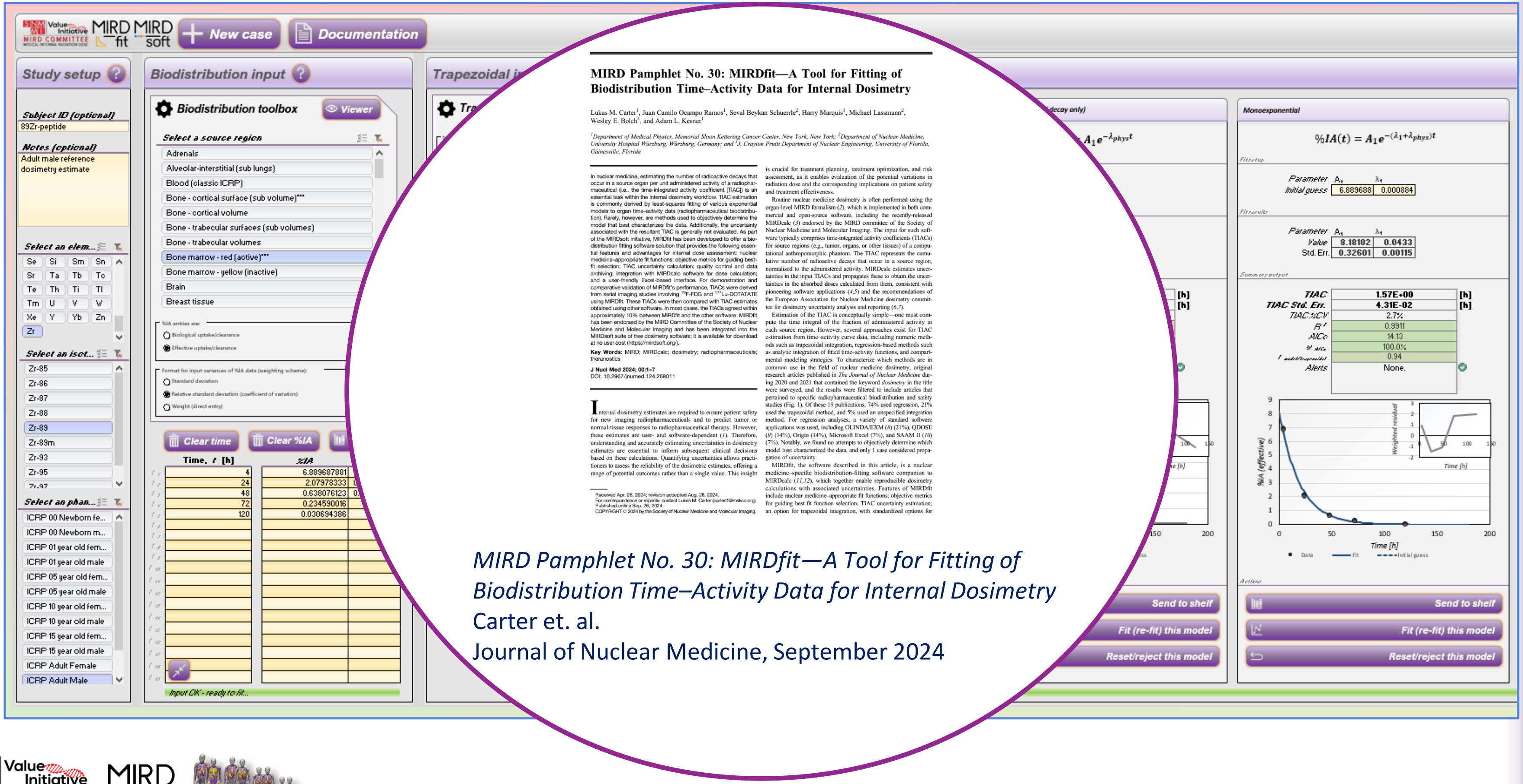
Adam Kesner, PhD

Uncertainty estimation in TAC fitting

- State of the field: all JNM publications with “dosimetry” in the title and filtered for biodistribution studies
  - Of 19 articles, 74% utilized regression, 21% utilized the trapezoidal method, and 5.1% did not specify
  - For regression analyses: EXM module of OLINDA (21%), QDOSE (14%), Origin Pro (14%), Microsoft Excel (7%), and SAAM-II (7%).
  - No publications objectively compared fitting models
  - Only 1 publication considered uncertainty



MIRDfit interface



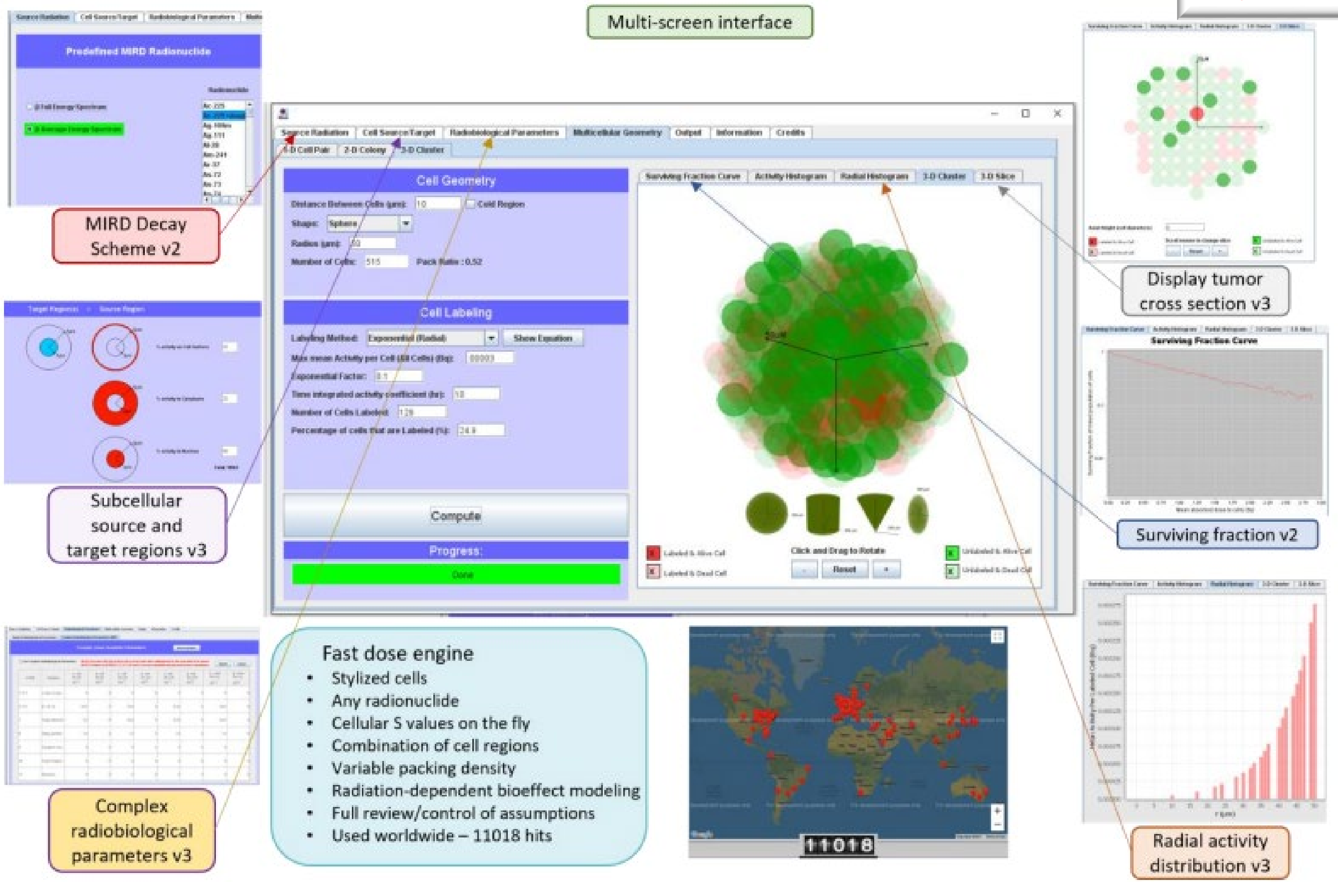
MIRD Pamphlet No. 30: MIRDfit—A Tool for Fitting of Biodistribution Time–Activity Data for Internal Dosimetry
Carter et. al.
Journal of Nuclear Medicine, September 2024

MIRDcell

- PI – Roger Howell (Rutgers)
- Radionuclide Cell-level dosimetry and bioeffect modeling software
  - Sub-cell, single cells, multi-cell clusters - Sources and Targets
  - B particles: Average E or Full E spectrum
  - LQ modeling
- Available now for download

MIRD Pamphlet No 25: MIRDcell V2, Software Tool for Dosimetric Analysis of Biologic Response of Multicellular Populations
Varizi et al. JNM 55: 1-8, 2014

MIRD Pamphlet No 27: MIRDcell V3, a revised software tool for multicellular dosimetry and bioeffect modeling
Katugampola et al. JNM 63, 2022



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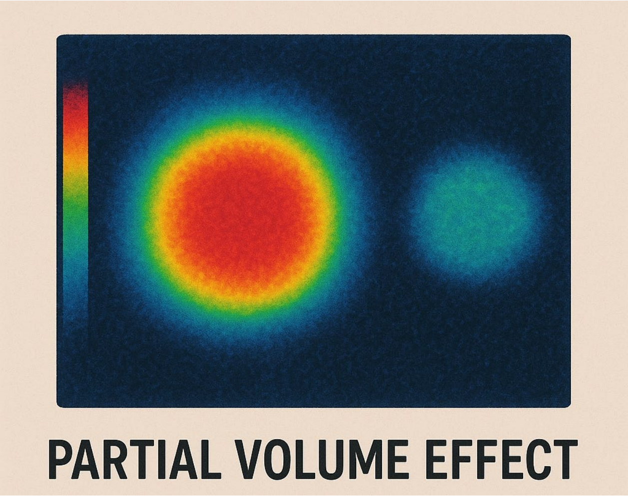
MIRDpvc - *A Software Tool for PET & SPECT Resolution Characterization and Shape-Specific Partial Volume Correction*

Module driven by
Harry Marquis, PhD

- **The partial volume effect (PVE)** *is a significant factor prohibiting accurate dosimetry of target volumes in radiopharmaceutical therapy (RPT)*
- The PVE is a phenomenon that results in the loss of apparent activity in small objects or regions
- Partial volume correction (PVC) methods aim to restore the loss in signal due to limited resolution of our imaging systems
- Why PVC? Improved quantitative accuracy will allow us to better understand treatment responses and outcomes from RNT – and will facilitate personalized therapies in RNT.



MIRDpvc – The RC Model

- Theoretical recovery coefficients for spheres:

$$\mathrm{RC}_{out} = \mathrm{erf}\left(\frac{R\sqrt{2}}{\sigma}\right) - \frac{1}{\sqrt{2\pi}}\frac{\sigma}{R}\left(3 - e^{-\frac{2R^2}{\sigma^2}}\right) + \frac{1}{\sqrt{2\pi}}\left(\frac{\sigma}{R}\right)^3\left(1 - e^{-\frac{2R^2}{\sigma^2}}\right)$$

Presented by De Nijs, Physica Medica, 2023

Reformulated from Gabiña et al, PMB, 2023

- **3-PL** function (empirical model) fit to theoretical RCs:

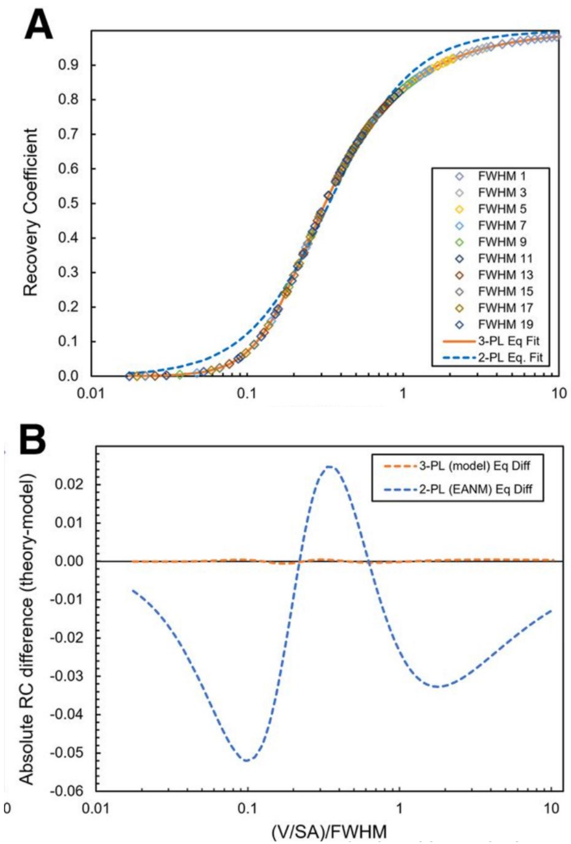
$$RC_{out} = 1 - \frac{1}{\left[1 + \left(\frac{Vol}{SA \times FWHM \times \beta}\right)^{\gamma}\right]^{L}}$$

  - Beta, gamma, & "L", are the fitting parameters → ***Excellent*** fit to theory allows us to measure RCs and solve for FWHM:

→
$$FWHM = \frac{R}{3\beta\left[\left(\frac{1}{1-\mathrm{RC}_{out}}\right)^{\frac{1}{L}} - 1\right]^{\frac{1}{\gamma}}}$$

where R is the radius of the sphere

Main takeaway point:
Our approach finds the resolution (Gaussian – FWHM mm) that is required produce the measured recovery given the known volume and SBR



MIRD Pamphlet No. 32: A MIRD Recovery Coefficient Model for Resolution Characterization and Shape-Specific Partial-Volume Correction

Harry Marquis[1], C. Ross Schmidtlein[1], Robin de Nijs[2], Pablo Mínguez Gabiña[3], Johan Gustafsson[4], Gunjan Kayal[1], Juan C. Ocampo Ramos[1], Lukas M. Carter[1], Dale L. Bailey[5], and Adam L. Kesner[1]

[1]*Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, New York;* [2]*Department of Clinical Physiology and Nuclear Medicine, Copenhagen University Hospital–Rigshospitalet, Copenhagen, Denmark;* [3]*Department of Medical Physics and Radiation Protection, Gurutzeta-Cruces University Hospital/Biocruces Bizkaia Health Research Institute, Barakaldo, Spain;* [4]*Medical Radiation Physics, Lund, Lund University, Lund, Sweden; and* [5]*Department of Nuclear Medicine, Royal North Shore Hospital, Sydney, New South Wales, Australia*

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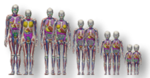
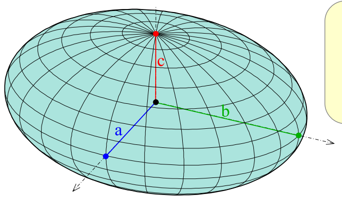


MIRDpvc – RECOVER-GM

- Extending the model to non-spherical shapes:
  - When RCs for ellipsoids are plotted as Vol/SA vs RC, the data collapses onto a single curve (for RCs>0.7)
  - Through simulations of ellipsoids, and prolate/oblate spheroids we were able to extend the model



By Ag2gaeh - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=45585493

REcovery **CO**efficient equi**V**al**E**nt **R**esolution (RECOVER)

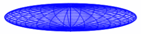
$$\mathrm{RC}_{abc} \approx (\mathrm{RC}_a \cdot \mathrm{RC}_b \cdot \mathrm{RC}_c)^{\frac{1}{3}}$$

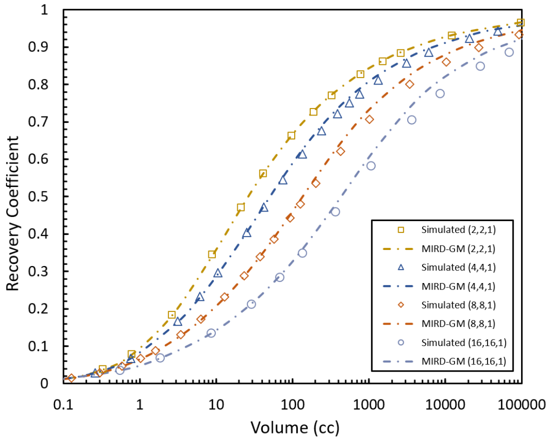
^ Geometric mean of:

$$\mathrm{RC}_a = \mathrm{erf}\left(\frac{a\sqrt{2}}{\sigma}\right) - \frac{1}{\sqrt{2\pi}}\frac{\sigma}{a}\left(3 - e^{-\frac{2a^2}{\sigma^2}}\right) + \frac{1}{\sqrt{2\pi}}\left(\frac{\sigma}{a}\right)^3\left(1 - e^{-\frac{2a^2}{\sigma^2}}\right),$$

$$\mathrm{RC}_b = \mathrm{erf}\left(\frac{b\sqrt{2}}{\sigma}\right) - \frac{1}{\sqrt{2\pi}}\frac{\sigma}{b}\left(3 - e^{-\frac{2b^2}{\sigma^2}}\right) + \frac{1}{\sqrt{2\pi}}\left(\frac{\sigma}{b}\right)^3\left(1 - e^{-\frac{2b^2}{\sigma^2}}\right),$$

$$\mathrm{RC}_c = \mathrm{erf}\left(\frac{c\sqrt{2}}{\sigma}\right) - \frac{1}{\sqrt{2\pi}}\frac{\sigma}{c}\left(3 - e^{-\frac{2c^2}{\sigma^2}}\right) + \frac{1}{\sqrt{2\pi}}\left(\frac{\sigma}{c}\right)^3\left(1 - e^{-\frac{2c^2}{\sigma^2}}\right),$$





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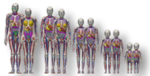
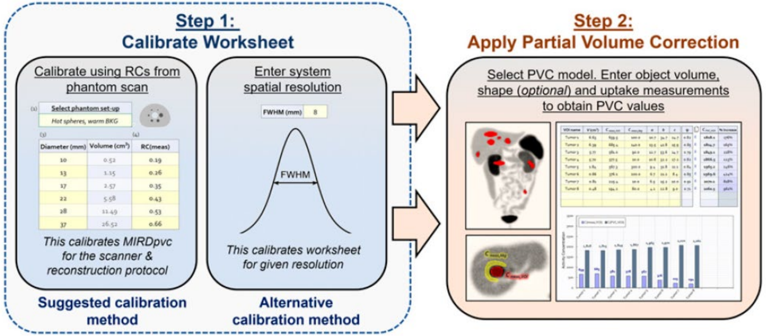


Figure 6: Simulated RC for spheres, prolate (1,1,4) & (1,1,8), and oblate (4,4,1) & (8,8,1) as a function of V:SA/FWHM (left) and its inverse (right) showing the linear regime.

MIRDsoft.org collaboration

Adam Kesner, PhD

MIRDpvc – Worksheet overview

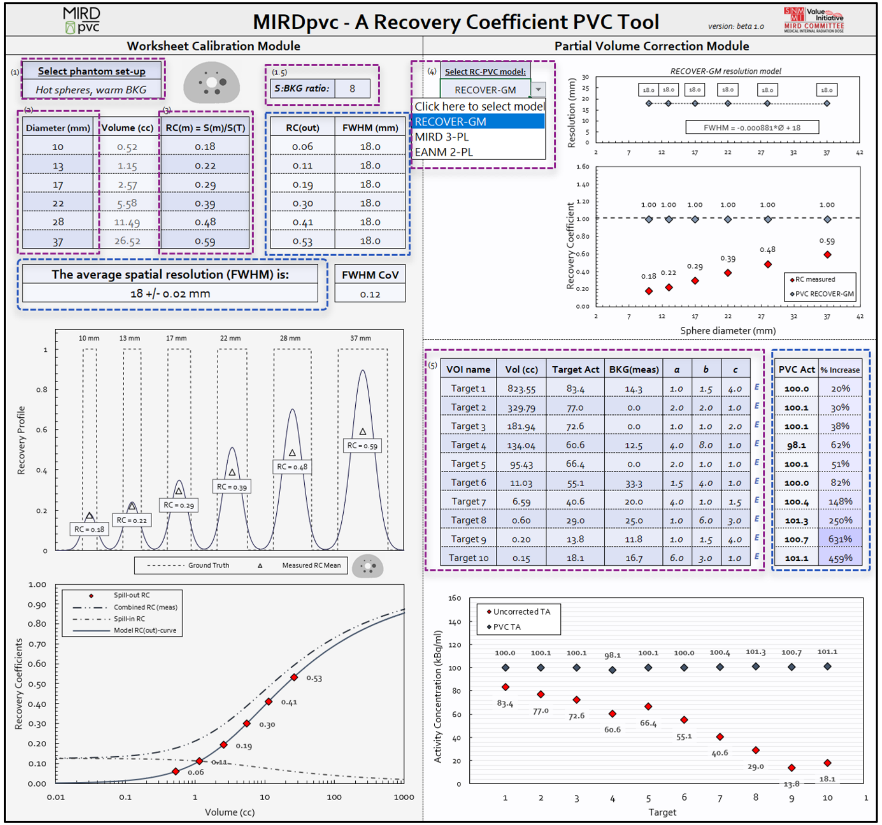


SPECIAL CONTRIBUTION

MIRD Pamphlet No. 33: MIRDpvc—A Software Tool for Recovery Coefficient–Based Partial-Volume Correction

Harry Marquis[1], Johan Gustafsson[2], C. Ross Schmidtlein[1], Robin de Nijs[3], Pablo Mínguez Gabiña[4], Gunjan Kayal[1], Juan C. Ocampo Ramos[1], Lukas M. Carter[1], Dale L. Bailey[5], and Adam L. Kesner[1]

[1]Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, New York; [2]Medical Radiation Physics, Lund, Lund University, Lund, Sweden; [3]Department of Clinical Physiology and Nuclear Medicine, Copenhagen University Hospital–Rigshospitalet, Copenhagen, Denmark; [4]Department of Medical Physics and Radiation Protection, Gurutzeta-Cruces University Hospital/BioBizkaia Health Research Institute, Barakaldo, Spain; and [5]Department of Nuclear Medicine, Royal North Shore Hospital, Sydney, New South Wales, Australia

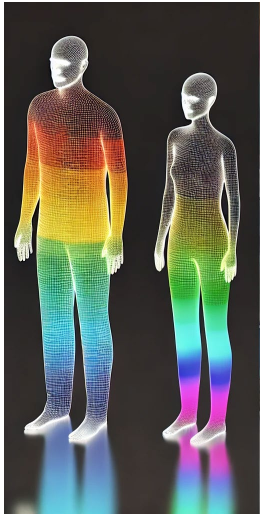


Adam Kesner, PhD

MIRDct CT dosimetry software

Front end module driven by Dr. Ocampo Ramos backend supported by UF

- MIRDct has been developed to provide organ model-based CT dosimetry
- The software enables quick estimation of organ absorbed dose and whole body effective dose
- MIRDct is intended to support:
  - Evaluation of CT dosimetry
  - Optimization of CT protocols, techniques, and procedures
  - Comparison of CT techniques, procedures, technologies
  - Numerical quantification of risk for providers and patients
  - Support for diagnostic reference levels (DRLs)
  - Educational use



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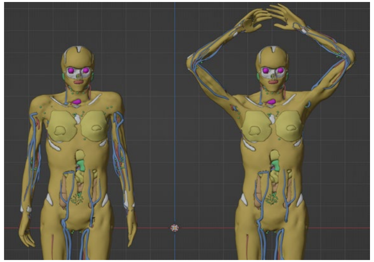
MIRDsoft

MIRDct CT dosimetry software



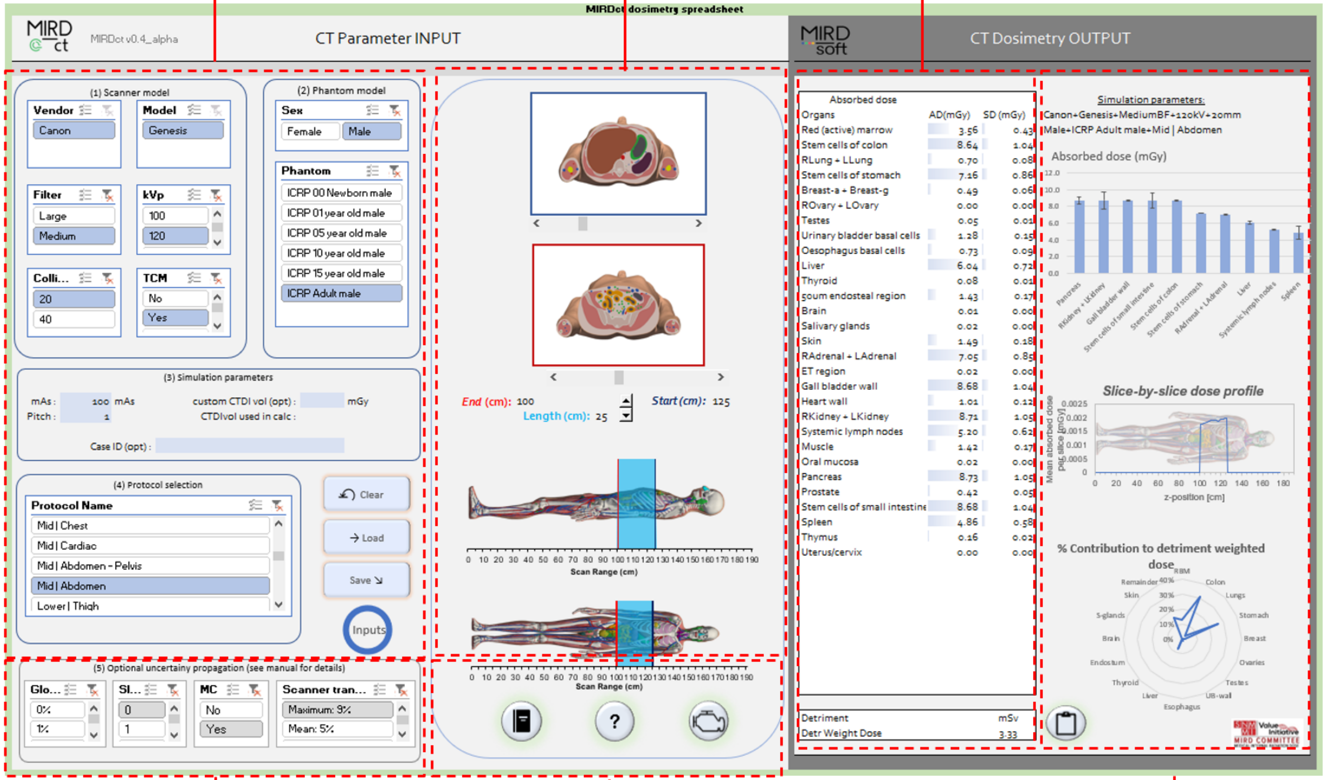
- Key components:
  - Realistic anatomical models
    - ICRP Publication 145 – Adult mesh-type phantoms
    - ICRP Publication 156 – Pediatric mesh-type phantoms
    - arms up/down
  - New dose coefficient database
    - Heavy processing pre-calculated
  - Robust model options:
    - 1 cm CT-slice-specific organ dose coefficients, CT manufacturer, model, collimations, kVp, bowtie filters, and support for Tube Current Modulation (TCM).
  - Single screen graphical user interface
  - Uncertainty evaluation:
    - Software identifies and quantitates sources of error and allows users to propagate these into the calculational results (optional).

MIRDct – GUI

Input parameters panel

Graphical selection/guidance

Dosimetry estimate output



Uncertainty for error propagation

Control panel

Informative graphical results

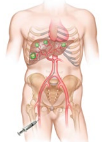
MIRDsoft.org collaboration

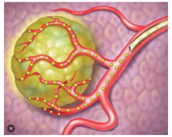
Adam Kesner, PhD

MIRDy90

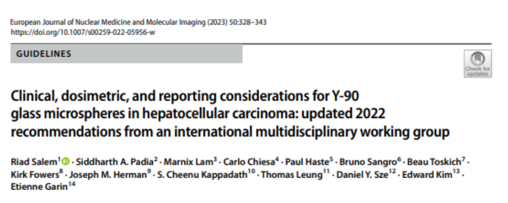
Module driven by
Harry Marquis, PhD

- <u>MIRDy90</u>
  Yttrium 90 microsphere radioembolization





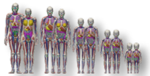
- Dosimetry


European Journal of Nuclear Medicine and Molecular Imaging (2023) 50:328–343
https://doi.org/10.1007/s00259-022-05956-w

GUIDELINES

Clinical, dosimetric, and reporting considerations for Y-90 glass microspheres in hepatocellular carcinoma: updated 2022 recommendations from an international multidisciplinary working group

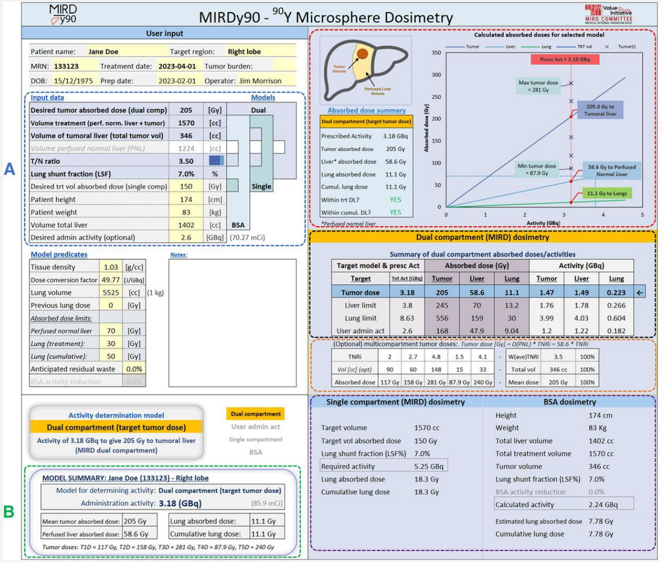
Riad Salem[1] · Siddharth A. Padia[2] · Marnix Lam[3] · Carlo Chiesa[4] · Paul Haste[5] · Bruno Sangro[6] · Beau Toskich[7] · Kirk Fowers[8] · Joseph M. Herman[9] · S. Cheenu Kappadath[10] · Thomas Leung[11] · Daniel Y. Sze[12] · Edward Kim[13] · Etienne Garin[14]



<u>MIRDy90</u>

Implements 3 models for dose prescription

- BSA (SIRTeX)
- Single compartment (TheraSphere)
- Partition model (dual, multi compartment)



MIRD pamphlet 29
(JNM 2024)


MIRD Pamphlet No. 29: MIRDy90—A ^{90}Y Research Microsphere Dosimetry Tool

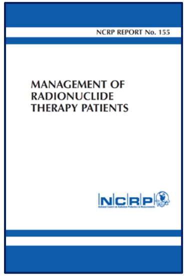
MIRDsoft.org collaboration

Adam Kesner, PhD

MIRDrelease

Module driven by Juan Camilo Ocampo Ramos, PhD and Harry Marquis, PhD

- MIRDrelease
  - Safe release of patients
    - Safety
    - Regulations
  - NCRP report 155 patient release guidelines



Operational Equation

$$\dot{E}(r_j,t) = \dot{K}_a(r_j,t)\,(E/K_a) = \sum_{i=1}^{n} \dot{K}_a(r_j,0)_i\,(E/K_a)\,e^{\frac{-(\ln 2)t}{T_{e_i}}} \qquad (5.7)$$

- $\dot{E}(r_j,t)$ is the effective dose rate (mSv/h) at index distance r_j (meters) from patient at time t post-administration (days),
- $\dot{K}_a(r_j,t)$ is the air kerma rate (Gy/h) at an index distance r_j (m) from the patient at time t (days) post-administration,
- (E/K_a) is the effective dose per air kerma coefficient (Sv/Gy),
- $\dot{K}_a(r_j,0)_i$ is the zero-time intercept of the exponential component i of the time-dependent air kerma rate,
- T_{e_i} is the effective half-life (days) of the non-decay corrected total-body activity for compartment i of a multi-exponential function,
- n is the number of exponential compartments required to describe the time-dependent total-body activity.

MIRDrelease

- Single screen patient release worksheet

MIRDrelease patient release calculation worksheet

Instructions - complete all yellow cells

Treatment		Clinic	
Patient Name:	John Q. Patient	Institution :	AAPM
Patient Number:	222-22-222	Physician :	Doc Holiday
Disease/Condition:	Neuroendocrine Tumors	Contact phone :	555-5555
Treatment date:	6/1/2024	Patient Releasable Dose Limits (/regulations)	
Radionuclide:	Lu-177	Adult family:	125 mrem
Radiopharmaceutical	Lu-177 DOTATATE	Child/pregnant woman/public :	25 mrem

Physics calculations

Administered activity: 7400 [MBq]; 200.0 [mCi]

Assumed Exposure Factors, E(rj) [units: fraction, 0-1]

Family member (1m)	0.25	Co-Worker (1m)	0.33
Sleeping partner (0.3m)	0.33	Held child (0.3m)	0.2

Exposure rate at time zero

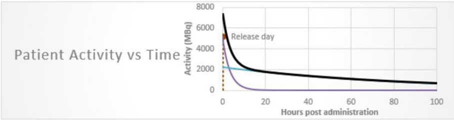
mR/h at 1 m	mR/h at 0.3 m
5.66	62.888889

Release day: 0 (select from dropdown)

Total-Body-Activity-Retention [units: days]

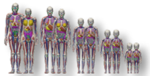
A(t) = F1*exp(ln(2)/T_{e1}) + F2*exp(ln(2)/T_{e2}) + F3*exp(ln(2)/T_{e3})

	amplitude		half time [days]
F1	0.7	T_{e1}	0.1
F2	0.3	T_{e2}	2.4
F3		T_{e3}	



	Release instructions	Days (post administration)
1)	Avoid close contact [less than 1 meter (3 feet) away from] with pregnant women and children until 2 days after the administration of the radionuclide therapy; that is, there are no restrictions on such activity.	2 Days
2)	Do not hold or embrace children for more than 10 minutes a day until 15 days after the administration of the radionuclide therapy.	15 Days
3)	Do not return to work until 3 days after the administration of the radionuclide therapy; that is, you may return to work immediately.	3 Days
4)	Do not sleep in the same bed with your adult sleeping partner until 7 days after the administration of the radionuclide therapy.	7 Days
5)	If your sleeping partner is pregnant, do not sleep in the same bed with your sleeping partner until 16 days after the administration of the radionuclide therapy.	16 Days

SNMMI Value Initiative MIRD COMMITTEE MEDICAL INTERNAL RADIATION DOSE



MIRDsoft.org collaboration

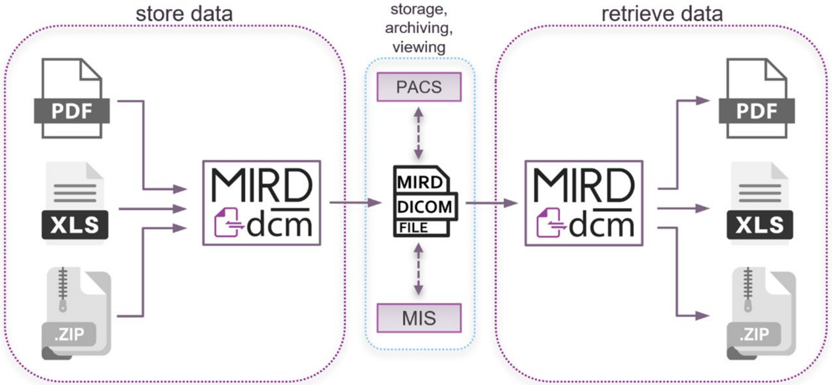
Adam Kesner, PhD

MIRDtools

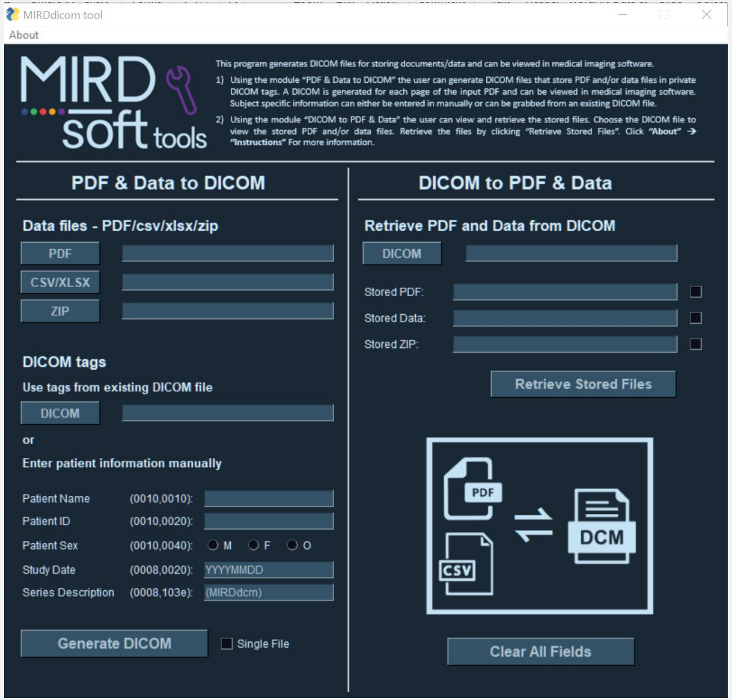
Module driven by
Harry Marquis, PhD

MIRDdcm

- Compile (dosimetry) reports to DICOM format
  - Data -> Single DICOM file
  - Software also reverts DICOM-> data



MIRDdcm

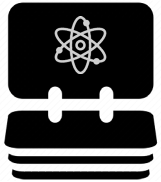


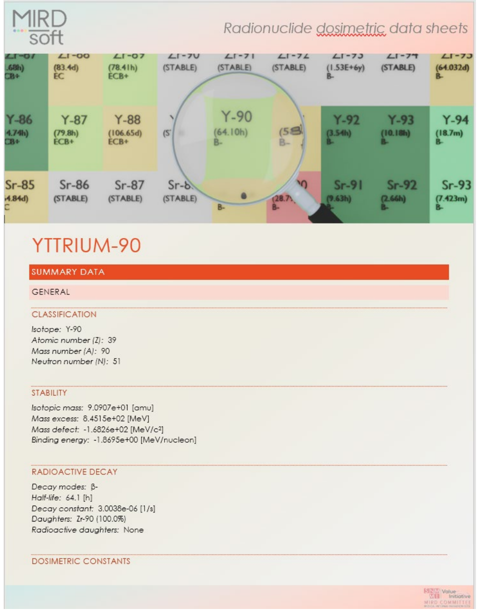
MIRDtools

Module driven by Lukas Carter, PhD

MIRDspecs

- Reference material for MIRDsoft.org website
- 1000+ isotopes





Radionuclide dosimetric data sheets

YTTRIUM-90

SUMMARY DATA

GENERAL

CLASSIFICATION

Isotope: Y-90
Atomic number (Z): 39
Mass number (A): 90
Neutron number (N): 51

STABILITY

Isotopic mass: 9.0907e+01 [amu]
Mass excess: 8.4515e+02 [MeV]
Mass defect: -1.6826e+02 [MeV/c²]
Binding energy: -1.8695e+00 [MeV/nucleon]

RADIOACTIVE DECAY

Decay modes: β-
Half-life: 64.1 [h]
Decay constant: 3.0038e-06 [1/s]
Daughters: Zr-90 (100.0%)
Radioactive daughters: None

DOSIMETRIC CONSTANTS

Radionuclide dosimetric data sheets

Mean alpha energy: 0.0 [MeV]
Mean electron energy: 0.9331 [MeV]
Mean photon energy: 0.0 [MeV]
Air kerma rate constant, Γ_{10}: 1.653e-21 [Gy·m²/Bq·s]
Air kerma coefficient, K_{air}: 1.653e-21 [Gy·m²/Bq·s]
Equilibrium dose constant for weakly-penetrating radiations (α and/or electrons), Δ_{wp}: 1.495e-13 [Gy·kg/Bq·s]

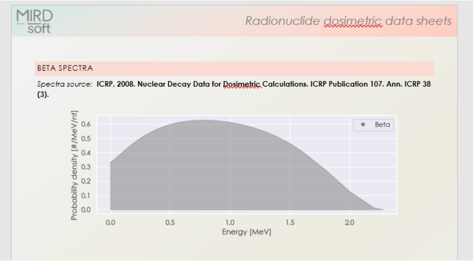
DOSE POINT KERNELS

Dose point kernel source: **Graves, et al. Medical Physics. 2019 Nov.; 46(11):5284-5293.**

Note: Bins are spaced every 0.1 mm until a radius of 10 cm, and every 1 mm until a radius of 2 m.

SUMMARY SPECTRA

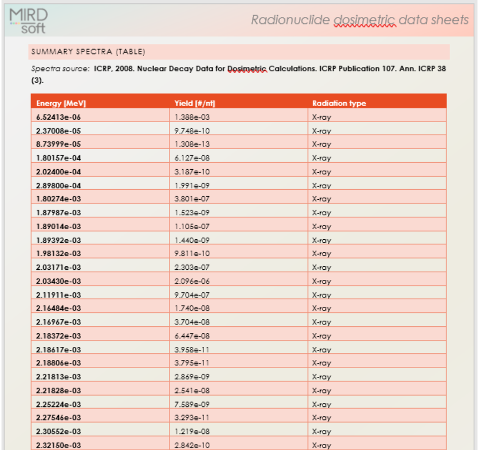
Spectra source: **ICRP, 2008. Nuclear Decay Data for Dosimetric Calculations. ICRP Publication 107. Ann. ICRP 38 (3).**



Radionuclide dosimetric data sheets

BETA SPECTRA

Spectra source: **ICRP, 2008. Nuclear Decay Data for Dosimetric Calculations. ICRP Publication 107. Ann. ICRP 38 (3).**



Radionuclide dosimetric data sheets

SUMMARY SPECTRA (TABLE)

Spectra source: **ICRP, 2008. Nuclear Decay Data for Dosimetric Calculations. ICRP Publication 107. Ann. ICRP 38 (3).**

Energy [MeV]	Yield [#/nt]	Radiation type
6.52413e-06	1.388e-03	X-ray
2.37008e-05	9.748e-10	X-ray
8.73999e-05	1.308e-13	X-ray
1.80157e-04	6.127e-08	X-ray
2.02400e-04	3.187e-10	X-ray
2.89800e-04	1.991e-09	X-ray
1.80274e-03	3.801e-07	X-ray
1.87987e-03	1.523e-09	X-ray
1.89014e-03	1.105e-07	X-ray
1.89392e-03	1.440e-09	X-ray
1.98132e-03	9.811e-10	X-ray
2.03171e-03	2.303e-07	X-ray
2.03430e-03	2.096e-06	X-ray
2.11911e-03	9.704e-07	X-ray
2.16484e-03	1.740e-08	X-ray
2.16967e-03	3.704e-08	X-ray
2.18372e-03	6.447e-08	X-ray
2.18617e-03	3.958e-11	X-ray
2.18806e-03	3.795e-11	X-ray
2.21813e-03	2.869e-09	X-ray
2.21828e-03	2.541e-08	X-ray
2.25224e-03	7.589e-09	X-ray
2.27546e-03	3.293e-11	X-ray
2.30552e-03	1.219e-08	X-ray
2.32150e-03	2.842e-10	X-ray

SNMMI Value Initiative
MIRD COMMITTEE
MEDICAL INTERNAL RADIATION DOSE

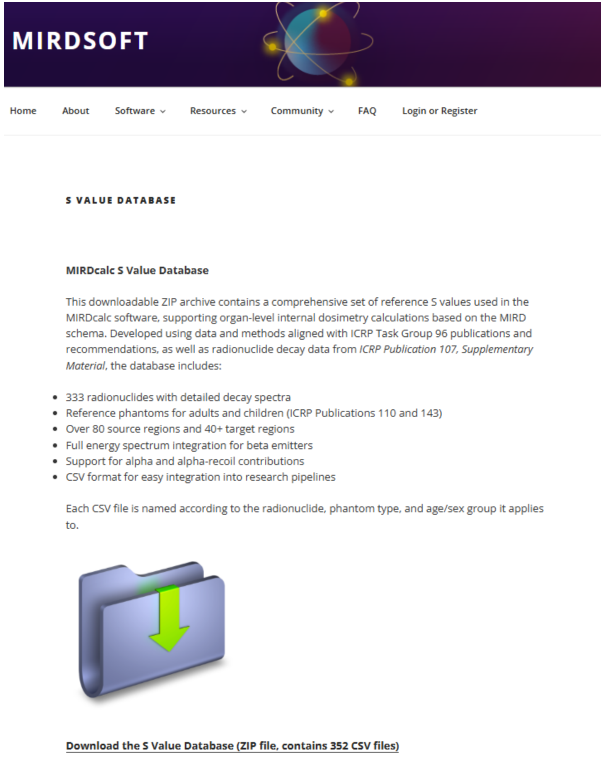
MIRDsoft.org collaboration

Adam Kesner, PhD

MIRDtools

Module driven by Lukas Carter, PhD

MIRDcalc S value database



MIRDSOFT

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S VALUE DATABASE

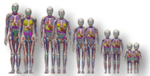
MIRDcalc S Value Database

This downloadable ZIP archive contains a comprehensive set of reference S values used in the MIRDcalc software, supporting organ-level internal dosimetry calculations based on the MIRD schema. Developed using data and methods aligned with ICRP Task Group 96 publications and recommendations, as well as radionuclide decay data from *ICRP Publication 107, Supplementary Material*, the database includes:

- 333 radionuclides with detailed decay spectra
- Reference phantoms for adults and children (ICRP Publications 110 and 143)
- Over 80 source regions and 40+ target regions
- Full energy spectrum integration for beta emitters
- Support for alpha and alpha-recoil contributions
- CSV format for easy integration into research pipelines

Each CSV file is named according to the radionuclide, phantom type, and age/sex group it applies to.

Download the S Value Database (ZIP file, contains 352 CSV files)

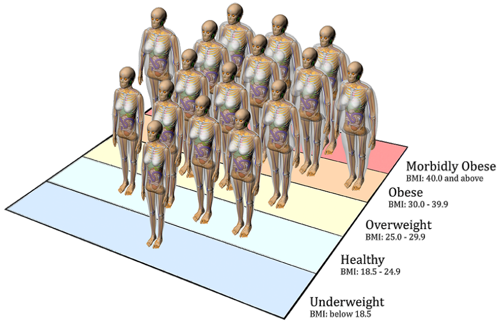


MIRDsoft.org collaboration

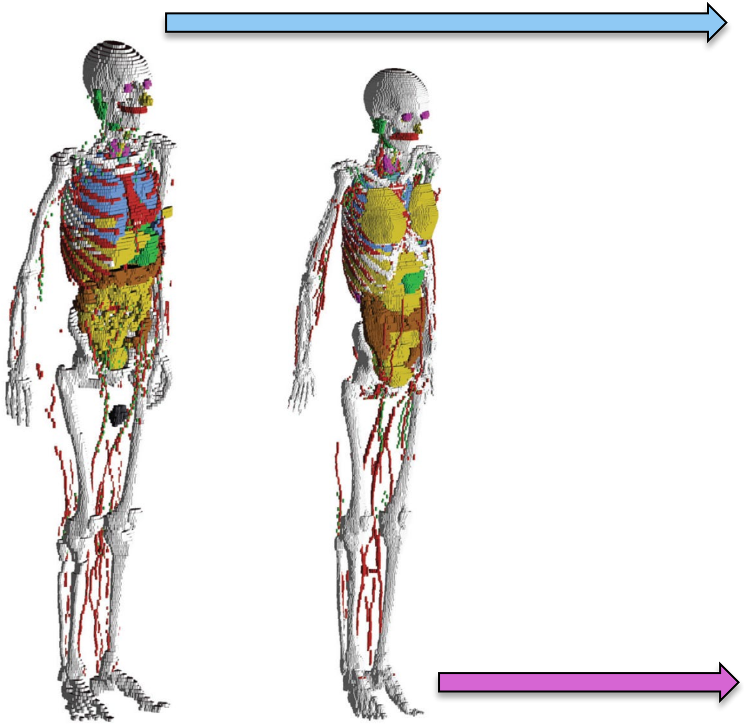
Adam Kesner, PhD

Development of computational phantoms

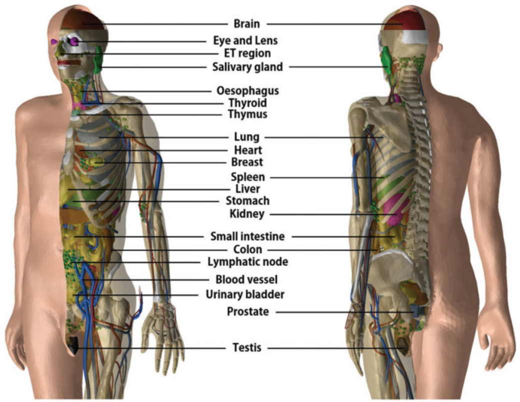
- Grant effort powered by MSK/UF partnership
  - Co-PI Wes Bolch, PhD
- Bolch lab has significant experience with developing computational phantoms
- As (significant) part of grant we are creating the UF/MSK computational phantom library
  - Powers MIRDsoft tools
  - Many other uses



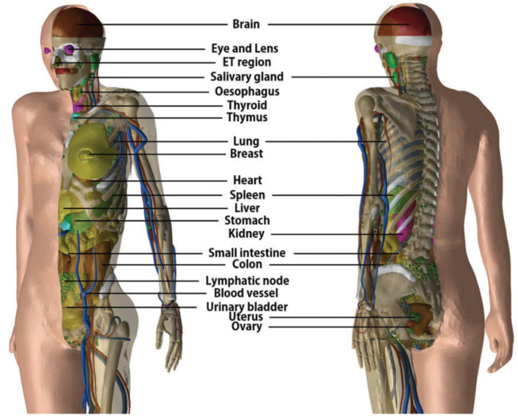
Changes in phantom technology: Voxel → Mesh



ICRP Publication 110



ICRP Publication 145



Note - In 2023, ICRP will release a companion document on the pediatric mesh-based reference phantom series

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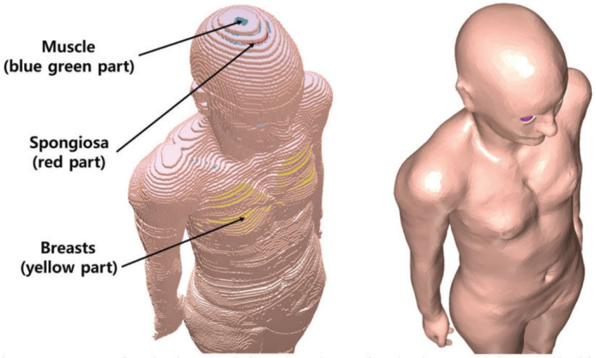
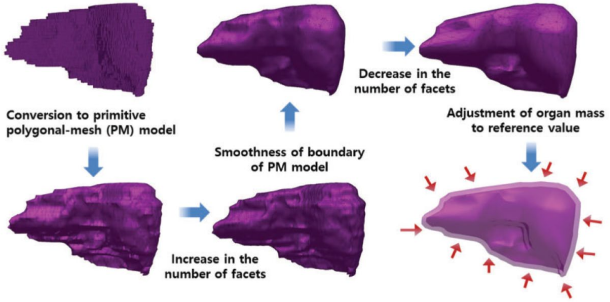
Key advantages of mesh-based over voxel-based phantoms

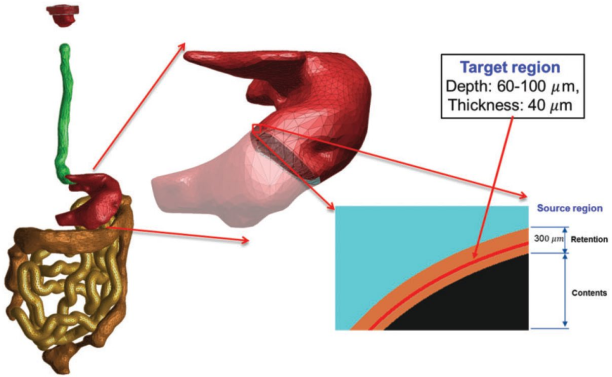
1. Avoidance of stair-step artifacts



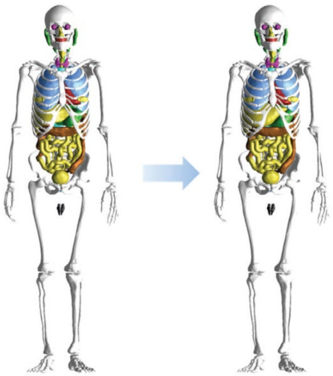
2. Nonuniform scaling of mesh surfaces



3. Ability to model very thin tissue layers



4. Proper accounting of in-vivo organ volumes

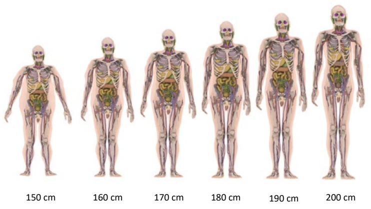


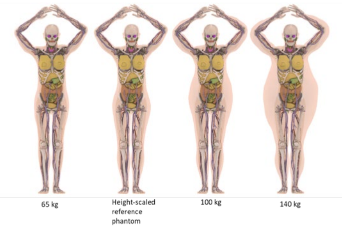
Previously, phantom modelers assumed that ICRP reference masses were inclusive of blood content – they were not!

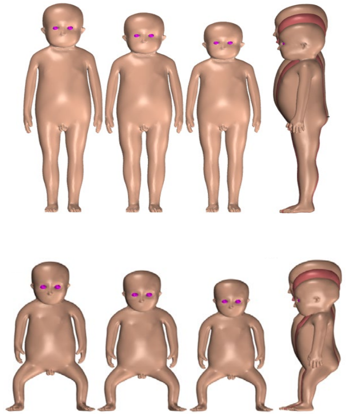
Development of computational phantoms

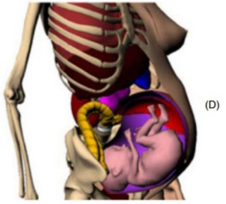
Summary

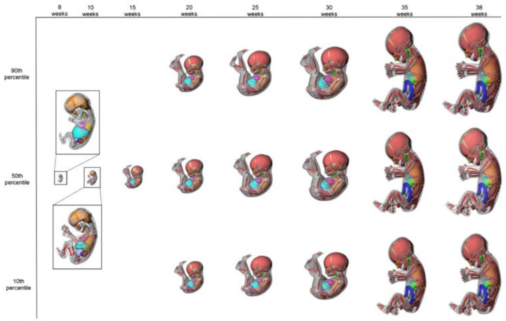
- Phantom development under MIRDsoft initiative will set new standard for digital phantoms
- UF/MSK (combined with UF/NCI) library is now 732 phantoms in total
- Include variety of sizes/shapes/postures
- Powers MIRDsoft products
- To be distributed on MIRDsoft.org











SNMMI Value Initiative MIRD COMMITTEE MEDICAL INTERNAL RADIATION DOSE
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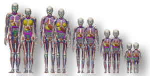
MIRDsoft.org collaboration

Adam Kesner, PhD

Presentation overview

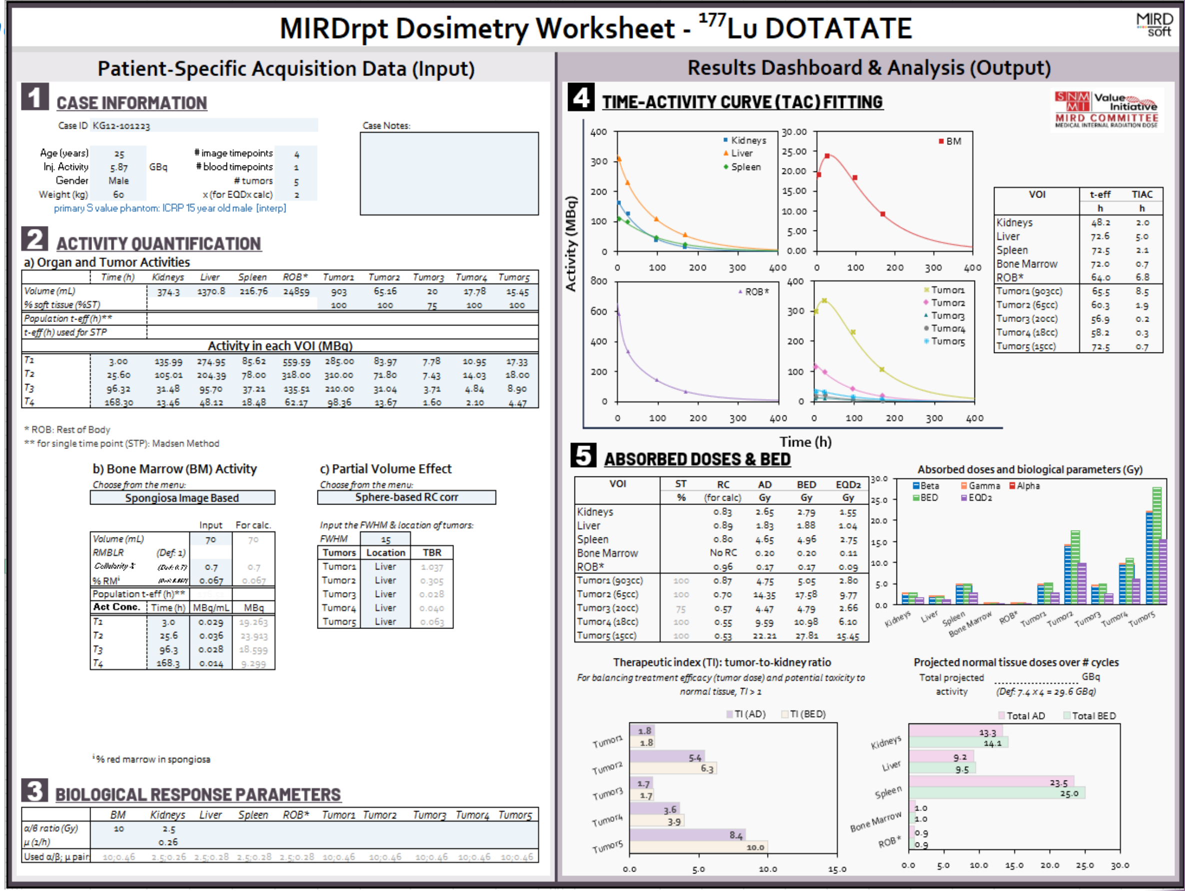


Coming soon MIRDrpt series

Module driven by Gunjan Kayal, PhD

A *radiopharmaceutical - specific organ level dosimetry worksheet* developed to perform patient-specific dosimetry in RPT

- Single page calculation workflow
  - Minimal inputs & user complexity
  - Standardized parameters
- Effort to support
  - Access
  - Standardization
  - Transparency
- Integrates
  - Single/muti timepoint dosimetry
  - Partial volume correction
  - Automatic curve fitting
  - Tumor dosimetry
  - Bone marrow (BM) dosimetry
  - Absorbed dose, BED (EQD0), EQDx
- To be freely distributed at MIRDsoft.org



MIRDrpt Dosimetry Worksheet - ^{177}Lu DOTATATE

Patient-Specific Acquisition Data (Input)

1 CASE INFORMATION

Case ID KG12-101223

Case Notes:

Age (years)	25		# image timepoints	4
Inj. Activity	5.87	GBq	# blood timepoints	1
Gender	Male		# tumors	5
Weight (kg)	60		x (for EQDx calc)	2

primary S value phantom: ICRP 15 year old male [interp]

2 ACTIVITY QUANTIFICATION

a) Organ and Tumor Activities

	Time (h)	Kidneys	Liver	Spleen	ROB*	Tumor1	Tumor2	Tumor3	Tumor4	Tumor5
Volume (mL)		374.3	1370.8	216.76	24859	903	65.16	20	17.78	15.45
% soft tissue (%ST)						100	100	75	100	100
Population t-eff (h)**										
t-eff (h) used for STP										
Activity in each VOI (MBq)										
T1	3.00	135.99	274.95	85.62	559.59	285.00	83.97	7.78	10.95	17.33
T2	25.60	105.01	204.39	78.00	318.00	310.00	71.80	7.43	14.03	18.00
T3	96.32	31.48	95.70	37.21	135.51	210.00	31.04	3.71	4.84	8.90
T4	168.30	13.46	48.12	18.48	62.17	98.36	13.67	1.60	2.10	4.47

* ROB: Rest of Body

** for single time point (STP): Madsen Method

b) Bone Marrow (BM) Activity

Choose from the menu: Spongiosa Image Based

		Input	For calc.
Volume (mL)		70	70
RMBLR	(Def: 1)		
Cellularity		0.7	0.7
% RM¹		0.067	0.067
Population t-eff (h)**			
Act Conc.	Time (h)	MBq/mL	MBq
T1	3.0	0.029	19.263
T2	25.6	0.036	23.913
T3	96.3	0.028	18.599
T4	168.3	0.014	9.299

¹% red marrow in spongiosa

c) Partial Volume Effect

Choose from the menu: Sphere-based RC corr

Input the FWHM & location of tumors:

FWHM 15

Tumors	Location	TBR
Tumor1	Liver	1.037
Tumor2	Liver	0.305
Tumor3	Liver	0.028
Tumor4	Liver	0.040
Tumor5	Liver	0.063

3 BIOLOGICAL RESPONSE PARAMETERS

	BM	Kidneys	Liver	Spleen	ROB*	Tumor1	Tumor2	Tumor3	Tumor4	Tumor5
α/β ratio (Gy)	10	2.5								
μ (1/h)		0.26								
Used α/β; μ pair	10;0.46	2.5;0.26	2.5;0.28	2.5;0.28	2.5;0.28	10;0.46	10;0.46	10;0.46	10;0.46	10;0.46

Results Dashboard & Analysis (Output)

4 TIME-ACTIVITY CURVE (TAC) FITTING

VOI	t-eff	TIAC
	h	h
Kidneys	48.2	2.0
Liver	72.6	5.0
Spleen	72.5	2.1
Bone Marrow	72.0	0.7
ROB*	64.0	6.8
Tumor1 (903cc)	65.5	8.5
Tumor2 (65cc)	60.3	1.9
Tumor3 (20cc)	56.9	0.2
Tumor4 (18cc)	58.2	0.3
Tumor5 (15cc)	72.5	0.7

5 ABSORBED DOSES & BED

VOI	ST	RC	AD	BED	EQD2
	%	(for calc)	Gy	Gy	Gy
Kidneys		0.83	2.65	2.79	1.55
Liver		0.89	1.83	1.88	1.04
Spleen		0.80	4.65	4.96	2.75
Bone Marrow		No RC	0.20	0.20	0.11
ROB*		0.96	0.17	0.17	0.09
Tumor1 (903cc)	100	0.87	4.75	5.05	2.80
Tumor2 (65cc)	100	0.70	14.35	17.58	9.77
Tumor3 (20cc)	75	0.57	4.47	4.79	2.66
Tumor4 (18cc)	100	0.55	9.59	10.98	6.10
Tumor5 (15cc)	100	0.53	22.21	27.81	15.45

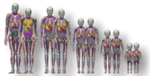
Absorbed doses and biological parameters (Gy)

Therapeutic index (TI): tumor-to-kidney ratio

For balancing treatment efficacy (tumor dose) and potential toxicity to normal tissue, TI > 1

Projected normal tissue doses over # cycles

Total projected activity .... GBq (Def: 7.4 x 4 = 29.6 GBq)



www.mirdsoft.org

MIRDsoft.org collaboration

Gunjan Kayal

Future of MIRDsoft - grant renewal

- **Specific aims:**

1. Enhancing MIRDcalc and MIRDct to Accommodate Variable Human-Body Morphometry
2. Development of a Mouse and Rat Phantom Library for Preclinical Dosimetry
3. Development of Advanced Model-Based Tumor Dosimetry
4. Simplified Bioeffect Modeling Tools for Clinical Dosimetry

MIRDsoft presentation summary

- **MIRDsoft.org** is a new initiative from the SNMMI MIRD committee to support accessible electronic infrastructure for NM community
- Projects address gap in idea translation
  - Community access tools not profitable, but crucial for education, benchmarking standards, innovation
- Projects/accomplishments have been true collaborative effort
- Currently available for download:
  - MIRDcalc, MIRDcell, MIRDy90, MIRDdcm, MIRDfit, MIRDct, MIRDspecs
- **More innovations to come**
  - Efforts currently underway
  - Application for funding renewal has been submitted

Closing remarks on skyscrapers

What was the final ingredient to send skyscrapers higher and higher?

Net positive value proposition – i.e. profitability

Closing remarks on being relevant

- What if there is a “Bessemer process” for radiopharmaceutical dosimetry?

Closing remarks on being relevant

- What if there is a “Bessemer process” for radiopharmaceutical dosimetry?

EDITORIAL

A Cures Act–Forged Pathway to Patient-Tailored Radiopharmaceutical Therapy and Call for Regulatory Transparency

Adam L. Kesner[1], Nikki Batista[2], Pat Zanzonico[1], and Cathy S. Cutler[3]

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Radiopharmaceutical therapy (RPT) offers molecular-targeted treatment strategies and presents an ideal model for advancing precision medicine. As the field grows, a long-standing question gains renewed relevance: What role will personalized dosimetry play in shaping its future? Dosimetry-guided patient management has long been recognized as a key objective in therapeutic nuclear medicine, enabling patient-specific optimization of radiation delivery. The promise of theranostics—seeing what we treat and using that information to tailor the treatment of what we see (*1*)—largely hinges on this capability. Yet despite decades of technical advancements, including the development of dosimetry software tools, their use in guiding treatments remains largely limited to research domains and has yet to become a routine element of clinical care.

Implementing personalized dosimetry in RPT depends on practical, clinically integrated software that can translate quantitative data into actionable decision support. Although the intent of Software as a Medical Device (SaMD) regulation is laudable—protecting patients and ensuring reliability—the current framework may be misaligned with the realistic capacity of routine RPT. In practice, it has produced no Food and Drug Administration (FDA)–cleared tools for prospective planning, even as guidelines increasingly endorse dosimetry-guided management; it leaves planning to in-house or noncleared solutions, limiting standardization; it imposes opaque, costly clearance pathways that raise barriers for clinicians and patients; and it stands in contrast to ^{90}Y radioembolization, where simple, transparent, professionally governed tools proved safe and scalable only because they operated outside the current SaMD pathway and where widespread, iterative use in routine care generated real-world evidence (RWE) that strengthened clinical confidence and informed best practices. In parallel, the U.S. Congress provided a mandate to modernize medical device regulation—via the 21st Century Cures Act (*2*) and later codified in the FDA’s 2022 Clinical Decision Support (CDS) guidance (*3*)—providing a route by which qualifying dosimetry calculators could be translated to the community, supporting individualized care and the generation of RWE—a pathway still underrecognized and unused.

This gap underscores the need for a constructive, field-wide effort to ensure that RPT has access to safe, scalable, and standardized tools for individualized treatment planning. We propose a pragmatic distinction between full-featured dosimetry platforms and transparent model calculators, and we explore how CDS classification—already available under current regulations—offers a viable means to enable such calculators to support individualized care through assumption-based modeling. This is not a perfect solution, but it could represent a substantial improvement over the current default in which many RPTs proceed without any dosimetry guidance.

DE FACTO BARRIERS TO DOSIMETRY SOFTWARE IN RADIOPHARMACEUTICAL THERAPY

Under current policies, RPT dosimetry software is classified as SaMD (*4*). Retrospective dose estimation tools have generally been cleared as moderate-risk class II devices through the 510(k) premarket notification pathway (*5*)—“clearance” being distinct from formal “approval” in regulatory terminology—whereas prospective treatment-planning tools are presumed to fall into the high-risk class III category, triggering the most stringent regulatory requirements.

The added dimensionality of regulation (spanning drug, radioactive material, and software domains), combined with the complexity of internal dose calculations, sets apart the translation of RPT dosimetry software from analogous tools in radiation oncology (Supplemental Table 1; available at http://jnm.snmjournals.org). Consequently, regulatory pathways used in other fields are not directly transferable, and the commonly used 510(k) pathway—though less costly than class II de novo or class III premarket approval—still poses significant hurdles, especially for smaller companies and academic institutions. Its requirement to demonstrate “substantial equivalence” to an existing marketed device is known to discourage innovation—an effect well recognized in the regulatory community (*6,7*). These burdens, together with high development costs and overlapping requirements across the 3 domains, incentivize simplified “one-size-fits-all” dosing strategies, as seen in recent approvals such as Lutathera and Pluvicto (both Novartis) (*8,9*).

Implicitly, there is a presumption that prospective treatment planning requires high-risk software and that population-based dosing—the one-size-fits-all protocols designed to minimize toxicities in the average patient populations—provides an adequate lower-risk default. This approach supplants patient-specific biokinetics and personal priorities—and the goal of optimizing therapy

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Table 1 - Comparison of FDA-defined regulatory pathways for medical software: CDS, Class II (510(k)) clearance, and Class III (Premarket Approval).

Characteristic	Clinical Decision Support (CDS)	Class II 510(k) Clearance	Class III (Premarket Approval)
Regulatory Classification	Supportive, not standalone medical devices	Moderate-risk medical devices	High-risk medical devices
Primary Focus	Assist clinicians with decision-making	Independent diagnostic or treatment devices	Standalone treatment or diagnostic tools with significant risk
Approval Process	Exempt if meeting FDA criteria	Requires 510(k) premarket notification	Requires PMA
Timeline for Clearance	No formal review timeline—tools meeting CDS exemption criteria can be implemented without FDA review.	Longer (~12-18 months)	Longest (~1.5-3 years)
Cost to Developers	Lower	Higher	Highest
Flexibility for Updates	High, iterative updates allowed	Low, requires regulatory re-approval for updates*	Very low, requires new PMA for any changes*
Innovation Potential	High, promotes faster integration	Moderate, constrained by approval process	Low, due to high regulatory barriers
Clinical Adoption	Promotes adoption via lower barriers	Slow adoption due to regulatory hurdles	Slowest, with limited use due to costs and complexities

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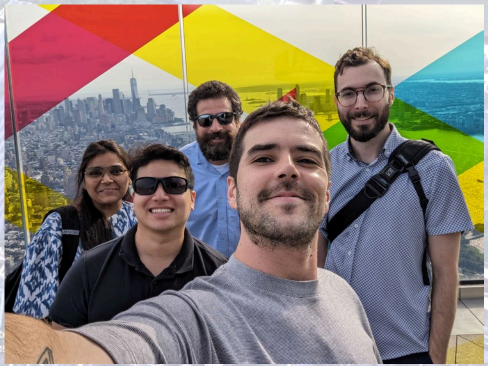

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