

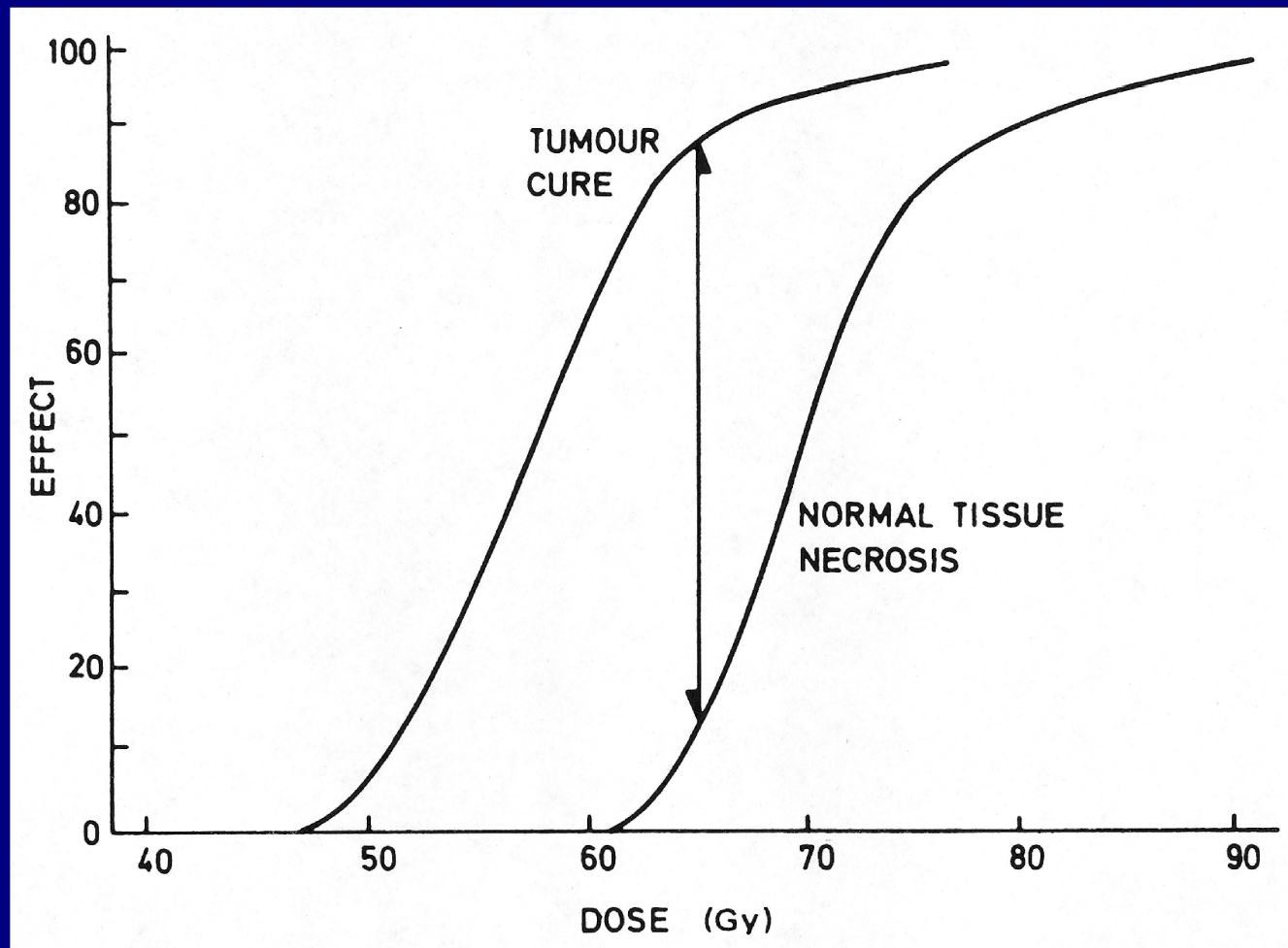
Individual Patient Dosimetry for Radionuclide Therapy

Erin McKay

Dept. Nuclear Medicine

St. George Hospital, Sydney

What do we want?



Tumour Control Probability

- TCP is the likelihood of sterilising every clonogenic cell in a tumour.
- In other words, it's the probability that the population of viable clonogens will eventually fall to zero.
- TCP is a complex variable that depends on the relationship between clonogen birth and death rates.
- Often approximated by the so-called Poisson model of TCP:

$$TCP = e^{-SF \cdot n}$$

Surviving Fraction

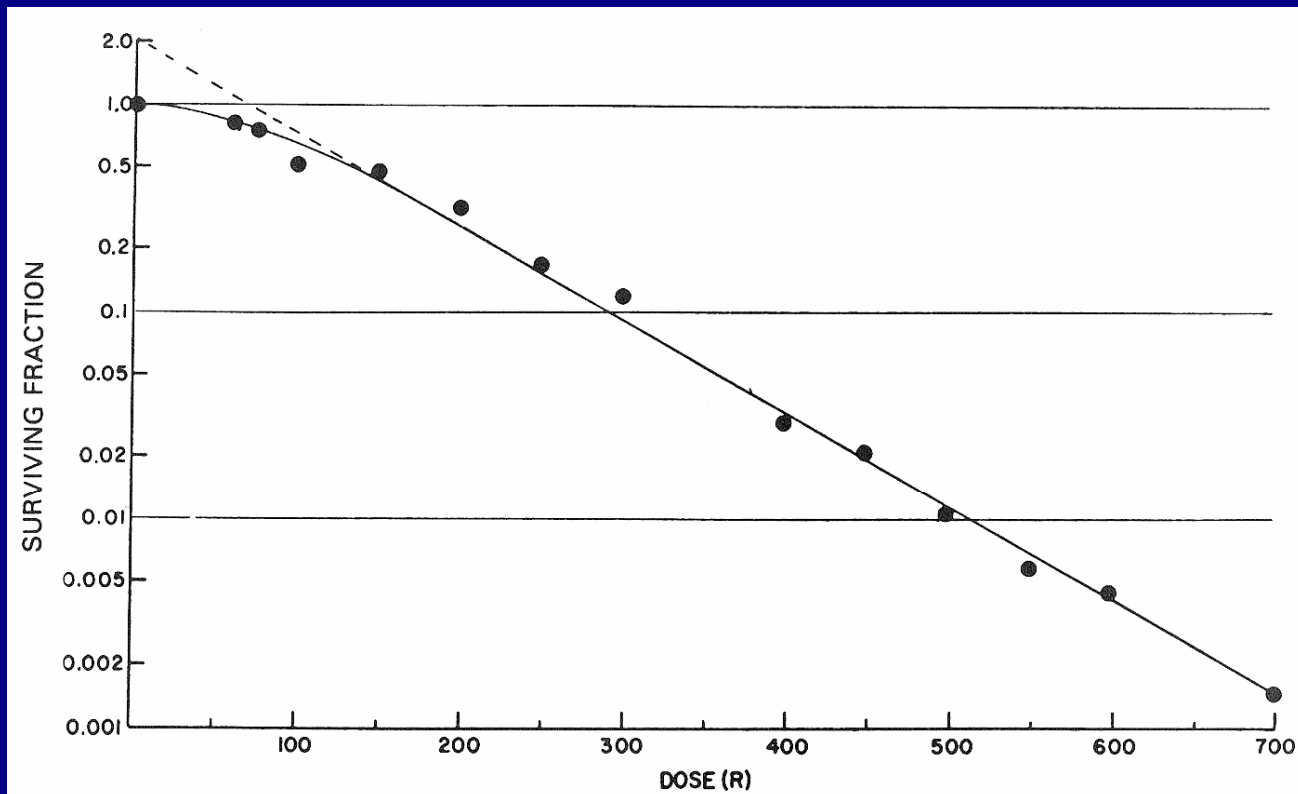
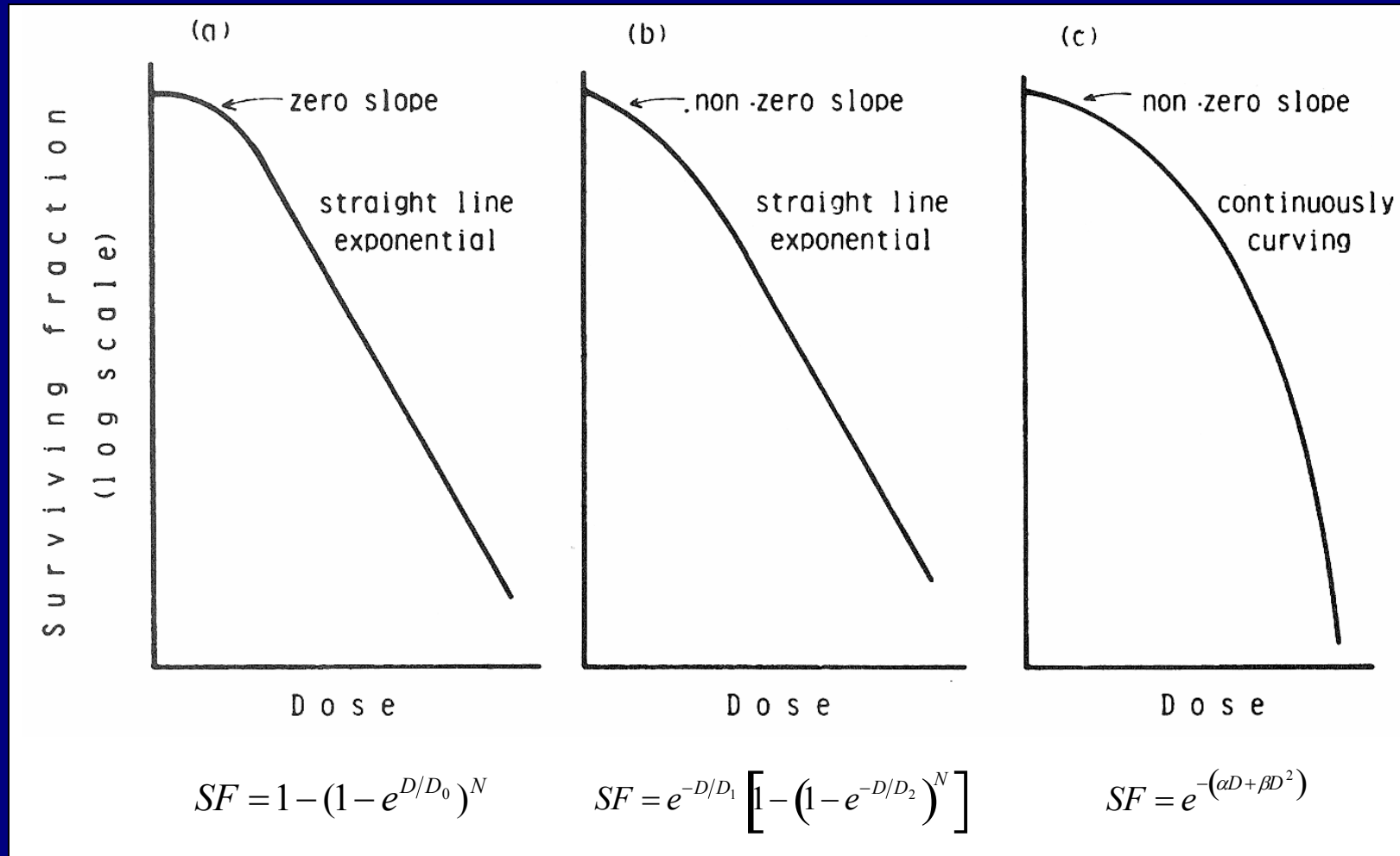
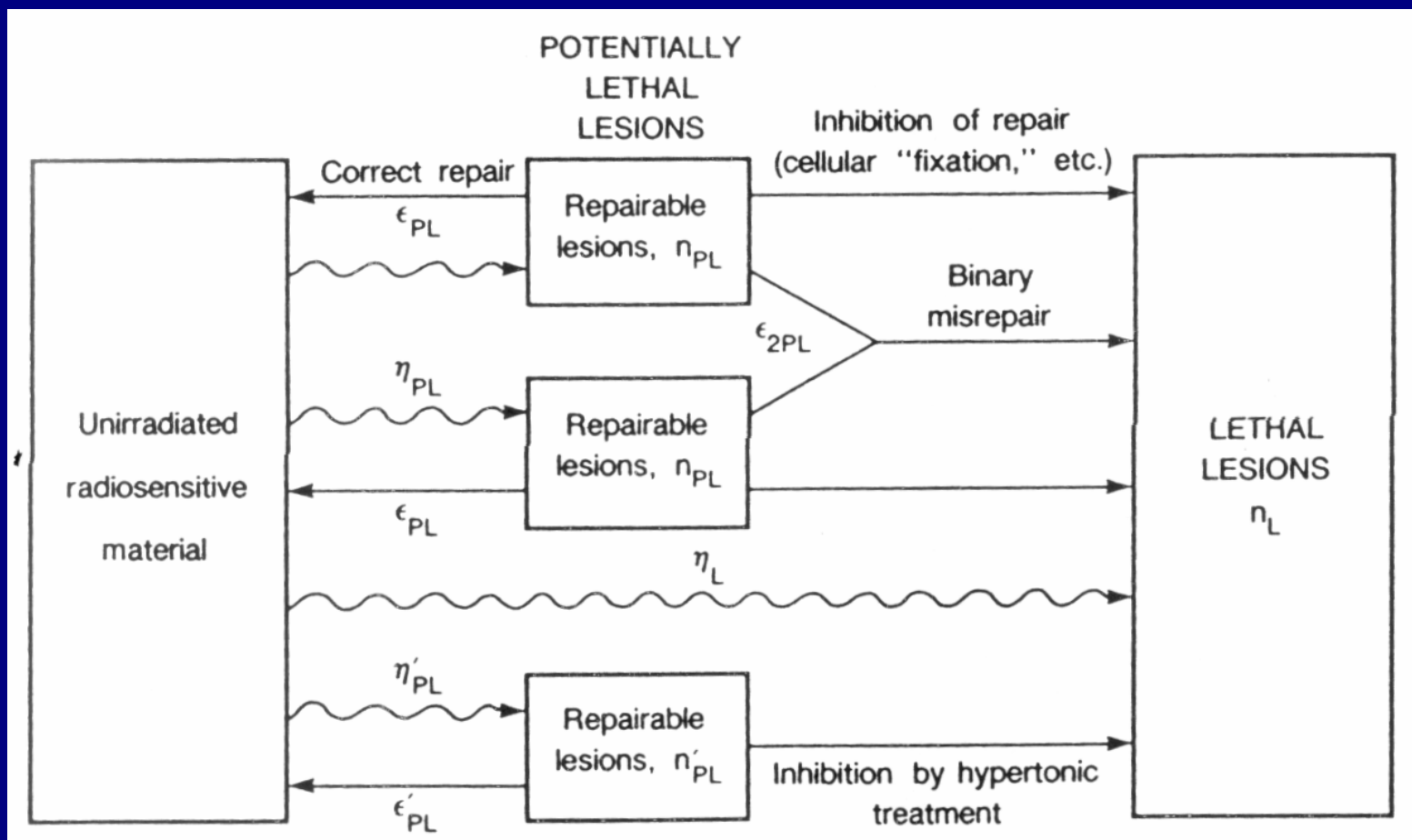


Figure 8.1. Radiation dose-response of human cancer cells *in vitro*. (Reproduced from Puck and Marcus, 1956, by copyright permission of The Rockefeller University Press.)

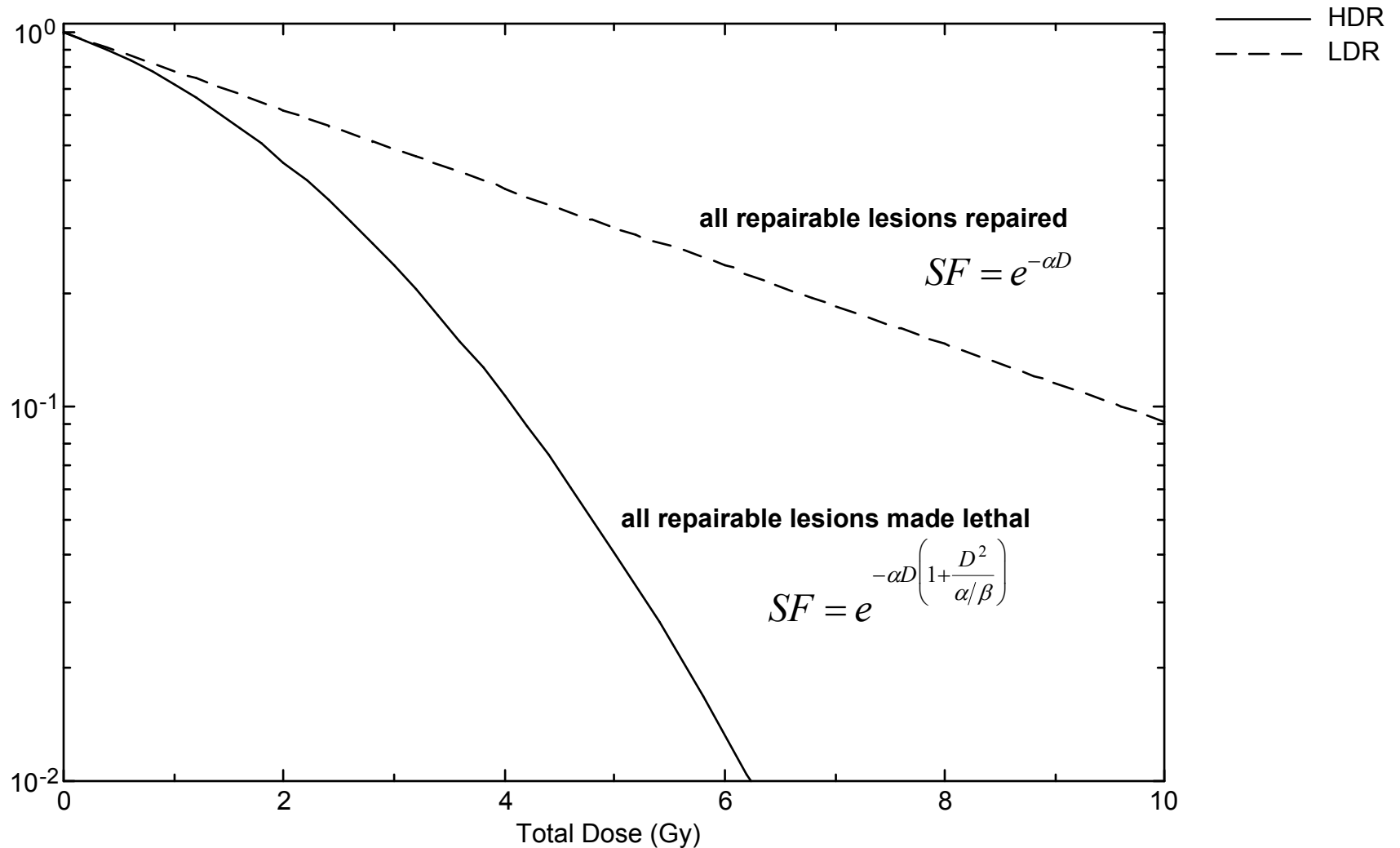
The LQ Approximation



Unified Repair Model



Repair Capacity



Repair of Sub-lethal Damage

Amount of repair $q(t)$ is time-dependent:

$$SF(t) = e^{-\alpha D(t) \left(1 + q(t) \frac{D(t)}{\alpha/\beta} \right)}$$

Where source is decaying exponentially:

$$q(t) = \frac{2(\lambda t)^2}{(\mu t)^2 (1 - \lambda^2/\mu^2) (1 - e^{-\lambda t})^2} \left[e^{-(\lambda+\mu)t} + \mu t \left(\frac{1 - e^{-2\lambda t}}{2\lambda t} \right) - \frac{1 + e^{-2\lambda t}}{2} \right]$$

and:

$$D(t) = \frac{R_0}{\lambda} [1 - e^{-\lambda t}]$$

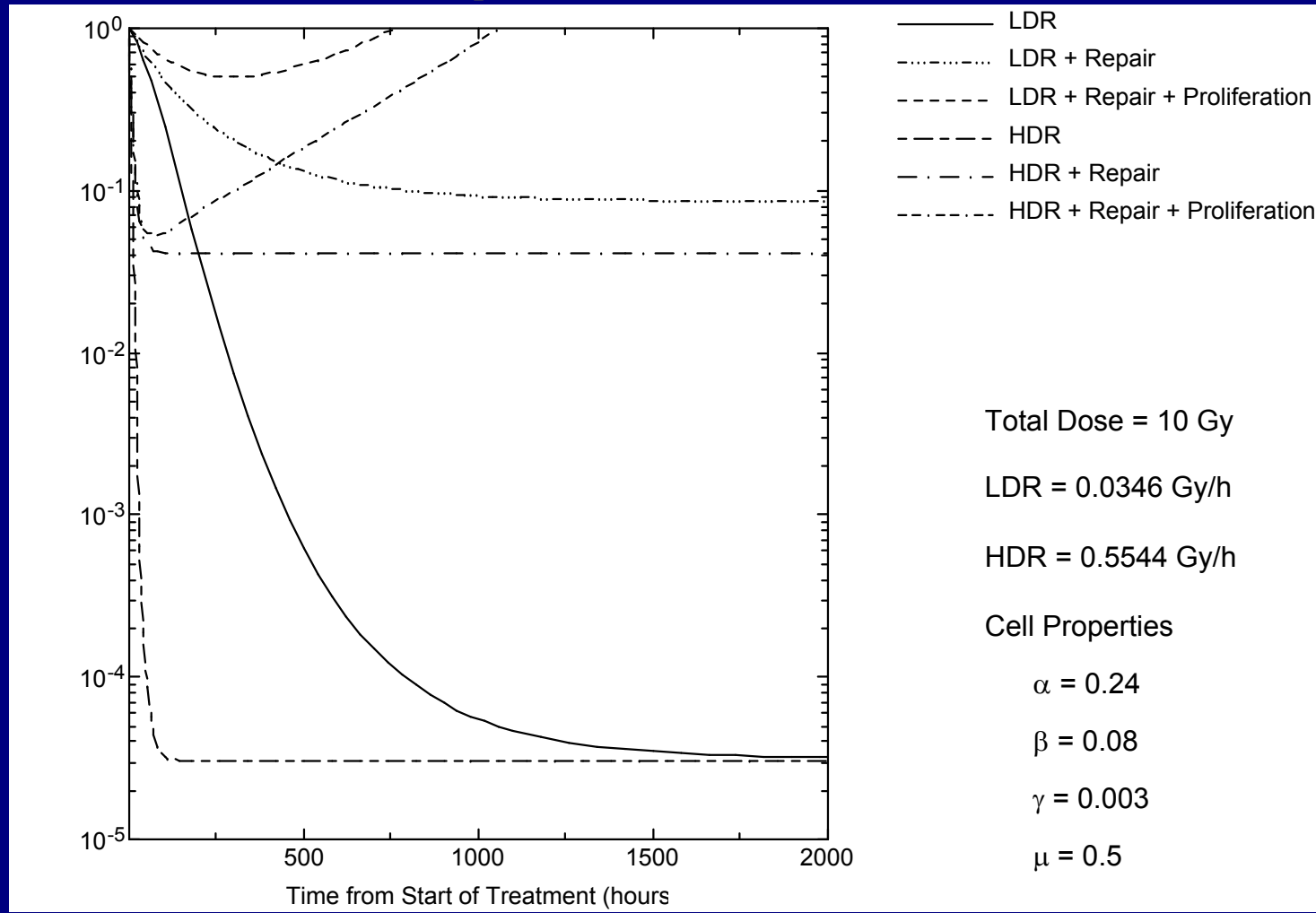
with λ the decay rate and μ the rate of repair.

Target Cell Proliferation

- Proliferation during irradiation will diminish the overall effectiveness of the delivered dose.
- It may be approximated by an exponential growth term:

$$n(t) = n(0)SF(t)e^{\lambda t}$$

Tissue Response to Irradiation

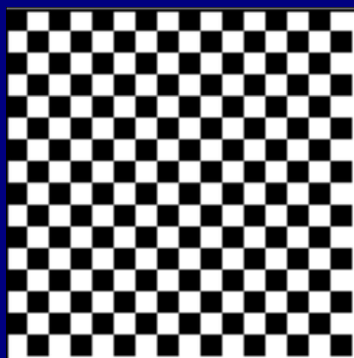


Dose Uniformity

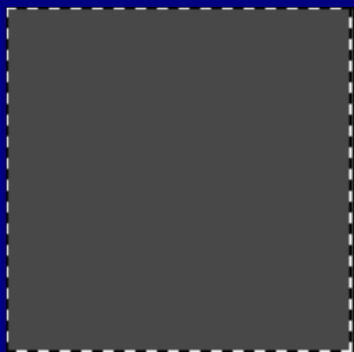
- Gamma camera resolution ~1 cm.
- Beta-ray mean range ~1 mm.
- Standard scintigraphic imaging may fail to adequately sample spatial distribution of activity for (therapeutic) dosimetry purposes.

Matrix Size vs Dose Distribution

3 mm
voxels



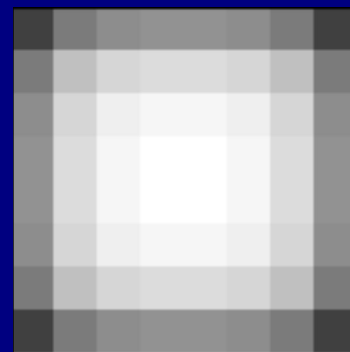
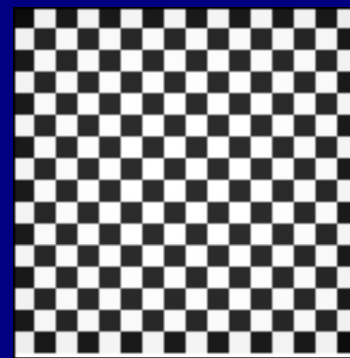
6 mm
voxels



activity

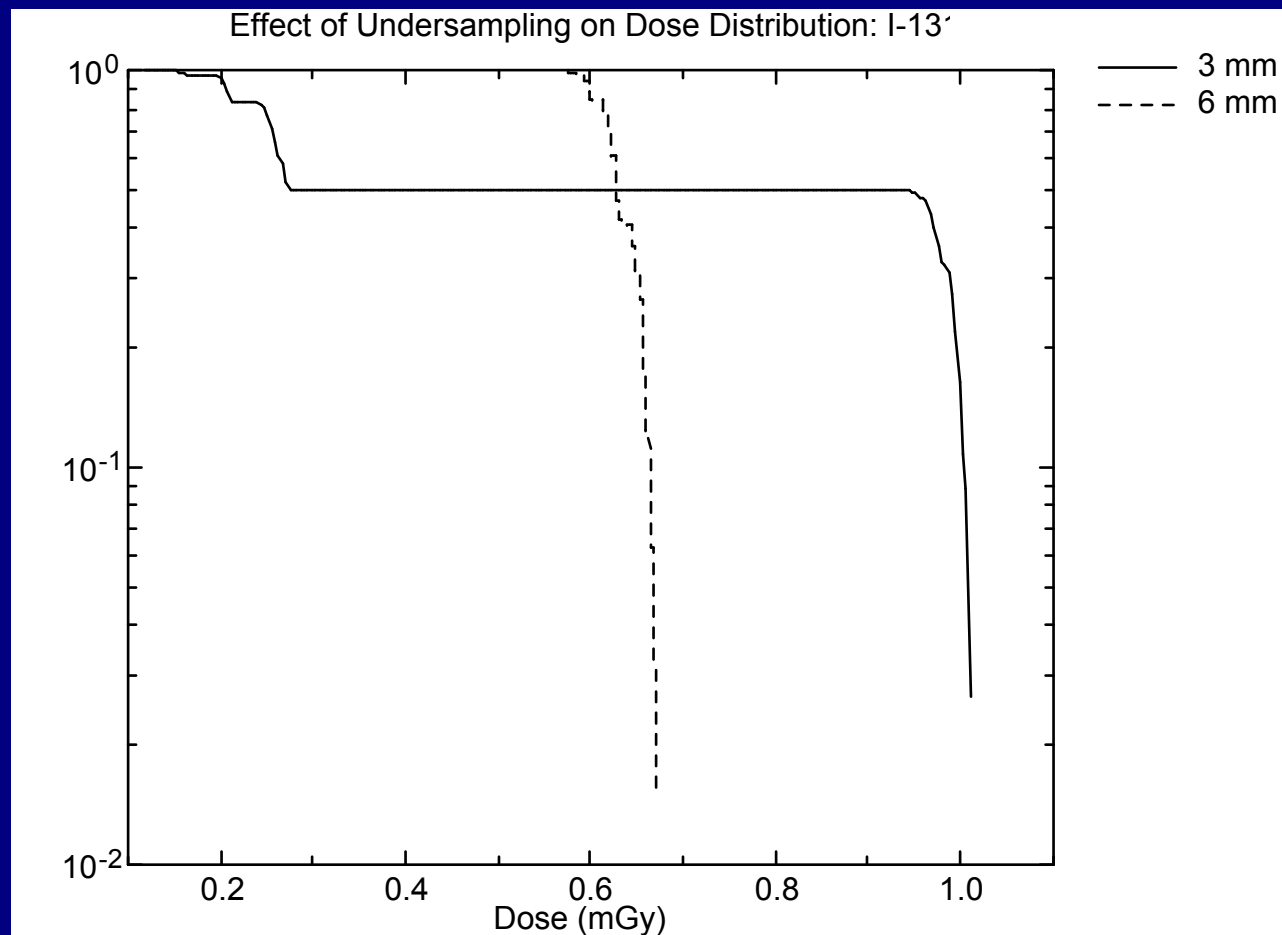
I-131 VDK
Convolution

*Fine structure
lost due to
undersampling*

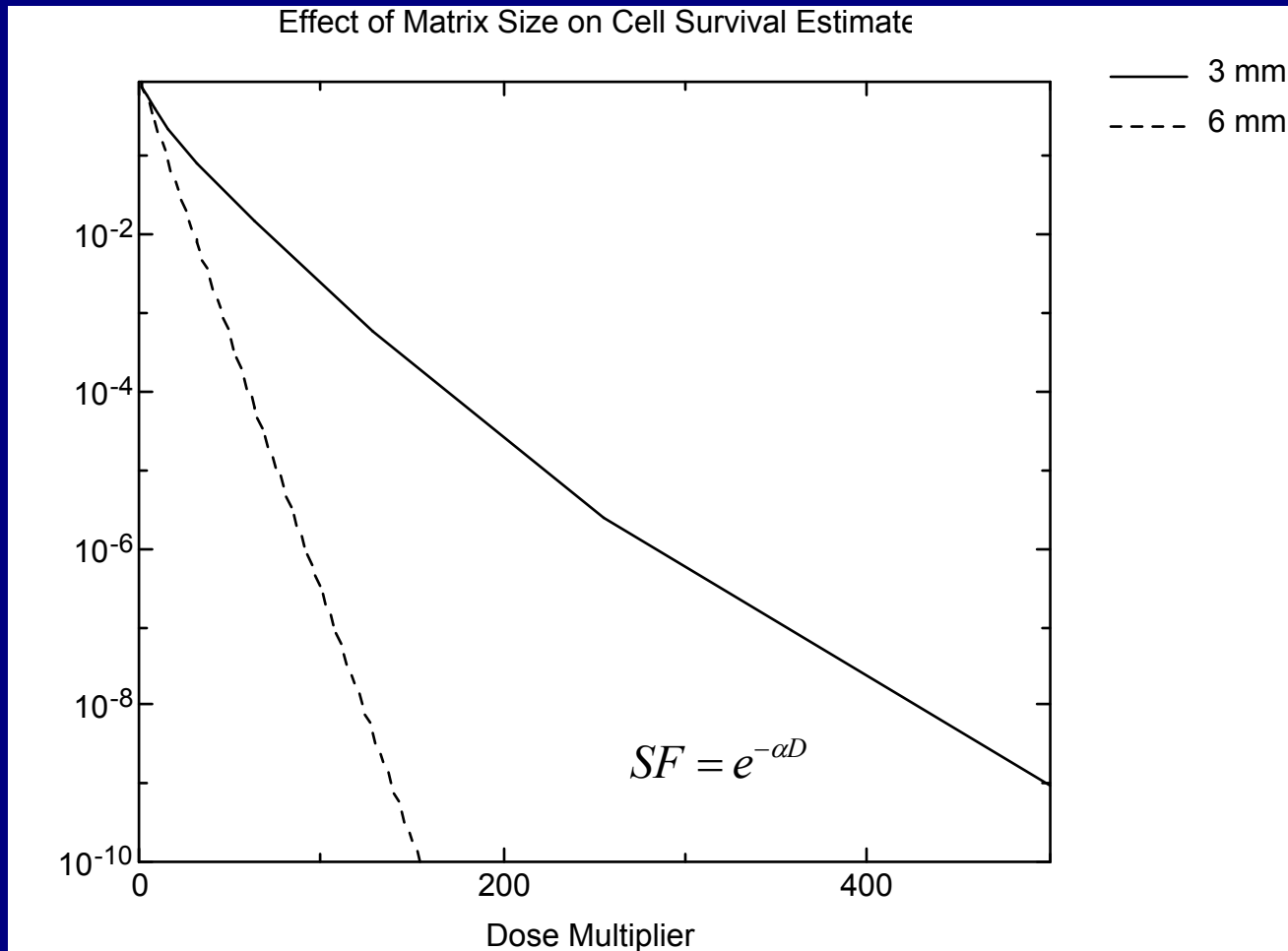


dose

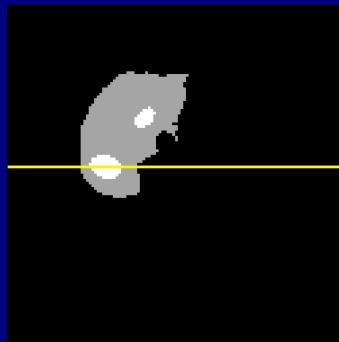
DVH: Impact of Undersampling



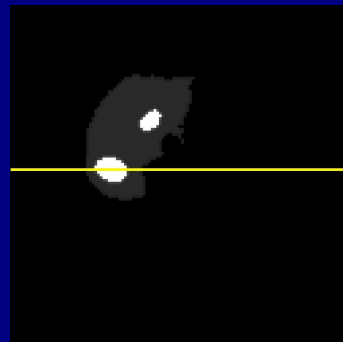
Surviving Fractions



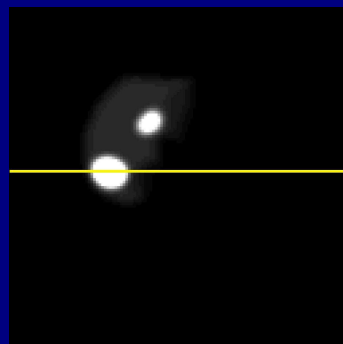
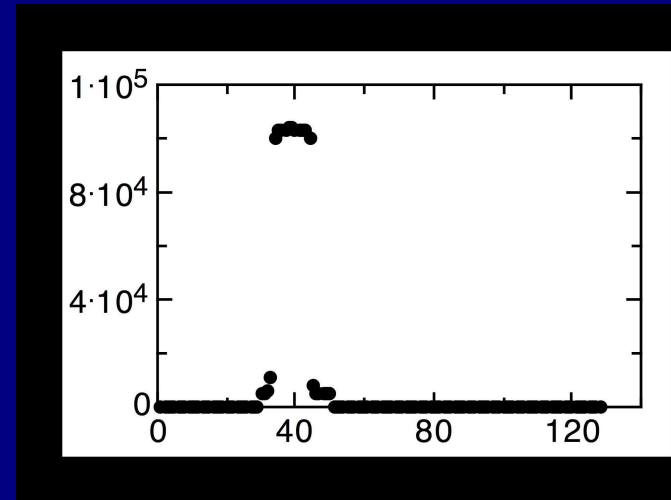
Partial Volume Effect



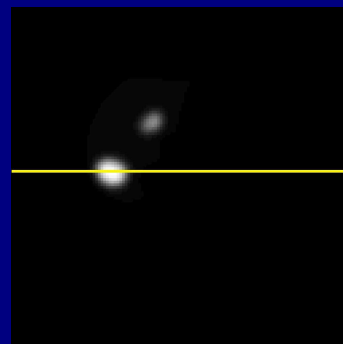
True Activity



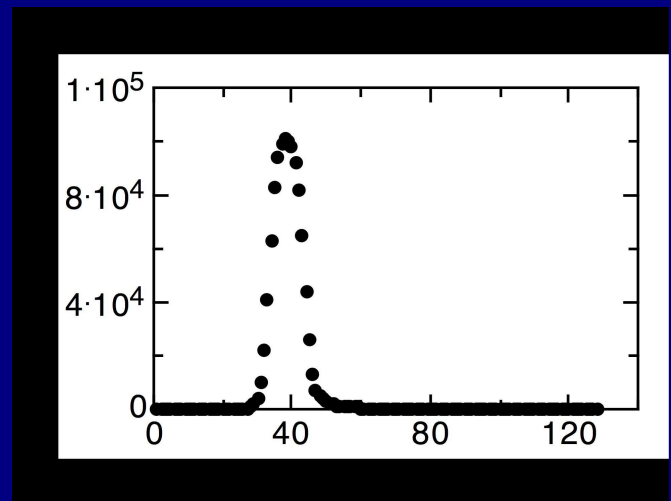
True Dose



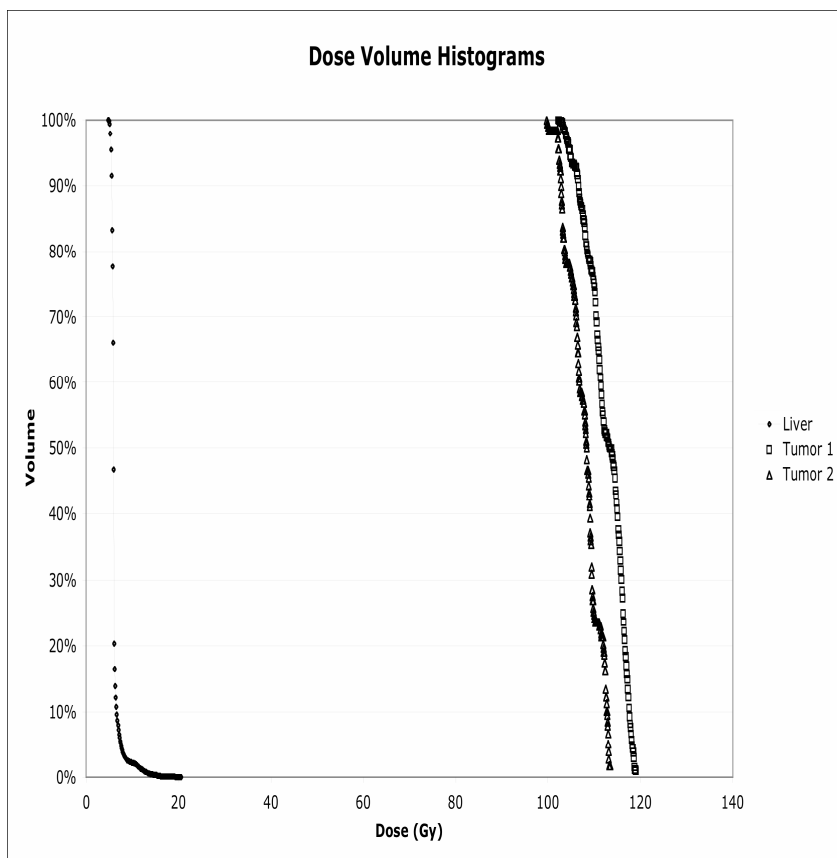
Measured Activity



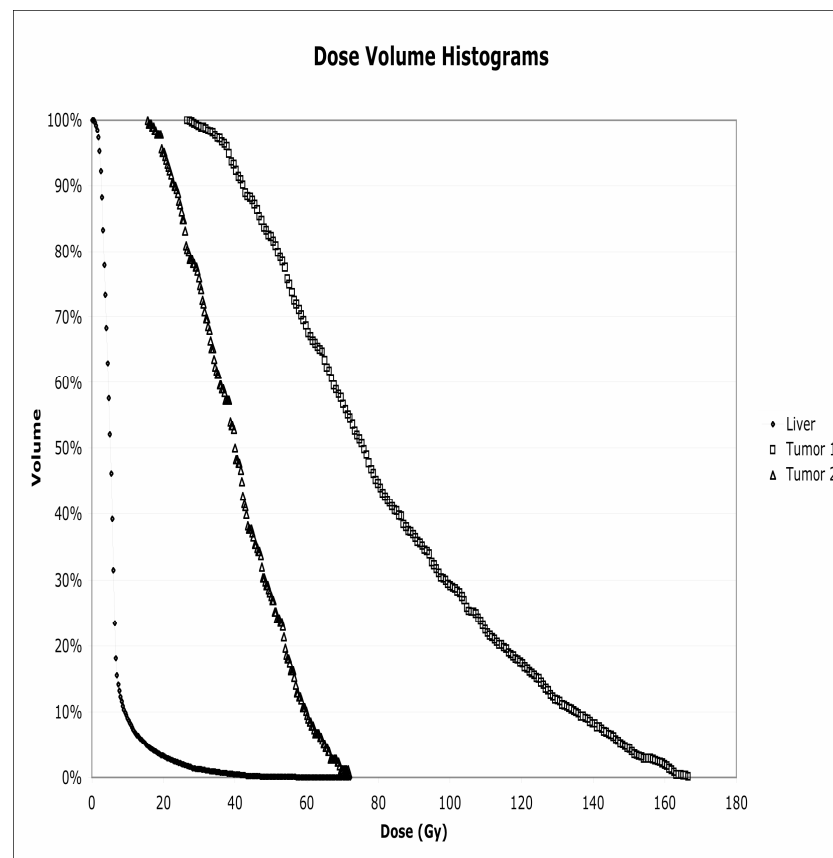
Estimated Dose



DVH vs Partial Volume Effect



True DVH



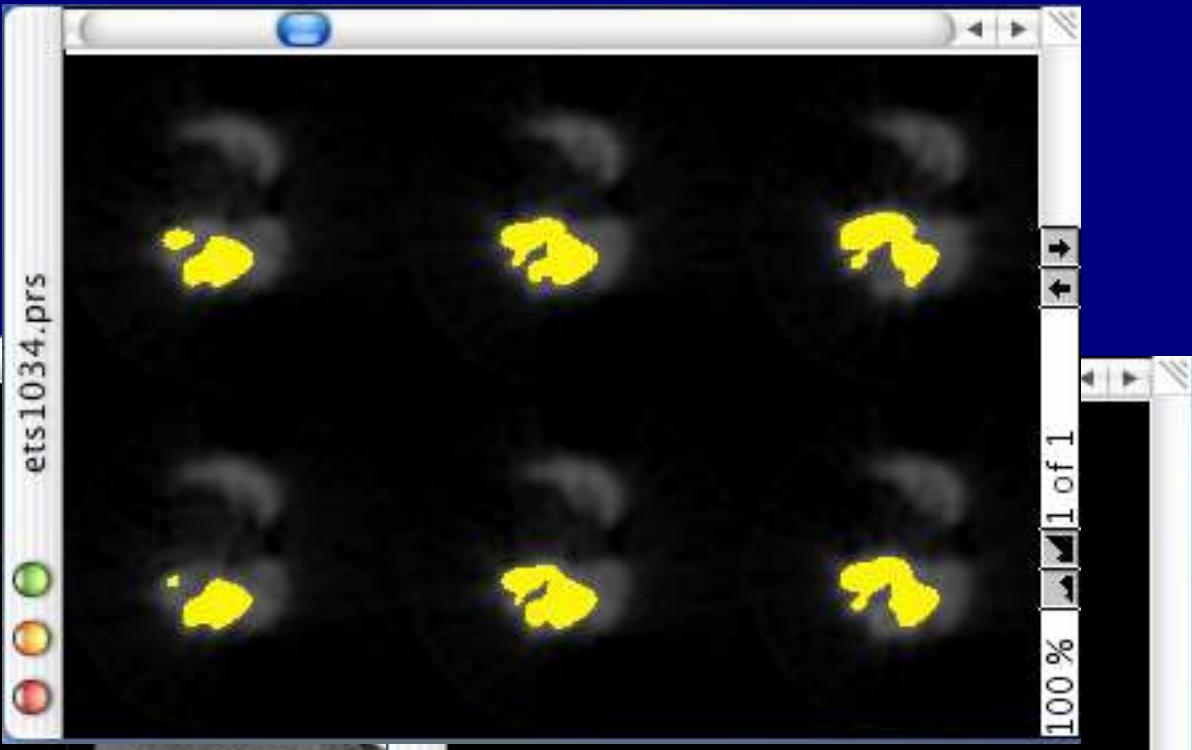
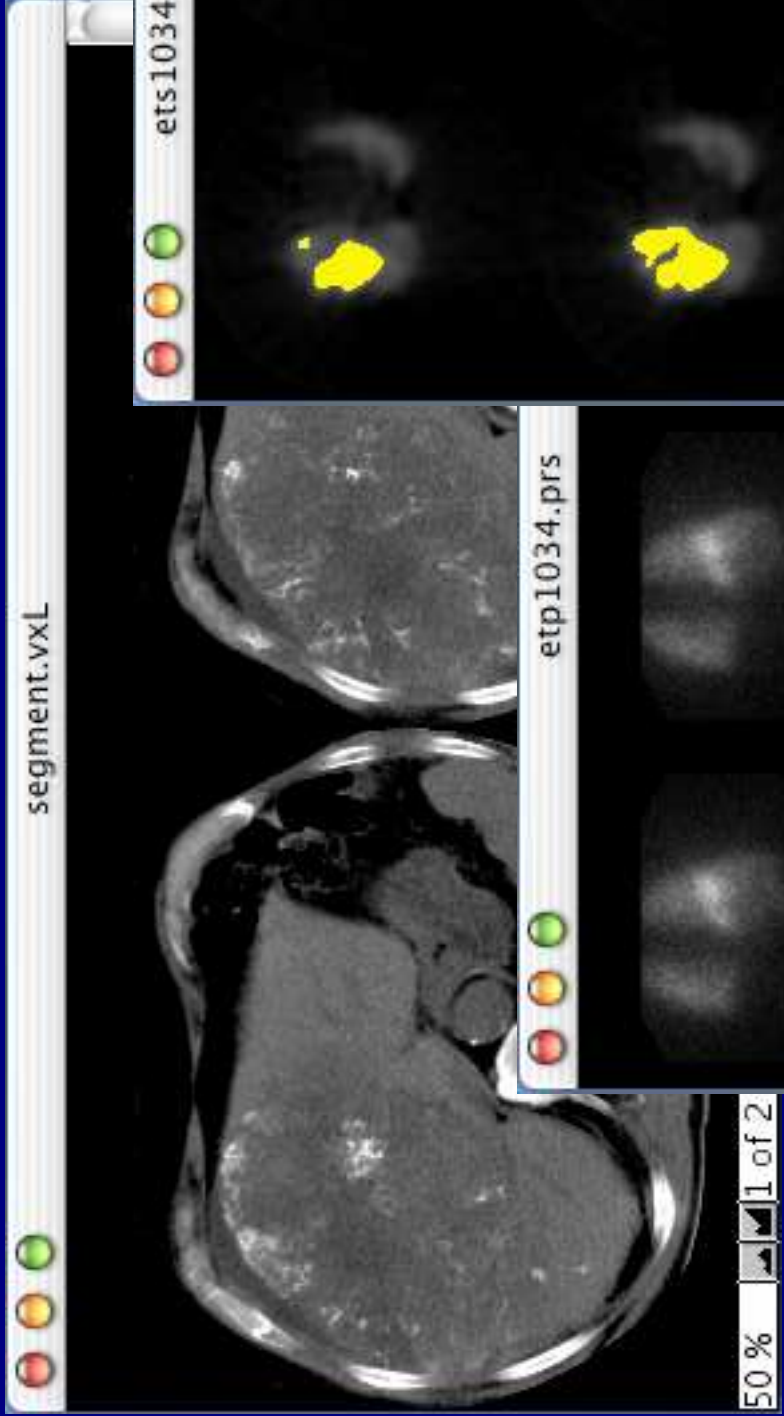
Estimated DVH

The Bottom Line

- Therapeutic dosimetry requires both total dose and dose rate distributions.
- May need very small (even cellular) scale spatial and temporal distribution.
- Will be relying on ~~fudge~~ calibration factors for the foreseeable future.

St. George Dosimetry Suite

- MrVoxel
 - Flexible tool for interactive medical image registration and segmentation
- VOXnova
 - Monte Carlo code for radiation transport in voxel geometries
- Millstone
 - Software system for building protocol-specific dosimetry tools



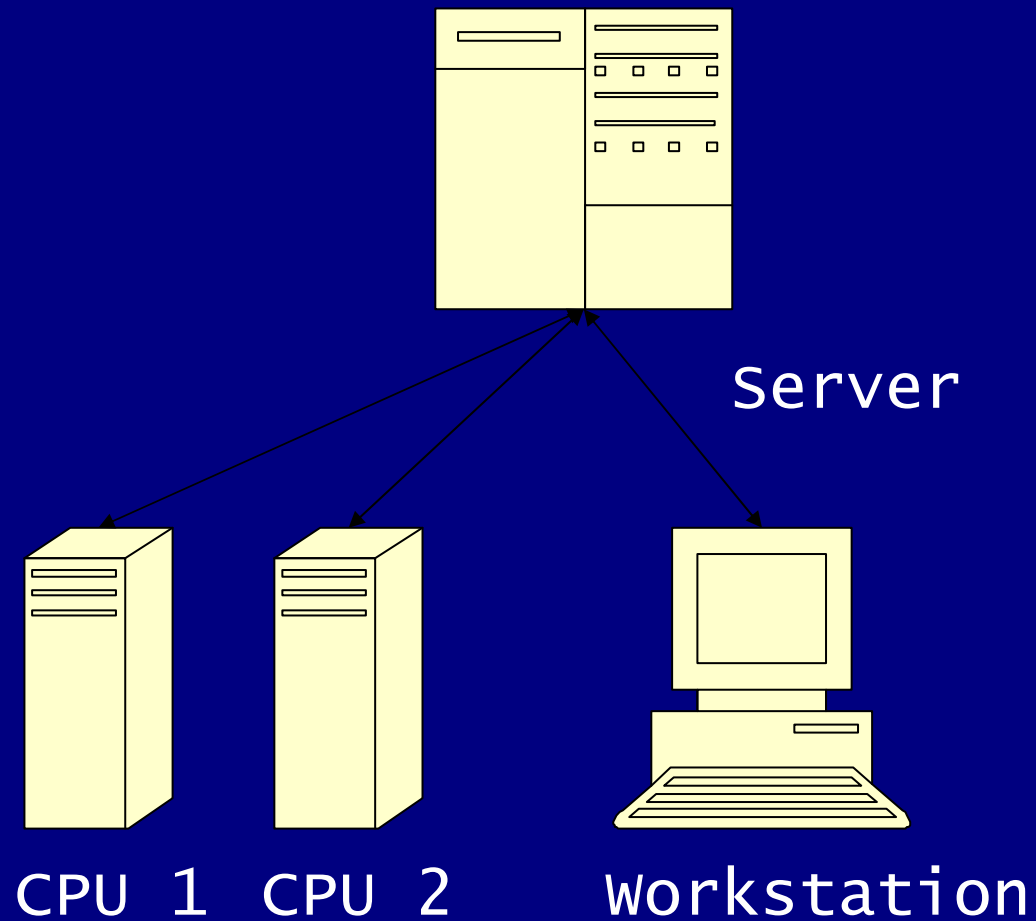
Millstone

- Extends the Tcl/Tk scripting tool by providing a data model and function library suitable for medical imaging & radionuclide dosimetry.
- Uses a relational database instead of a traditional in-memory data model.
- Supports image data, text tables and unstructured binary data.
- Imports and exports Interfile (3.3) files.

Millstone: Multi-Layer Design

Tcl	Tcl is an extensible scripting language with a C-like syntax. It is available on most common platforms and can be combined with Tk to build graphical user interfaces.
Millstone	Millstone is a C++ library used to manage and manipulate medical imaging data. It is designed for extensibility and robustness.
PostgreSQL	PostgreSQL is an industrial-strength, open-source relational database management system (RDBMS) with full transactional semantics.

Millstone: Client-Server Architecture



Therapy Dosimetry: HCC

Acquire Transmission, Whole Body, SPECT & CT images

Smooth and scale Co-57 transmission image to desired energy

Fuse reconstructed SPECT (non-quant) to CT slices

Register whole body emission image to fused SPECT slices

Register and merge Whole body emission & transmission images

Manual segmentation of CT into attenuation classes (lung, bone, etc)

Manual segmentation of CT into regions of interest (liver, tumor)

Regions of interest drawn on planar whole body images

Non-quant SPECT reconstruction for calculating CTF

Automated registration of reconstruction with SPECT fusion template

Attenuation map and ROI map sampled into reconstructed slices

Quantitative SPECT reconstruction (not scatter corrected)

Voxel-by-voxel curve fitting for cumulated activity map

On-the-fly generation of voxel dose kernel for SPECT matrix

VDK convolution of activity and cumulated activity maps

ROI analysis to extract source activity & dose volume histograms

Total dose map fused with CT slices for dose distribution review

MrVoxel

Millstone

VOXnova

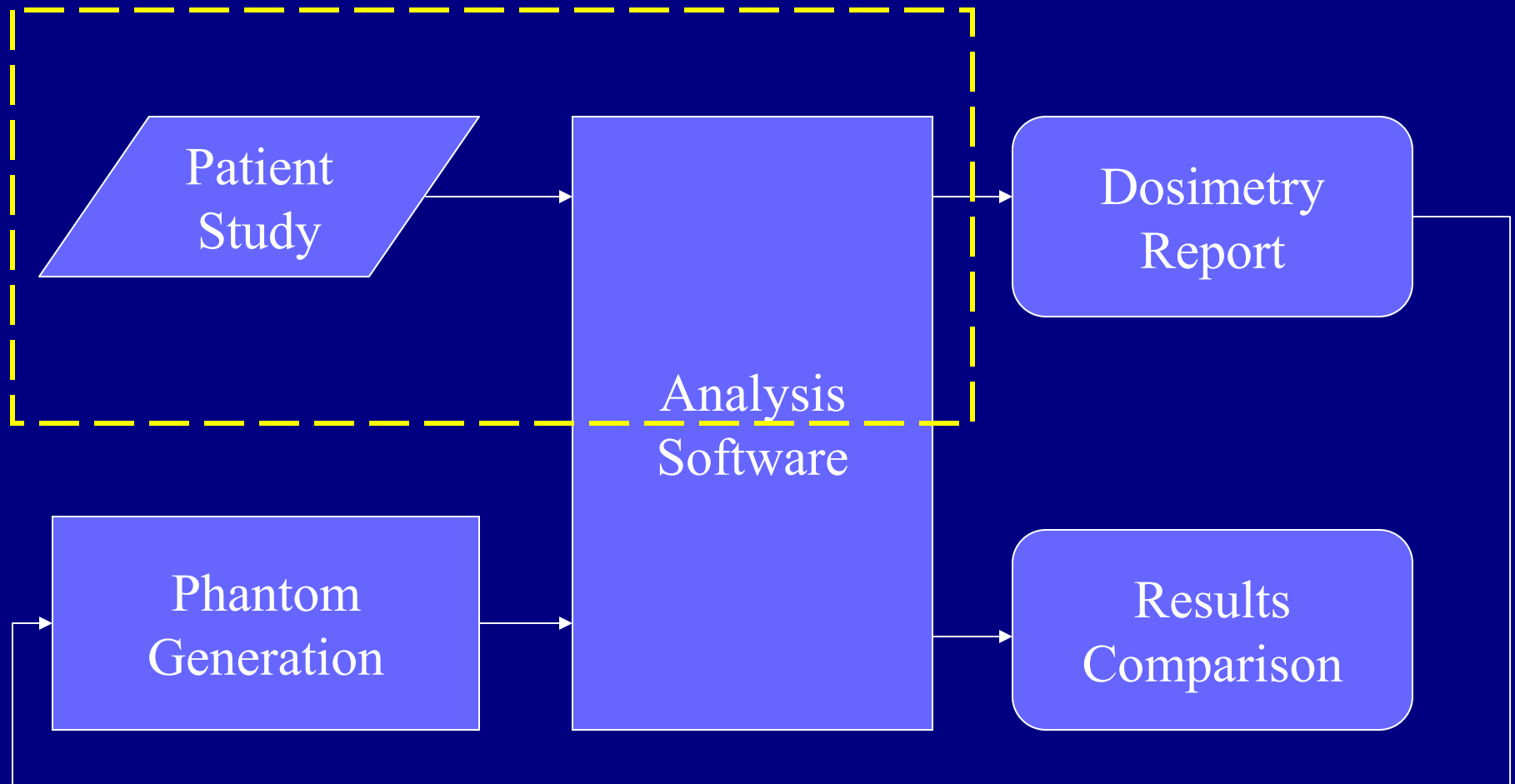
Validating Dosimetry Systems

- Dosimetry protocols can be complex and time consuming to perform.
- Physical phantom studies are valuable but don't test all aspects.
- Simulation studies are getting cheaper to perform but can be challenging to set up.
- Millstone' original purpose: make it easier to set up simulation studies.

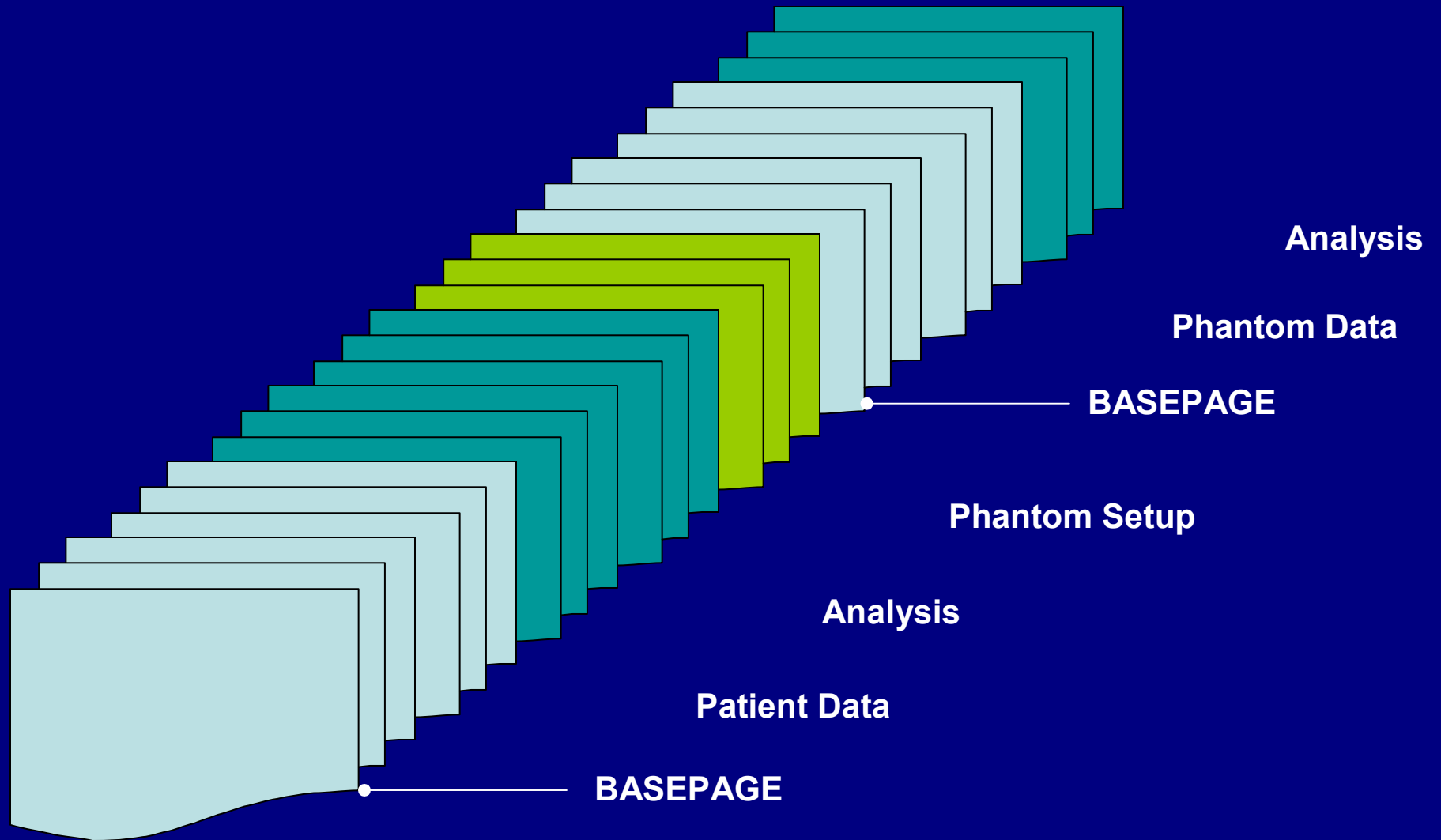
Millstone: designed for testing

- Data model comprises Albums and Editors
- Editors are independent modules encapsulating single, well-defined transformations to albums
- Tests are scripted using Tcl
- Multiple unit test scripts per module
- Tests are automated, returning ok, fail or no response
- Test inputs and outputs can be exported in Interfile format
- Database is preserved at end of each unit test run

Automated Cross-check



Internal Validation: Structure



Summary

- Therapeutic dosimetry requires calculating a 4D dose-rate distribution.
- Much of the work can be automated, including some elements of validation.
- Not every problem is a nail: build tools to suit protocols, not vice-versa.