

## RIT and Leukaemia: Dosimetry and Modelling



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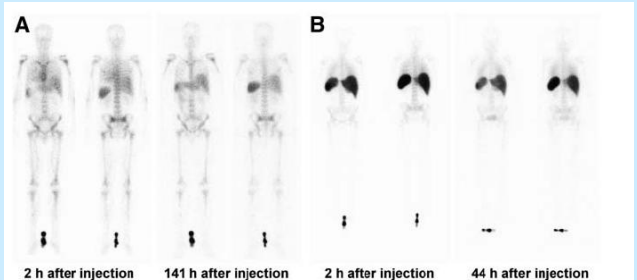
## TRNT in Ulm

- Radioimmunotherapy is performed since 1998
  - Conditioning before stem cell transplantation in leukaemia
- Antibodies
  - anti-CD66, anti-CD45, anti-CD20
- Nuclides
  - $^{188}\text{Re}$ ,  $^{111}\text{In}/^{90}\text{Y}$ , ( $^{213}\text{Bi}$ )
- Dosimetry
  - ULMDOS (Glatting et al. 2005)

## Objectives

- Development of a physiologically based pharmacokinetic model to describe radioimmunotherapy (RIT) using monoclonal antibodies
- Predict the optimal amount of unlabelled anti-CD45 antibody

## Introduction: Anti-CD45



0,5 mg/kg KG unlabelled Ab

no unlabelled Ab

G. Glatting et al. J Nucl Med 2006;47:1335-41

## Method I: Patients

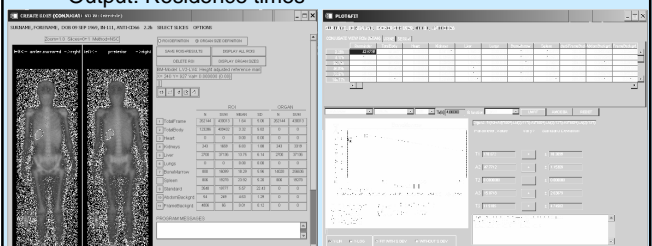
Patient no.	Disease	Age (y)	Sex	Unlabelled Ab	
				mg	mg/kg
1	AML, refractory	61	F	0	0.00
2	AML, relapsing	56	M	10	0.16
3	ALL, refractory	48	M	10	0.14
4	AML, relapsing	54	F	30	0.48
5	AML, refractory	44	M	45	0.49
6	AML, refractory	58	M	47	0.51
7	AML, refractory	53	M	42.5	0.48
8	AML, relapsing	49	M	43	0.51
Mean $\pm$ SD		—	—	53 $\pm$ 6	—

### Measurements:

- Gamma camera: E.CAM (Siemens), scatter correction: TEW
- Sample times: 2 and 4 h and 1, 2, 3 and 6 d p.i.
- Blood Sample times: 5 and 30 min, 1, 2 and 4 h and 1, 2, 3 and 6 d p.i.

## Method II: Dosimetry

- ULMDOS
- IDL 6.1 (Interactive Data Language), Windows 2000 / XP
- Input: Interfile, DICOM
- Output: Residence times



Glatting G et al. Internal radionuclide therapy: The UlmDos software for treatment planning. Med Phys 2005; 32(7): 2399-2405.

## Method III: Model

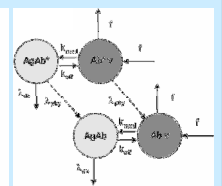
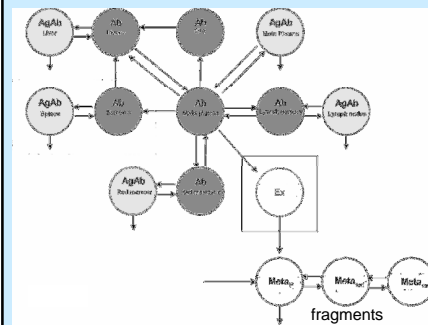
### Model development:

- SAAM II: Simulation, Analysis and Modelling Software
- Model selection AICc (corrected Akaike Information Criterion)

### Model:

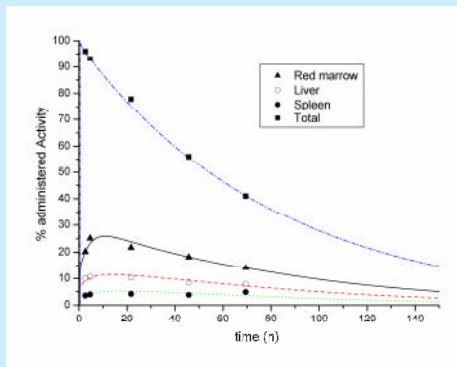
- Antibody distribution via blood flows
- Competitive binding of unlabelled und labelled Ab
- Degradation of Antigen-Ab complexes
- Degradation of unbound Ab

## Results I: Model

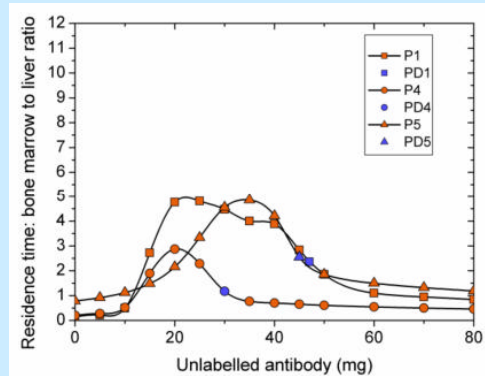


Connected via the same number of antigens in the organs and the decay!

## Results II: Example



## Results III: Potential improvement



## Summary / Outlook

- Model could adequately describe the biodistribution of anti-CD45 antibody (validation is ongoing)
- Modelling can help improving RIT (for some antibodies)