SAR Distribution in Test Animals Exposed to RF Radiation

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Background & Motivation

- *in vivo* studies need to be optimized with respect to the sensitivities of the hypothesis being tested, for ethical, time and cost reasons
- one key parameter is a well defined dose of the chemical or physical agent
- detailed and accurate dosimetric information is a basic precondition to enable interpretations and valuations of the results of histopathology

Example of a Possible Misinterpretation

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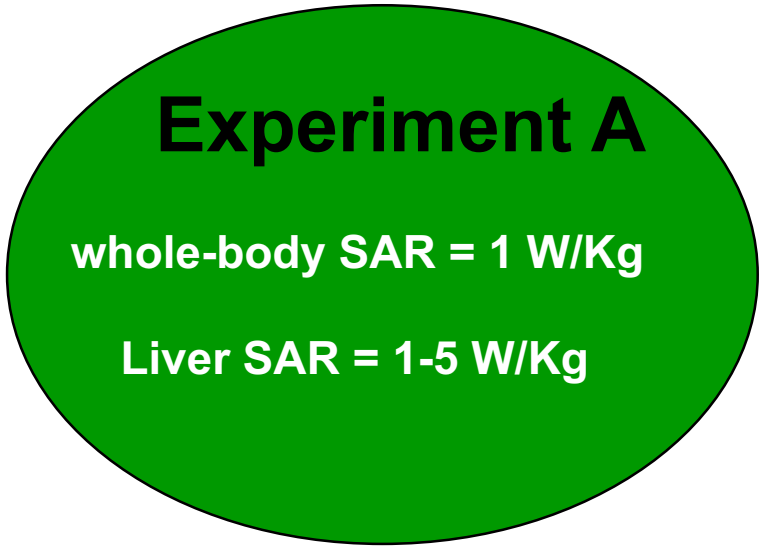
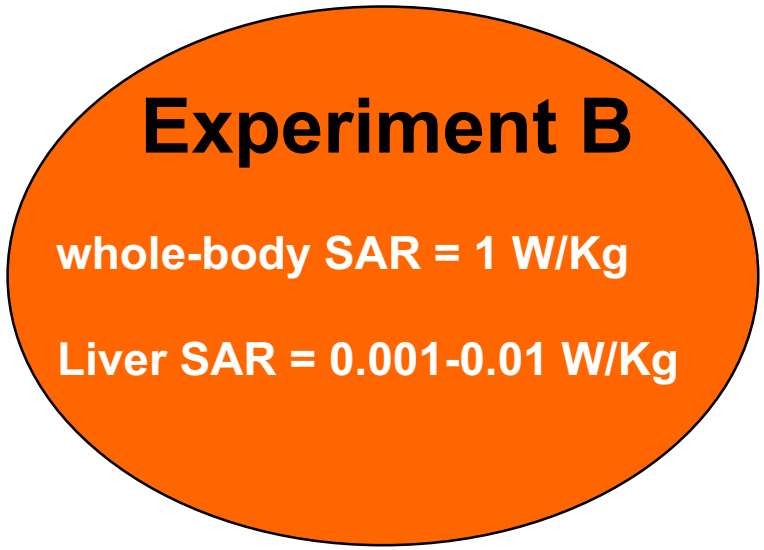




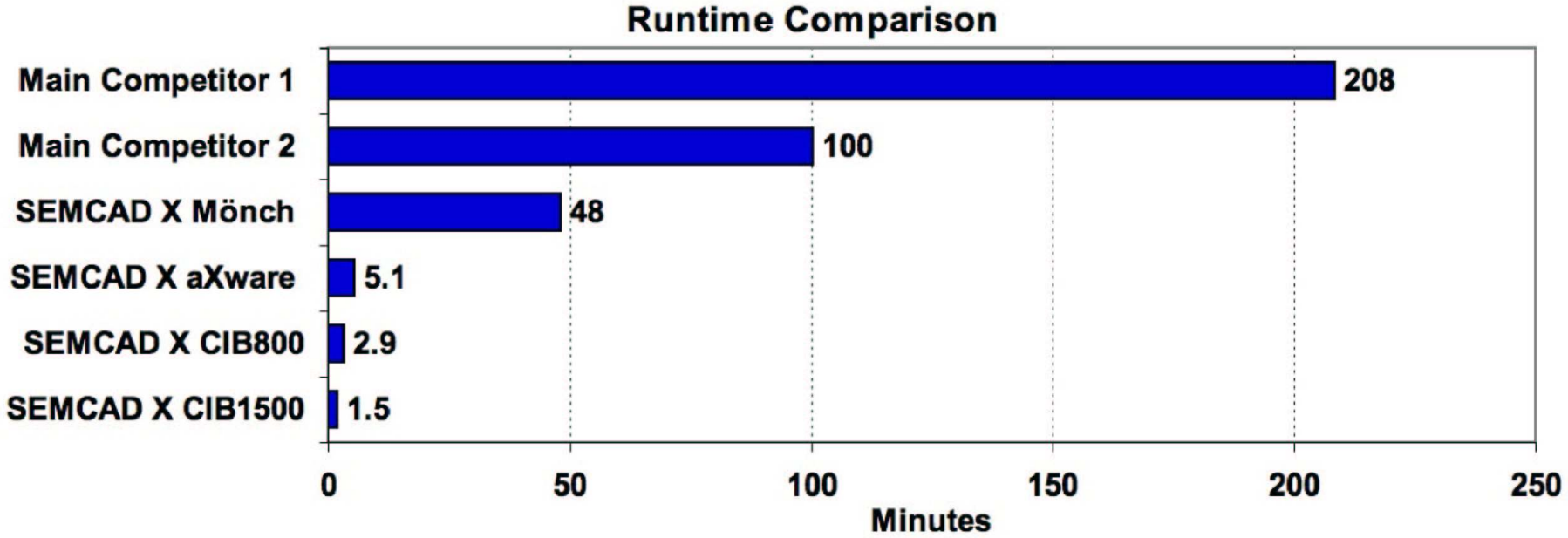
Objectives

- generation of high resolution anatomical models of animals
- dependence of SAR values and distribution on different factors: frequency, polarization, resolution
- identification of relevant parameters for the comparison of animal studies
- to develop a universally applicable methodology for the complete, detailed dosimetric analysis of ***in vivo*** experiments

Methods

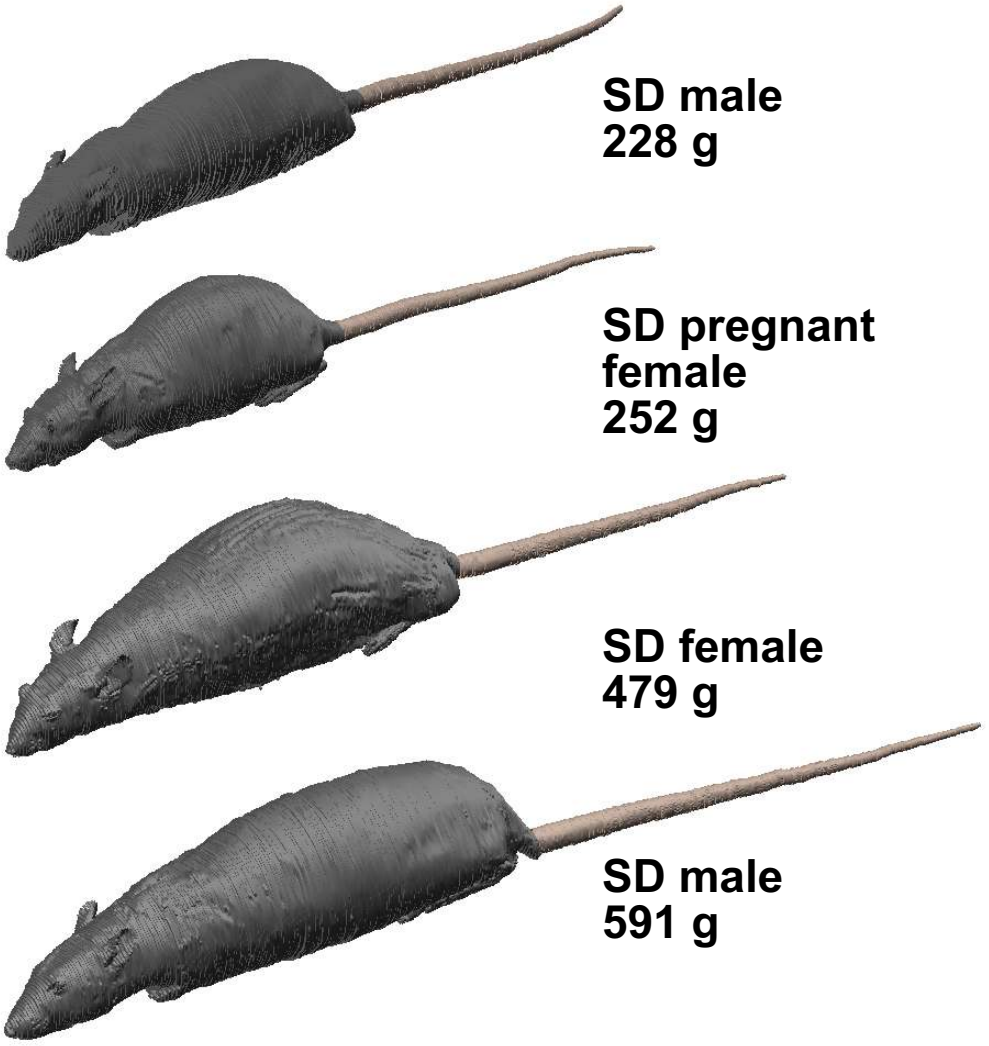
Simulation Tool SEMCAD X

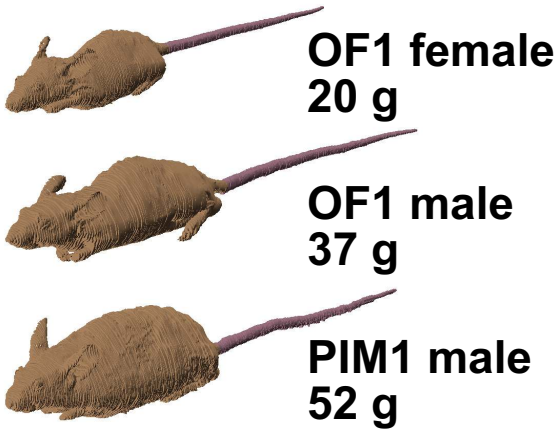
- import and handling of complex CAD data (several 10'000 CAD parts)
- non-uniform and conformal grids (>1 billion voxels)
- highly efficient EM and thermal solvers incl. blood flow
- availability of high resolution anatomical models (CAD based)
- extraction of required quantities (E- and H-field, SAR and temperature distributions, whole-body and organ-specific average SAR, peak spatial average SAR, etc.)



Anatomical Model Requirements

- high resolution anatomical models development based in Microtom slices
- manual identification of tissues supported by software for imaging and segmentation
- anatomical resolution <<1 % of total length (d_slice: 0.5 mm for mice & 1.2 mm for rats)





Measurement Tools DASY4 & EASY4

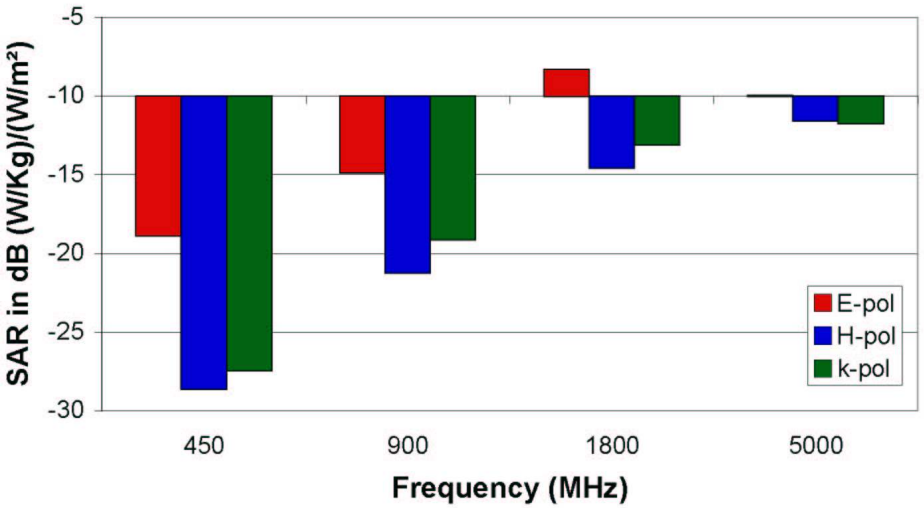
- E- and H-field probes (d < 5 mm, isotropic response of better than 0.5 dB)
- dosimetric probes (d < 1.5 mm, sensitivity of < 1 mW/kg, isotropic response of better than 0.5 dB)
- temperature probes (response time of < 1s, sensitivity of < 10 mK)
- position accuracy (<< 1 mm)

Relevant Parameter for the Comparison of Animal Studies

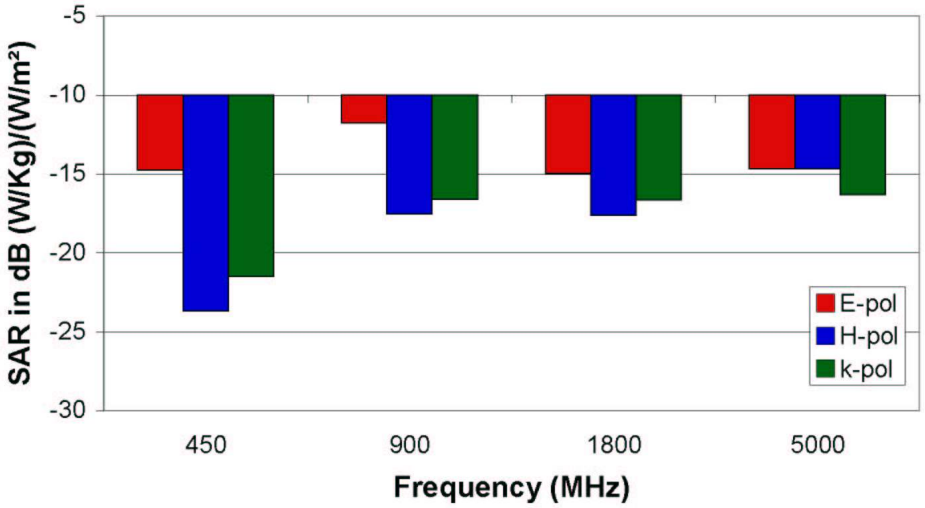
Polarization and Frequency Denpendence of WB SAR

- Whole-body averaged SAR in dB (W/Kg)/(W/m^2)

Mouse

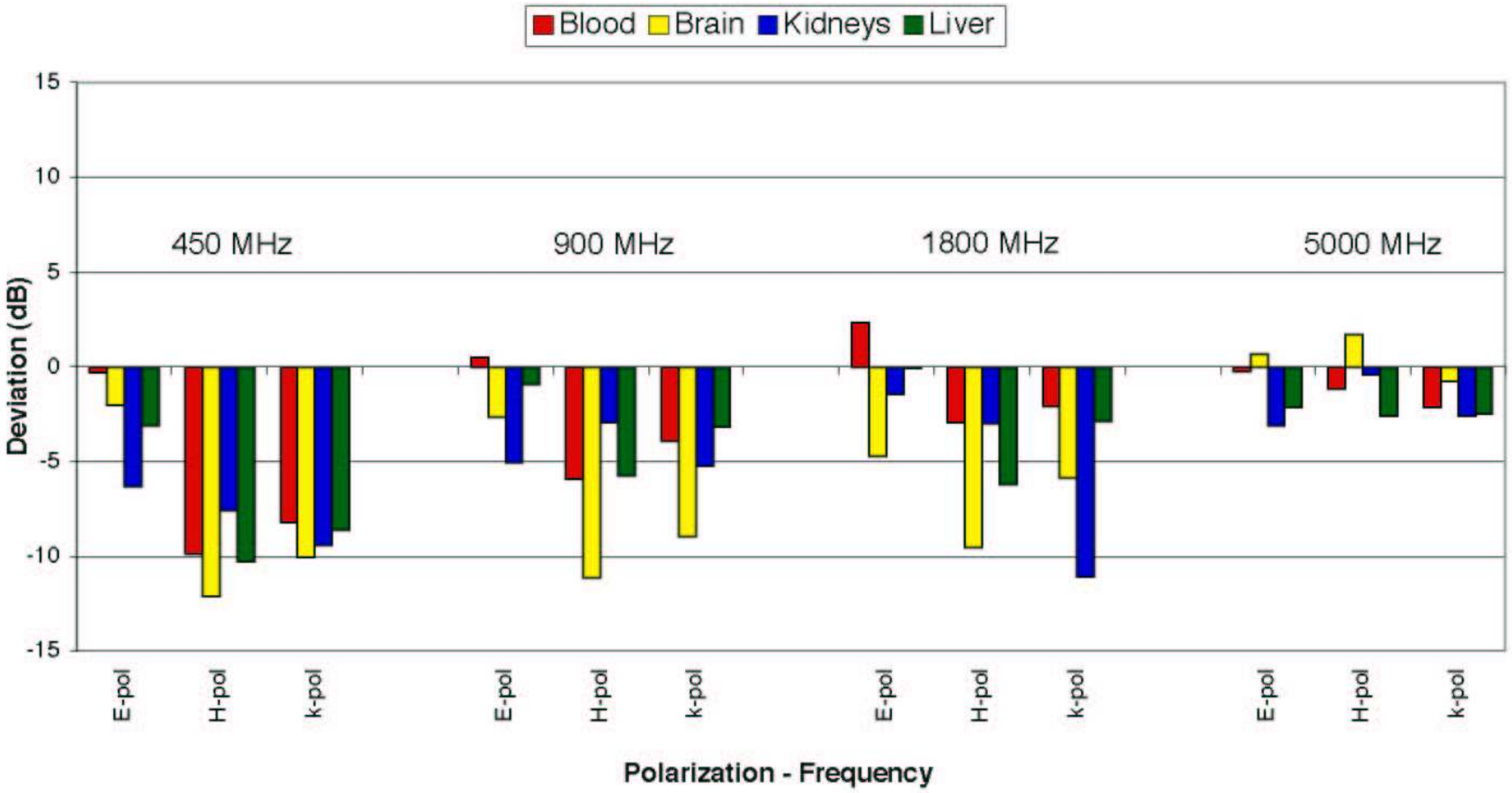


Rat



Mouse Organ-Specific SAR Variations

- deviation organ-specific avgeraged SAR of E-, H- and k-polarization vs. WB average SAR of E-pol



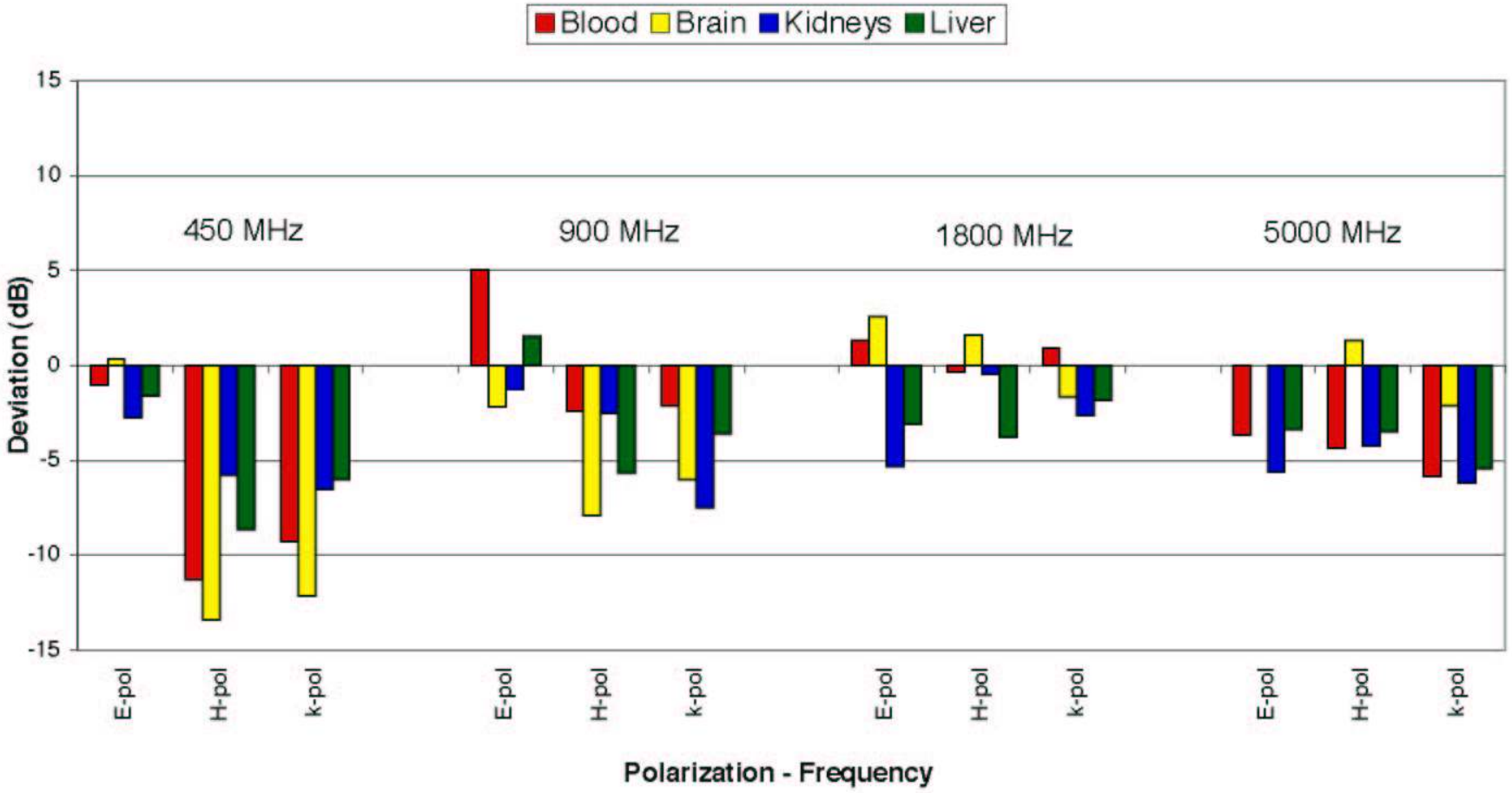
Mouse Organ-Specific SAR Variations

- maximal deviation in dB of mouse organ-specific average SAR among polarizations

Frequency	Brain (dB)	Kidneys (dB)
450 MHz	10	3
900 MHz	8	2
1800 MHz	5	10
5000 MHz	2	3

Rat Organ-Specific SAR Variations

- deviation organ-specific averaged SAR of E-, H- and k-polarization vs. WB average SAR of E-pol



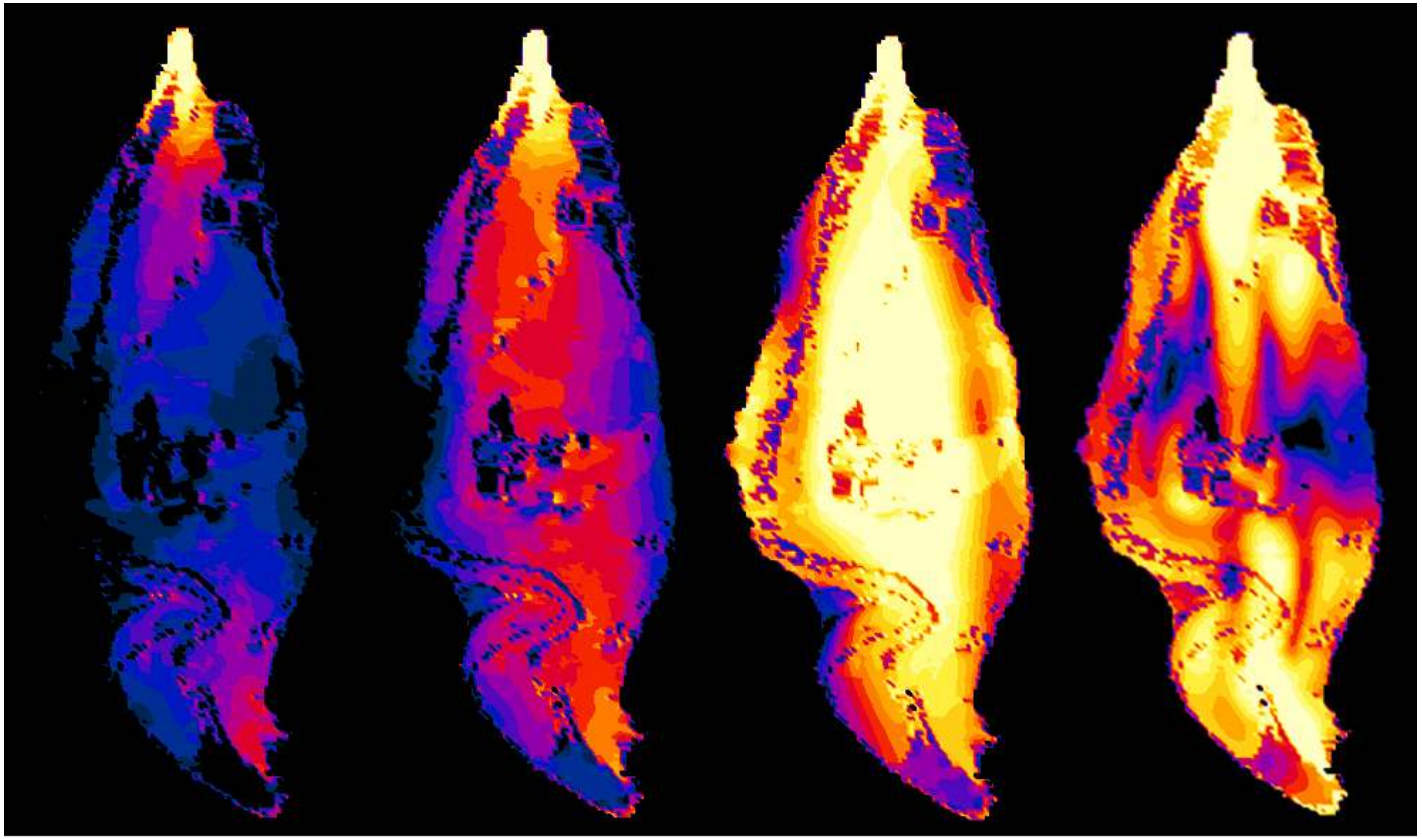
Rat Organ-Specific SAR Variations

- maximal deviation in dB of rat organ-specific average SAR among polarizations

Frequency	Brain (dB)	Kidneys (dB)
450 MHz	14	4
900 MHz	6	6
1800 MHz	4	5
5000 MHz	3	2

Mouse: SAR Distribution (E-polarization)

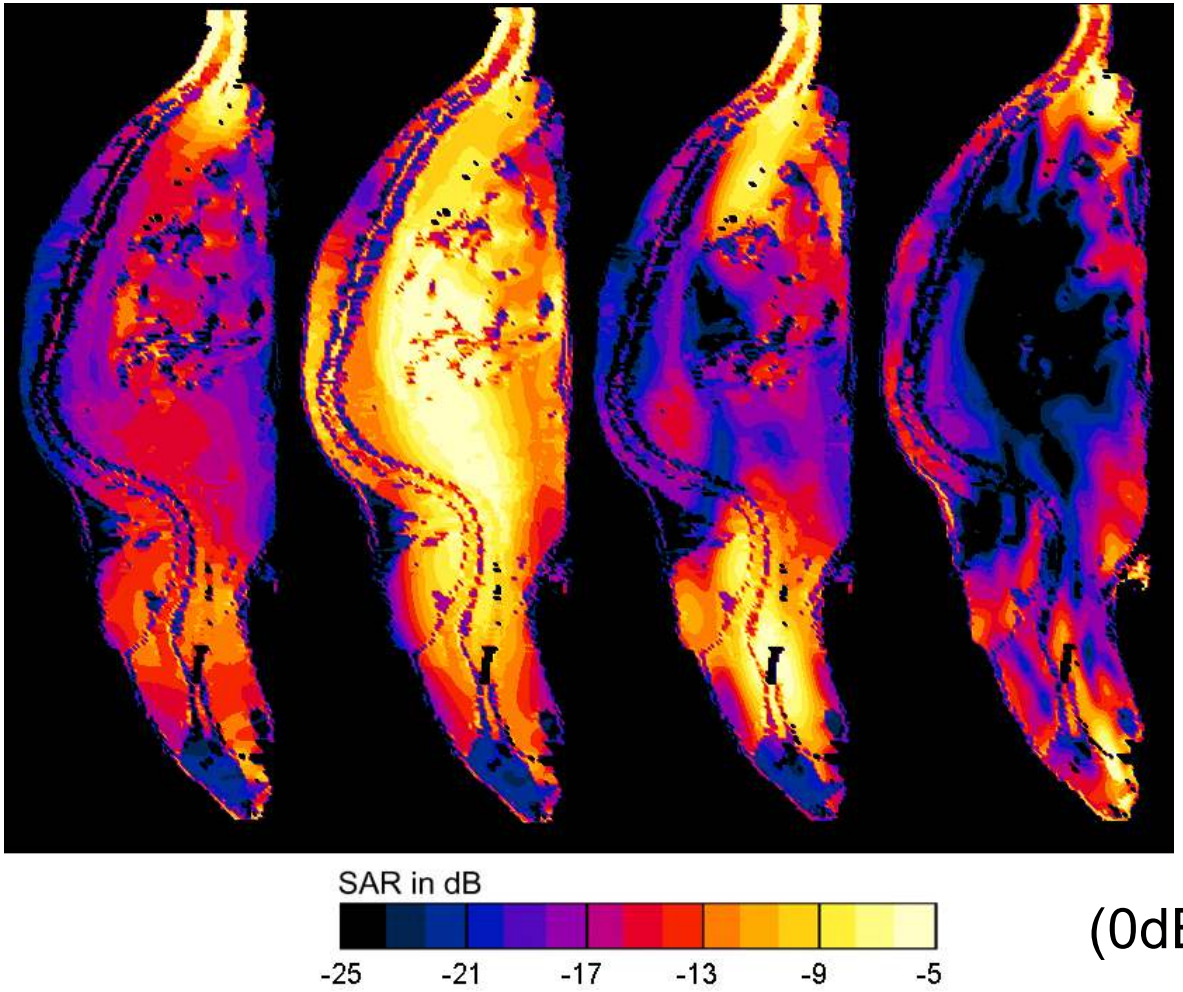
450MHz 900MHz 1.8GHz 5GHz



(0dB=1W/kg)

Rat: SAR Distribution (E-polarization)

450MHz 900MHz 1.8GHz 5GHz

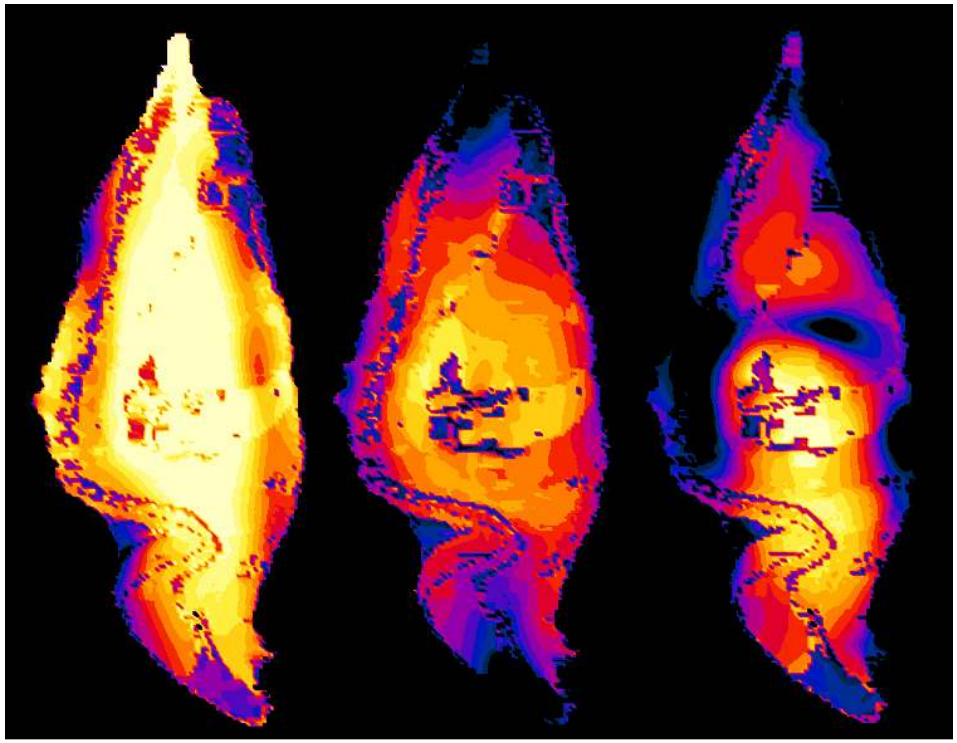


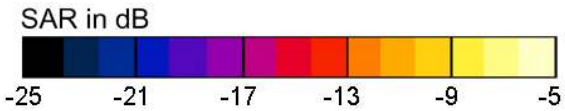
(0dB=1W/kg)

Comp. of SAR Distributions (close to body res.)

Mouse @ 1.8GHz

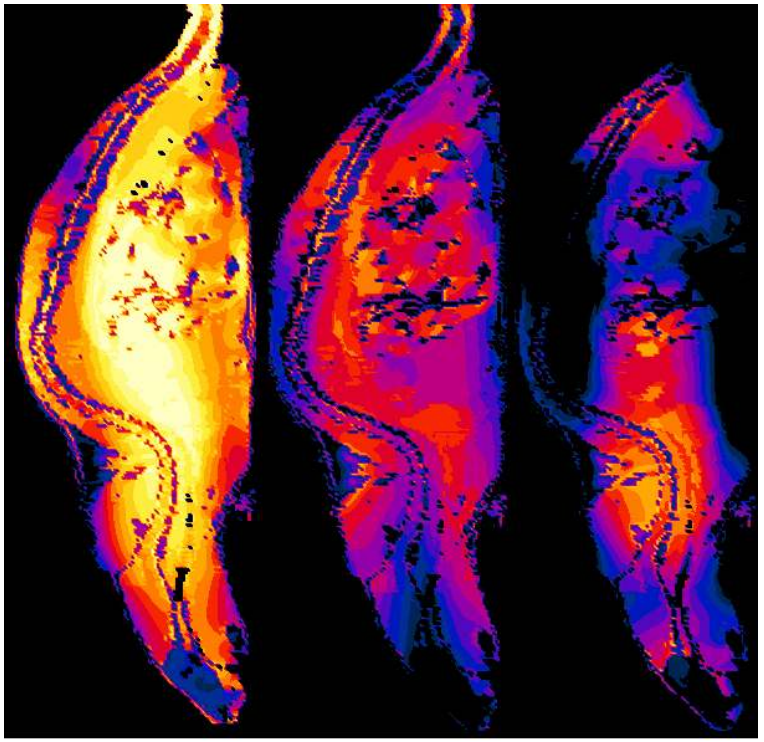
E-pol H-pol k-pol

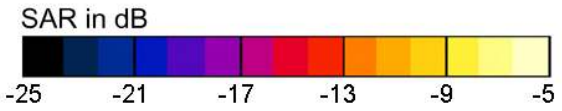




Rat @ 900MHz

E-pol H-pol k-pol

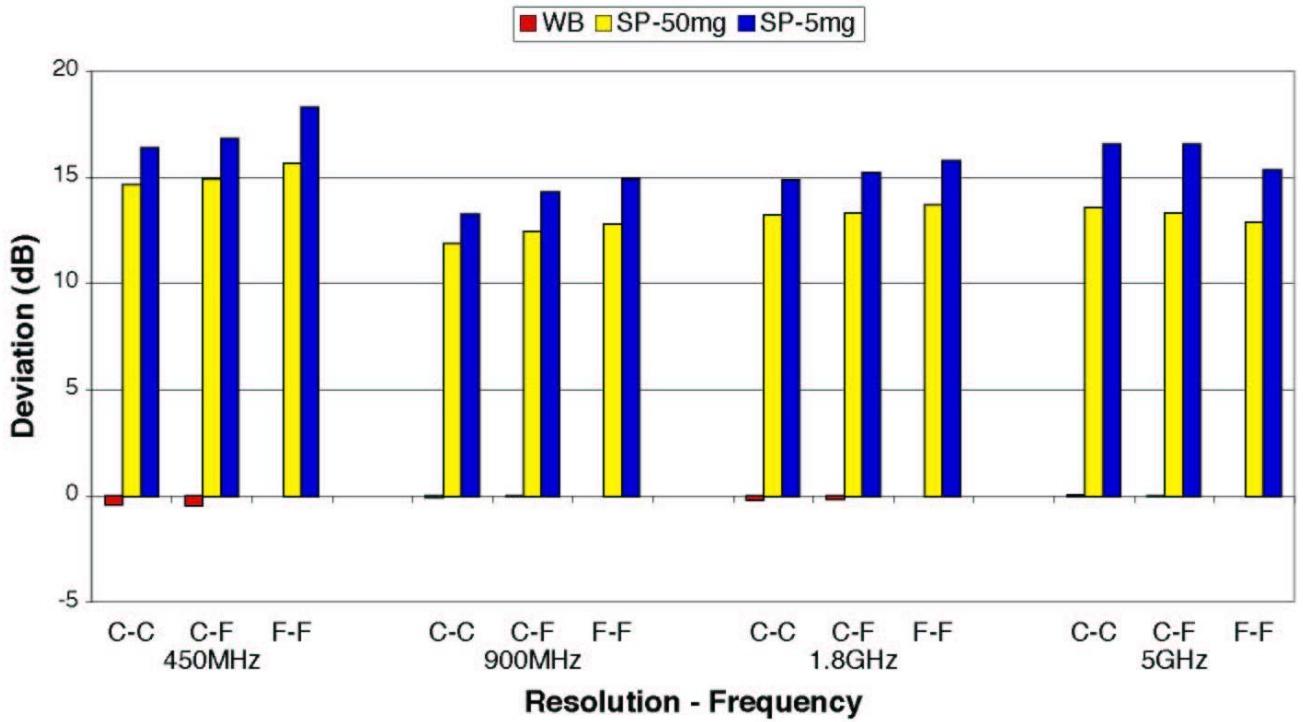




(0dB=1W/kg)

SAR values as a function of voxel resolution

- Rat deviation of SAR values vs. WB avg. SAR of F-F case



- CC: coarse anatomical resolution (1.2 mm) - coarse grid resolution (1.7mm^3)
- CF: coarse anatomical resolution (1.2 mm) - fine grid resolution (0.2mm^3)
- FF: fine anatomical resolution (0.6 mm) - fine grid resolution (0.2mm^3)

Discussion

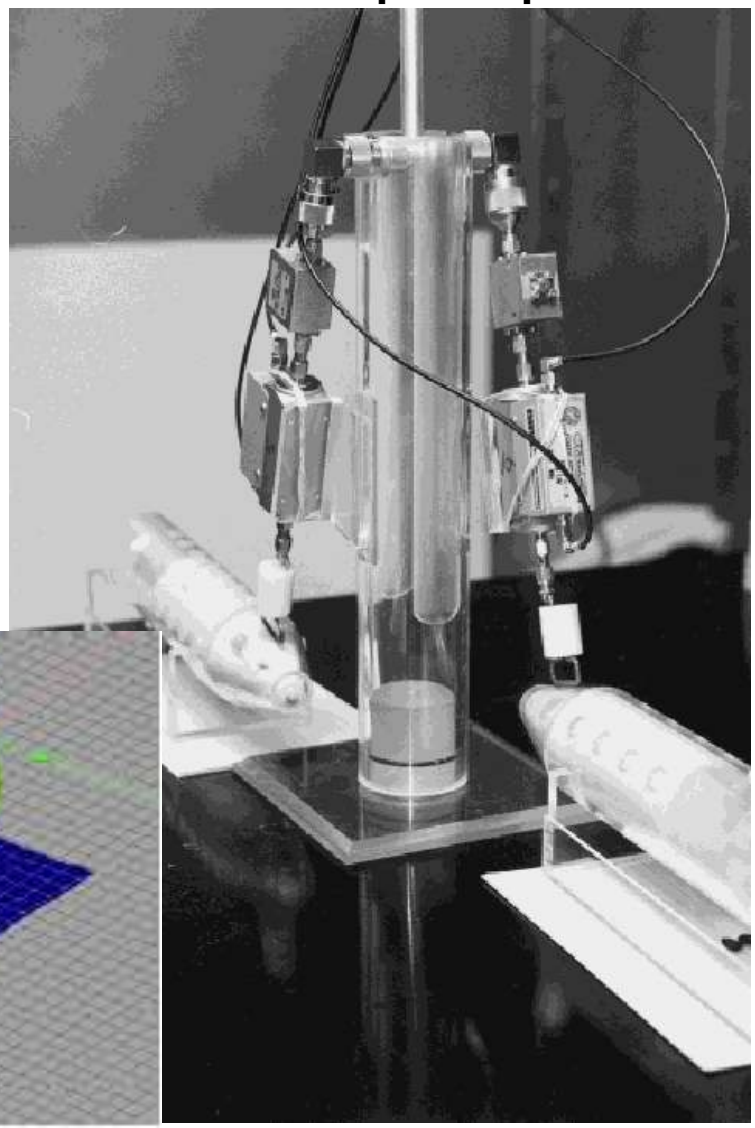
- SAR distributions highly depend on the frequency and polarization
- organ-specific SAR significantly vary, even with respect to whole-body averaged SAR
- comparable SAR distributions for mice @ 1.8GHz and rats @ 900MHz (that led NIEHS to use this scenario for their large scale studies)
- the uncertainty for WB SAR due to resolution is less than 0.5 dB
- the uncertainty at a grid resolution of 1.7mm^3 is bigger than 2 dB for peak spatial SAR

Overview of Exposure Concepts

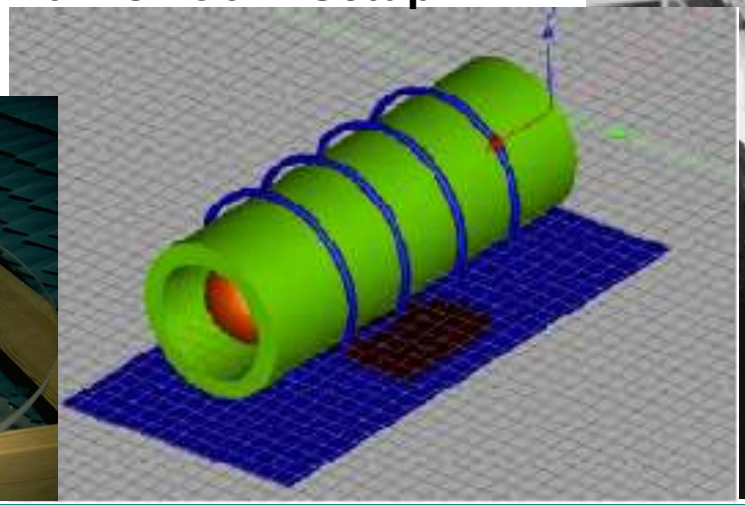
Concept: Open Systems (Near-Field Exposures)

- reasonable efficiency
- poor uniformity
- good variability
- small space requirements
- one exciter per one or two animals
- poor to medium isolation

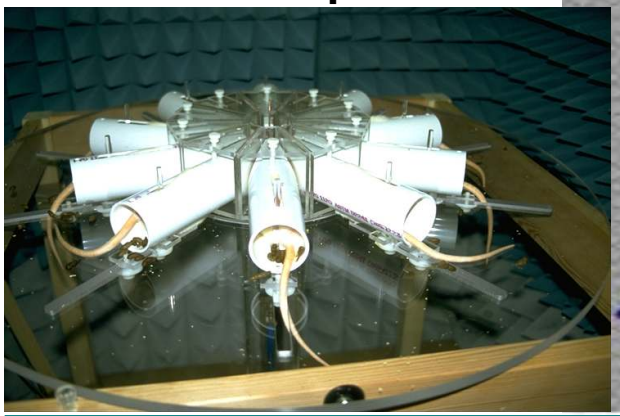
C.K. Chou's Loop Setup



Kain's "Coil" Setup



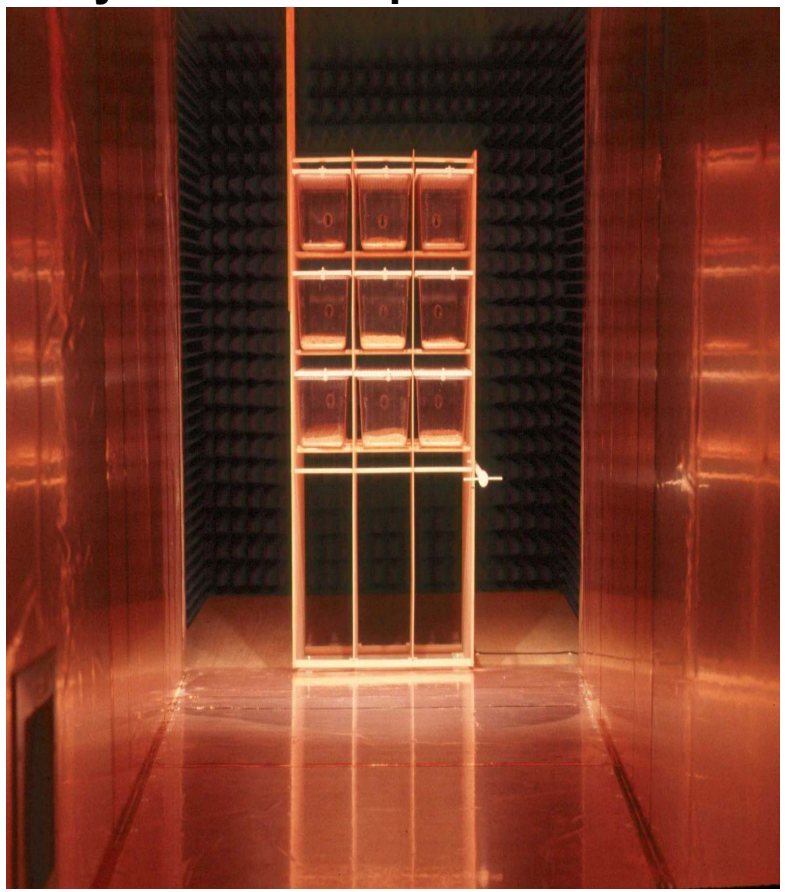
Carousell Setup



Concept: Open Systems ("Far"-Field)

- poor to medium efficiency
- good to reasonable uniformity
- medium variability (non-uniform incident exposure & higher modes)
- large space requirement
- one exciter per group or subgroub
- excellent isolation

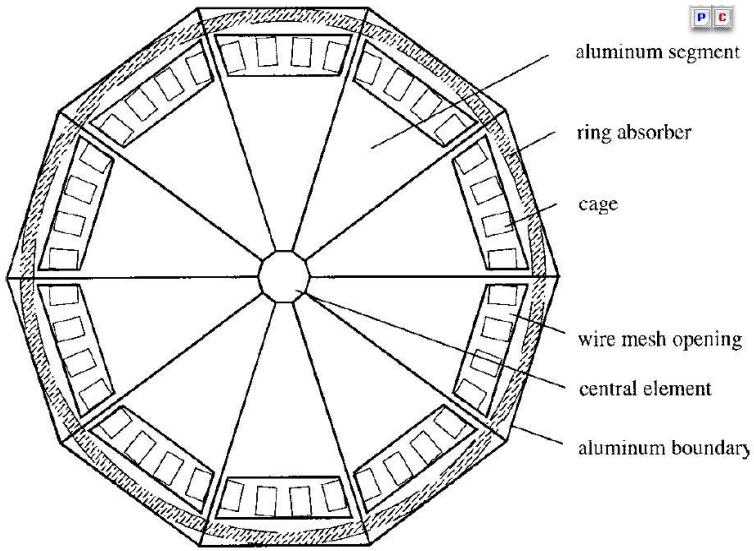
Adey's Horn Setup



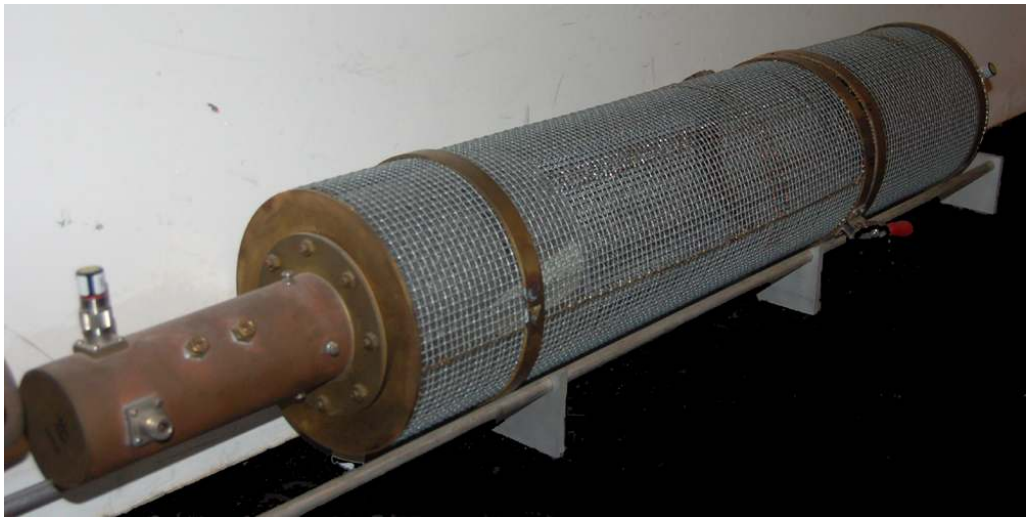
Concept: Quasi-Open Waveguide Systems

- medium efficiency
- reasonable uniformity
- medium variability
- medium to large space requirements
- good isolation

“Hansen’s” RTL Setup



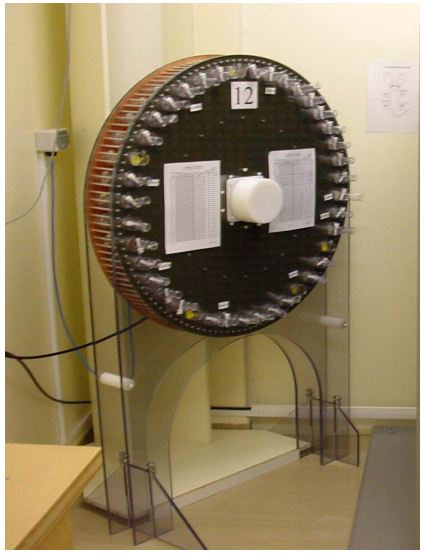
Guy and Chou’s Circularly Polarized WG Setup



Concept: Multi-Mode Resonant Systems

- high efficiency
- medium to good uniformity
- considerable variability due to higher modes (> +/- 3dB)
- small space requirements
- one exciter per group or subgroub
- good isolation

Motorola's Ferris-Wheel Setup

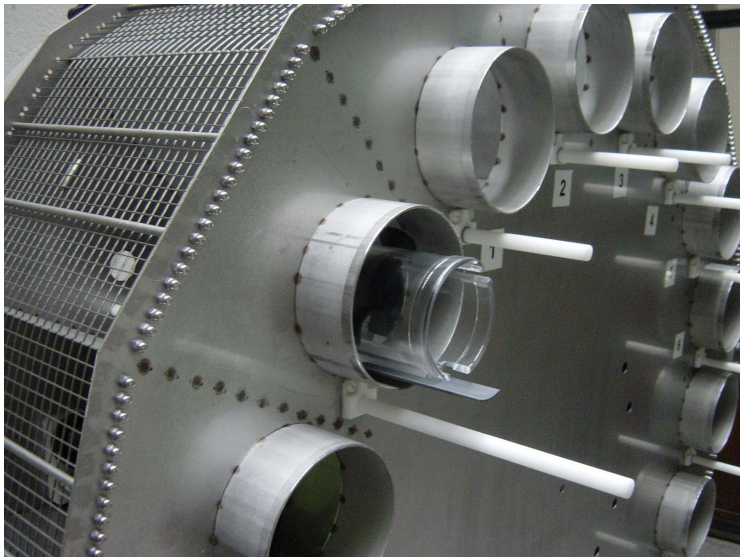


PERFORM A's Mouse Setup

Concept: “Mono-Mode” Resonant Systems

- high efficiency
- good uniformity
- small variability
- small space requirements
- one exciter per animal group
- good isolation

Restrainer tube & loading mechanism



PERFORM A’s Rat Setup

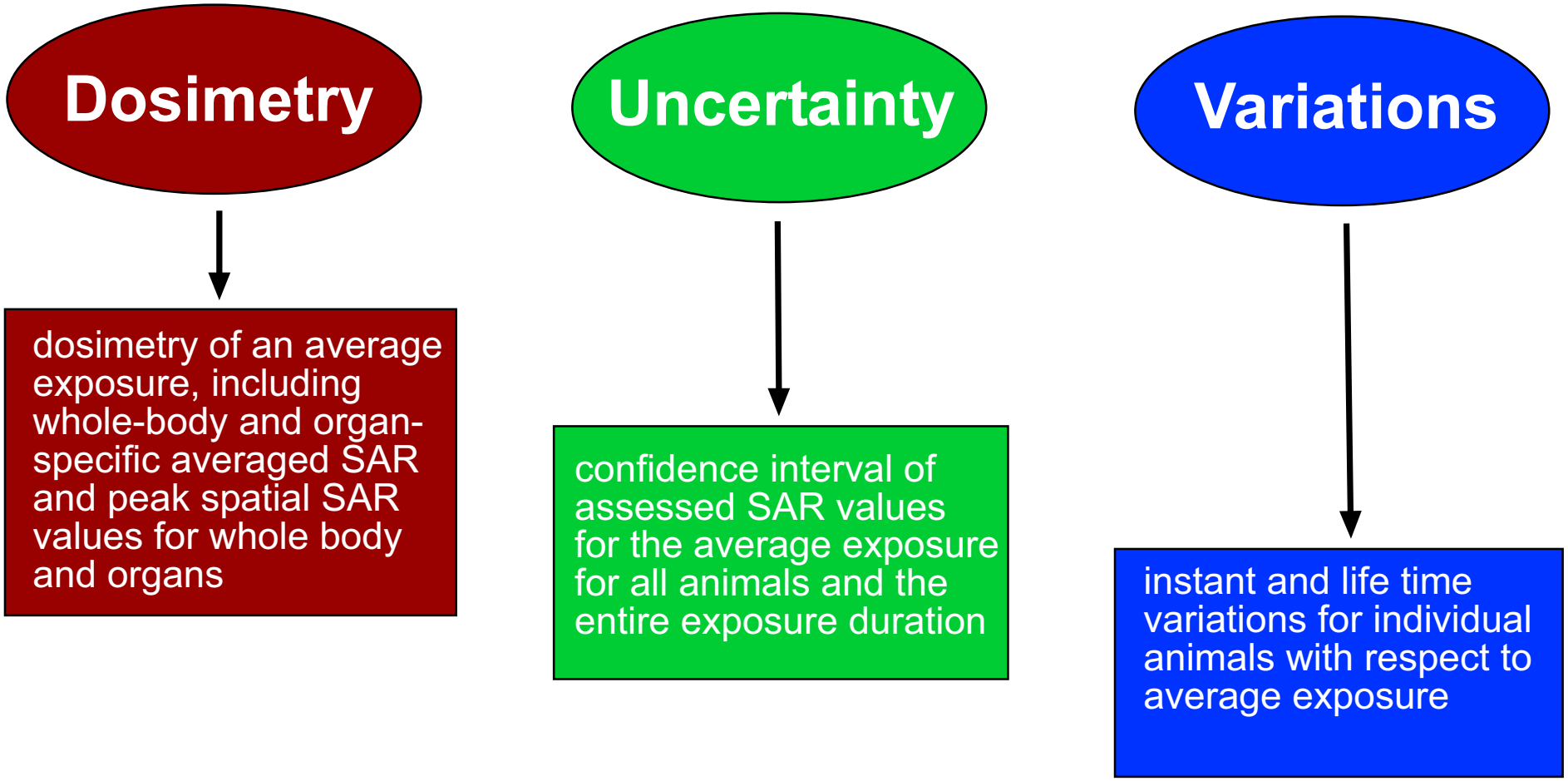
Concept: Statistical Multi-Mode Resonant Systems

- medium-high efficiency
- statistically uniform (<2 dB deviation) and isotropic field distribution
- small variability (for distances >λ/2)
- high space requirements
- large number of exposed animals per chamber
- 1 to 12 exciters per animal group

NIEHS's RC Prototype at IT'IS

Minimal Requirements for Dosimetry and SAR Uncertainty and Variation Assessment

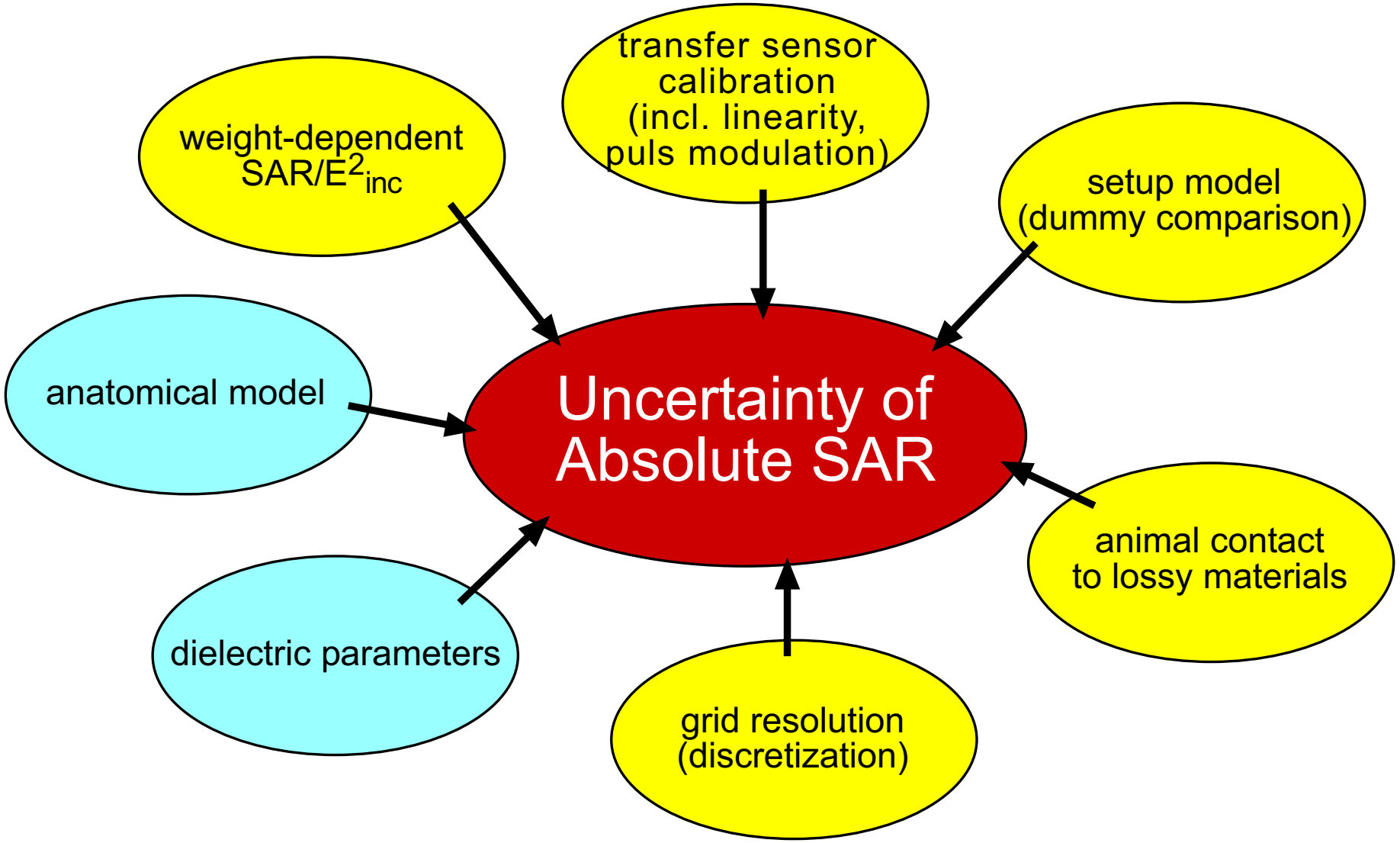
Detailed Dosimetry, Uncertainty and Variations



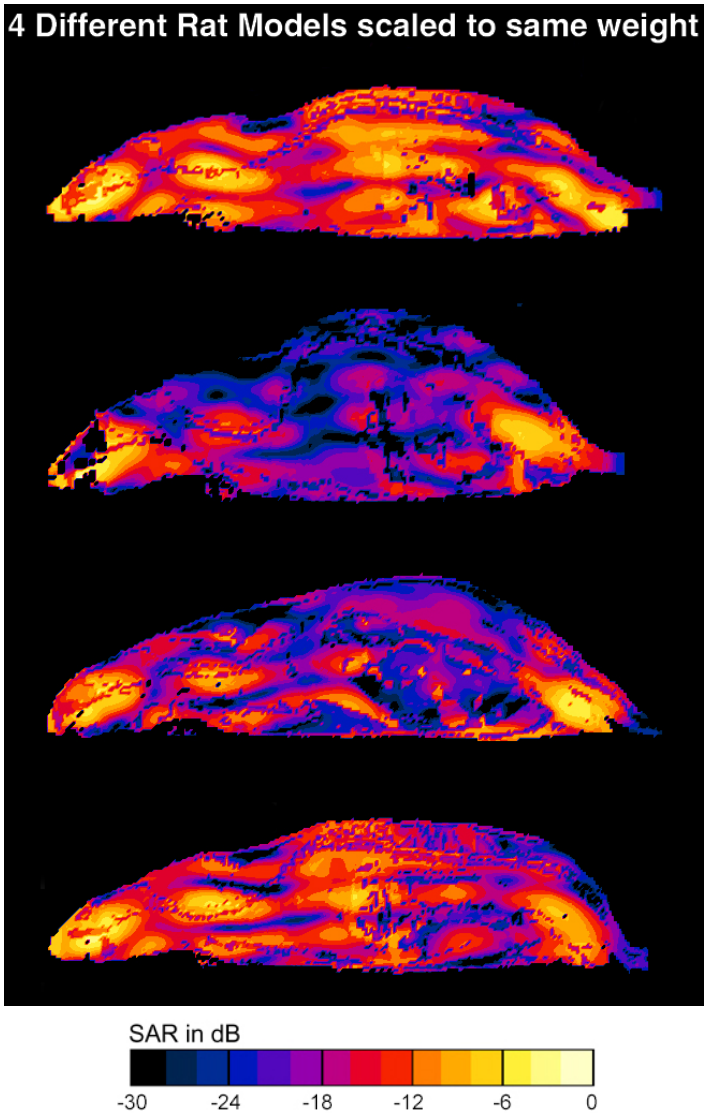
Dosimetry & Uncertainty Assessment

- a complete dosimetry has to be performed for an average exposure or standard situation:
  - average exposure setup
  - average animal model in weight and age
  - target/average position in the setup
  - target/average posture
  - average dielectric parameters
  - verified grid resolution
- the setup model and the uncertainty analysis need to be verified/determined by a combination of experimental and numerical means
- experimental verification of the animal model is very limited, and the uncertainty needs to be assessed by inter-numerical comparison

Evaluation of Uncertainty Assessment



SAR Uncertainty Rat 1747 MHz: Anatomy



- example from PERFORM A dosimetry
- 4 rat models scaled to average weight
- whole-body averaged SAR difference: 2.5 dB

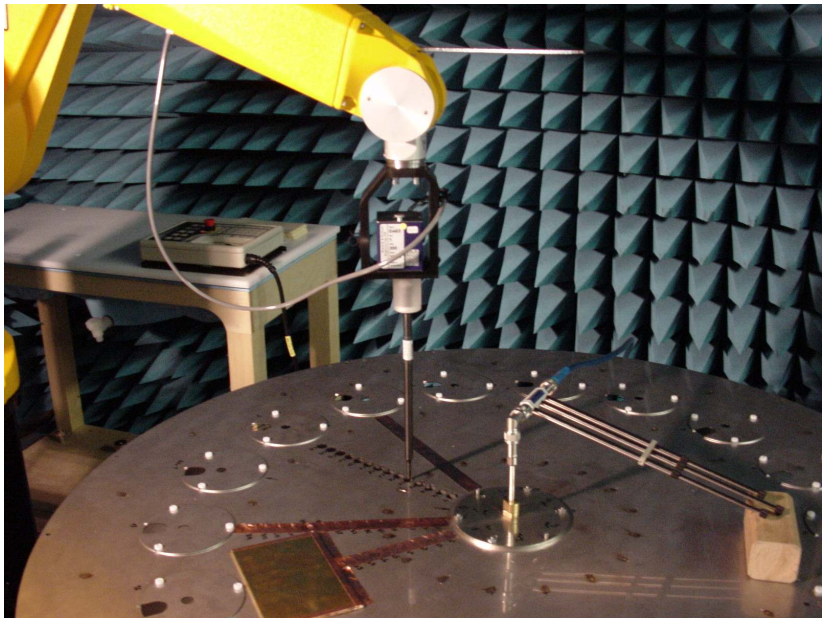
Experimental Validation of Numerical Model

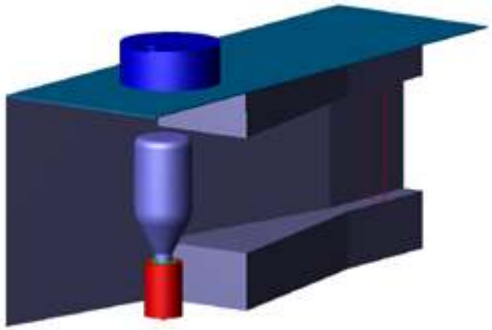
- validation is performed by loading the setup with animal phantoms that closely represent the load by animals in terms of size and absorption
- this requires an additional uncertainty analysis including the phantom and the experimental evaluation
- the dosimetry is reliable if the difference between experimental and numerical results is within the uncertainty boundary

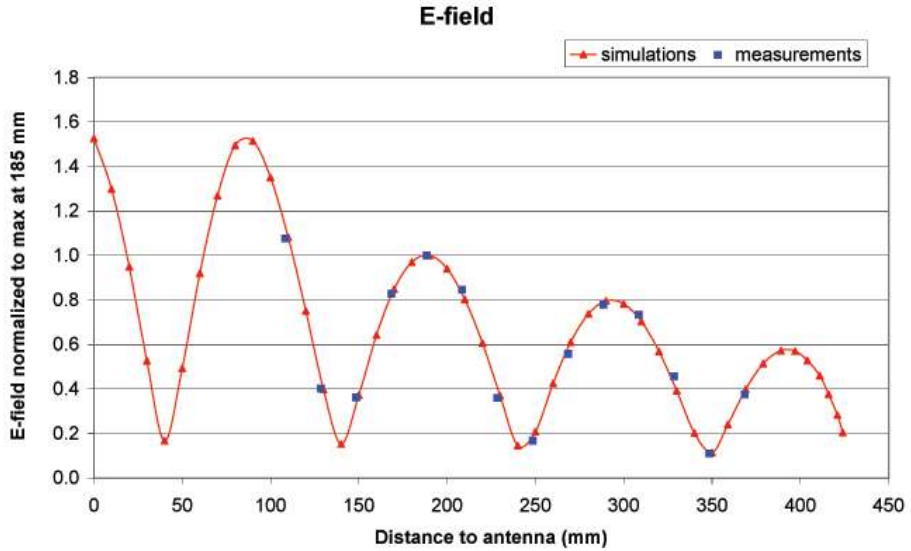
$$E_n = \sqrt{\frac{(v_{sim} - v_{meas})^2}{[v_{sim} u_{sim}(k=2)]^2 + [v_{meas} u_{meas}(k=2)]^2}} < 1$$

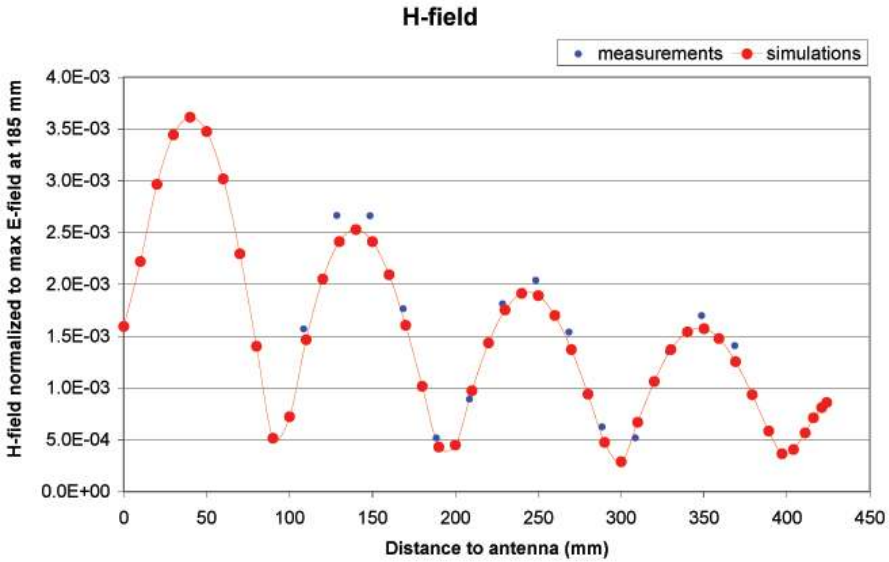
Example Validation: Rat Exposure Setup 1747 MHz

- E- and H-field comparison



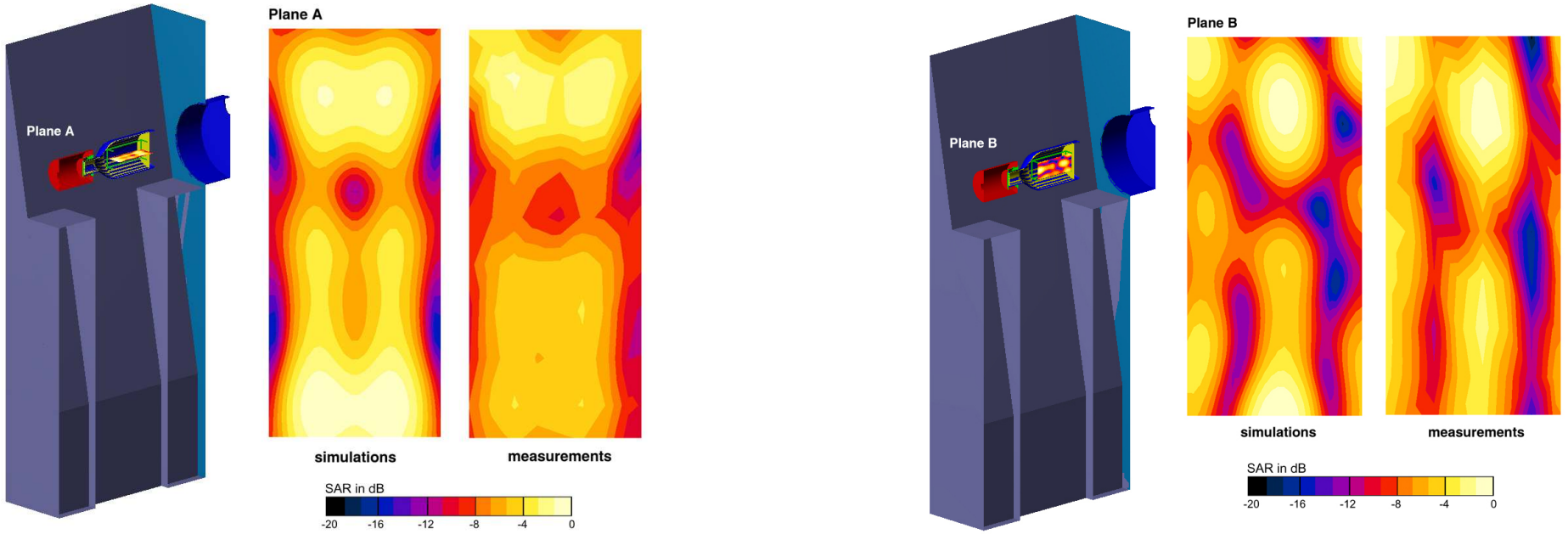






Example Validation: Rat Exposure Setup 1747 MHz

- SAR pattern comparison



- the final deviation E_n for averaged SAR validation was determined to be

$$E_n = \sqrt{\frac{(v_{sim} - v_{meas})^2}{[v_{sim} u_{sim}(k=2)]^2 + [v_{meas} u_{meas}(k=2)]^2}} = 0.34$$

Instant & Lifetime SAR Variations

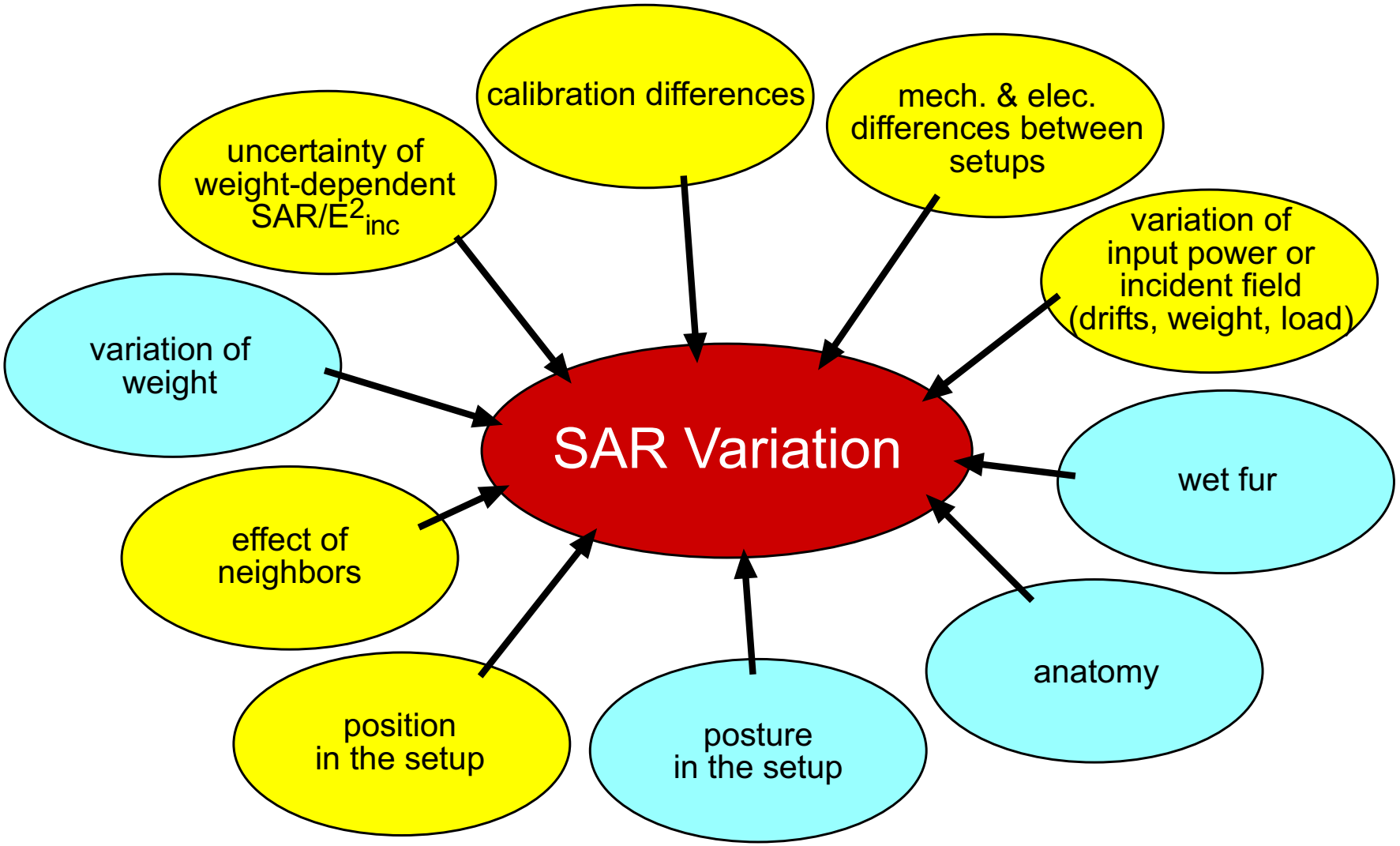
SAR Variations Caused by Exposure Setup

- input power / incident fields (drift of amplifiers/measurement equipments, load differences, etc.)
- calibration differences
- mechanical and electrical differences between setups
- position ocupied by the animal within the setup
- dependence on neighboring animals

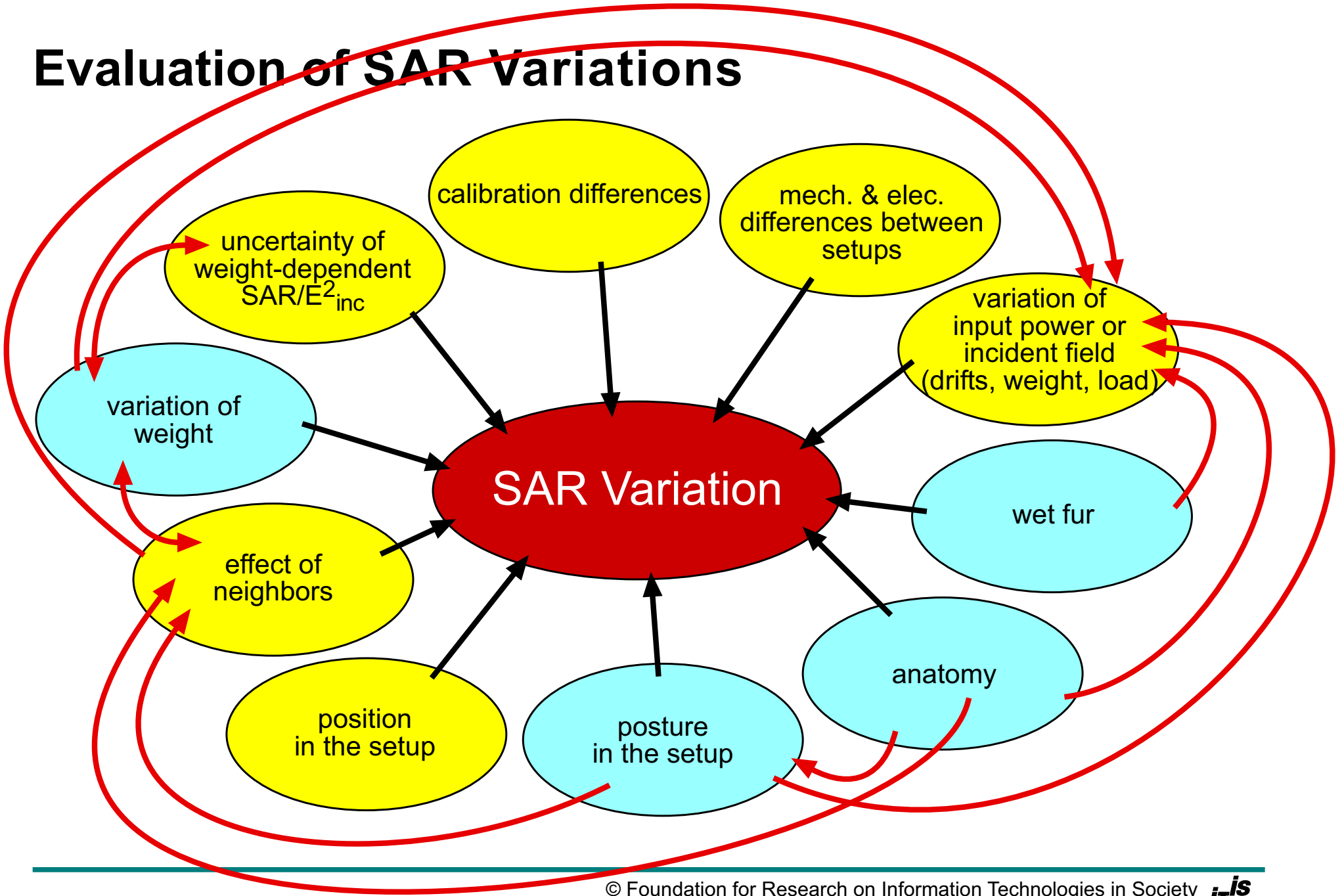
SAR Variations Caused by Animals

- size/weight (highly compensated by applying weight-dependent incident power)
- anatomy (age, strain, gender)
- orientation of the animal within the field (highly compensated by using a restrainer tube)
- posture and position within the waveguide
- position of the waveguide in the setup
- wet fur (water, urine, etc.)

Evaluation of SAR Variations

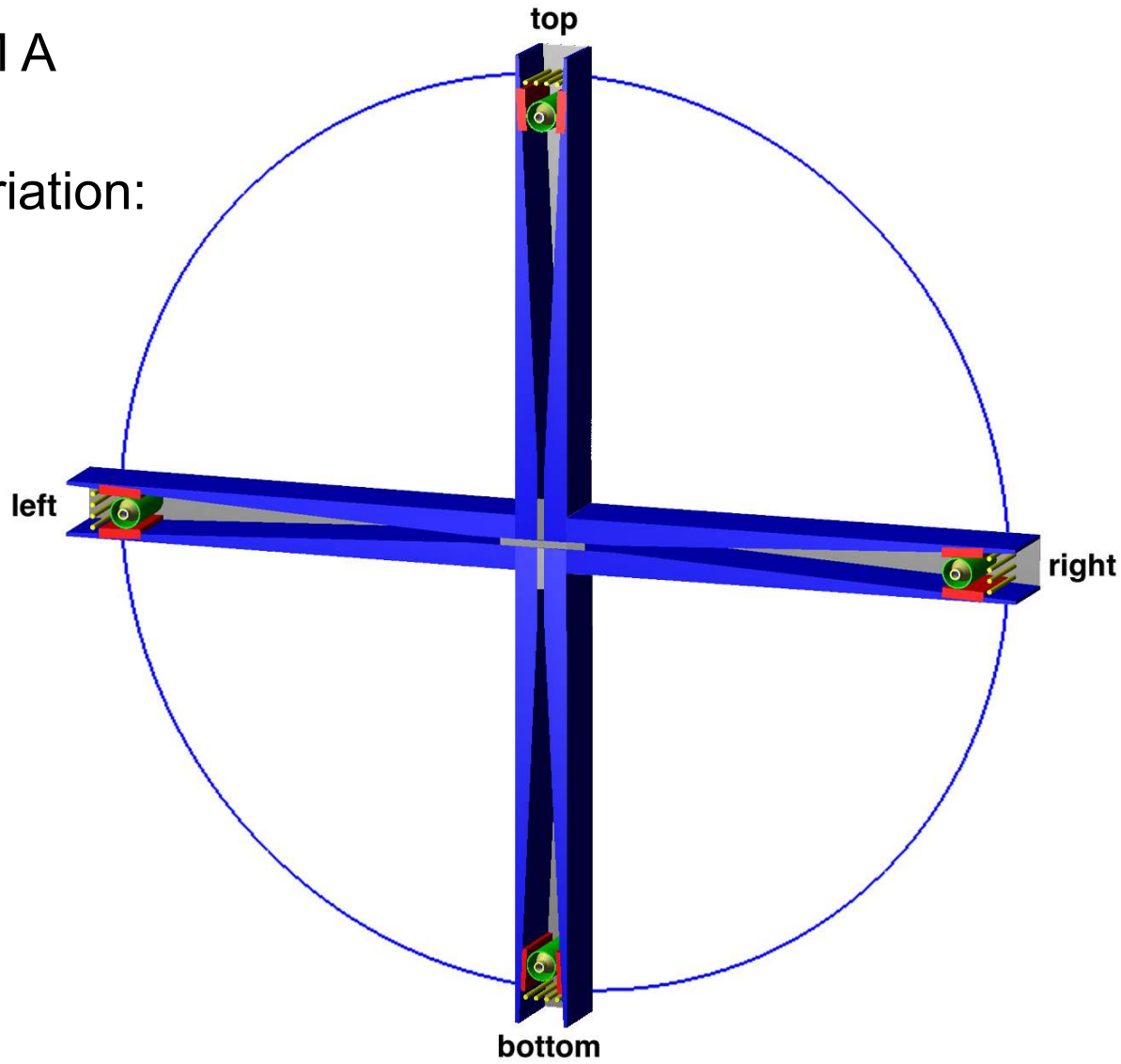


Evaluation of SAR Variations



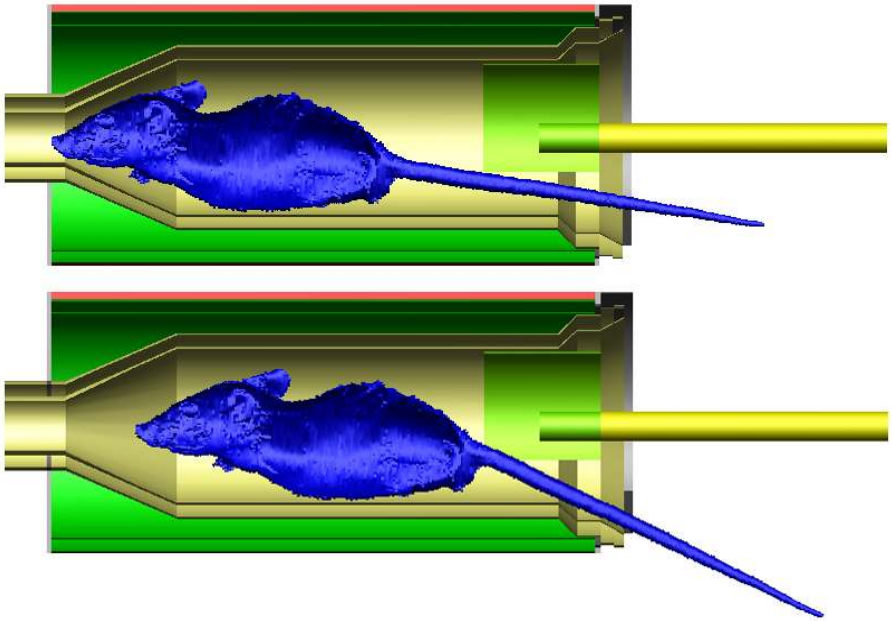
SAR Variations Mouse 902 MHz: Position in the Setup

- example from PERFORM A dosimetry
- whole-body avg. SAR variation: 2.5 dB

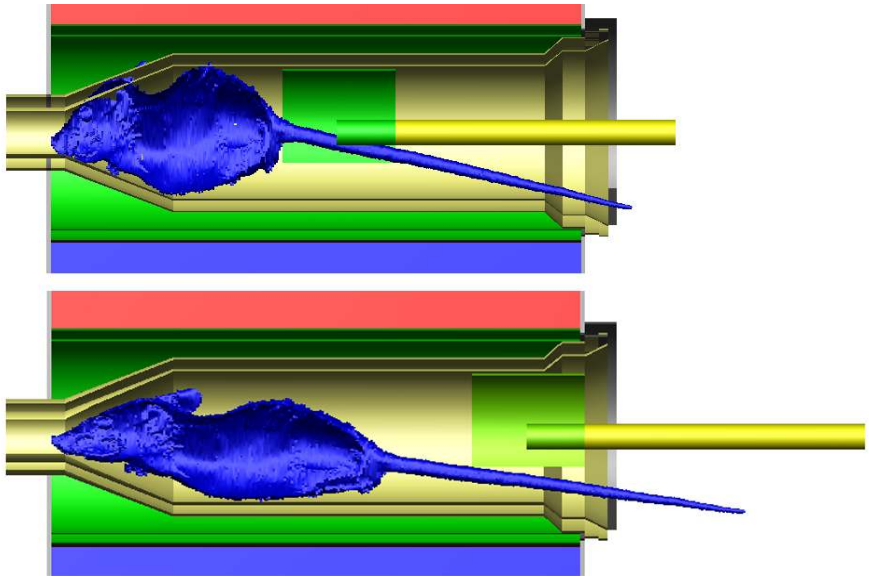


SAR Variations Mouse 902 MHz: Posture and Position

- example from PERFORM A dosimetry
- WB SAR variation: 0.6 dB



- WB SAR variation: 4.9 dB



Whole-body Averaged SAR Variations

- example of whole-body averaged SAR, absolute uncertainty, instant variation and lifetime variation, from PERFORM A dosimetry

Animal / Frequency	Uncertainty (k=2) (dB)	Instant Variation (k=1) (dB)	Lifetime Variation (k=1) (dB)
Mouse / 902 MHz	2.7	2.5	1.5
Mouse / 1747 MHz	2.2	2.0	1.0
Rat / 902 MHz	1.9	0.8	0.7
Rat / 1747 MHz	1.7	1.8	1.2

Spatial Peak Average SAR Variations Rat 1747 MHz

- example of whole-body peak spatial averaged SAR, absolute uncertainty, instant variation and lifetime variation, from PERFORM A dosimetry for rats exposed at 1747 MHz

Averaging Mass	Dev. SP SAR vs. WB avg SAR (dB)	Uncertainty (k=2) (dB)	Instant Variation (k=1) (dB)	Lifetime Variation (k=1) (dB)
50 mg	9.5	4.0	1.7	1.4
5 mg	10.3	4.5	1.9	1.7

Organ SAR Variations: Blood, Brain, Liver

- example of organ-specific averaged SAR, absolute uncertainty, instant variation and lifetime variation, from PERFORM A dosimetry

Animal / Frequency	Materials	Dev. Organ versus WB SAR (dB)	Uncertainty (k=2) (dB)	Instant Variation (k=1) (dB)	Lifetime Variation (k=1) (dB)
Mouse / 902 MHz	Blood	1.6	2.7	2.9	2.1
	Brain	-2.1	2.6	2.8	1.3
	Liver	0.2	2.7	2.6	1.7
Mouse / 1747 MHz	Blood	5.2	2.3	2.3	1.4
	Brain	1.0	2.3	3.1	2.0
	Liver	1.0	2.6	2.2	1.3
Rat / 902 MHz	Blood	2.6	1.6	1.1	0.9
	Brain	-4.3	5.0	2.4	1.7
	Liver	1.1	2.8	1.7	1.6
Rat / 1747 MHz	Blood	3.3	1.8	1.4	0.8
	Brain	2.9	2.5	3.3	1.4
	Liver	1.4	2.3	1.4	1.1

Discussion

- a methodology to obtain detailed dosimetric information for *in vivo* studies has been developed
- it includes:
  - whole-body and organ-specific averaged and spatial peak averaged SAR values
  - uncertainty of each assessed value
  - instant variations, variations of the averaged exposure of a single session as well as the entire lifetime
- reliable dosimetric data with reasonable effort can only be obtained if the concept of the exposure setup is well chosen
- the suggested methodology increases the reliability and credibility of the dosimetric results and provides a basis for high quality interpretations and valuations of the histopathological results (dose-effect relation)

Conclusions

- high resolution anatomical models, i.e., < 0.2 mm^3 are necessary
- SAR distribution strongly depend on animal, frequency, polarization
- whole-body and organ-specific SAR is required for the interpretation and inter-study comparison
- the dosimetry of animal studies should at least include:
  - whole-body averaged SAR
  - organ-specific averaged SAR
  - peak spatial SAR (averaging masses have to be appropriately scaled)
- a comprehensive uncertainty and variation analysis is a fundamental part of good science

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