Joint ICTP-IAEA Advanced School on Internal Dosimetry

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BASIC PLANAR DOSIMETRY

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Toxicity oriented vs efficacy oriented dosimetry

Toxicity oriented dosimetry

- The first organ which exhibits toxicity in activity escalation study is called the critical organ
- Red marrow is the critical organ in most treatments
- Administering the maximal activity under safety conditions for the critical organ is one possible planning stategy
- BUT maximizing the injected activity does not guarantee the therapeutic success

Efficacy oriented dosimetry

- Lesion destruction requires dose threshold overcoming
- Poor data about threshold values
- Necessity of imaging
- Lesion dosimetry alone is not safe

Ideally both approaches should be pursued

Pre/post treatment dosimetry

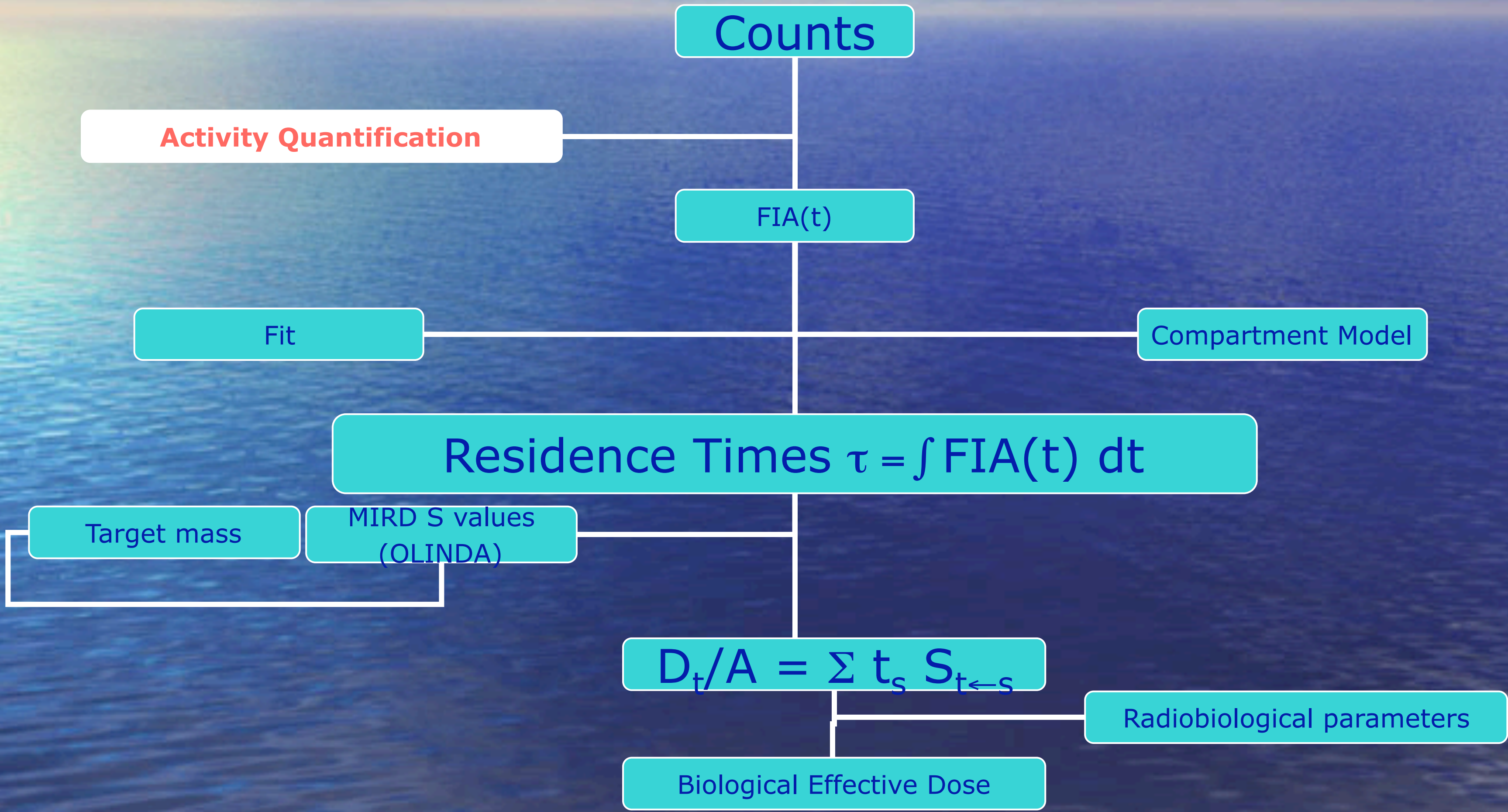
PRE-treatment

- Ideal treatment planning
- Mandatory in phaseI studies
- Possible mismatch between prevision & actual kinetics during therapy (data are lacking !)
- (Demanding for out patients)

POST-treatment

- No prevision
- Prevision in multiple administration therapies (not for tumor)
- Useful as a first historical step for data collection
- Exact kinetics during therapy
- Ethical when toxicity is known
- Dead time problems
- Easy for hospitalised patients

MIRD based dosimetry



Total body , planar , SPECT , PET

- **Total Body dosimetry**
  - Allows for TB quantification
  - Easiest to put in practice
  - For red marrow dose, additional blood sample are necessary

- **Planar imaging for dosimetry:**
  - Allows for WB quantification
  - Easier to put in practice than SPET
  - Most often based on the conjugate views method

TOTAL BODY

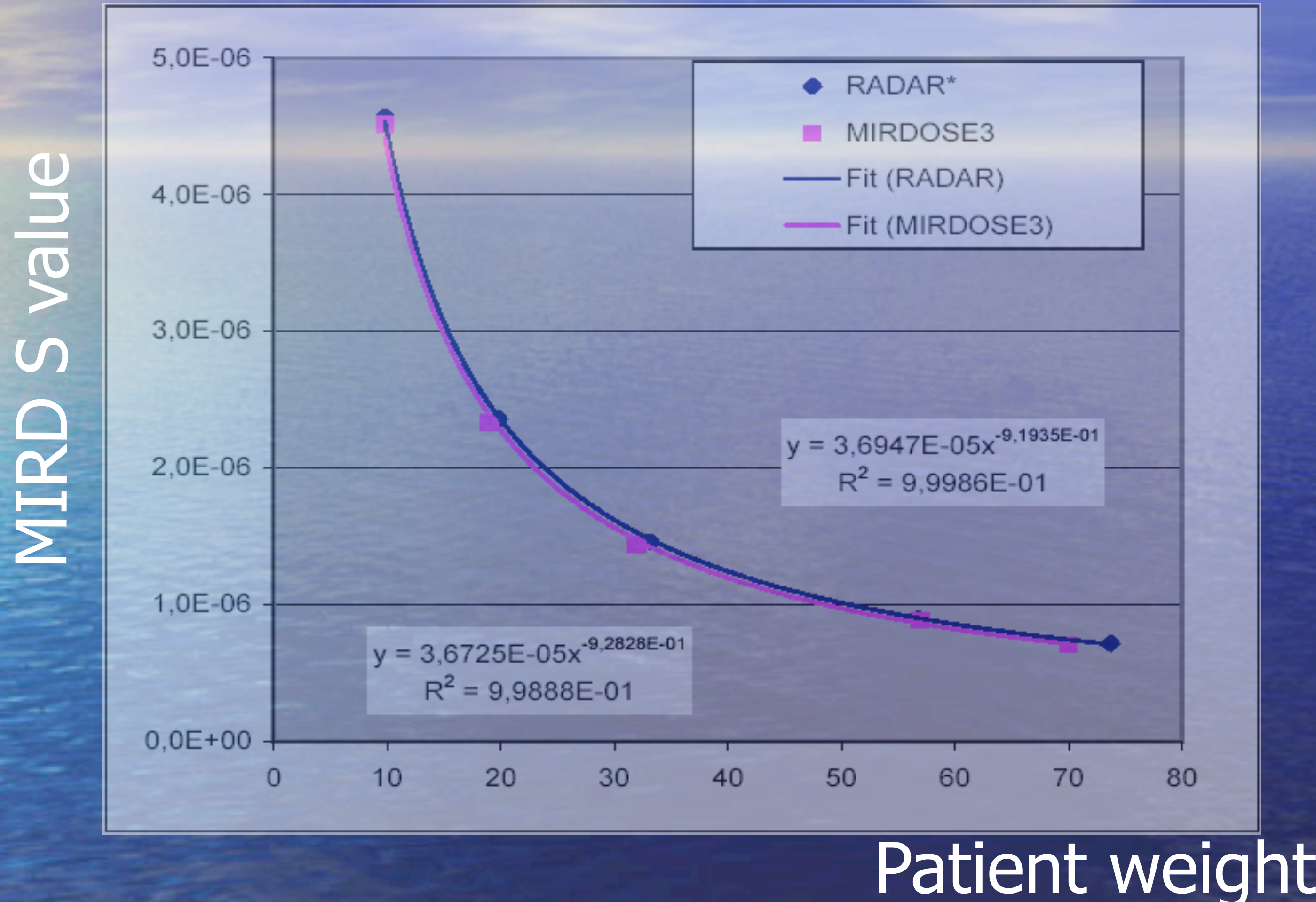
DOSIMETRY

TB dosimetry: theory & methods

$D_{TB} = \tilde{A}_{TB} \, S_{TB \leftarrow TB}$ very simple theory !

- Pre-treatment: spectroscopic probe, gammacamera WB counts
- Post-treatment: 10 mm Pb shielded spectroscopic probe with GBq of 131-I; low sensitivity Geiger
- Calibration:: 1st count without micturition after administration of known (measured) activity corresponds to FIA(0)=1
- Subsequent counts give activity proportional to cps
- Geometric mean of ANT/POST
- Fixed geometry (> 2 m distance) & background subtraction are mandatory
- Fixed biological conditions: count immediately after micturition (except 1st count)
- Choose proper count duration to get low statistical error (< 5%)

$S_{TB \leftarrow TB}$ values



S values should be interpolated to provide patient specific values

TB dosimetry: Geiger counter fixed on ceiling

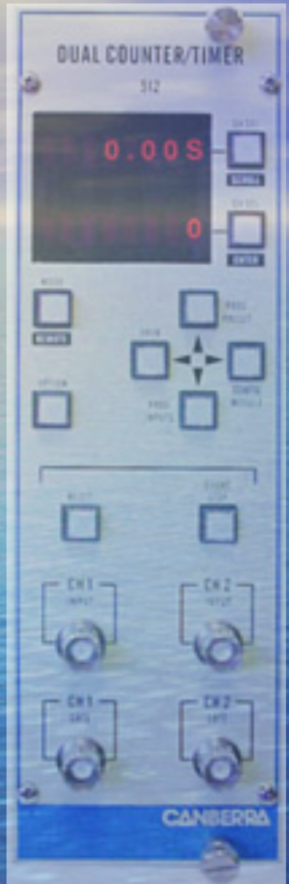
Easy to perform

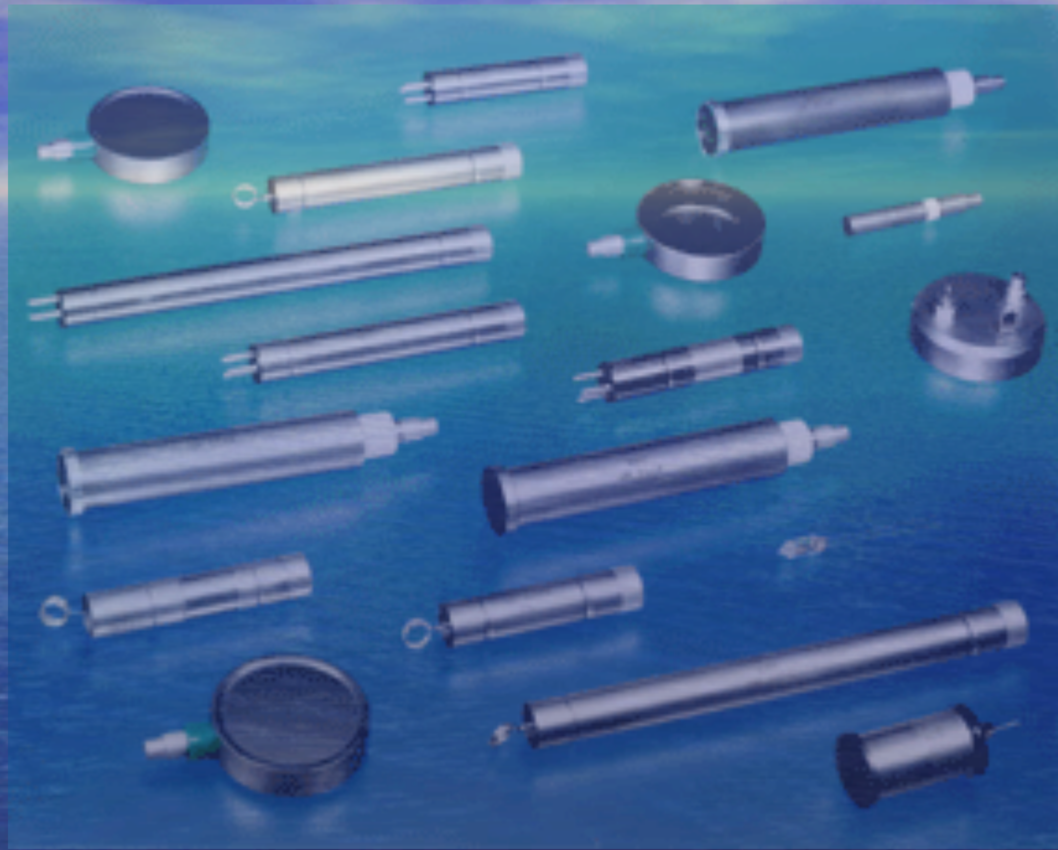
<u>Advantages:</u>
Imaging not necessary

Ward staff, carers can take measurements, without entering the shielded room

Courtesy of G. Flux - Royal Marsden Hospital - Sutton (UK)

TB counting: Geiger counter and ratemeter



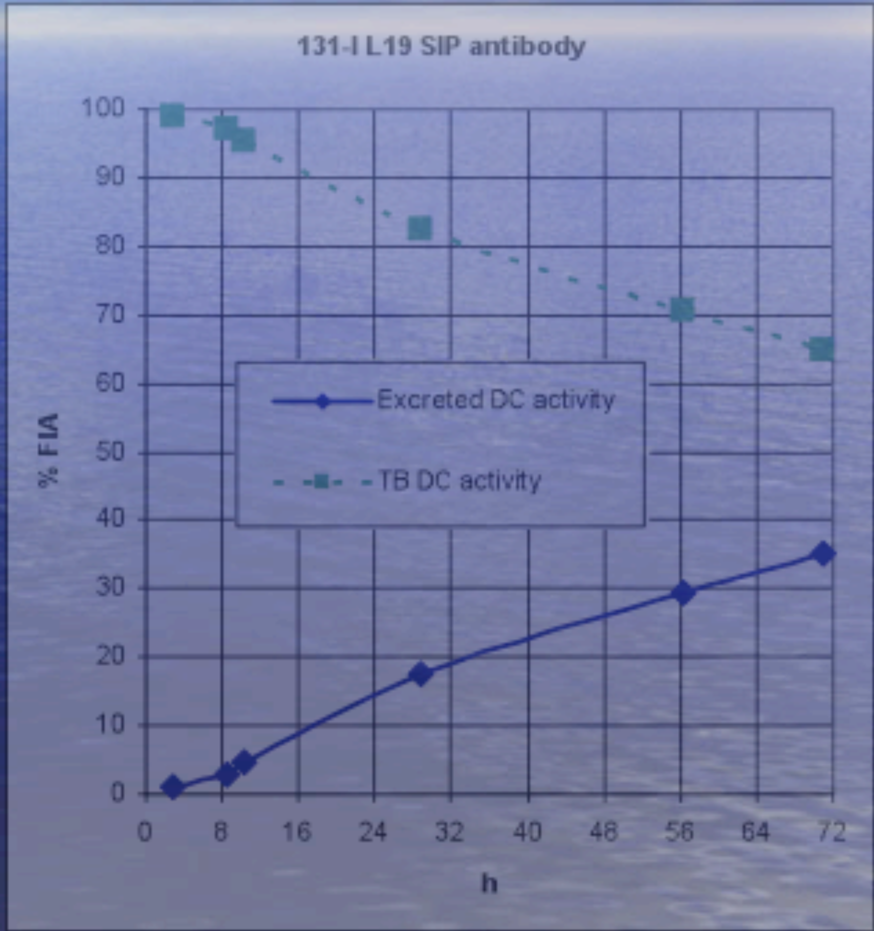


Cost for high activity measurements - <€1000
(eg mini-instruments MC70 low sensitivity + scale ratemeter)

Courtesy of G. Flux - Royal Marsden Hospital - Sutton (UK)

TB dosimetry and urinary excretion

- **If fecal excretion is negligible**
- TB decay corrected activity and cumulative urinary decay corrected activity are complementary
- TB DC FIA(t) + URINE DC FIA(t) = 1
- The evaluation of urinary bladder residence time allows dosimetry to pelvic organ:
  - Urinary bladder wall
  - Uterus (fetus)
  - Ovaries
  - Lower large intestine



PLANAR

QUANTIFICATION

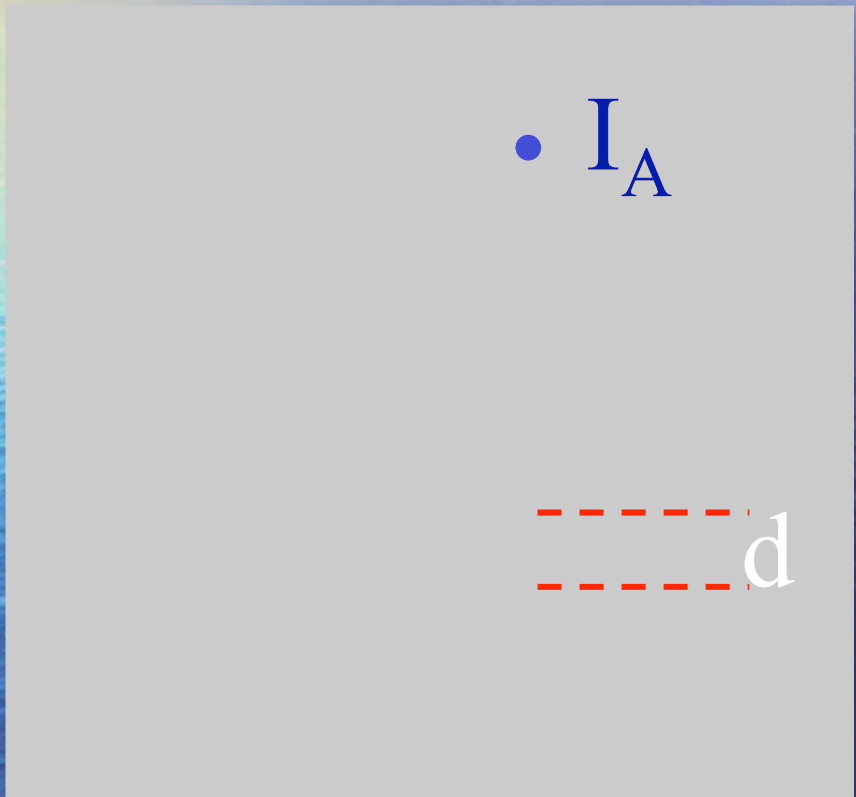
Gamma-camera is not meant to MEASURE activity

Calibration & Corrections are required
MIRD 16: Siegel et al J Nucl Med 1999; 40:37S-61S

1. Photon attenuation in patient body
2. Background of overlapping structures
3. Scatter
4. Self absorption of source object
5. Partial volume effect for small objects
6. Dead time count losses (only after therapeutic activity)

Calibration of gammacamera

1.A Attenuation correction in a single view



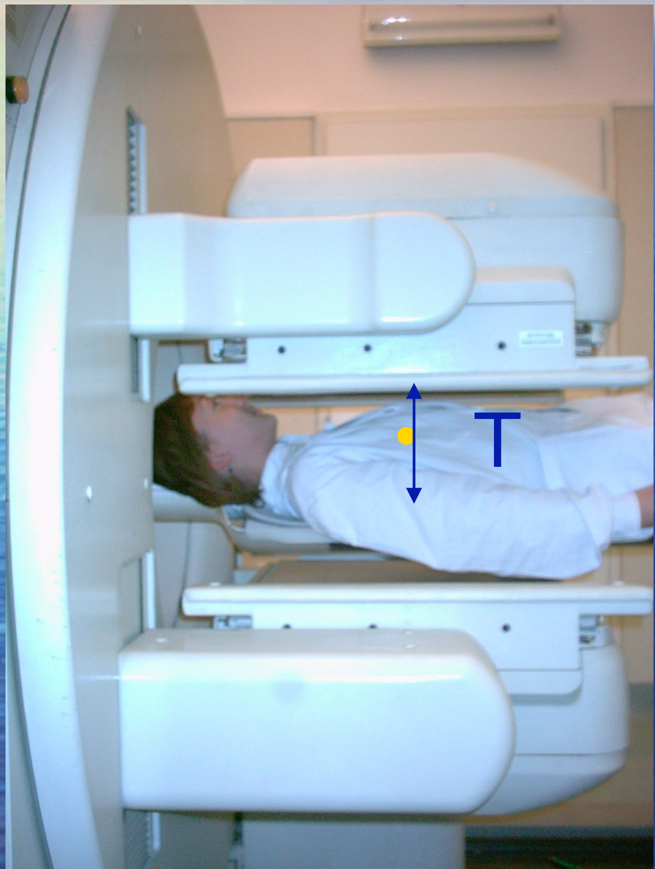
$$I_A = I_0 \cdot e^{-\mu_e d}$$

$$A = I_0 \cdot \frac{1}{C}$$

$$A = I_A \cdot e^{\mu_e d} \cdot \frac{1}{C}$$

- Very critical dependence on d
- d is often unknown

1.B Attenuation correction in conjugate view technique



- Conjugate view technique was developed to remove the dependece on d
- G (geometrical mean) is independent on the depth of the source
- This is true is under ideal conditions (MIRD 16) of absence of scatter, conditions never met in reality

Conjugate view formula

$$I_A = I_0 \, e^{-\mu_e d}$$

$$I = I_0 \, e^{-\mu_e (T-d)}$$

$$I_0 = \sqrt{\frac{I_A \; I_P}{e^{-\mu_e T}}}$$

$$A = \sqrt{I_A \; I_P} \; e^{\mu_e T/2} \; \frac{1}{C}$$

Attenuation correction factor ACF

- This formula is valid for point sources
- It removes dependency on d
- Still requires μ_e, T, C

Attenuation correction in conjugate view Example with 131-I

- We need the attenuation factor ACF

$$ACF(^{131}I) = I_0/I = \exp(\mu(^{131}I)\ T/2)$$

- MIRD 16 asks a transmission with ^{131}I, which is cumbersome
- A much more practical approach is to use a flood source (^{99m}Tc fillable source or even better, ^{57}Co flood source)
- Perform a blank and a trasmission scan with ^{57}Co

$$ACF(^{57}Co) = I_0/I = \exp(\mu(^{57}Co)\ T/2)$$

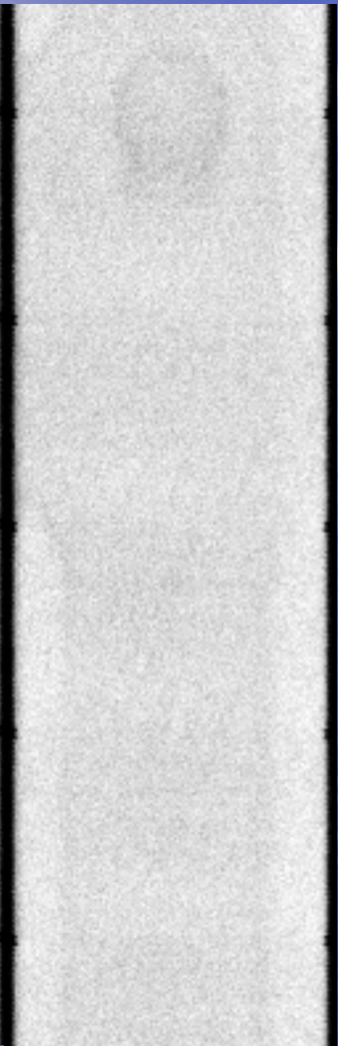
Attenuation correction in conjugate view

57Co blank scan

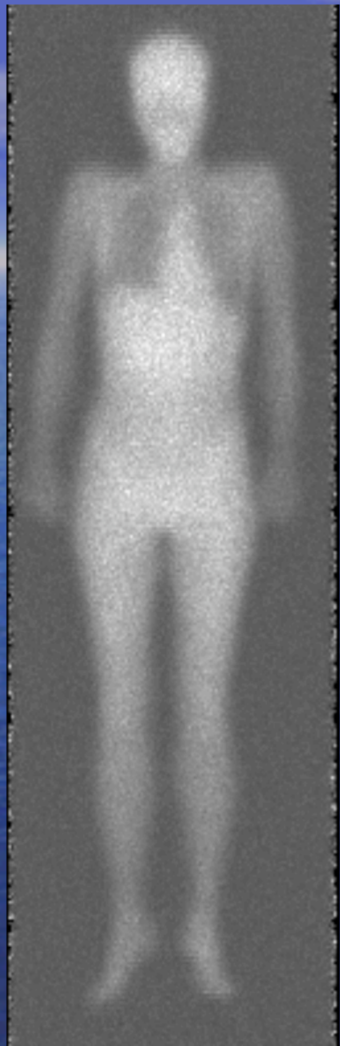
57Co trasmission scan

Example of transmission scan

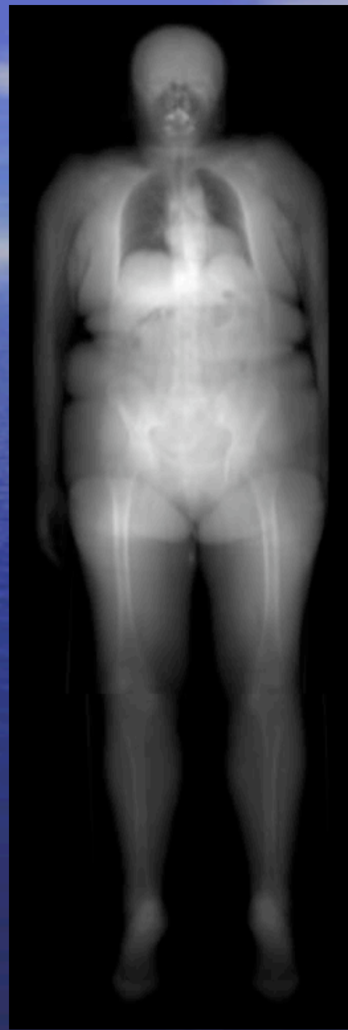
Transmission scan



Blank scan



ACF



Alternate possibility: CT scan...

^{57}Co Attenuation correction in conjugate view

57Co blank scan

For Cobalt-57

Liver ACF = √7.1

Lung ACF = √3.3

57Co transmission scan

Example 131-I Liver attenuation correction in conjugate view

- ACF(57Co)=√7.1 = exp(μ(^{57}Co) T/2)
- Known μ(^{57}Co) → T
- Known μ(^{131}I) → ACF (^{131}I)

- The goal of the blank&trasm scan is to get the water equivalent patient thickness T averaged over the organ

- Equivalent relationship

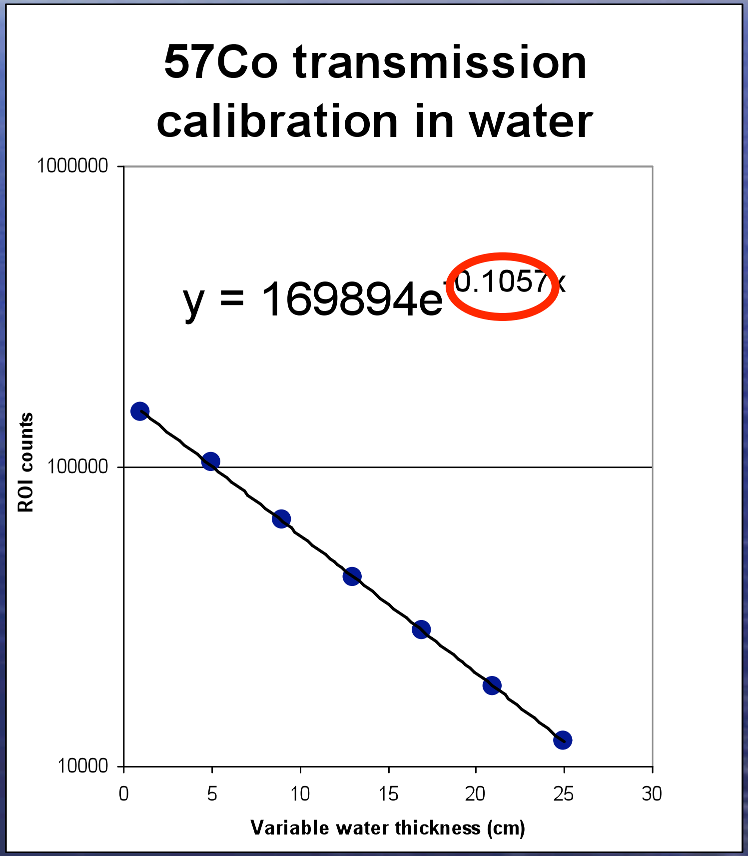
$$ACF(^{131}I) = [ACF(^{57}Co)]^{\mu(131I) / \mu(57Co)}$$

- μ(^{57}Co) must be experimentally determined for each system
- μ(^{131}I) must be experimentally determined for each system

- Two preliminary transmission calibration are necessary

Preliminary transmission calibration

- Cylindrical phantom positioned as a pot
- 57Co flood on the bottom head
- Add water at fixed step
- Draw ROI on the sequence of transmission images



Linear attenuation coefficients: never use tabulated data !

- Table values of $\mu(^{57}Co)$, $\mu(^{131}I)$, are always measured is good geometry conditions, i.e. narrow beam
- Gammacamera and extended organs give bad geometry, i.e. broad beam
- Build up effects (scatter) decrease the attenuation coefficient
- $\mu(^{57}Co)$, $\mu(^{131}I)$ must be measured for each equipment
- Additional problem: there is evidence of dependence upon shape and dimension of the used source
- This derives again from the presence of the SCATTER

2. Background of overlapping activity

- The second and potentially most serious drawback of quantification with planar images
- The amount of background activity is strongly dependent upon the kinetics of the radiopharmaceutical, and on the object/BKG ratio
- Worst case: antibodies (slowest kinetics)
- A ROI adjacent to the object gives the BKG counts
- Normalization for object and BKG ROI areas are necessary

ROI drawing method

- The method of ROI drawing, both on organs and their background, strongly affects the planar quantification
- Dependence upon operator is known
- In conjugate view technique, anterior and posterior ROIs should be identical and mirrored
- Background ROI should be a narrow C shaped border averaging background over the sources of high or low background

ROI DRAWING METHOD

^{111}In-hLL2 ANTI CD22

24 h

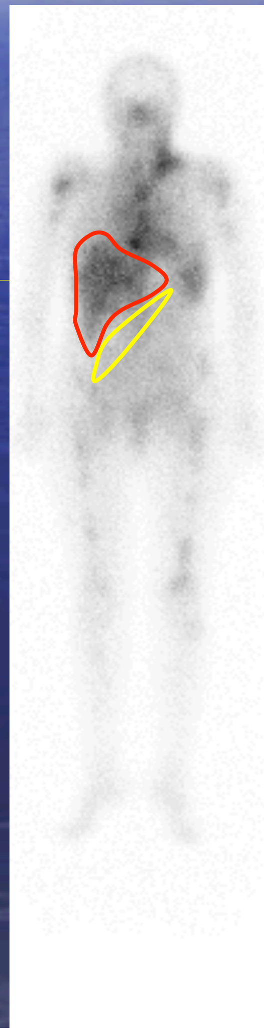
48 h

4 ROIs

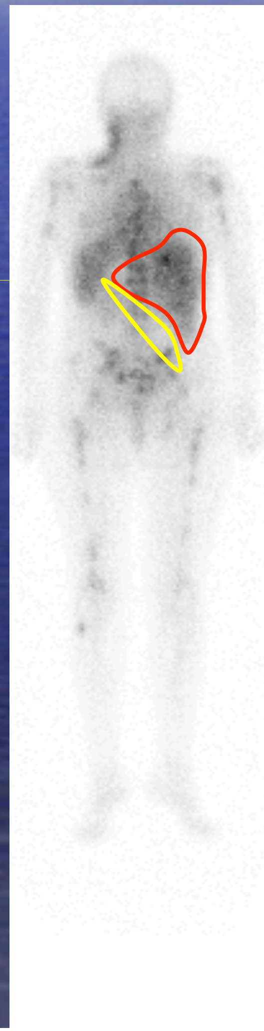
For each source organ

for each time point

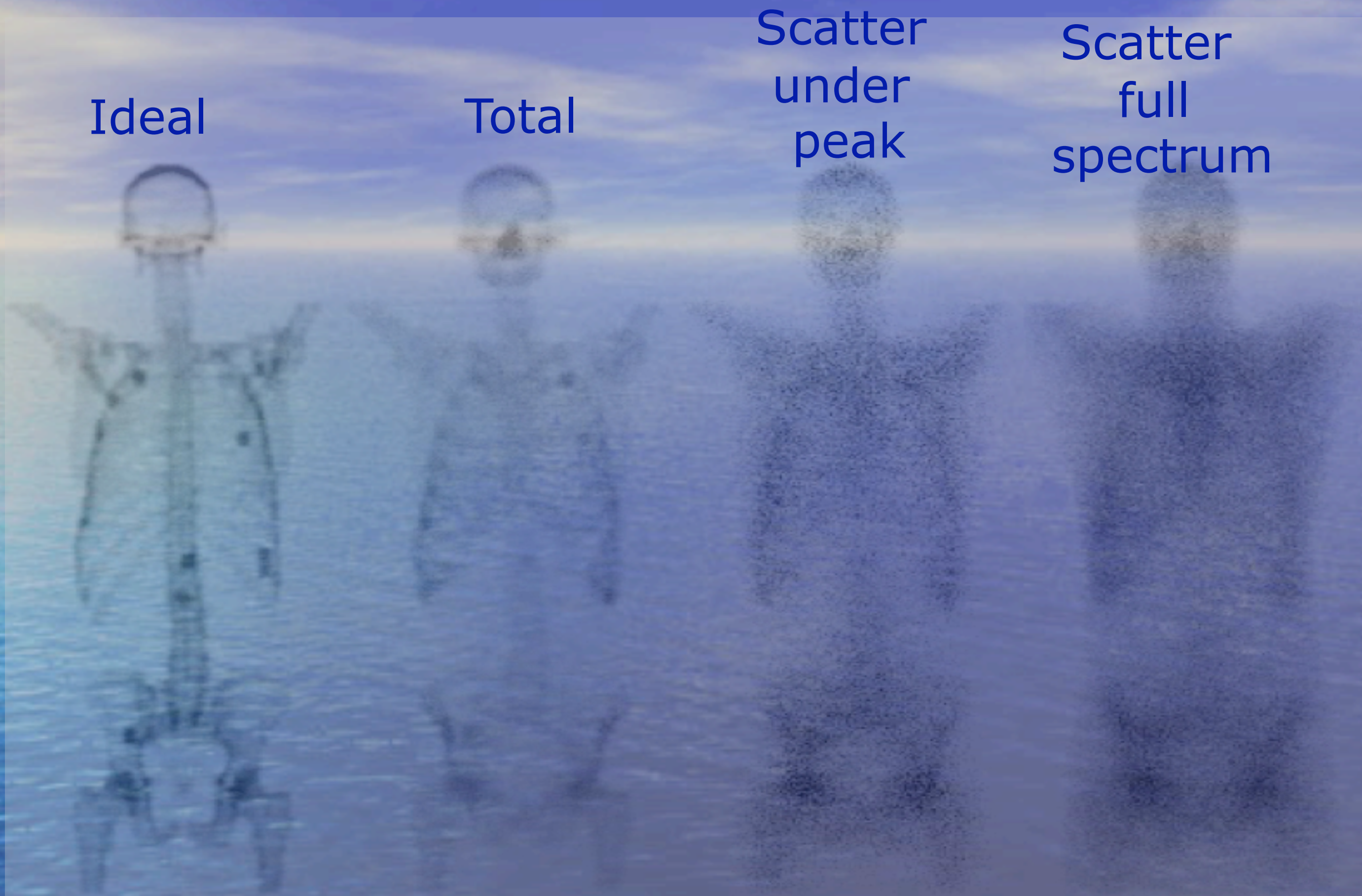
72 h



96 h

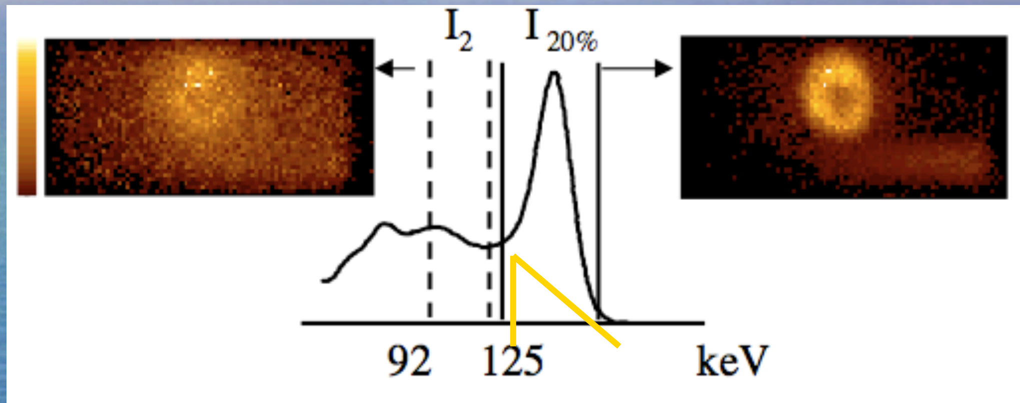


3. Scatter correction



Montecarlo simulation of scatter effects 99mTc
Michael Ljungberg (Lund - Sweden), 1998

Practical scatter correction Dual Energy Window (DEW)

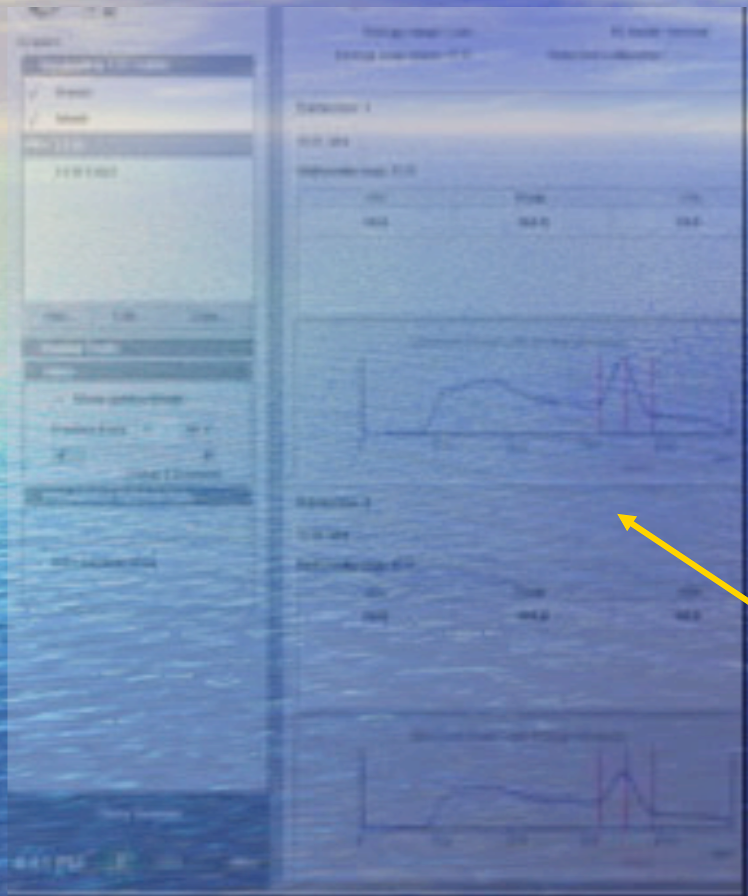


- Counts in the triangular area are subtracted from the peak

  - $I_{sc\ corrected} = I_{20\%} - k\ I_2$

- K is usually ½ (rather arbitrary choice)
- Proper correction when there is nothing beyond the peak

Problem with ^{131}I imaging



High energy gamma emissions:

364 keV: 81.7%

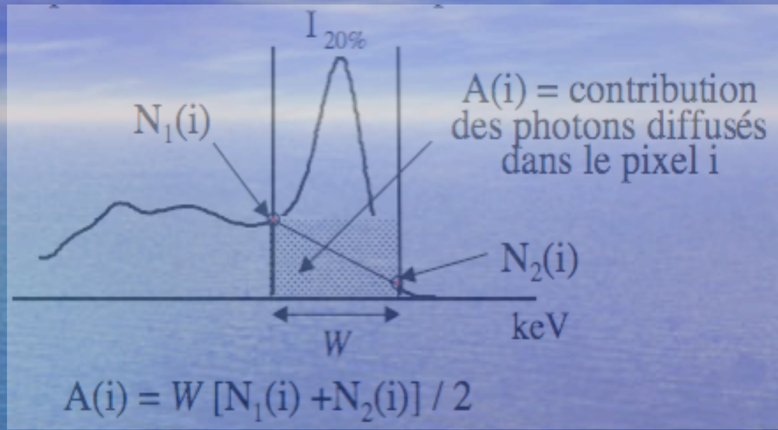
637 keV: 7.2%

723 keV: 1.8%

Septal penetration !!

Spectrum tail beyond the peak

Practical scatter correction
Triple Energy Window (TEW)



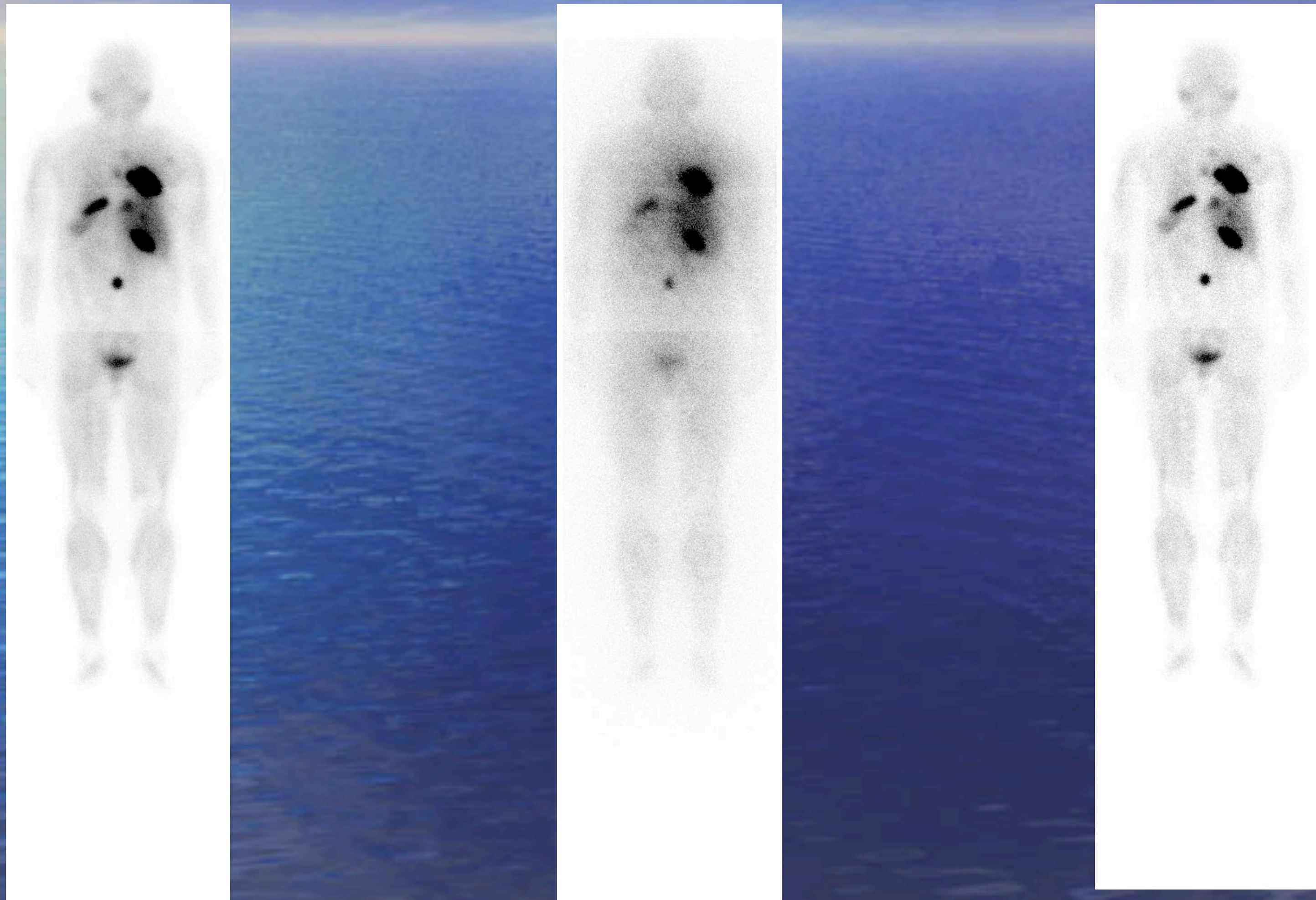
- Counts in the trapezoidal area are subtracted from the peak
  - $I_{sc\ corrected} = I_{15\%}$ - ½ Isc Wpeak/Wscatter
- Isc is the sum of counts in the two lateral windows
- If the total scatter window amplitue Wscatter = 2 Wpeak
  - $I_{sc\ corrected} = I_{15\%}$ - Isc
- Proper correction when there is something right of the peak

Scatter correction

- Drawbacks: image noise amplification following images subtraction
- No problem in high statistics post therapy images
- Accurate scatter correction with multi peak emitters is more complicated

Example of TEW Scatter correction

131-I mIBG therapy of thyroid medullar CA p.i.



4. Self absorption

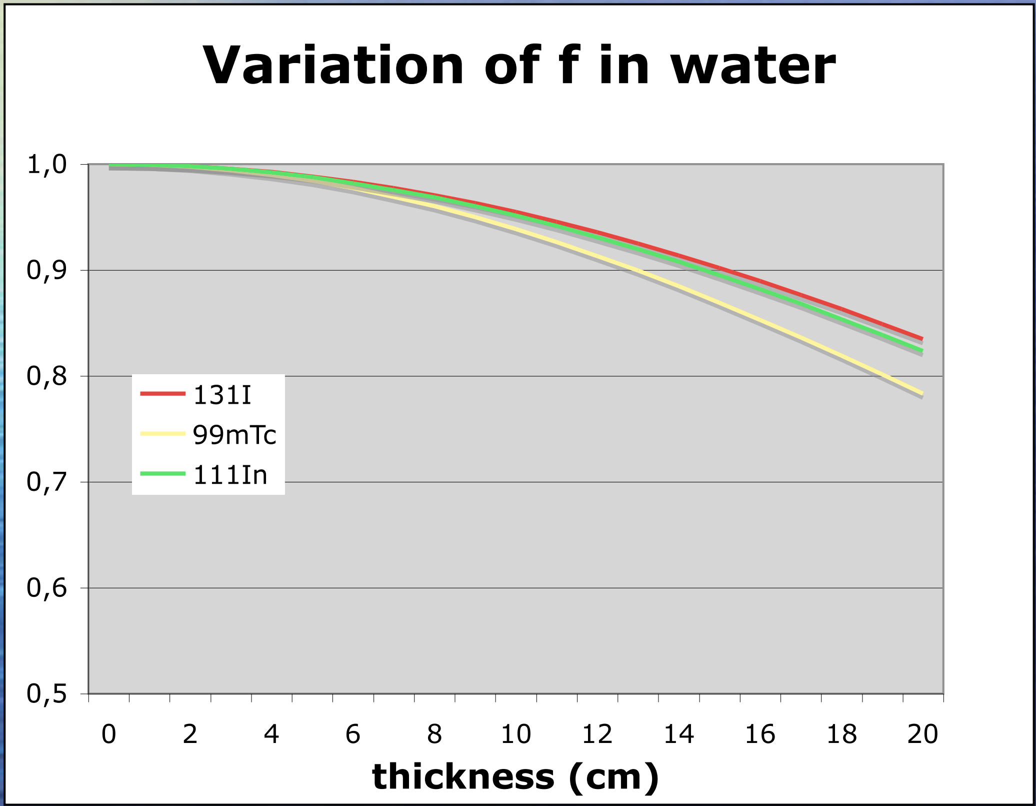
$$A = \sqrt{I_A \quad I_P} \quad e^{\mu_e T/2} \quad f \quad \frac{1}{C}$$

- For larger sources:
  - thickness t
  - linear attenuation coefficient μ

$$f = \frac{(\mu t/2)}{\sinh(\mu t/2)}$$

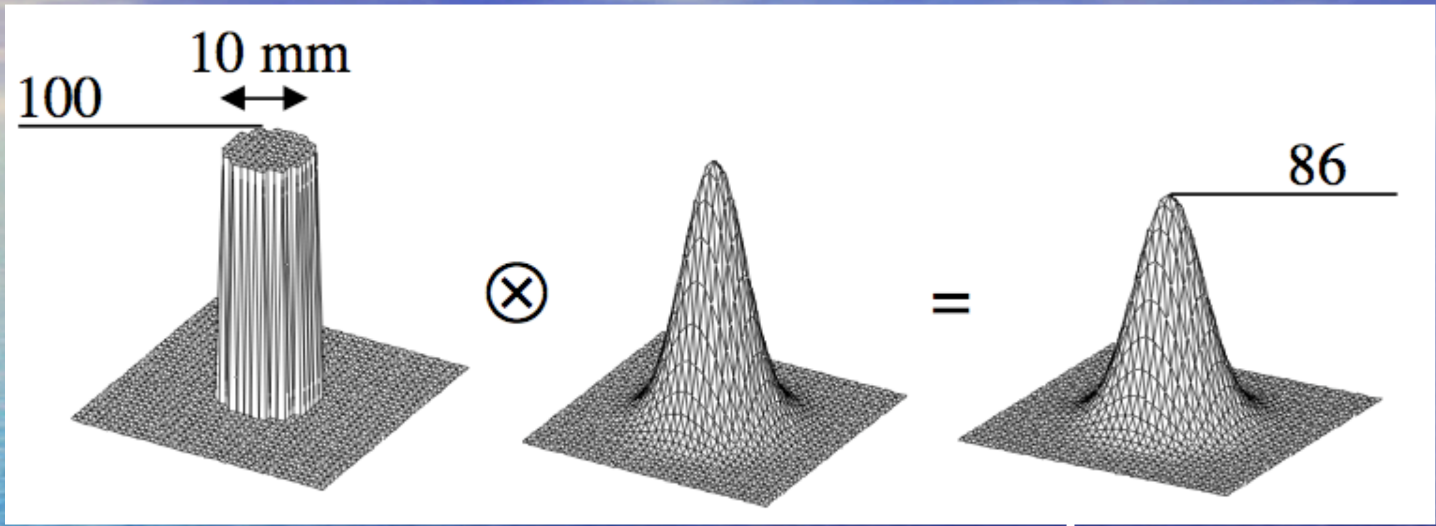
- And the effective linear attenuation coefficient μ_e is:

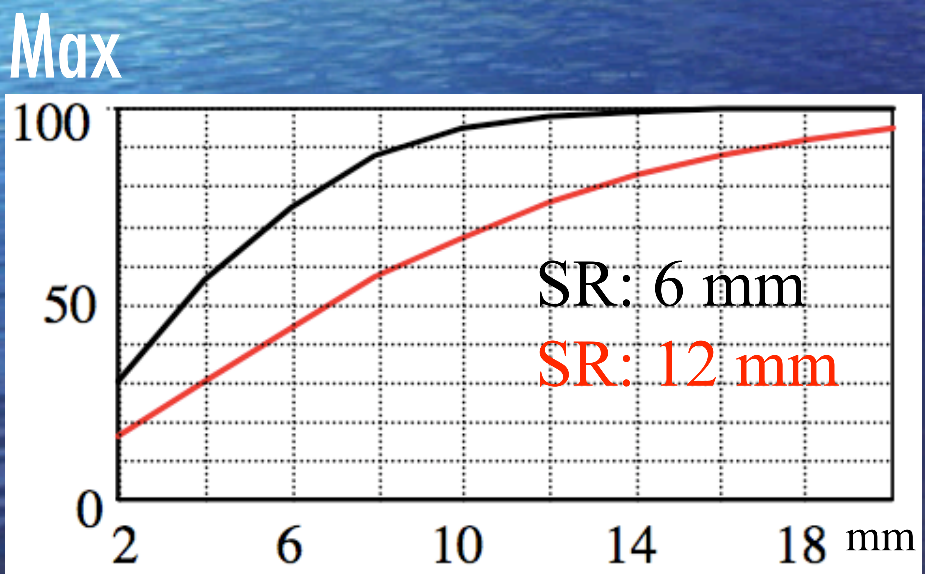
4. Self absorption important only for large objects



LUND DATA	μ (cm^{-1})
^{131}I	0.106
^{111}In	0.11
^{99m}Tc	0.124

5. Partial volume effect

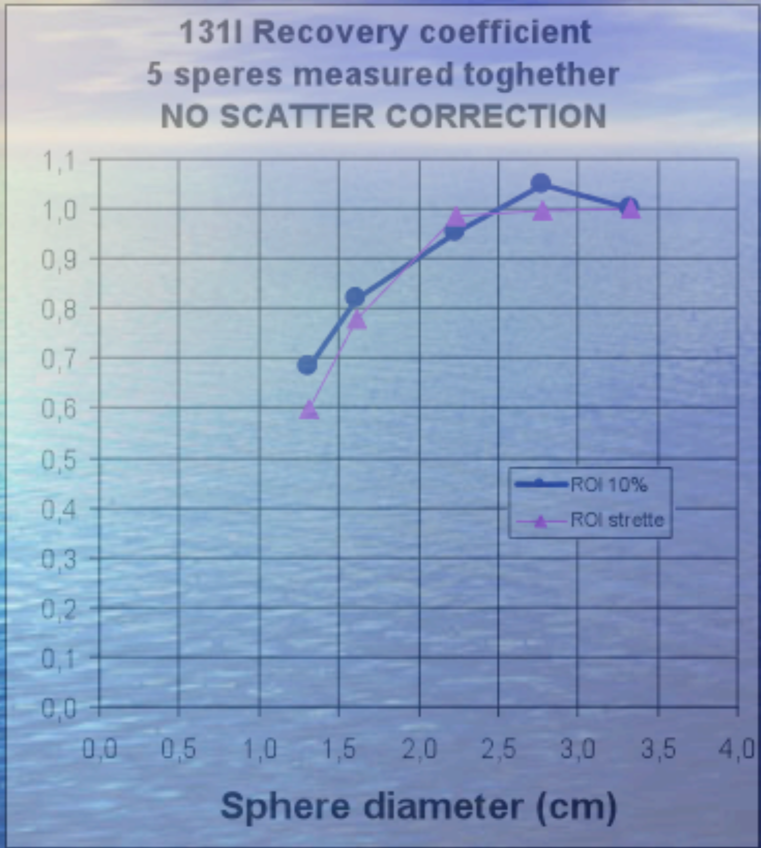


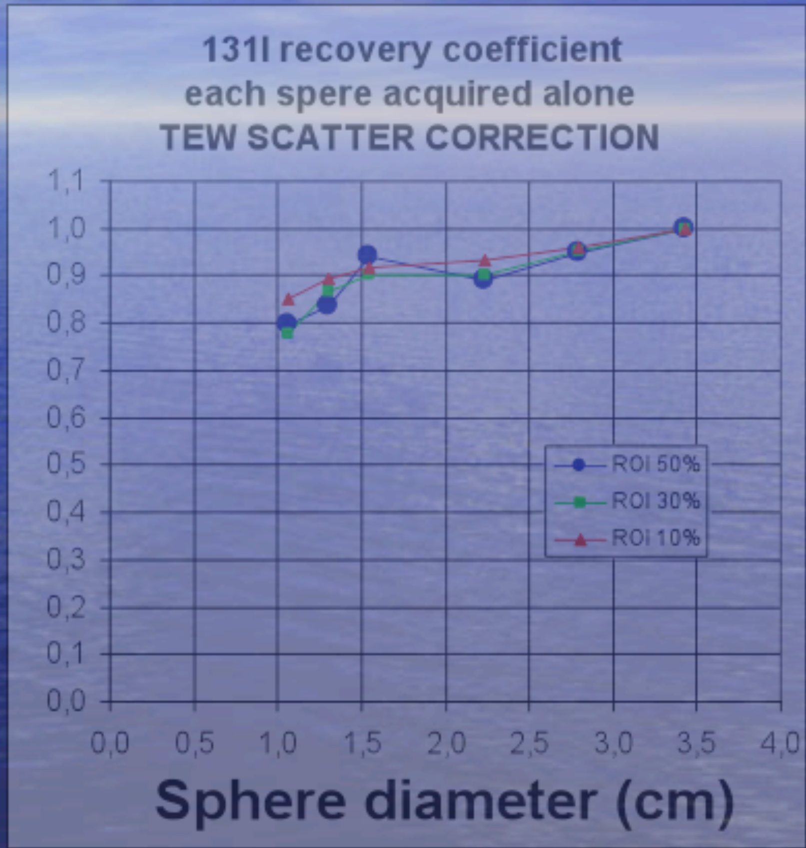


Depends on:

- Contrast
- Object dimension
- Spatial resolution
- Structures <2-3 FWHM

5. Partial volume effect in planar

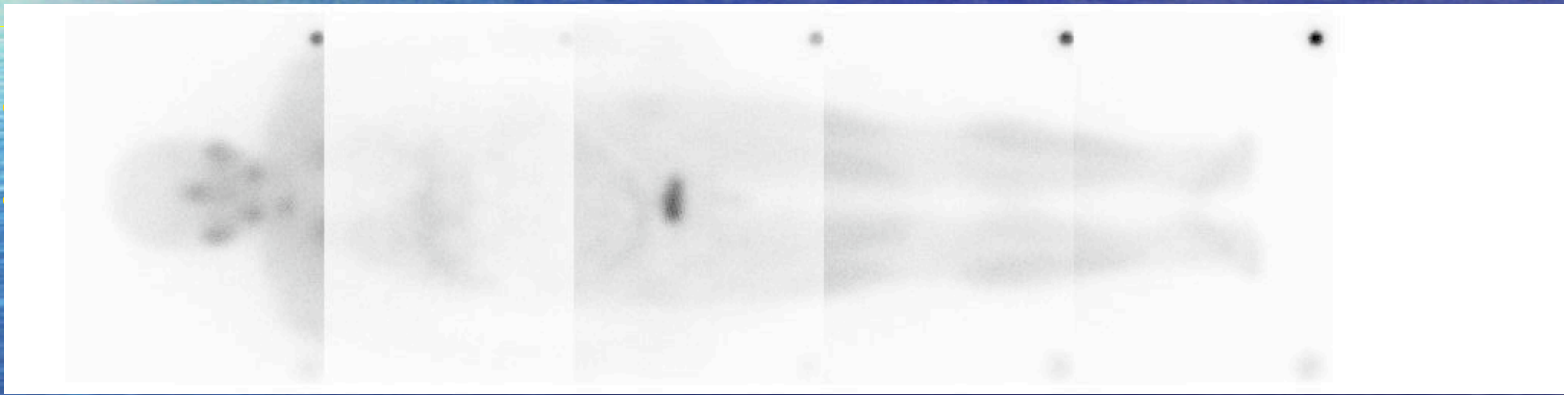




Reduced effect after scatter correction

6. Count losses caused by gammacamera dead time (DT) during therapy scans

Peri-therapy dosimetry in necessary as historical step: we must be sure to have identical diagnostic & therapy phase behaviors



131-I mIBG 6 h p.i. 8.9 GBq

1st DT naive correction method: standard source (point source)

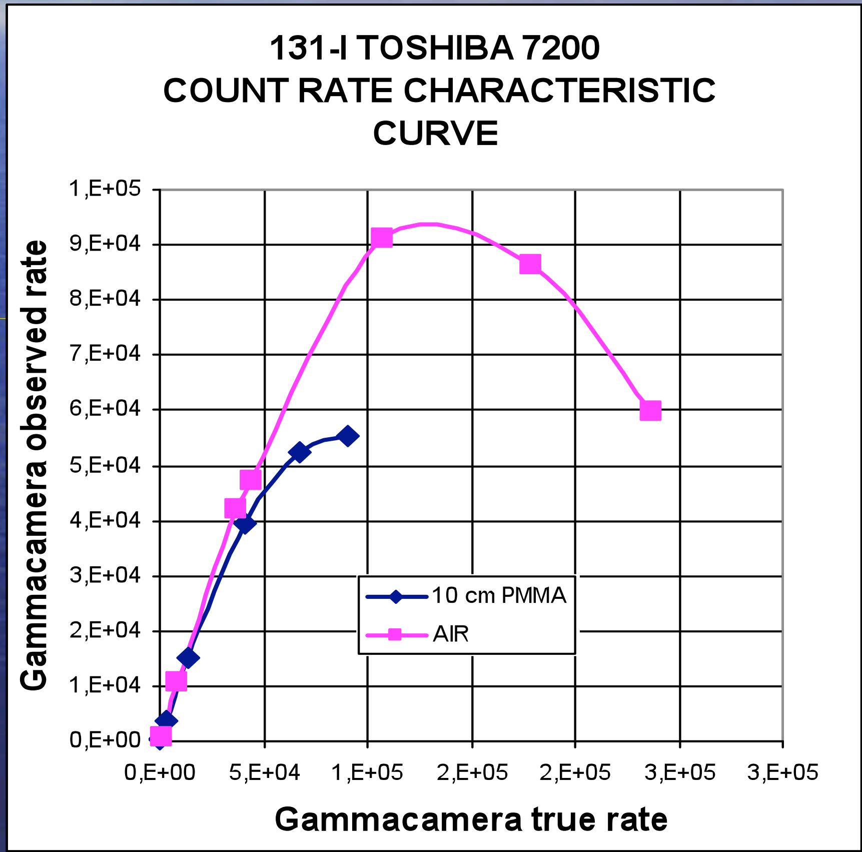
- CF = N without DT / N with DT
- Quite simple method
- Inaccuracy: CF overestimates true counts of large objectes
- The error increases with activity
- Practical drawback: overlapping with patient's arm
- Problem of ROIs across 2 FOVs

A (MBq)	CF	*E* (%)
37	1.00	0.00
190	1.04	0.74
373	1.11	2.18
557	1.17	3.39
750	1.26	6.77

2nd DT Correction method: modelling the count rate characteristic curve with phantom studies

Delpon G, Ferrer L, Lisbona A, Bardies M Phys Med Biol 47 (2002) N79-N90

- The goal is derive the true count rate from the observed count rate
- A preliminary calibration with high activity on phantom is necessary
- The characteristic curve depends upon the spectrum shape, i.e. on the scatter fraction, i.e. upon the geometry of the phantom vs patient
- The use of 2 energy window in demanding LIST mode gave the best results
- Not applicable beyond the peak
- Applicable only if WB step & shoot is available (GE gamma-cameras)

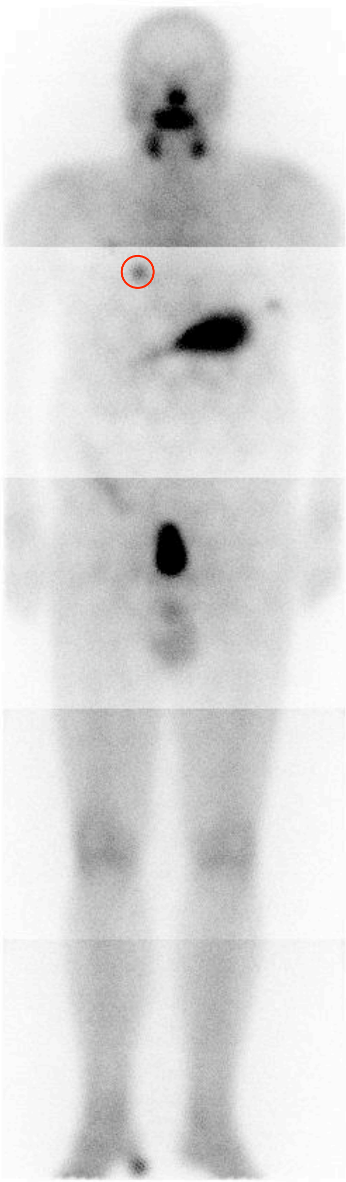


3rd: "Continuity" DT correction method: image manipulation to get continuos variations of counts

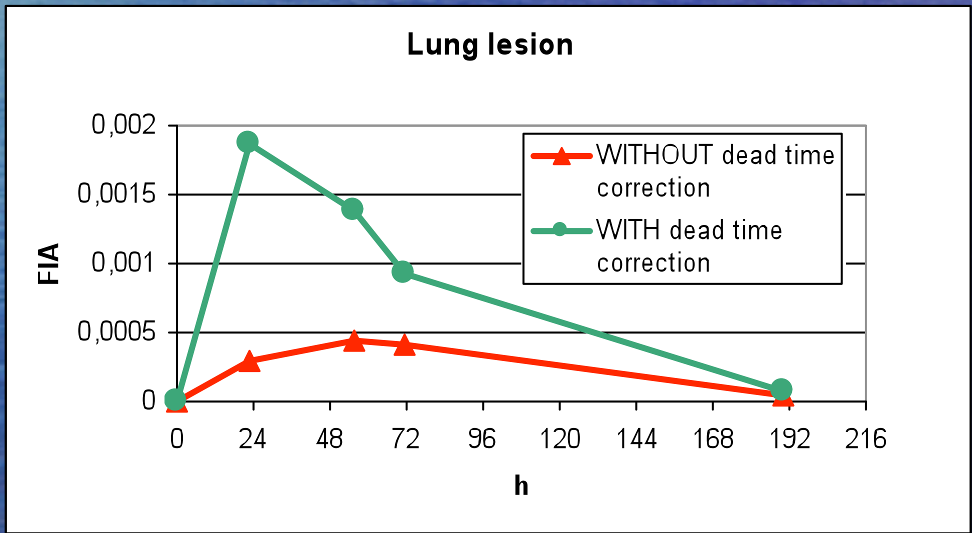
Chiesa C, Negri A, Albertini C et al Q J Nucl Med Mol Im (2009) vol 53 546-561

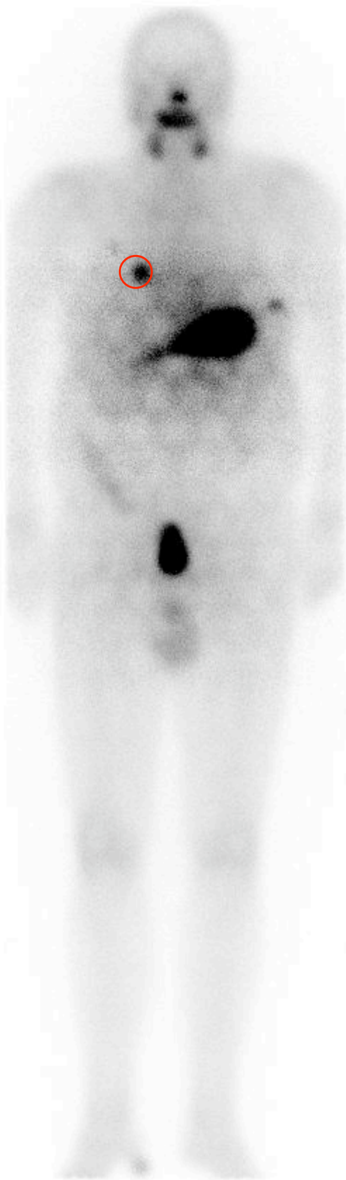
- Only image manipulation
- No need of high activity phantoms
- No need of list mode
- A sequential correction is applied to each FOV starting from feet, where no deadtime is present
- The ratio of counts the last rows of pixel in the n and n+1 FOV is taken as correction factor
- Applicable beyond the peak
- **Applicable only if WB step & shoot is available (GE gamma-cameras)**

APPLICATION:
Thyroid CA metastasis
131-I A_0 = 11.1 MBq



DT corr.





Dose difference with/without dead time correction: 3 times

4th DT correction method

RF Hobbs, S Baechler, S Senthamizhchlvan, AR Prideaux, CE Esaias, M Reinhardt, EC Frey, DM Loeb and G Sgouros

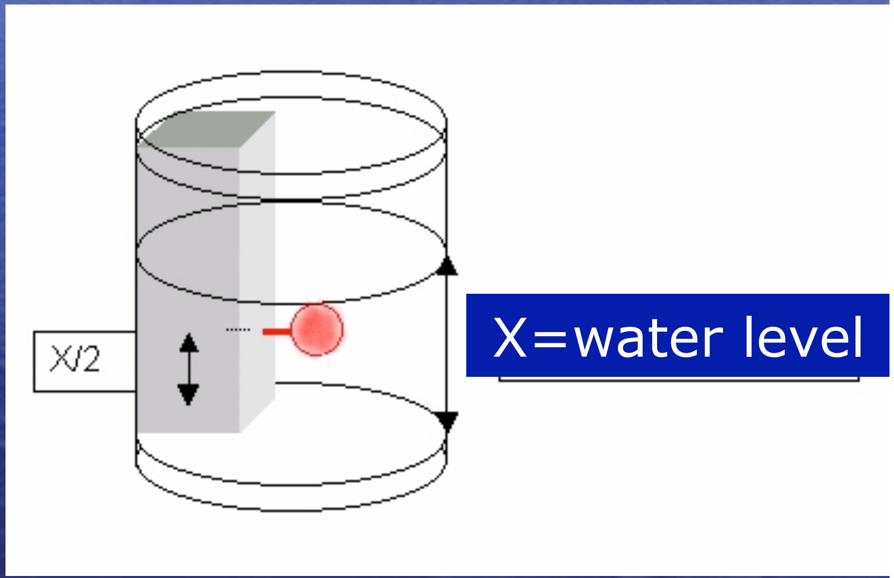
A gamma camera count rate saturation correction method for whole body planar imaging

Phys Med Biol 55 (2010) 817-831

Applicable to WB continuos modality

Absolute gammacamera calibration
MIRD 16 pseudoextrapolation number

- Different methods are proposed by MIRD 16
- Basically the main difference using a known source in air or water
- The latter approach (pseudoextrapolation number) is closer to the clinical condition
- Scan for T_n = 0, 4, 8 ….cm

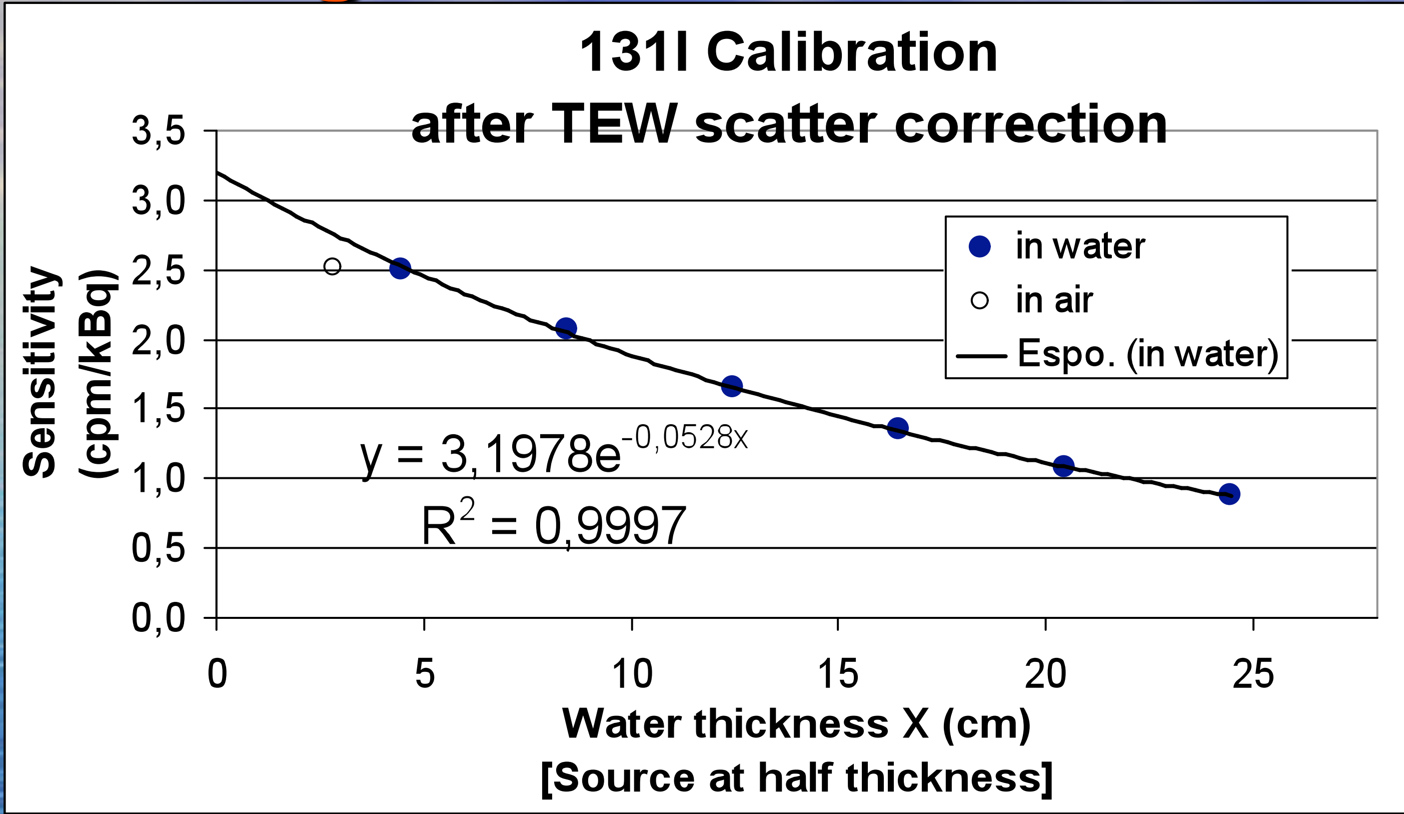


Absolute gammacamera calibration
MIRD 16 pseudoextrapolation number
Coniugate view formula resolved for C

$$C[T_n;\mu(^{131}I)]\exp(-\mu(^{131}I)/2*T_n)=\sqrt{\frac{I_A(T_n)\,I_P(T_n)}{}\frac{f}{\Delta t}}*1/A$$

- Given A_0 (kBq), plot $\sqrt{I_A(Tn)I_P(Tn)}/\Delta t$
- Δt = static scan duration (min); $I_A(Tn)I_P(Tn)$ counts
- An exponential is obtained
- The value for T=0 is the extrapolated calibration factor in water, which includes the scatter contribution
- The value of μ(131I) is twice the exponent coefficient

Absolute gammacamera calibration



The sphere in air still is out of the curve:

TEW scatter correction cannot solve the scatter problem

Gammacamera relative calibration

- Some author obtain the calibration factor C as ratio between total cpm in the first scan (without micturition) and the known injected activity, without considering WB ACF
- WB ACF must be included, but……
- This calibration factor depends on the biodistribution, through the attenuation
- Slow organ uptake (antibodies): arms & legs with low attenuation overestimate C to be applied to trunk
- Fast organ uptake (radiopeptides): dependence of C on the first scan time

Planar quantification: conclusions

- Main advantage: low cost (it's easy !)
- Corrections feasible by most centres
- Main limitations: overlapping activity

Acknowledgements

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