Chapter 17: Quantitative Nuclear Medicine

**Set of 28 slides based on the chapter authored by
J. Ouyang and G. El Fakhri
of the IAEA publication (ISBN 92-0-107304-6):**
*Nuclear Medicine Physics:
A Handbook for Teachers and Students*

Objective:

To familiarize with absolute quantification of radionuclide distributions methods in nuclear medicine.
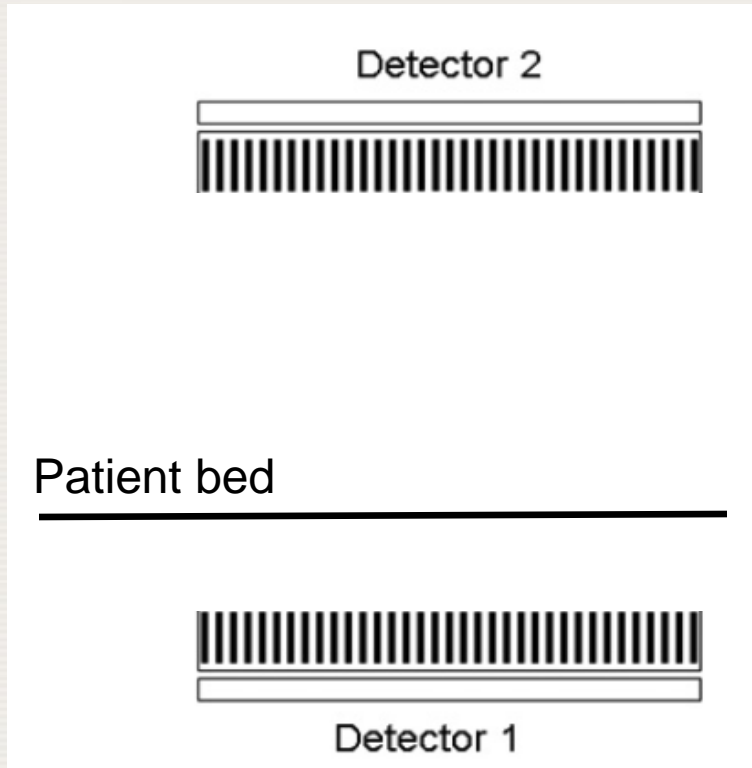
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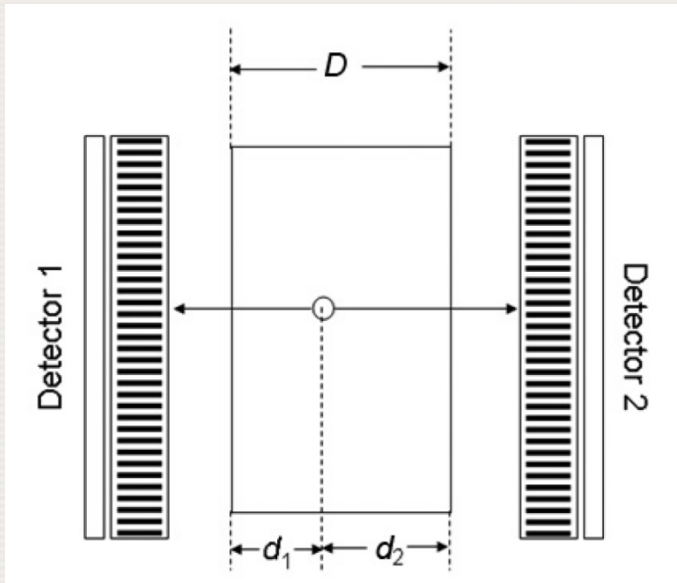**International Atomic Energy Agency**

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Planar whole body imaging:

- dual-head gamma camera: one detector above the patient, one detector below the patient

- each detector provides a 2D image representing a 2D projection of the radionuclide distribution in the patient.

Photon attenuation

- when reaching one of the detectors, photons have been attenuated by the patient body

- For a uniform attenuator, attenuation depends on the length of the path travelled by detected photons before reaching the detector (e.g. d_1, d_2 in the figure), and by the material(s) encountered

- attenuation can be compensated for

Conjugate views method

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Conjugate views method - 1

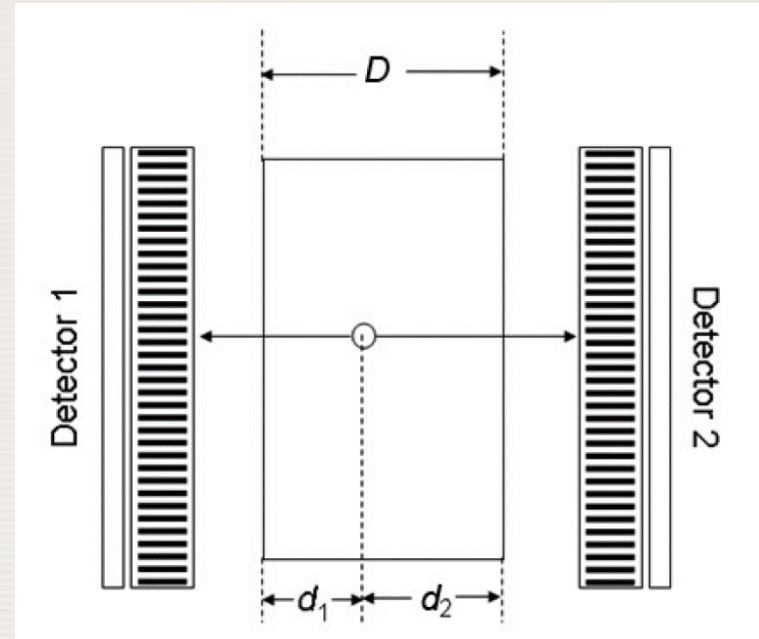Consider a point source placed inside an uniform attenuating body at depths d_1 and d_2

I_o = the number of counts that would be measured by the detectors in absence of attenuation

μ = attenuation coefficient of the material

The detectors will reveal a lower number of counts, P_1 and P_2 :

Detector 1 $\qquad P_1 = I_o \cdot \exp(-\mu \cdot d_1)$

Detector 2 $\qquad P_2 = I_o \cdot \exp(-\mu \cdot d_2)$

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Conjugate views method - 2

The geometric mean of the counts:

$$P_G = \sqrt{P_1 P_2} = I_0 \exp(-\mu D / 2)$$

only depends on the object thickness, D, and not on the source position (which is unknown in the case of patients)

For a non-uniform attenuator, line integral at each point through the attenuator can be computed.
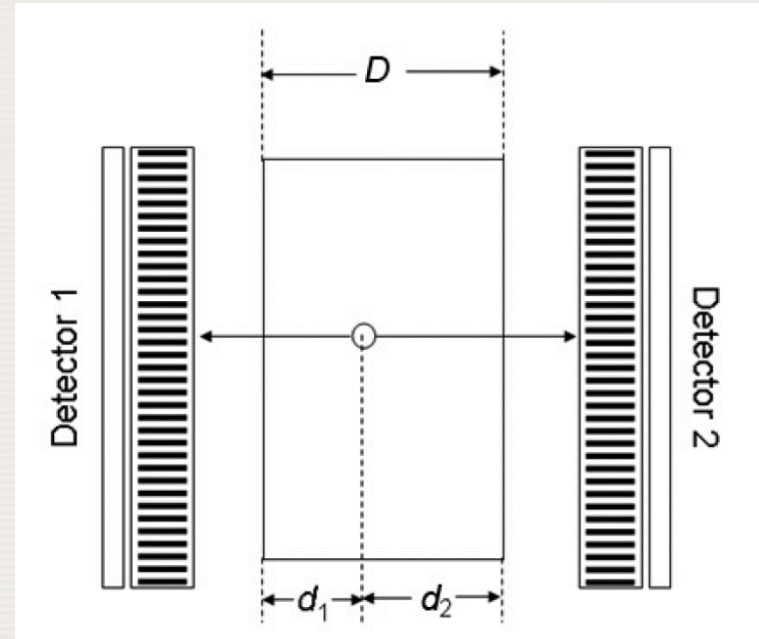
→ the number of counts I_o, unaffected by attenuation, can be obtained

→ attenuation has been compensated for.

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Conjugate views method - 3

- Geometric mean using conjugate views is a method commonly adopted when performing planar imaging quantification

- The formulation reported here is exact in the case of point sources only

- In case of extended sources (as is normally the case of patients) further corrections need to be applied

    Many references exist on this topic, e.g.:

    Sorenson JA, "Quantitative measurement of radioactivity in vivo by whole-body counting", Instrumentation of Nuclear Medicine (HINE, G.J., SORENSON, J.A., Eds), Academic Press, New York 2 (1974) 311-348

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17.2 QUANTITATION IN EMISSION TOMOGRAPHY

17.2.1 Region of Interest

ROI = Region Of Interest

= the region where tracer uptake needs to be quantified

How to define it on images?

- Manual drawing slice by slice:

    difficult to determine the object edge, operator dependent

- Semi-automatic and automatic methods using edge detection techniques:

    count threshold

    isocountours

    maximum slope or maximum count gradient

    factor analysis of dynamic sequences (to study volumes with specific time-activity behaviour in a dynamic acquisition)

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17.2 QUANTITATION IN EMISSION TOMOGRAPHY

17.2.2 Use of standards

A possible method to **convert counts into activity concentration**:

to image a **standard activity** (= a small object containing a known, measured amount of radiotracer) along with the patient projection

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a factor can be derived converting the counts in the projection into activity concentration (MBq/mL)

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when applied to the counts within a ROI, it allows quantification of the activity in the ROI itself

! Use of standards **does not guarantee** accurate absolute quantification because the standard activity is not affected by scatter, attenuation and partial volume effects in the same way as the activity distribution in the patient

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Ideal situation:

images properly corrected for

      scatter

      attenuation

      randoms (PET)

      dead time

the count intensity within a region in a reconstructed image is proportional to the real activity present in the object

Real situation:

even if proper correction is applied

there is no proportionality between counts and true activity when considering objects of different sizes
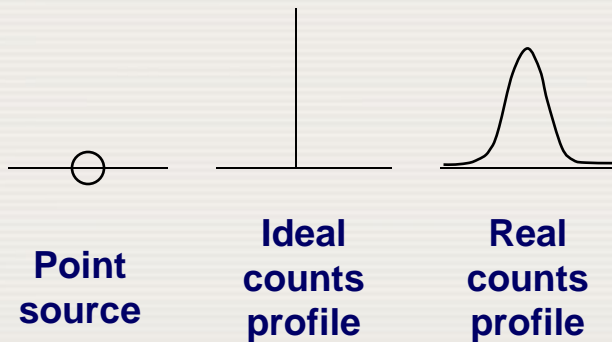
Partial Volume Effect

![IAEA logo] **IAEA**

Causes of Partial Volume Effect

Image Blurring

due to the finite spatial resolution of the imaging system, which cannot be fully compensated for

A point source is imaged as a spot, larger and dimmer

Point source   **Ideal counts profile**   **Real counts profile**

Tissue fraction effect

due to the fact that digital images sample at the voxel size

The boundaries of the voxel may not match the underlying activity distribution

PVE results in:

- reduced contrast between the object and the surrounding areas due to the summed effect of spill-out (object counts attributed to the surrounding background) and spill-in (background counts attributed to the object)

- reduced absolute uptake in a hot region

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Factors affecting PVE

- size and shape of the region

- activity distribution in the surrounding background

- image spatial resolution

- pixel size

- method used to evaluate the uptake

- spill-out and spill-in usually do not balance, making it difficult to predict the overall PVE

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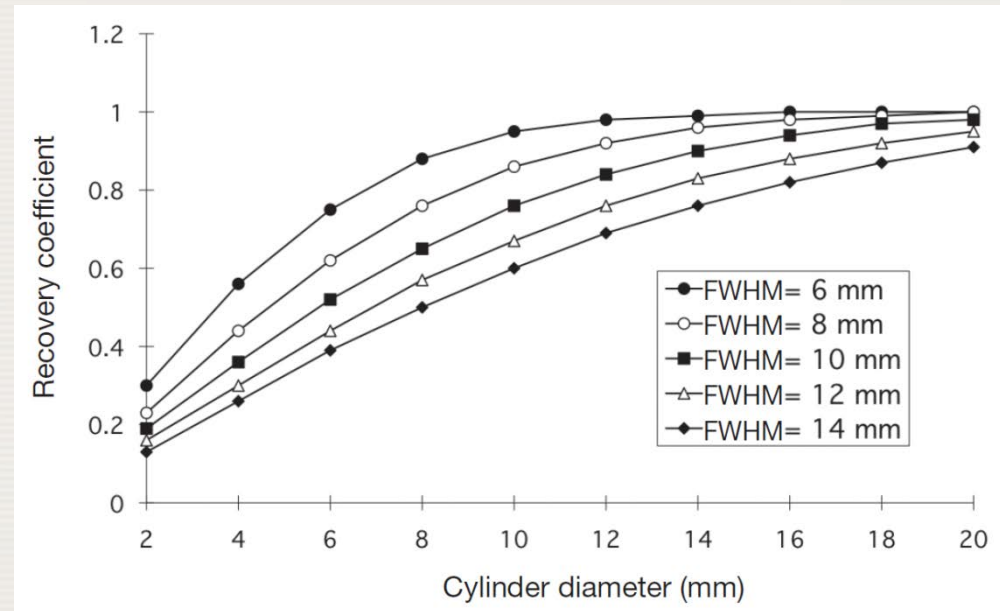## 17.2.3 Partial Volume Effect and the Recovery Coefficient

Recovery coefficient **RC** = ratio of the apparent concentration to true concentration

RC can be pre-calculated if the spatial resolution as well as the size and shape of a region are known.

RC approaches 1 when

object size > 2· FWHM

RC will vary according to:

• object size

• system resolution

• object-background concentration ratio

A simple, common method for PVE correction inside regions:

1. Obtain the RC curve for the scanner

2. Obtain the size of the object for which activity quantification is needed (e.g. from other imaging modalities, CT or MRI)

3. Obtain the system FWHM at the location where the object is placed (the dependence of spatial resolution on location is normally known for SPECT and PET scanners)

    → Derive the RC value and apply it to the measured concentration to obtain the true concentration

    This will only correct the spillover between two structures

Other methods: geometric transfer matrix (spillover among many structures)

deconvolution (not requiring any assumptions on tumour size, shape, homogeneity or background activity)

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Quantitative image assessment

- target to background contrast

    = the ratio between concentration in the target region and the surrounding background (**Relative method**)

- radiotracer concentration (Bq/mL)

    = amount of activity per unit volume within a ROI

    Sometimes it is normalized by patient-specific data:

    e.g. Standardized Uptake Value (SUV) is the radiotracer concentration normalized by the injected activity and the patient weight (**Semi-quantitative metric**)

- kinetic parameters

    = parameters describing the interaction between the tracer and the physiological processes, derivable by dynamic quantitative PET acquisition (**Absolute metric**, the most accurate achievable from PET measurements)
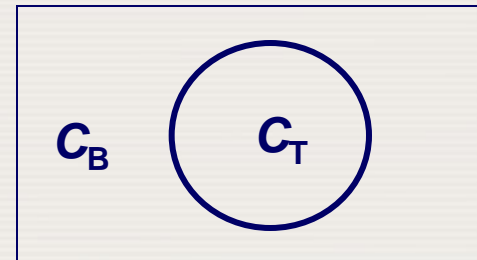
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17.2.4.1 Relative quantification using contrast ratio

Contrast Ratio, CR

$$\text{Image contrast} = \frac{\text{signal level of a target}}{\text{signal level in the surrounding background}}$$

$$CR = \frac{C_T - C_B}{C_B}$$

where C_T = mean concentration within the defined target

C_B = mean concentration within the background region

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Standardized Uptake Value (SUV)

For a single voxel:
$$\text{SUV} = \frac{C_i \,(\text{kBq/mL})}{\mathcal{A}\,(\text{kBq}) \,/\, W\,(\text{g})}$$

being C_i = decay-corrected activity concentration (kBq/mL)

   $\mathcal{A}$ = injected activity (kBq)

   W = patient weight (g)

Assuming tissue density equal to 1 g/mL, SUV becomes dimensionless.

It allows to assess the uptake in a ROI irrespective of the administered activity and the patient weight.

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Different SUV definitions inside a ROI

SUV_{mean} = mean SUV among the voxels included in the ROI

SUV_{max} = maximum SUV among the voxels included in the ROI

+ Less sensitive to PVE than SUV_{mean}

+ Avoids including necrotic or other non-tumour elements

- Lower reproducibility and larger bias than SUV_{mean} because it is computed over a small number of voxels (or only one)

SUV_{peak} = mean SUV in a group of voxels surrounding the voxel with highest SUV

+ Meant to be a more robust parameter than SUV_{max}

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Factors affecting SUV - 1

<u>Physical</u>
- image noise
- reconstructed activity concentration
- reconstruction algorithm
- method for ROI delineation
- PVE

<u>Biological</u>
- a part of the administered dose could infiltrate interstitially: if not taken into account, resulting SUV is artificially low

- in case of FDG: glucose avidity – and thus SUV – is affected by insulin and glucose level, which varies widely depending on the most recent meal

- in presence of diabetes, further fluctuations occur according to the moment of insulin administration

- impaired renal function causes a slow FDG extraction from the bloodstream, yielding higher SUV (more FDG available in the tissue)

- in patients with a large number of ascites, body mass can be elevated by the presence of fluid, artificially lowering SUV

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Factors affecting SUV - 2

Physical

Biological

- low reproducibility of SUV measurement

- up to 50% variations can be observed due to one or more of the factors reported (physical, biological)

The SUV should be properly corrected for all these effects

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Total Lesion Glycolysis, TLG

Another metric commonly used to assess tumour response to therapy:

TLG = SUV$_{mean}$ · V

being V the lesion volume (mL) that can be obtained using 3D contour software

TLG provides a measurement of the total relative uptake in the tumour region, reflecting the total rather than the average tumour metabolism

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17.2 QUANTITATION IN EMISSION TOMOGRAPHY

17.2.4.3 Absolute quantification using kinetic modeling

Dynamic imaging → Time-activity curve in each voxel → Possibility to quantify tracer kinetics in-vivo

Dynamic imaging data

+

Understanding of the physiological factors controlling the level of tissue radioactivity

Mathematical kinetic models can be constructed.

The model parameters describe the radiotracer distribution in the body as a function of time

Models in Nuclear Medicine

based on compartments where the radiotracer nearly instantly distributes uniformly

= the models describe a system which is time variant but not space variant

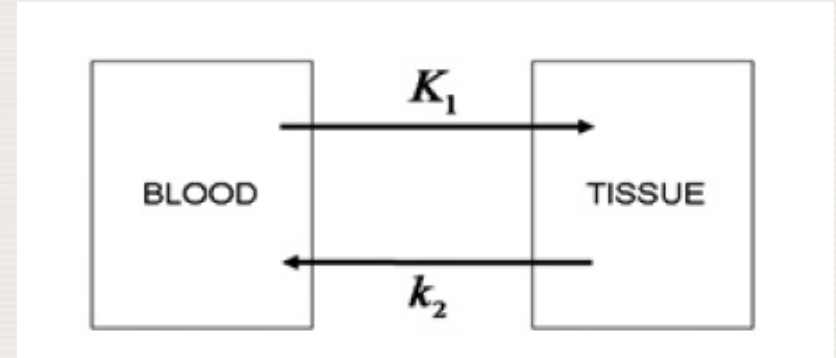Spatial gradients are normally not applicable due to the poor image resolution.

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17.2.4.3 Absolute quantification using kinetic modeling

Example: single tissue compartment

Rate of change of tracer concentration in a tissue:

$$\frac{dC_t(t)}{dt} = K_1 C_a(t) - k_2 C_t$$

being C_t = tracer concentration in the tissue (derived from ROIs on the images)

       C_a = tracer concentration in the blood (measured from blood samples)

       K_1, k_2 = first order rate constant for the fluxes into and out of the tissue

The equation solution is:

$$C_t(t) = K_1 C_a(t) \otimes \exp(-K_2 t) \longrightarrow$$

knowing both C_t and C_a, regression analysis is applied to solve both K_1 and k_2, whose values can be used to interpret the underlying physiology

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17.2 QUANTITATION IN EMISSION TOMOGRAPHY

17.2.5 Estimation of activity

Parameters assessing the performance of the quantification procedure

<u>BIAS</u> = mean of the differences between the measured data and an accepted reference or true value

The presence of bias is mainly due to faulty measuring devices or procedures

$$\text{BIAS} = \frac{1}{N}\sum_{i=1}^{N}(x_i - t)$$ where

N: the number of measurements

x_i: the ith measurement

t: the true value

<u>PRECISION</u> = defined as the inverse of the variance σ^2 (random error), which expresses the fluctuations of the measurements

$$\sigma^2 = \frac{1}{N}\sum_{i=1}^{N}(x_i - \bar{x})^2$$ where $$\bar{x} = \frac{1}{N}\sum_{i=1}^{N}x_i$$

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17.2.5 Estimation of activity

Parameters assessing the performance of the quantification procedure

Combining <u>BIAS</u> and <u>PRECISION</u> it is possible to assess the measurement performance:

$$\downarrow \text{BIAS and} \uparrow \text{PRECISION} = \uparrow \text{ACCURACY}$$

<u>ACCURACY</u> being the overall difference between the measured and the true value

quantified by the MEAN SQUARE ERROR (MSE):

$$\text{MSE} = \frac{1}{N} \sum_{i=1}^{N} (x_i - t)^2$$

$$\text{MSE} = \sigma^2 + \text{BIAS}^2$$

Alternatively, precision can be quantified by $\sqrt{VAR}$, and accuracy by $\sqrt{MSE}$

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17.2.6 Evaluation of image quality

What defines image quality?

<u>Quantitative parameters</u> cover just one aspect

However, they are very useful when first assessing a new system or a quantification method

In particular:

- resolution
- contrast
- point spread function
- bias
- precision
- accuracy

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17.2.6 Evaluation of image quality

What defines image quality?

For a more rigorous evaluation or for definitive optimization of data acquisition strategies:

assessment of <u>Image utility</u> = the usefulness of an image for a particular detection or quantification task

- Task based estimation
- Detection task

possible measures of image utility, the most clinically relevant bases to evaluate or optimize imaging systems

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17.2.6 Evaluation of image quality

What defines image quality?

<u>Human-observer studies</u> are the most conclusive assessment of image quality

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resource consuming, not routinely performed clinically

As an alternative:

<u>Numerical (or mathematical)-observer studies</u> are often used.

Examples:
- non-prewhitening matched technique
- channelized Hotelling observer

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