PET Interpretation Issues:
Quantitative Analysis
(Problems and Reproducibility)

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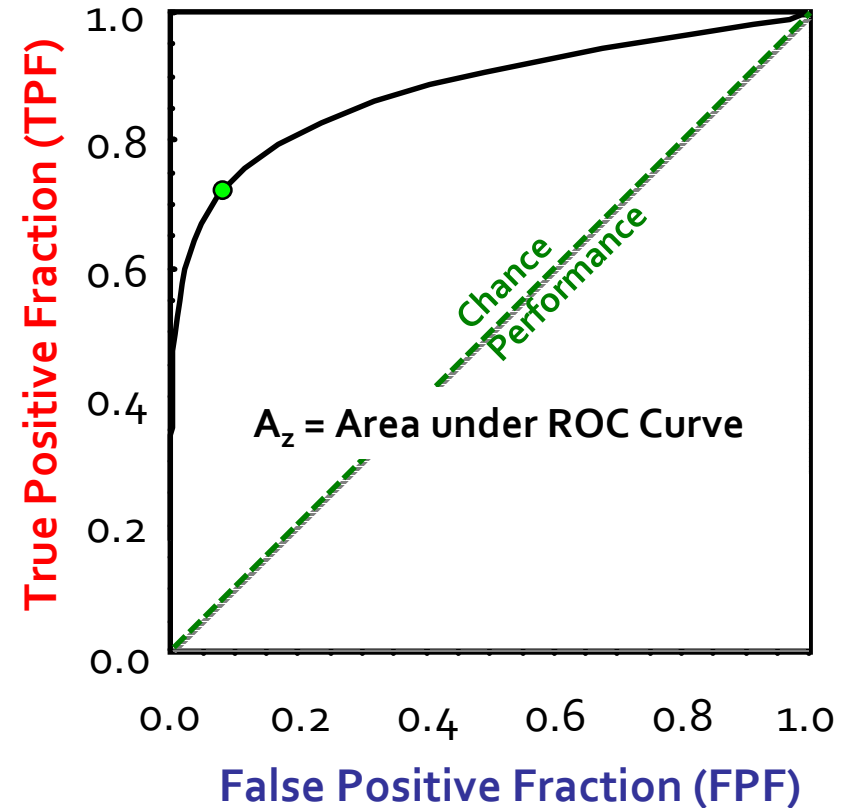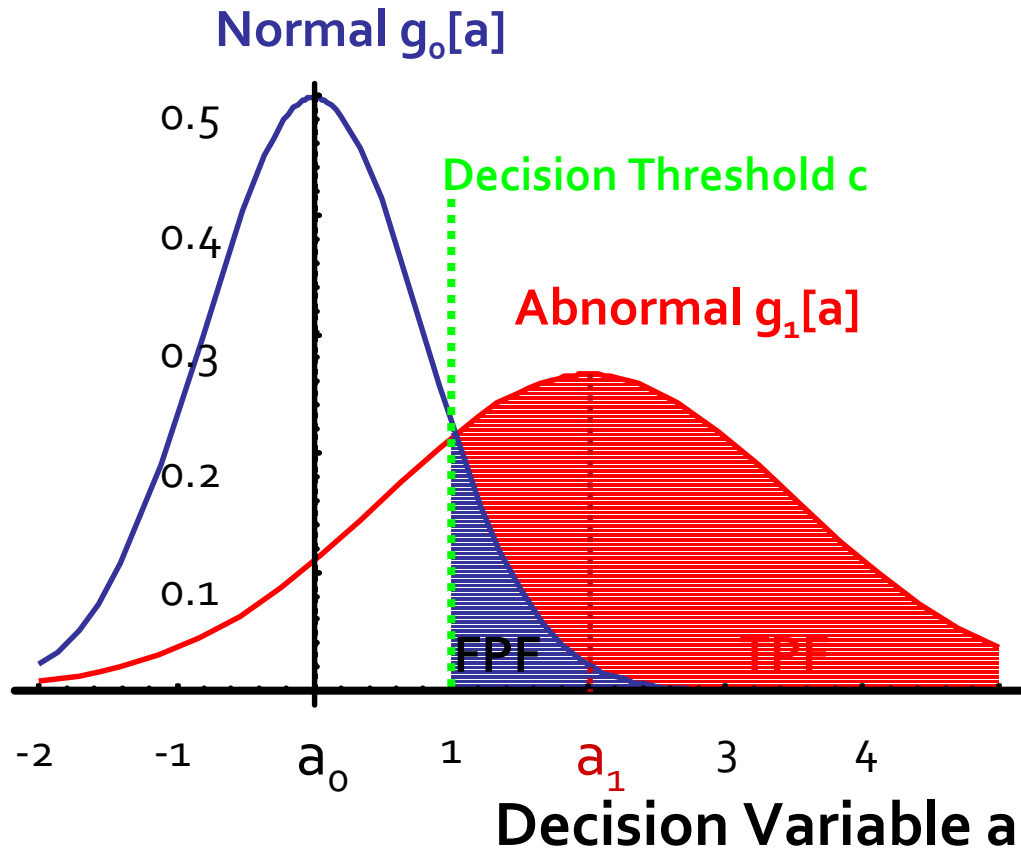Germany

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Interim-PET Interpretation Issues

- FDG metabolism predictor of response
- PET FDG uptake reflects FDG or glucose metabolism
- Deauville Consensus: "Preservation of the continuous nature of the data is recommended instead of just reporting a binary decision"
  - Quantitative: interval scale, e.g. SUV, ΔSUV, SUV ratio, …
  - Visual: ordinal, e.g. Deauville 5-point scale
    1. No uptake
    2. Uptake ≤ mediastinum
    3. Uptake > mediastinum but ≤ liver
    4. Uptake moderately more than liver uptake
    5. Markedly increased uptake at any site

Clinical Decision Making and ROC

Normal $g_0[a]$

Decision Threshold c

Abnormal $g_1[a]$

FPF

TPF

a_0

a_1

Decision Variable a

True Positive Fraction (TPF)

False Positive Fraction (FPF)

Chance Performance

A_z = Area under ROC Curve

$$FPF[c] = \int_c^\infty g_0(a)\,da \qquad TPF[c] = \int_c^\infty g_1(a)\,da$$

CE Metz: Invest.Radiol. 21,720,1986;   CE Metz: Invest.Radiol. 24,234,1989

Required Validation

- Optimal decision variable
  - Suitable reference
    - Within study: reference organ, $SUV_{body\ weight}$, SUV_{BSA}, …
    - Between studies: SUV ratio, ΔSUV, …
  - Cover all relevant decision thresholds
  - Stable decision variable: measurement issues
  - Stable operating points: observer issues
- Optimal decision threshold
  - Minimize "misclassification"
  - Based on outcome
- Validation required regardless of scale

Standardized Uptake Value - SUV

$$\text{SUV} = \frac{\text{PET-Tissue Concentration}\ [MBq\,/\,kg]}{\text{Injected Activity}\ [MBq]\,/\,\text{Body Weight}\,[kg]}$$

- Requires absolute scanner calibration
  - Normalisation, cross-calibration dose calibrator
  - Attenuation correction
  - Scatter correction

- Correlated with metabolic rate of glucose consumption

Factors affecting FDG SUV

- Biology – affects also visual assessment
  - Time between injection and PET scan
  - Blood glucose concentration
  - Distribution volume of FDG (body composition)
  - FDG – Elimination (kidneys)
- Physics
  - Corrections (attenuation, scatter, detector response, …)
  - Reconstruction (Filter, Regularisation, …)
    - Resolution: Recovery and Spillover
    - Image noise characteristics
  - Region-of-Interest (ROI)
    - Form, size, shape, and position of ROI
    - Form, size, shape, and position of object
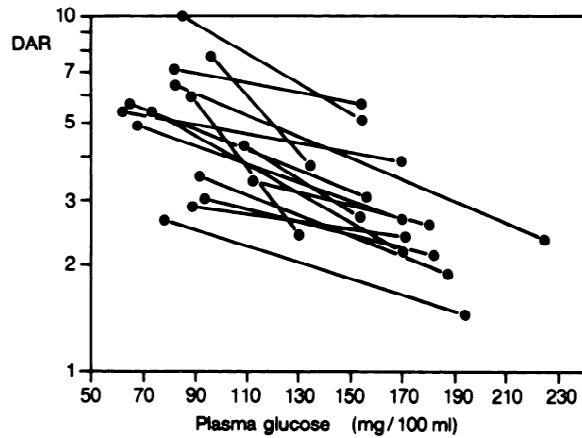   - Reproduceability of ROI segmentation
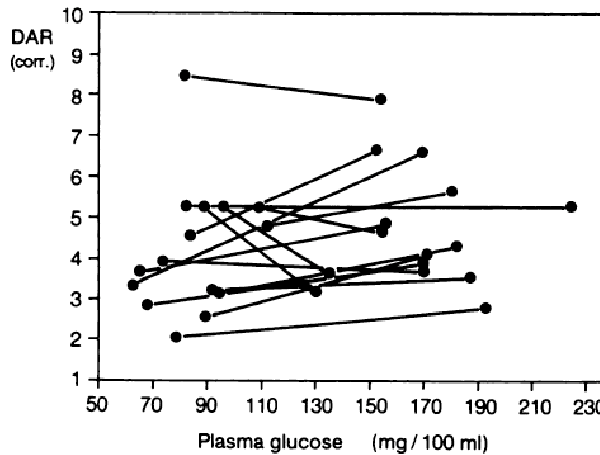- **Standardization required**

Interval Injection – PET Scan

FDG-Kinetics in different Tissues
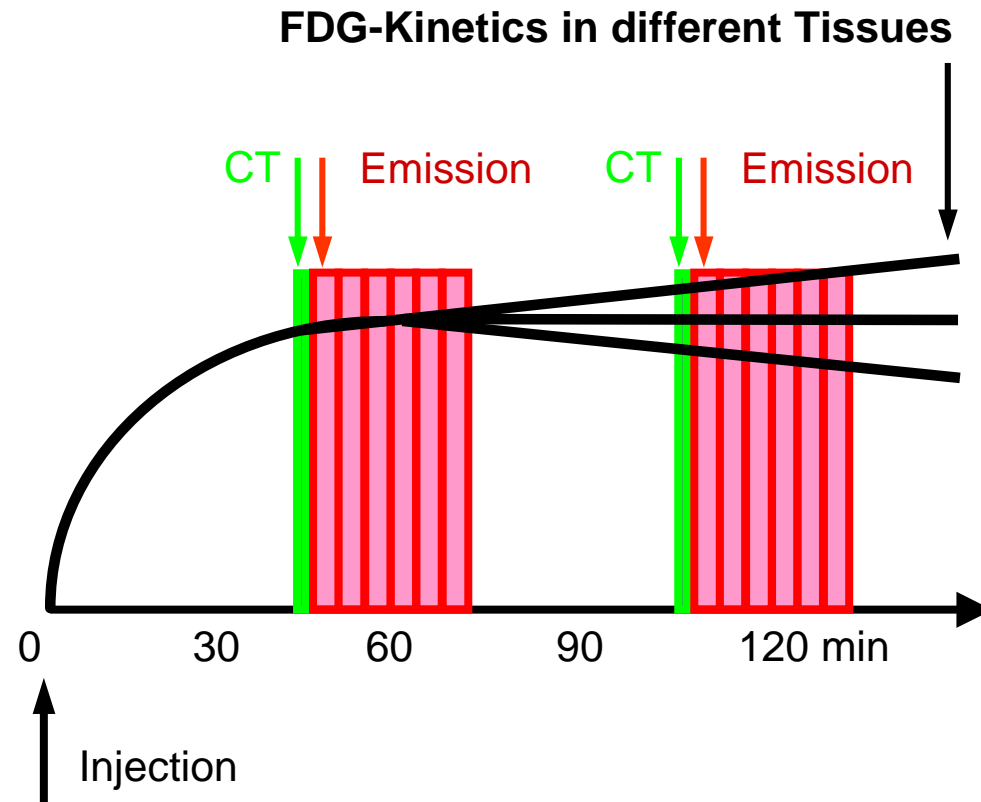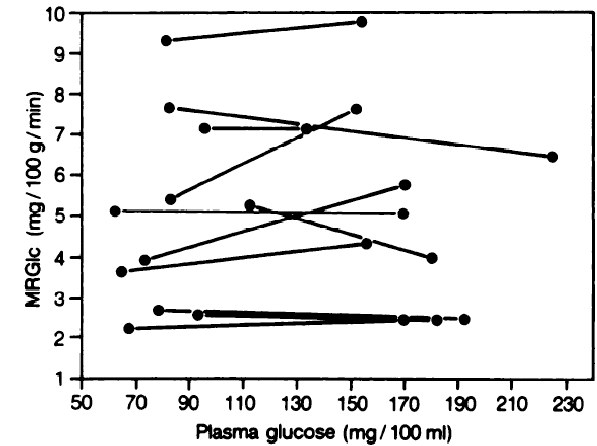
Blood Glucose Concentration

FDG Uptake in NSCLC

SUV $SUV_{gl} = [Glc]/100*SUV$ $MRGI_{Patlak-Plot}$
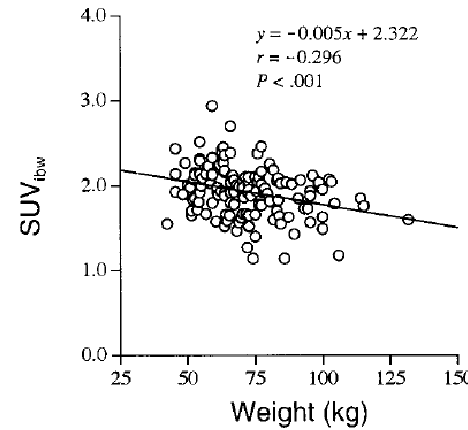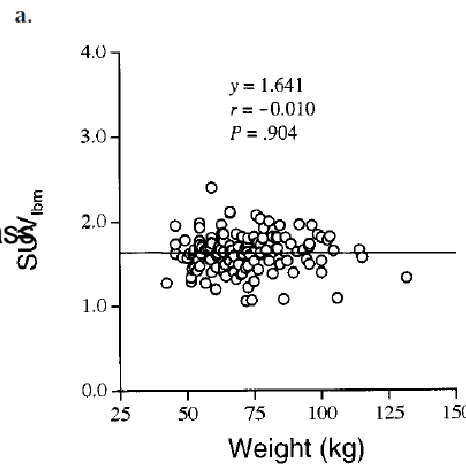
Insulin sensitivity different in various tissues

Langen J Nucl Med 34, 355, 1993

Distribution Volume

SUV$_{\text{Body Weight}}$
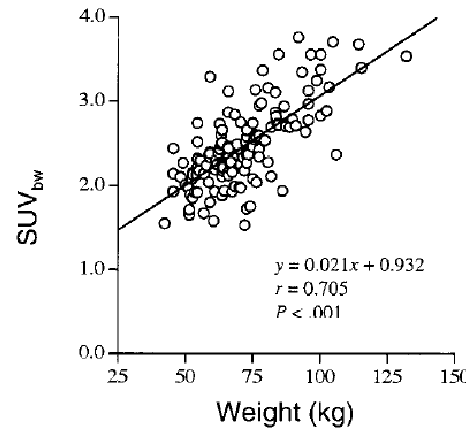
SUV$_{\text{Ideal Weight}}$

SUV$_{\text{Lean Body Mass}}$

SUV$_{\text{BSA}}$
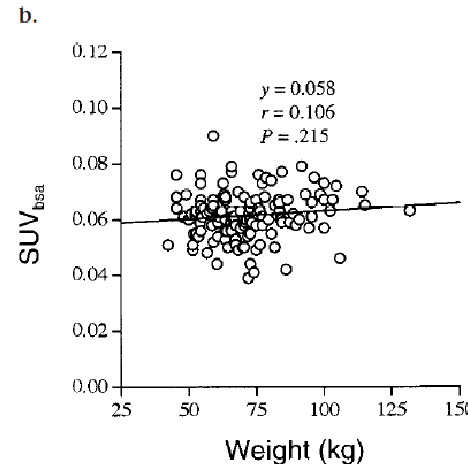
No major change between Staging and Interim PET

Sugawara Radiology 213, 521, 1999

Influence of Time Point for Interim-PET

Max. SUV = 17.4   Max. SUV = 7.3   Max. SUV = 3.2

Staging PET   **Interim PET
12 d post cycle 2**   **Interim PET
19 d post cycle 2**
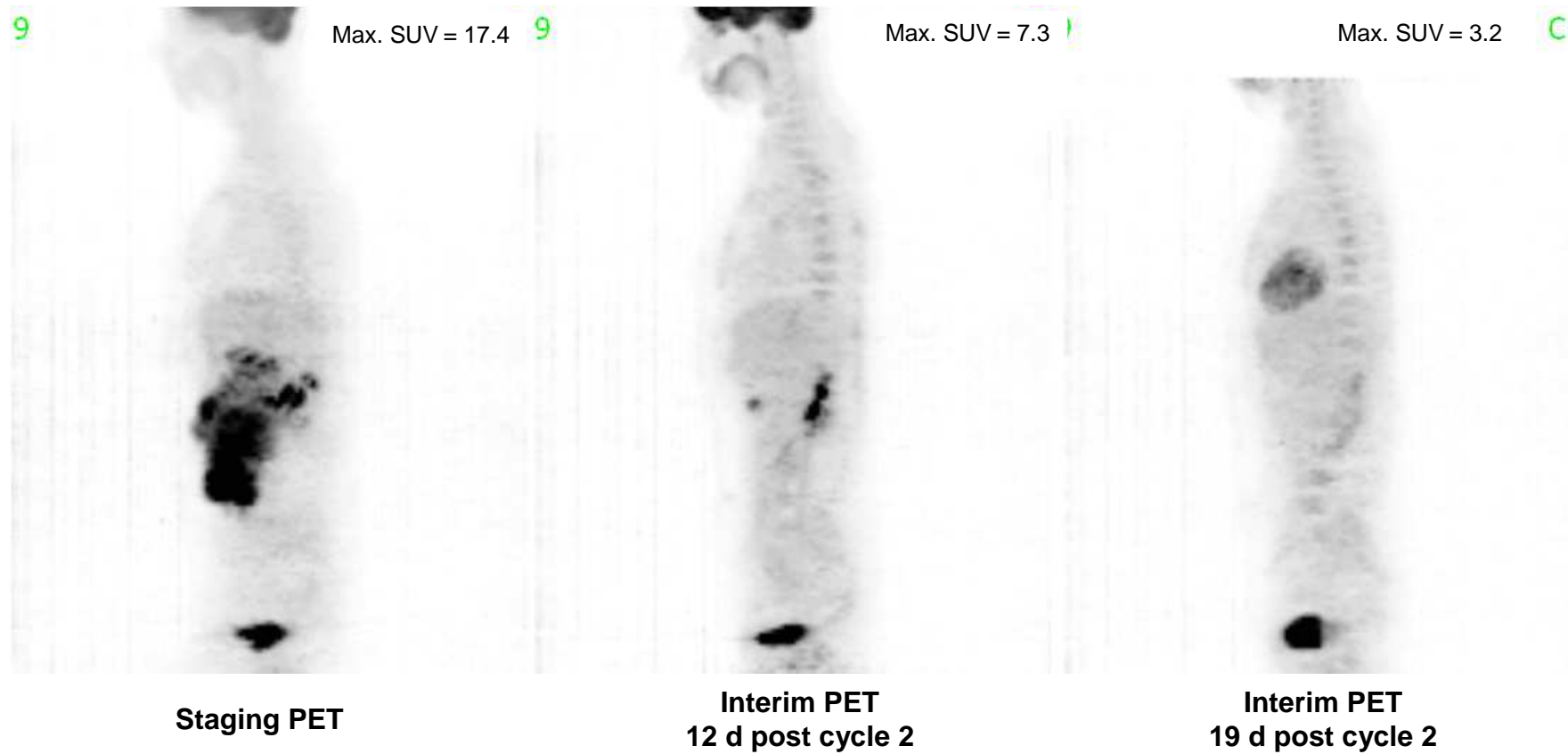
- Optimal time point
- Standardization (PETAL Resp.: 19.5±4.2 d, Non-Resp.: 19.5±4.3 d

Visual vs. Quantitative Analysis

- Most biological determinants of SUV also affect visual analysis
- Standardization required for both analyses
- Protocols for
  - Time of PET after last cycle
  - Patient preparation
  - Scanner calibration
  - Data acquisition
  - Data analysis
- Similar to clinical routine PET protocols

Reproducibility
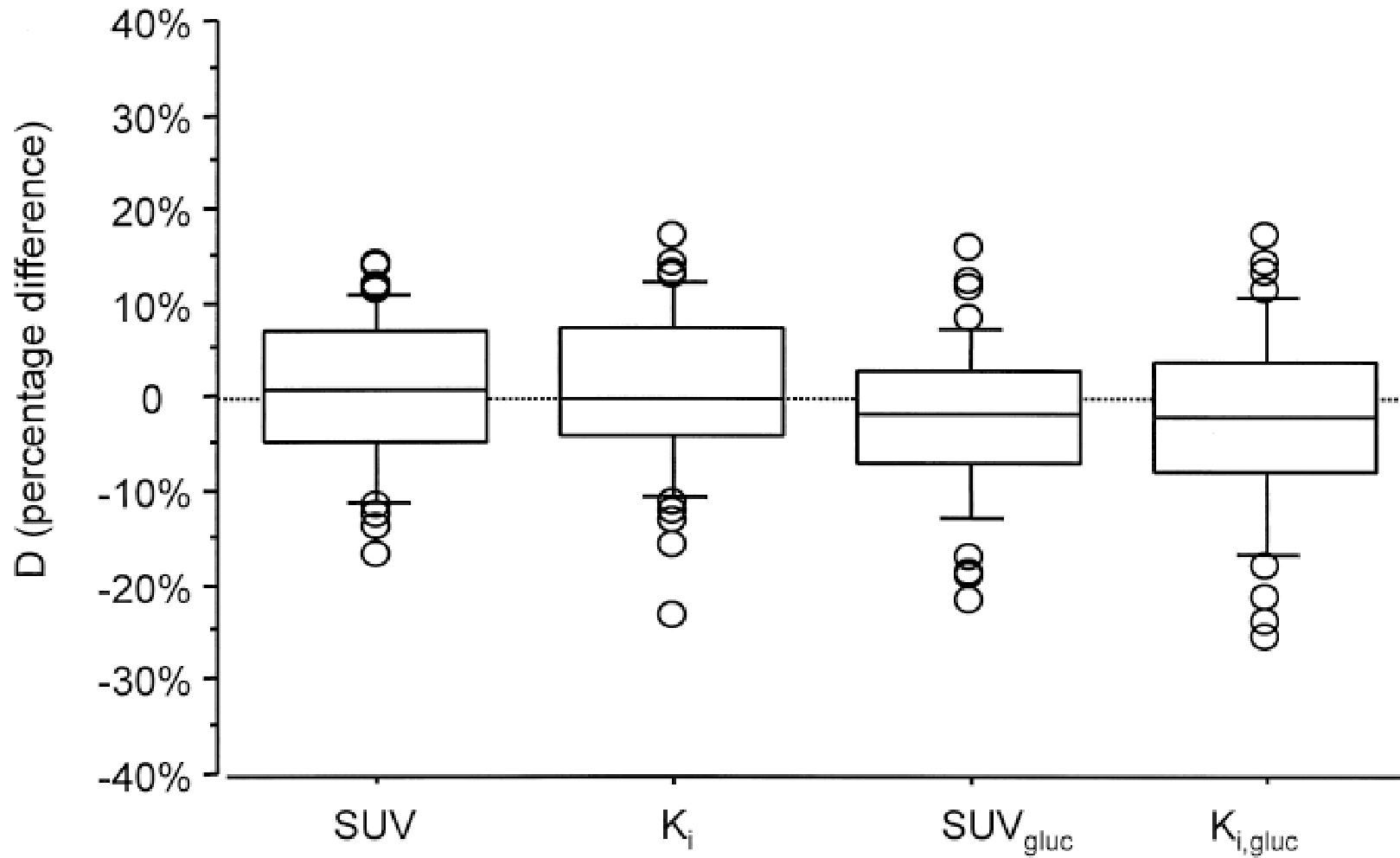
Quantitative Analysis

- Quantitative analysis easily feasible

- Eliminates inter- and intra-observer variability
  - Particularly important for multicentric trials
  - Standardized protocols similar to clinical routine

- Interval scales allow any decision threshold

- Outcome based validation ongoing
  - May be more advanced than visual scales