


Modality specific QI: PET/CT

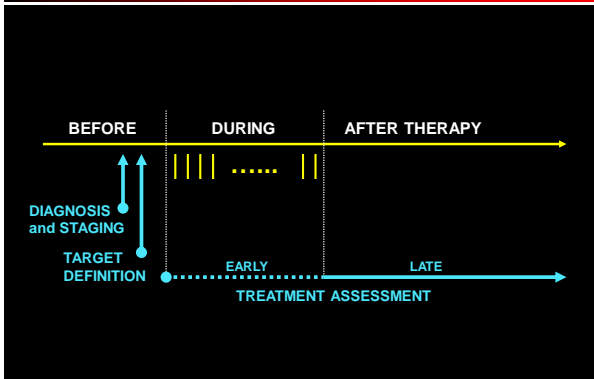
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University of Wisconsin Carbone Cancer Center

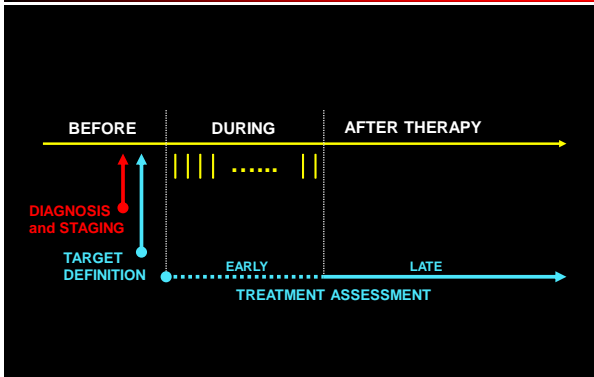
 rjeraj@wisc.edu



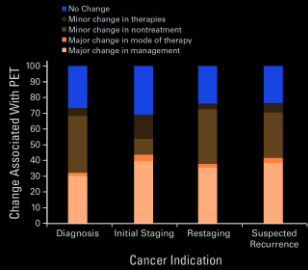
PET/CT during therapy



PET/CT for diagnosis and staging



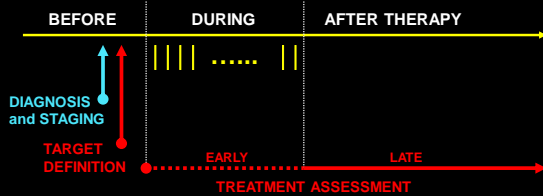
PET/CT for diagnosis and staging



- **Qualitative FDG PET/CT** has had a tremendous impact in oncology

Hillner et al 2008, J Clin Oncol 26: 2155

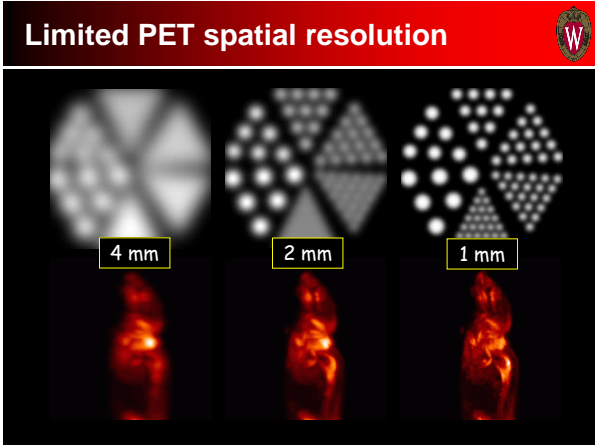
Use of PET/CT

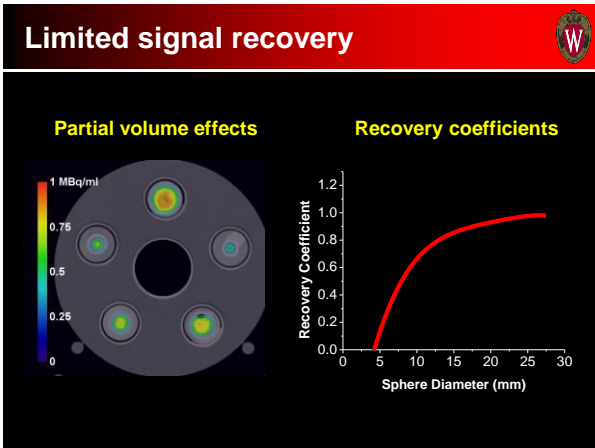


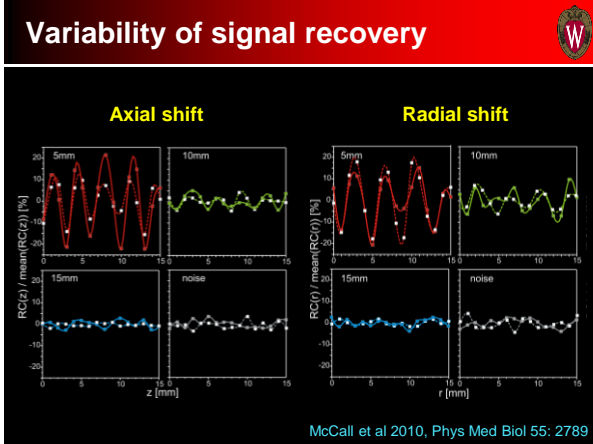
Need for quantitative PET/CT

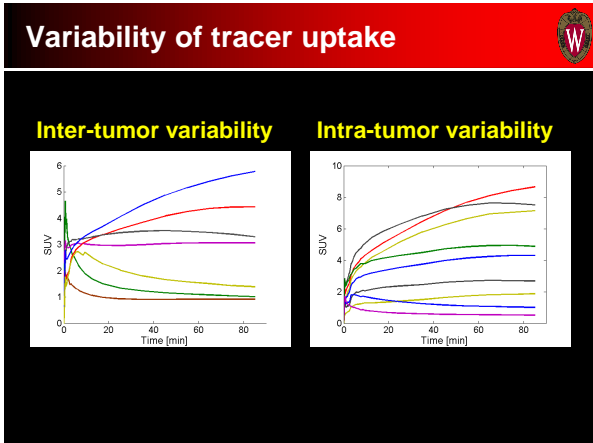
- **Where is the tumor?**
 - **SPATIAL** accuracy
- **What kind of the tumor is there?**
 - **SPECIFIC** accuracy
- **How much of the tumor is there?**
 - **ABSOLUTE** accuracy
- **How much has the tumor changed?**
 - **RELATIVE** accuracy

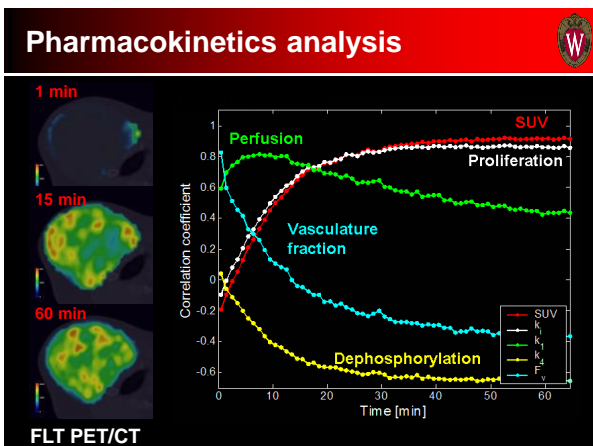
WHAT LIMITS PET/CT QUANTITATIVE ACCURACY?











PET imaging uncertainties



- **Technical factors**
 - Relative calibration between PET scanner and dose calibrator
 - Residual activity in syringe
 - Incorrect synchronization of clocks
 - Injection vs calibration time
 - Quality of administration
 - **Physical factors**
 - Scan acquisition parameters
 - Image reconstruction parameters
 - Use of contrast agents
 - **Analytical factors**
 - Region of interest (ROI) definition
 - Image processing
 - **Biological factors**
 - Patient positioning
 - Patient breathing
 - Uptake period
 - Blood glucose levels
- Jeraj et al. 2011, in Uncertainties in ext. beam RT*
Boellaard et al. 2009, J Nucl Med 50: 11S

PET imaging uncertainties

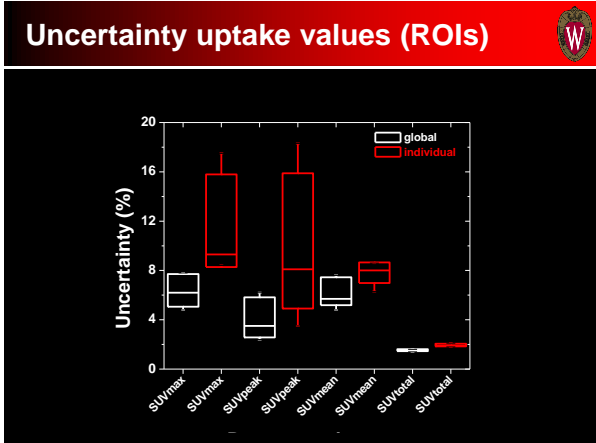


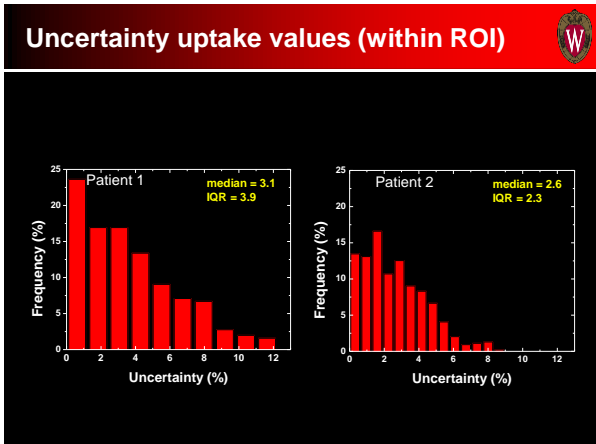
- **Technical factors**
 - Relative calibration between PET scanner and dose calibrator (10%)
 - Residual activity in syringe (5%)
 - Incorrect synchronization of clocks (10%)
 - Injection vs calibration time (10%)
 - Quality of administration (50%)
 - **Physical factors**
 - Scan acquisition parameters (15%)
 - Image reconstruction parameters (30%)
 - Use of contrast agents (15%)
 - **Analytical factors**
 - Region of interest (ROI) definition (50%)
 - Image processing (25%)
 - **Biological factors**
 - Patient positioning (15%)
 - Patient breathing (30%)
 - Uptake period (15%)
 - Blood glucose levels (15%)
- Jeraj et al. 2011, in Uncertainties in ext. beam RT*
Boellaard et al. 2009, J Nucl Med 50: 11S

IMPACT OF UNCERTAINTIES (Example of variable reconstruction parameters)

Reconstruction parameters

Reconstruction type	Acquisition	Recon Algorithm	Grid Size	Iterations	Post filter
A	3D	3D OSEM	256 x 256	2	3 mm
B					6 mm
C			128 x 128	4	6 mm
D					6 mm
E			2	3 mm	
F	2D	2D OSEM	256 x 256	2	3 mm
G					5 mm
H			128 x 128	4	5 mm
I					5 mm
J			2	3 mm	

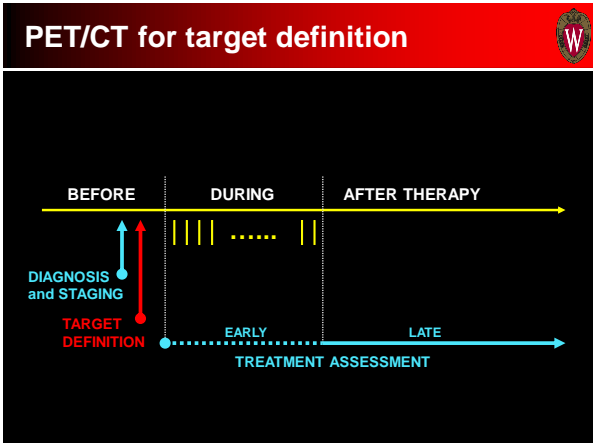







APPLICATIONS OF QUANTITATIVE PET/CT

Target definition and treatment assessment





Adding FDG PET/CT helps

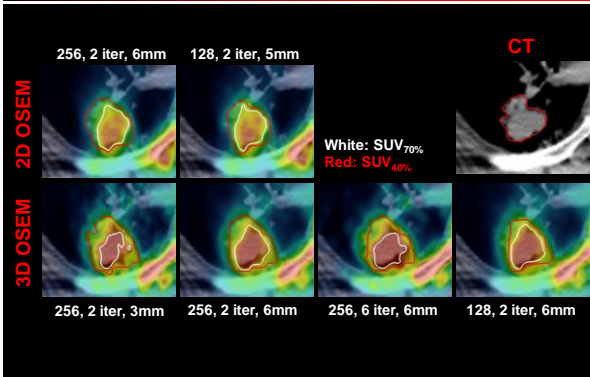
CT

FDG PET/CT

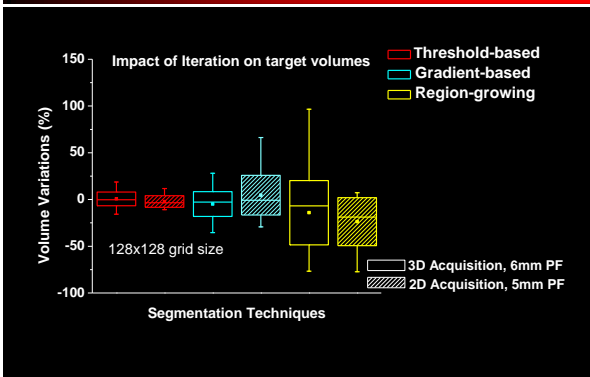
50% (30%-70%) decrease of the contouring standard deviation, but it still remains significant!

Steenbakkers et al 2006. Int J Rad Oncol Biol Phys 64: 435

Automatic segmentation needed



But still large uncertainties

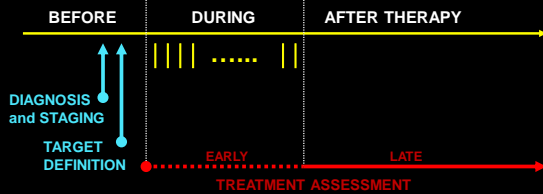


Standardization is essential



- **AAPM TG211** - Classification, Advantages and Limitations of the Auto-Segmentation Approaches for PET
 - **Manual segmentation** is NOT the way to go, but the final manual review required!
 - **Auto segmentation**
 - Threshold-based (Erdi 1997, Paulino 2004)
 - Gradient-based (Geets 2007)
 - Region-growing (Drever 2006)
 - Statistical-based (Yu 2009)
 - ...
 - **Reference benchmark dataset**

PET/CT for treatment assessment



PET-based response assessment



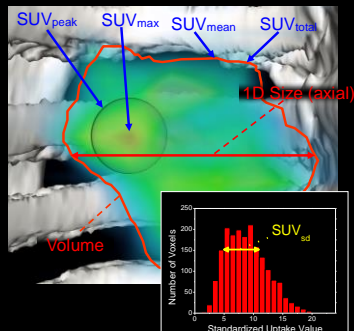
- **EORTC, NCI Recommendations** (1999, 2005) ^{1,2}
 - SUV-based approach
 - SUV_{mean} and SUV_{max}
 - Response categories with thresholds (CR, PR, SD, PD)
 - Problems
 - SUV_{mean} – collapses information, sensitivity issues
 - SUV_{max} – noise contamination
 - fails to use all available functional data
 - distribution
 - heterogeneity
 - no response threshold validation
 - few sensitivity studies
 - alternative measures
- **PET Response Criteria in Solid Tumors (PERCIST)** (2009) ³
 - SUV_{peak}

¹Young et al 1999, ²Shankar et al 2006, ³Wahl et al 2009

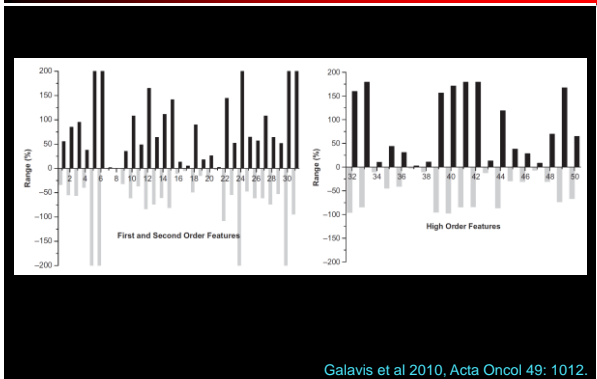
Multiple measures (radiomics)



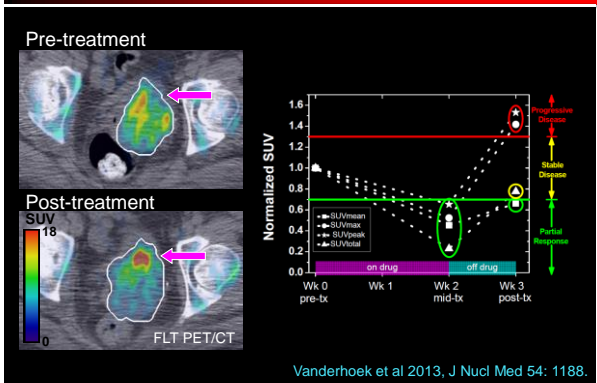
- Size measures
 - Volume
 - 1D size (axial)
- Standardized Uptake Value (SUV) measures:
 - SUV_{mean}
 - SUV_{total}
 - SUV_{max}
 - SUV_{peak}
- Uptake Non-uniformity measure:
 - SUV_{sd}
- ...



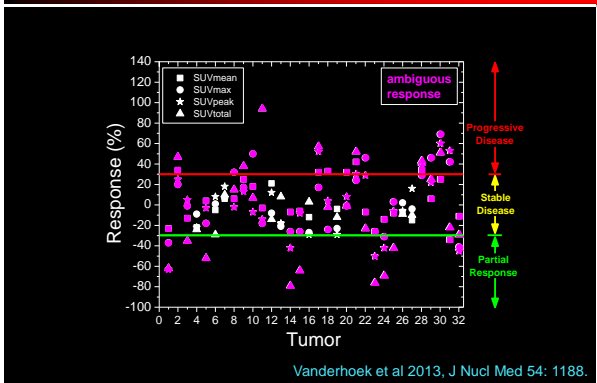
Uncertainty of the imaging features



Ambiguity of response evaluation



Ambiguity of response evaluation





WHAT CAN WE DO TO MAKE PET/CT MORE QUANTITATIVE?

Harmonization of PET/CT imaging

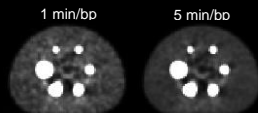


- **Harmonization of acquisition**
 - Minimize limitations due to different scanner hardware and software
- **Harmonization of scanning protocols**
 - Creating harmonized imaging protocols, which need to be tuned to specific scanners
- **Harmonization of image analysis**
 - Unifying image analysis protocols, which often means *centralized analysis*
- **Harmonization of reporting**
 - Standardized reporting, otherwise not comparable data

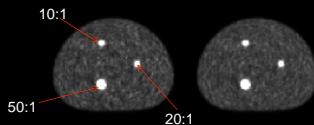
Harmonization of acquisition



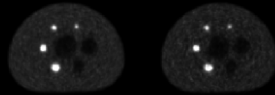
NOISE

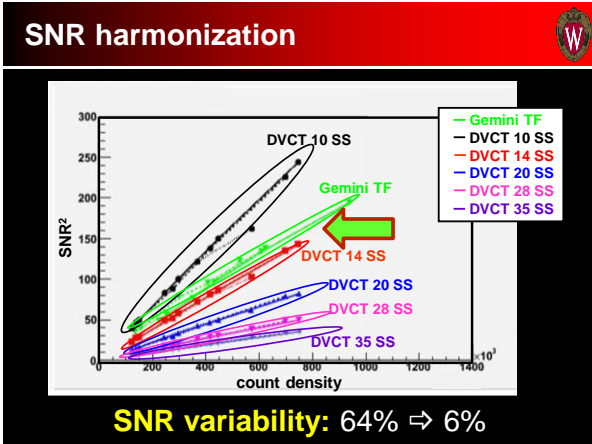


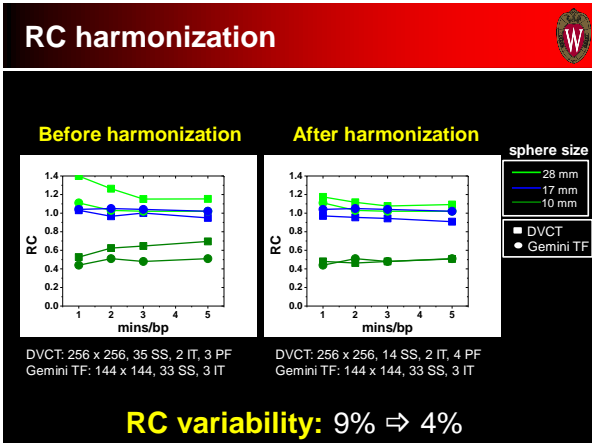
CONTRAST

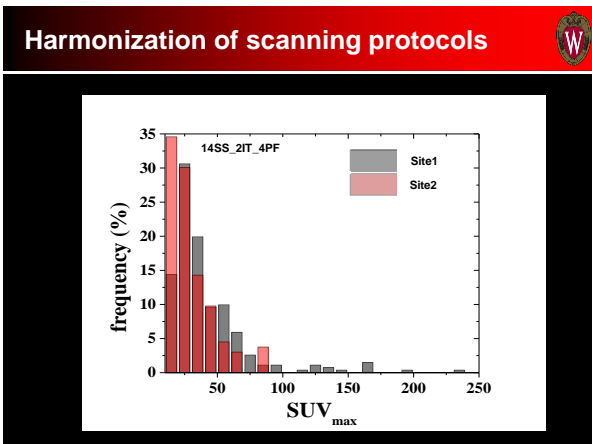


RESOLUTION

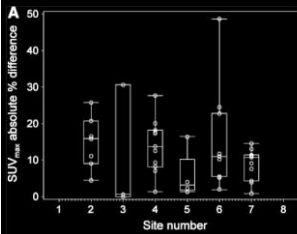








Harmonization of image analysis



- Repeatability results of double baseline ^{18}F -FDG PET scans were similar for all SUV parameters assessed

Centralized QA and centralized image analysis improved intra-subject CV from 15.9% to 10.7% for averaged SUV_{max}

Velasquez *et al.* 2009, J Nucl Med 50: 1646

Test/retest reproducibility



		SUV_{max}	SUV_{mean}	$\text{SUV}_{\text{total}}$
Site1	Mean diff	0.02	0.00	-0.01
	ICC	0.99	0.99	0.998
	CPD	9.1	5.1	20.8

$$\text{ICC} = \frac{\tau^2}{(\tau^2 + \sigma^2)} \times 100$$

τ ... inter-patient variation
 σ ... intra-patient variation

$$\text{CPD} = [\exp(Z_{0.975} \times \sqrt{2} \times \sigma) - 1] \times 100$$

$Z_{0.975}$... the 97.5th percentile of standard normal distribution
 σ ... standard deviation for variation due the repeated scans

Test/retest reproducibility



		SUV_{max}	SUV_{mean}	$\text{SUV}_{\text{total}}$
Site1	Mean diff	0.02	0.00	-0.01
	ICC	0.99	0.99	0.998
	CPD	9.1	5.1	20.8
Site2	Mean diff	0.01	0.01	0.08
	ICC	0.91	0.87	0.92
	CPD	19.5	5.8	70.1
Site3	Mean diff	0.03	0.01	0.12
	ICC	0.97	0.92	0.99
	CPD	2.9	2.1	18.0
Kurdziel 2012	Mean diff	0.09	0.06	0.20
	ICC	0.93	0.91	0.95
	CPD	52.7	33.2	135.3

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Test/retest reproducibility				
Patient reproducibility				
		SUV _{max}	SUV _{mean}	SUV _{total}
Site1	Mean diff	0.02	0.00	-0.01
	ICC	0.99	0.99	0.998
	CPD	9.1	5.1	20.8
Individual lesion reproducibility				
		SUV _{max}	SUV _{mean}	SUV _{total}
		min, max	min, max	min, max
Site1	Mean diff	-0.06, 0.06	-0.03, 0.01	-0.21, 0.17
	ICC	0.86, 0.99	0.84, 0.99	0.94, 0.99
	CPD	7.8, 23.8	2.9, 8.0	12.5, 151.0

Conclusions



- **Qualitative PET/CT** sufficient for *diagnosis* and *staging*
- **Quantitative PET/CT** essential for *target definition* and *treatment response assessment*
- **Harmonization of PET/CT** imaging necessary to increase quantitative accuracy:
 - Harmonization of acquisition
 - Harmonization of imaging protocols
 - Harmonization of image analysis
 - Harmonization of reporting
- **Test/retest reproducibility** essential to establish confidence intervals
