Quantitative Imaging Metrology: What Should be Assessed and How?

- Introduction: Why is Metrology Important in QI?
  - Maryellen Giger
- Methods for Technical Performance Assessment
  - Nicholas Petrick, FDA
- Methods for Algorithm Comparison Assessment
  - Nancy Obuchowski, Case Western
- Toward a Common Goal: Publication and Meta-Analysis
  - Paul Kinahan, U of Washington - Seattle

Quantitative Imaging Metrology:
What Should be Assessed and How?

Introduction: Why is Metrology Important in QI?

Maryellen Giger, Ph.D.

Chair, AAPM Technology Assessment Committee
Member, QIBA Steering Committee

Mission of QIBA

To improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, patients and time, i.e., build “measuring devices” rather than “imaging devices”.

As “measuring devices” is it important to incorporate into our studies, **metrology**, which is the **science of measurement**, embracing both experimental and theoretical determinations at any level of uncertainty in any field of science and technology.

Need to identify sources of bias and variance in these quantitative outputs.

What is a Biomarker?

A biomarker is defined generally as an objectively measured indicator of a biological/ pathobiological process or pharmacologic response to treatment.

What is a Biomarker?

- We focus on quantitative imaging biomarkers, defined as imaging biomarkers that consist
  - only of a **measurand** (variable of interest), or a measurand and other factors that may be held constant
  - AND
    - if the **difference** between two values of the measurand is meaningful.
    - OR
    - there is a clear definition of zero such that the **ratio** of two values of the measurand is meaningful.

What is a Biomarker?

- **Difference** between two values of the measurand is meaningful.
  - Temperature
  - Lung density
- **Ratio** of the two values of the measurand is meaningful and there is a clear definition of zero.
  - Tumor volume
  - PET SUV

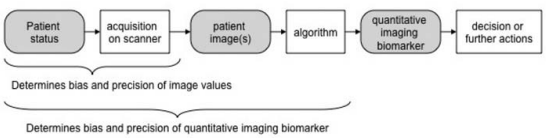
Example of a Biomarker - Lung nodule on CT being followed over time (ratio)

- (CT volumetry): A measured volume change of more than 30% for a tumor provides at least a 95% probability that there is a true volume change.
- P(true volume change > 0% | measured volume change >30%) > 95%

Example of a Biomarker – Tumor on DCE MRI

- Quantitative microvascular properties, specifically transfer constant (Ktrans) and blood-normalized initial-area-under-the-gadolinium-concentration curve (IAUGCBN), can be measured from DCE-MRI data obtained at 1.5T using low-molecular-weight extracellular gadolinium-based contrast agents with a 20% within-subject coefficient of variation for solid tumors at least 2 cm in diameter

Quantitative Imaging Biomarker

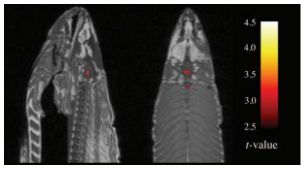


Obuchowski et al., Statistical Methods in Medical Research, 2014

Why is Metrology Important in QI?

Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction

C Bennett, A Baird, M Miller, G Wolford, University of California Santa Barbara, Santa Barbara, CA; Vassar College, Poughkeepsie, NY; Dartmouth College, Hanover, NH

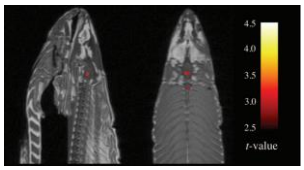


Investigators looked for significant signal change during the photo condition compared to rest.

The task administered to the salmon involved completing an open-ended mentalizing task. The dead salmon was shown a series of photographs depicting human individuals in social situations with a specified emotional valence. The salmon was asked to determine what emotion the individual in the photo must have been experiencing.

Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction

C Bennett, A Baird, M Miller, G Wolford, University of California Santa Barbara, Santa Barbara, CA; Vassar College, Poughkeepsie, NY; Dartmouth College, Hanover, NH



Found a change!

- Across the 130,000 voxels in a typical fMRI volume the probability of a false positive is almost certain.
- Correction for multiple comparisons should be completed with these datasets, but is often ignored by investigators.

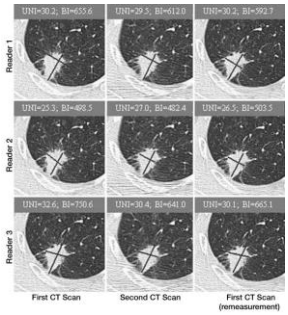
Why is Metrology Important in QI?

- In research – biomarker serves as a surrogate endpoint
  - e.g., May be used to indicate success or failure in a clinical trial of some pharmaceutical drug in curing cancer.
- In clinical care – biomarker contributes to the human decision making on patient management
  - e.g., May be used to continue or stop some therapy for a specific patient.

Example of a Biomarker - Lung nodule on CT being followed over time

- (CT volumetry): A measured volume change of more than 30% for a tumor provides at least a 95% probability that there is a true volume change.
- P(true volume change > 0% | measured volume change >30%) > 95%

Variability in Tumor Measurements from Same-day Repeat CT Scans of Patients with Non-Small Cell Lung Cancer



- Reproducibility of the radiologists was high.
- Changes in unidimensional lesion size of 8% or greater exceed the measurement variability of a computer **and might be significant when estimating the outcome of therapy.**

Zhao B et al. Radiology, 252:263-272

SUV Varies with Time After Injection in ^{18}F-FDG PET of Breast Cancer

Beaulieu et al. J Nucl Med 44:1044-1050, 2003

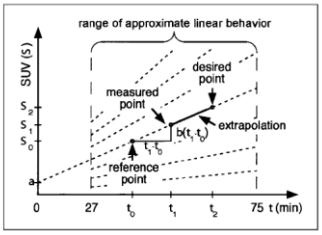


FIGURE 5. Illustration of proposed SUV correction method where SUV increases linearly with time, and rate of change (dS/dt) at any fixed time increases linearly with SUV value (S) at that time (dashed lines). From any measured point, a desired point can be extrapolated by use of a predetermined reference point as given in Equations 3 and 5 and Table 1.

Such variation hinders patient-to-patient comparisons as well as same patient over time comparisons.

Corrections necessary

Potential Problems

- Subjects imaged on different CT scanners
- Subjects imaged on same CT scanner but different protocol
- Subjects imaged at different institutions

Need for Standardization (Harmonization)

Potential Problems

- Investigator A does not correct for background
- Investigator B does not correct for multiple comparisons
- Investigator C compares to a different reference standard (truth)

Aspects of Metrology

- **Linearity -** The strength of the linear relationship of the biomarker to a known or related standard reference
- **Repeatability -** The measure of the biomarker performance to repeat the quantitative measurement on the same experimental unit
- **Reproducibility -** The measure of the biomarker performance to consistently measure image features in predetermined different clinical conditions (i.e., different scanners at different institutions)

Thank you

Quantitative Imaging Metrology: What Should be Assessed and How?

- Introduction: Why is Metrology Important in QI?
  - Maryellen Giger
- Methods for Technical Performance Assessment
  - Nicholas Petrick, FDA
- Methods for Algorithm Comparison Assessment
  - Nancy Obuchowski, Case Western
- Toward a Common Goal: Publication and Meta-Analysis
  - Paul Kinahan, U of Washington - Seattle