Beebe Symposium on AI and ML Applications in Radiation Therapy, Medical Diagnostics, and Radiation Occupational Health and Safety

Requisites and Challenges in Quantitative Imaging

Thursday, March 13

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Duke University School of Medicine

Outline

- Basic concepts:
  - Quantitative Imaging (QI)
  - Standardization
- Clinical implications
  - Quantitative Imaging Biomarkers (QIB)
  - Reproducibility
- Challenges and Impediments
  - QIB Implementation
  - Standardized Image Acquisition

Variability due to radiologists' subjective interpretations is a huge problem.

- Well-documented for decades.
- True for all modalities and all clinical applications
- But, the shift to digital imaging technologies made it possible to extract information from images in a consistent way.
- Reproducibility became possible!

ELSEVIER

CrossMark

The Spine Journal 17 (2017) 554–561

THE SPINE JOURNAL

Clinical Study

Variability in diagnostic error rates of 10 MRI centers performing lumbar spine MRI examinations on the same patient within a 3-week period

"… a patient should expect to receive the same radiological diagnosis regardless of which imaging center he or she visits, or which radiologist reviews the examination."

"Based on their extensive clinical experience, the authors believe that this assumption is not correct and that it can negatively impact patient care, outcomes, and costs."

STUDY DESIGN: This is a prospective observational study comparing the interpretive findings reported for one patient scanned at 10 different MRI centers over a period of 3 weeks to each other and to reference MRI examinations performed immediately preceding and following the 10 MRI examinations.

PATIENT SAMPLE: The sample is a 63-year-old woman with a history of low back pain and right L5 radicular symptoms.

Thought Experiment:

Employ a suite of AI algorithms for spine, providing each radiologist with quantitative results for:

Need VERY LARGE training datasets of standardized, population-relevant , high-quality scans.

- Gray matter cross-sectional areas
- Alignment vectors
- Bone density values
- Facet joint alignment
- Foraminal sizes
- Etc.

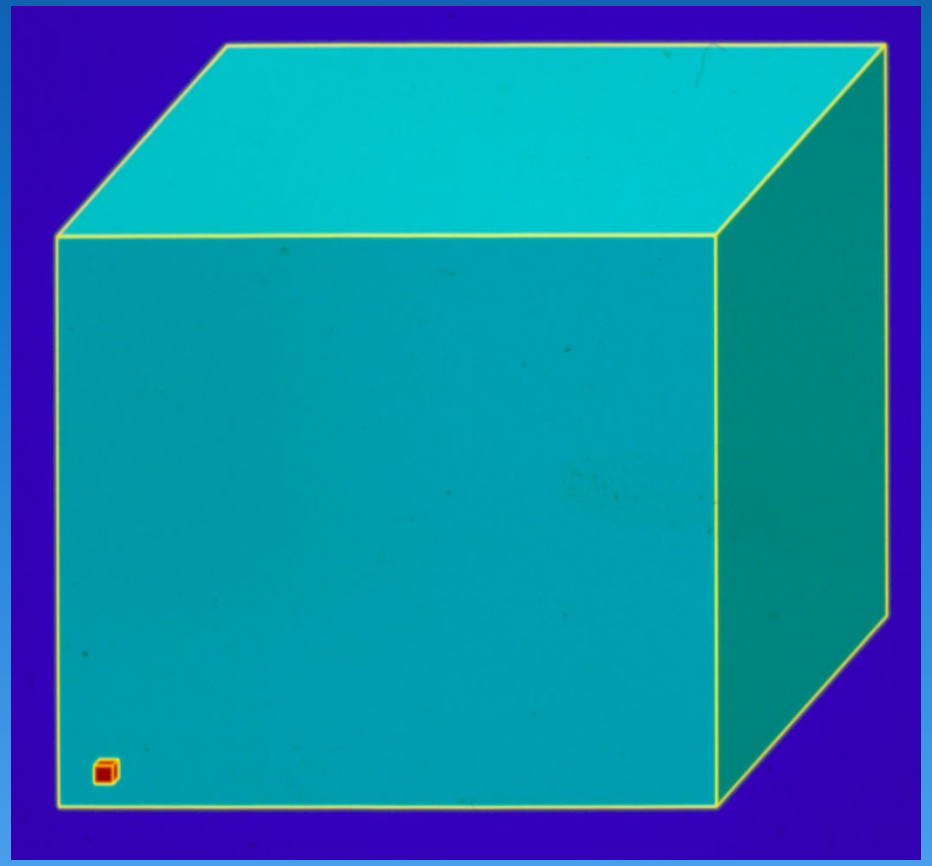
Clinical Imaging …

… provides spatially- and/or temporally-localized information about some property of matter with which the energy has interacted.

What is an Image?

- an *n*-D data set, where n>1;
- each pixel value provides spatially- and/or temporally localized information about some property of matter with which the energy has interacted;
- “interpretation”/quantification requires extracting a sub-set of data (“segmentation”);
- in biology, usually a noisy, blurry dataset.

Cell Size vs. Voxel Size



~ 1 Billion cells
(10^9) per mm^3

-784	-786	-774	-740	-681	-616	-559	-535	-501	-453	-396	-316	-238	-163	-103	-75	-31	8	32	64	111	121	97
-698	-706	-711	-665	-567	-474	-423	-436	-462	-452	-377	-281	-204	-150	-113	-85	-42	0	17	59	112	103	74
-700	-637	-589	-528	-415	-324	-298	-353	-421	-417	-341	-260	-205	-142	-91	-52	-11	23	38	125	157	103	74
-657	-498	-368	-285	-221	-181	-167	-222	-324	-332	-264	-212	-178	-121	-87	-47	-5	0	57	175	173	120	88
-602	-382	-208	-107	-78	-55	-34	-95	-218	-246	-222	-194	-153	-109	-83	-39	10	40	150	199	136	120	107
-512	-289	-127	-46	-21	-5	2	-44	-127	-169	-190	-171	-131	-103	-57	0	44	122	241	231	165	131	115
-454	-236	-89	-2	21	29	19	4	-25	-68	-105	-116	-106	-78	-26	9	80	221	281	218	168	134	130
-527	-298	-104	18	31	33	26	24	5	-34	-63	-79	-84	-37	13	57	198	334	297	196	166	153	151
-629	-450	-249	-100	-56	-23	14	29	4	-21	-45	-59	-53	-9	58	183	325	346	274	200	167	152	139
-663	-554	-357	-176	-90	-64	-40	-20	-36	-58	-83	-82	-40	27	180	348	367	286	243	201	147	127	120
-653	-602	-426	-224	-137	-119	-99	-69	-68	-74	-80	-50	45	189	333	355	273	234	241	209	172	146	127
-647	-624	-476	-277	-176	-161	-155	-146	-131	-107	-82	-11	145	299	334	285	252	236	199	170	150	130	92
-646	-625	-547	-420	-309	-246	-204	-191	-155	-110	-45	101	288	331	286	264	245	217	175	160	152	115	57
-631	-588	-513	-418	-334	-268	-223	-184	-118	-40	131	320	374	330	295	284	255	208	177	168	166	120	67
-625	-582	-498	-391	-321	-258	-197	-144	-67	69	285	391	332	296	275	248	212	166	143	145	111	49	18
-626	-567	-481	-379	-311	-257	-195	-99	63	253	346	333	307	299	274	228	190	179	175	138	84	41	24
-611	-553	-459	-339	-266	-218	-156	-8	209	336	337	308	317	311	283	229	190	186	171	101	59	34	17
-586	-523	-431	-300	-206	-162	-59	126	281	327	314	275	262	264	237	197	174	169	137	66	49	35	37
-538	-480	-357	-245	-167	-47	123	249	301	315	304	278	289	281	235	197	176	146	80	27	34	24	14
-471	-391	-262	-188	-63	137	276	308	307	299	273	281	295	243	189	172	158	124	67	43	37	9	1
-443	-335	-213	-45	149	305	345	318	295	260	246	259	233	192	188	164	110	74	41	35	19	-2	14
-332	-177	-1	203	335	343	315	303	277	242	251	246	200	178	168	128	78	50	40	42	23	-5	10
-174	14	197	312	343	305	279	269	258	259	250	213	185	176	122	74	52	42	36	32	19	2	20

Quantitative Imaging Biomarkers Alliance (QIBA): Background

- Started by RSNA in 2007
- Mission: Improve the value and practicality of quantitative imaging biomarkers by reducing variability across sites, devices, patients, and time.
- "Build measuring devices rather than imaging devices"

Imaging Assays

Assays are characterized by their:

- **Technical Performance**
- **Clinical Performance**
  - **Clinical validation**
  - **Clinical utility**

Metrology Working Group

- **Metrology** is the science of measurement:

- "A measurement result is complete only when it is accompanied by a statement of the associated uncertainty,."

  - NIST Policy Statement

NATIONAL INSTITUTE OF STANDARDS AND TECHNOLOGY
U.S. DEPARTMENT OF COMMERCE

QIB Technical Parameters

- QIBA Metrology Working Group advice –
- the three most important technical parameters to characterize for an imaging biomarker are:
- Bias
- Precision
- Linearity

Precision

- **Repeatability**
  - **precision that occurs with identical or near-identical conditions.**
- **Reproducibility**
  - **precision when location, operator, measuring system, or other factors differ.**

2017 Fleischner Society Guidelines for Management of CT Pulmonary Nodules

A: Solid Nodules*

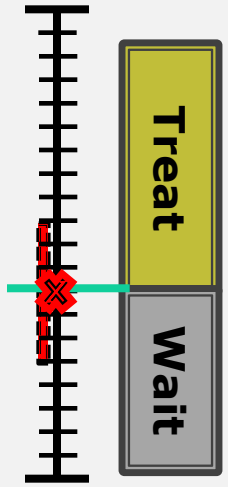
Nodule Type	Size			Comments
	<6 mm (<100 mm³)	6–8 mm (100–250 mm³)	>8 mm (>250 mm³)	
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up, but certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).

Radiology. 2017 Feb 23

Overall Goal of QIBA

Problem

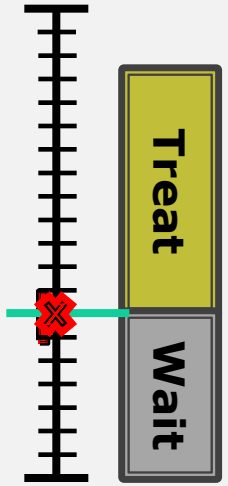
?



Measure = 7 ± 3

Goal

!



Measure = 7 ± 1

Analysis

Sources of Variance

Differences in:

- Patient Handling
- Acq. Protocols
- Reconstruction
- Segmentation

. . .

Solution

Requirements for:
Acquisition Params
Recon Params
Resolution

Processing Params

Patient Prep & Operation

Segmentation

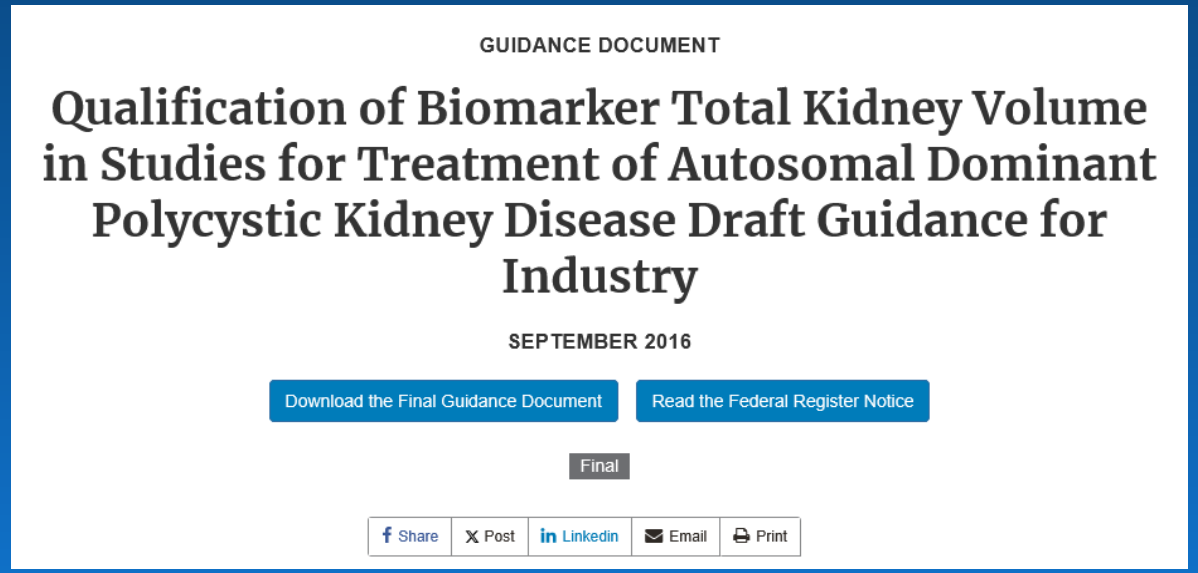
Calibration

When all participating components conform…

Quantitative Imaging Biomarkers Alliance RSNA

Image compliments of Kevin O'Donnell

FDA Biomarker Qualification Program
Sept 2016



GUIDANCE DOCUMENT

Qualification of Biomarker Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease Draft Guidance for Industry

SEPTEMBER 2016

Download the Final Guidance Document | Read the Federal Register Notice

Final

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"TKV [as measured by MRI, CT or ultrasound] as a prognostic biomarker for clinical trial enrichment in patients with ADPKD."

No specifications for precision were required, because the polycystic kidneys are so much larger than normal.

Radiology

Original Research
Genitourinary Imaging

Automated CT Measurement of Total Kidney Volume for Predicting Renal Function Decline after ^{177}Lu Prostate-specific Membrane Antigen–I&T Radioligand Therapy

Lisa Steinhelfer*, Friederike Jungmann*, Manuel Nickel, Georgios Kaissis, Marie-Luise Hofer, Robert Tauber, Christoph Schmaderer, Isabel Rauscher, Bernhard Haller, Marcus R. Makowski, Matthias Eiber**, Rickmer F. Braren**

TKV QIB (Steinhelfer)

- "A 10% or greater decline in TKV at 6 months … is an easily accessible imaging-derived marker for predicting a 30% or greater decline in eGFR at 12 months."
- "This imaging marker could be a …parameter in decision-making to continue or discontinue treatment after 4 cycles of ^{177}Lu-PSMA-I&T radioligand therapy."
- "Furthermore, it presents opportunities for adjusting the treatment cycle interval or intensity, implementing therapy pauses for stable disease, or exploring a de-escalation treatment strategy."

True Biologic Change …

… is approximately twice the variability

(Clinical Significance of that change needs to be determined by clinical studies.)

Radiology: Artificial Intelligence

Original Research

Free Access

TotalSegmentator: Robust Segmentation of 104 Anatomic Structures in CT Images

Jakob Wasserthal, Hanns-Christian Breit, Manfred T. Meyer, Maurice Pradella, Daniel Hinck, Alexander W. Sauter, Tobias Heye, Daniel T. Boll, Joshy Cyriac, Shan Yang, Michael Bach, Martin Segeroth

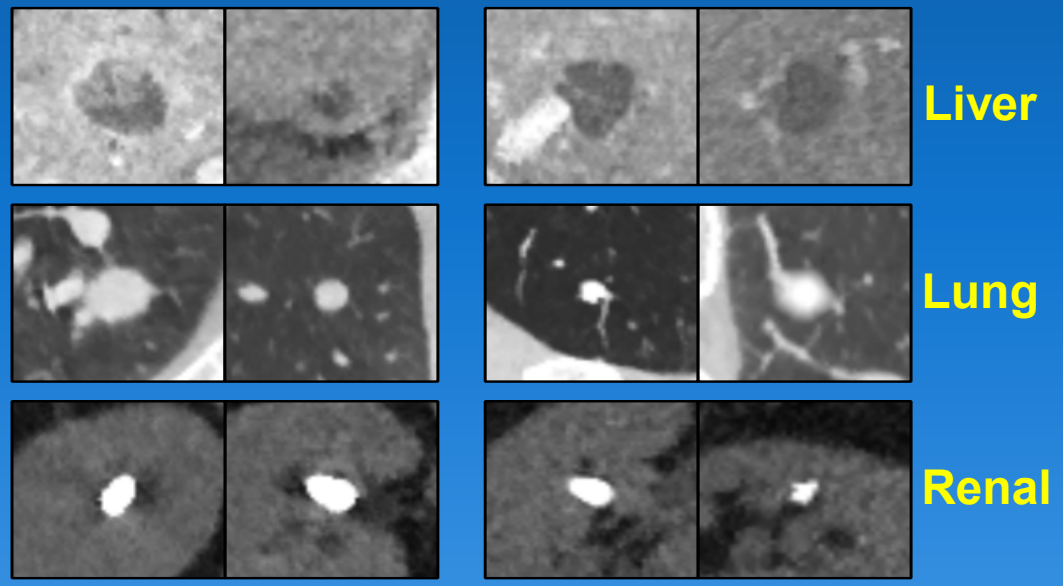
Author Affiliations

Published Online: Jul 5 2023 | https://doi.org/10.1148/ryai.230024

See related article

Synthetic Data

Which lesions are real?



Methodology and Reference Image Set for Volumetric Characterization and Compliance	Ehsan Samei, PhD – Duke

Radiology

ORIGINAL RESEARCH • CARDIAC IMAGING

Association of Epicardial Adipose Tissue Changes on Serial Chest CT Scans with Mortality: Insights from the National Lung Screening Trial

Isabel L. Langenbach, MD • Ibrahim Hadzic, MSc • Roman Zeleznik, PhD • Marcel C. Langenbach, MD • David Maintz, MD • Thomas Mayrhofer, PhD • Michael T. Lu, MD, MPH • Hugo J. W. L. Aerts, PhD • Borek Foldyna, MD, PhD

From the Cardiovascular Imaging Research Center, Massachusetts General Hospital, Harvard Medical School, 165 Cambridge St, Ste 400, Boston, MA 02114 (I.L.L., M.C.L., T.M., M.T.L., B.F.); Institute for Diagnostic and Interventional Radiology, University Hospital Cologne, Cologne, Germany (I.L.L., M.C.L., D.M.); Artificial Intelligence in Medicine Program, Mass General

Clinical data limitations (Langenbach)

- Two-year imaging follow-up was short
- Important covariates (eg, steroid or statin use) not collected in the NLST.
- Medical therapies, lifestyle risk factors, not collected.
- Body mass index and BSA available at baseline only.
- Need comprehensive longitudinal data collection to understand the dynamic changes in body composition.

RSNA®
Radiological Society of North America

Quantitative Imaging Committee (QUIC)

…And QIN, EIBALL, J-QIBA, EANM, AIUM, ALA, SNMMI, ISMRM, and others.

What is the Impediment to Implementation of QIB's?

- Few clinical treatment decisions are driven by a quantitative imaging result.
- Other contributing factors:
  - Inertia
  - Insufficient resources to collect clinical data
  - Perverse financial incentives in U.S. healthcare
  - Conservative (cautious) mindset

Challenges to adoption of standardization

- Inertia
  - Inherent; passive; subconscious
- Resistance to mandates or authority
  - Active; individuality; independence
- Skepticism about need or value
  - Will outcomes improve?
- Professional organization “turf” (territoriality)
  - Boundaries; ownership; credit
- Education; publicity; awareness
- Regulatory agency differences
  - Geographic; political
  - Absence of any national QA/QC program for QI.

Lessons learned in the Quantitative Imaging Biomarkers Alliance (QIBA)

Standards documents must:

1. Have a clear rationale,
2. Be based on published data as much as possible or expert consensus opinion when data are absent,
3. Reflect broad stakeholder input,
4. Reflect an open, consensus process, and
5. Evolve or be revised periodically.

Take-home Message?

Prioritize and Incentivize Reproducibility

!

Thank you.