Clinical Utility of Quantitative Imaging

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Quantitative imaging (QI) is increasingly applied in modern radiology practice, assisting in the clinical assessment of many patients and providing a source of biomarkers for a spectrum of diseases. QI is commonly used to inform patient diagnosis or prognosis, determine the choice of therapy, or monitor therapy response. Because most radiologists will likely implement some QI tools to meet the patient care needs of their referring clinicians, it is important for all radiologists to become familiar with the strengths and limitations of QI. The Association of University Radiologists Radiology Research Alliance Quantitative Imaging Task Force has explored the clinical application of QI and summarizes its work in this review. We provide an overview of the clinical use of QI by discussing QI tools that are currently used in clinical practice, clinical applications of these tools, approaches to reporting of QI, and challenges to implementing QI. It is hoped that these insights will help radiologists recognize the tangible benefits of QI to their patients, their referring clinicians, and their own radiology practice.

Key Words: Radiology; radiologist; quantitative imaging; biomarker.

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Quantitative imaging (QI) is becoming an increasingly common tool in modern radiology practice, advancing from research trials to clinical reading rooms. Today, methods that quantify imaging features assist in the clinical assessment of many patients, serving as biomarkers for disease states as diverse as brain ischemia, interstitial lung disease, and colorectal cancer. Because the potential impact of QI on patient care and on clinical outcomes is so great, the Radiological Society of North America has committed considerable resources to standardizing QI, most recently with the Quantitative Imaging Biomarkers Alliance (QIBA). The Association of University Radiologists' leadership, QIBA participants, and many others in the radiology community view QI as important to the future of radiology. Because it is anticipated that most practicing radiologists will eventually implement some QI tools to meet the specific patient care needs of their referring clinicians, it is important for radiologists of all subspecialties and practice types to become familiar with the various strengths and limitations of QI.

What is QI? According to QIBA (1):

> "Quantitative imaging is the extraction of quantifiable features from medical images for the assessment of normal or the severity, degree of change, or status of a disease, injury, or chronic condition relative to normal. Quantitative imaging includes the development, standardization, and optimization of anatomical, functional, and molecular imaging acquisition protocols, data analyses, display methods, and reporting structures. These features permit the validation of accurately and precisely obtained image-derived metrics with anatomically and physiologically relevant parameters, including treatment response and outcome, and the use of such metrics in research and patient care."

Although this definition is comprehensive, several practical aspects of QI must be highlighted: accuracy, precision, and clinical validity. When performing measurements, we must be certain that what we are measuring has a clinical correlate, a reference standard against which our measurement has been derived. In this regard, the accuracy of a measurement describes how close the measurement is to a correct answer and thus indicates whether our QI measurement fundamentally "works." Precision is also important, particularly given the role of QI in performing serial evaluation over time. A useful QI metric should provide the same value when

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measured in the same way multiple times. Precision (repeatability and reproducibility) allows us to discriminate measurement error from biologic change. Finally, QI tools that demonstrate good accuracy and reliability must ultimately have clinical validity; the results must be relevant to our practice, impacting patient care and improving outcomes.

QI has the greatest impact on patient care when the results help to: 1) inform the diagnosis or prognosis of a particular disease; 2) determine the choice of a particular therapy; or 3) monitor the course of therapy. To make a diagnosis using QI, a general consensus of normal versus abnormal QI values must be established. Similarly, monitoring the response to therapy with QI requires consensus on the amount of change that is considered both statistically and clinically significant. This article will present an overview of the clinical use of QI by presenting QI tools that are currently used in clinical practice, clinical applications of these tools, approaches to reporting that add value to clinical care, and challenges to implementing QI in a clinical radiology practice.

TOOLS FOR PERFORMING QI

Image Acquisition

QI currently has important clinical applications in ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and nuclear medicine, including positron emission tomography (PET), although theoretically QI can be applied to any digital imaging modality. QI is enhanced by volumetric data sets, which facilitate assessments of morphological, parametric, functional, and other quantitative features.

Ultrasound. Gray-scale ultrasound images are commonly used to obtain size and distance measures, providing the basis for diagnosis in much of obstetric and cardiac imaging. Doppler ultrasound, in which altered frequency of the reflected sound waves provides measurements of flow velocity, has been used for quantitative characterization of vascular disease for decades (2). Flow velocities are routinely used in the diagnosis of vascular stenoses of the carotid and renal arteries, transplant vasculature, and vascular shunts (2,3) (Fig 1). More sophisticated Doppler measures such as the intrarenal acceleration time and resistive index are used in diagnosing renal artery stenosis (4). Technical optimization of Doppler, including angle correction, gain, and gate position, is essential to avoid measurement errors (5).

CT. The standardization of CT pixel values with the Hounsfield unit (HU) scale allows for characterization of tissue density, a common QI application (6). HU measures allow lesion characterization using a region of interest (ROI)-based measurement of average density or voxel-counting based on a threshold value (7). For instance, improved characterization of renal lesions is achieved using ROI measurements rather than subjective visual assessment (8).

Recently, the advent of dual-energy CT scanners has bolstered the clinical role of QI. In particular, the differential absorption of x-rays by tissues of differing chemical composition at different energies allows for improved characterization of tissues (9) (Fig 2). For instance, dual-energy CT has greater accuracy than standard single-energy CT in determining the composition of renal calculi (10). This distinction helps determine whether a patient is treated medically or with an invasive procedure such as extracorporeal shockwave lithotripsy.

MRI. Given its ability to interrogate various properties of tissues using specific pulse sequences and various vascular and tissue-specific contrast agents, MRI is ideally suited for QI (6). MR signal intensity units lack inherent meaning, being influenced by sequence parameters as well as hardware and software selection. However, some advanced MRI sequences and postprocessing techniques allow for the computation of parametric maps in which the pixel values are used for diagnosis. For example, imaging the liver using varying echo times allows for computation of the tissue T2* relaxation time, used as a marker of the presence and severity of hepatic iron deposition (11) (Fig 3). Diffusion-weighted (DW) MRI using a rapid echo-planar sequence with motion-probing gradients of varying strength, as reflected by the b-value, allows for computation of the apparent diffusion coefficient (ADC) of tissue (12). Lower ADC values occur in more cellular tissues and serve as markers for the presence and aggressiveness of tumors, such as prostate cancer (12,13). Diffusion-tensor imaging is an extension of DW imaging that provides quantification of white matter tracts to guide surgery for brain tumors, allowing for better definition of surrounding neural pathways and improving functional outcomes (14). MRI spectroscopy provides information regarding the presence and concentration of chemicals in an ROI, such as brain metabolites that show characteristic alterations in conditions, including Alzheimer disease, infection, tumor, and radiation therapy (15). In addition, rapid MRI techniques, including real-time "segmented" sequences and velocity-encoded phase-contrast imaging, are used in cardiac imaging to calculate stroke volume and cardiac output (16).

Dynamic Contrast-Enhanced Imaging. Dynamic contrast-enhanced CT or MRI is often used to improve tissue characterization. Rapid contrast administration and imaging the same region at multiple time points allows a comparison of pixel values between pre- and postcontrast images and assessment of the rate and pattern of enhancement or washout over time. For example, after contrast administration, an increase in pixel values for a renal lesion of at least 20 HU on CT or of at least 15% on MRI indicates a solid lesion (17,18). Obtaining a larger number of postcontrast time points provides a more precise assessment of the temporal kinetics of contrast passage through a tissue. Although a lack of ionizing radiation with MRI generally allows acquisition of more time points than with CT, the nonlinear relationship between tissue gadolinium concentration and MRI signal intensity complicates the computation of kinetic parameters (19). Various approaches to postprocessing and quantification of multiphase postcontrast imaging are used. For example,

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