The impact of quantitative imaging in medicine and surgery: charting our course for the future

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Visual inspection and interpretation by radiologists or other physicians with adequate trainings are the currently acceptable clinical practices of exploring and utilizing the information generated by various medical imaging technologies. This approach is considered adequate for disease detection, diagnosis, and even for disease staging. Modern imaging techniques, however, can be employed to collect both quantitative anatomic information and in vivo metabolic or functional information. With the advancement of technologies, medical imaging's inherent quantitative characteristics are increasingly being recognized as providing an objective, more accurate, and less observer-dependent measure for prognosis and monitoring response as compared to visual inspection alone. Quantitative imaging methods that have been proven to correlate with clinical outcomes can play an important role in clinical decisions (1-3).

According to the Radiological Society of North America (RSNA), 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." In principle, the quantitative and

objectively assessed characteristics derived from imaging dataset should be superior to the traditional subjective (i.e., observer-based) assessments that often have high inter- and intra-observer variability. A classical application of quantitative imaging in clinical medicine is monitoring the therapy response of malignant tumors. Conventional criteria for monitoring the cytotoxic therapy of malignant tumors are defined by tumor shrinkage, generally measured by radiologic techniques. According to the criteria defined by the World Health Organization (WHO), the size of the tumor should be measured in 2 perpendicular diameters. Recently, DCE (dynamic contrast enhanced) MRI and SUV (Standard Uptake Index) FDG PET are used for early readout of therapy response of tumor. Visual interpretation of PET scans is frequently sufficient for assessment of tumor response after completion of therapy. However, quantification of Gadolinium-agents and FDG uptake potentially allows an early, accurate assessment of responses to stratify responding and non-responding patients (4-7). Moreover, quantitative FDG PET for early response assessment has created a paradigm shift in anticancer drug development.

Although quantification has been proven to be beneficial for patient care, several factors make routine quantitative imaging a challenge. Human visual perception is designed for pattern recognition, but rather limited at making complex quantitative assessments. Busy radiologists face "image overload" on a daily basis. A single cross-sectional imaging study may contain hundreds of images, thus imposing an extensive burden on reviewing physicians. A full understanding of the response characterized by the

potential surrogate imaging biomarkers (e.g., those used to monitor angiogenesis, hypoxia, and necrosis) may often require the use of physiological modeling and/or multi-parametric analysis of the image data to examine any quantitative correlation with clinical metadata and clinical outcomes (8,9). As a result of image measurement being time-consuming, useful quantitative information contained in these images is not routinely included in the radiological reports, negatively impacting clinical care and clinical research. The problem is further compounded by a need to develop consensus approaches for the standardization and the harmonization of quantitative and statistical methods. For studies involved with multi-centers and multi-vendors, it is even more critical to standardize patient preparation, image acquisition, post-processing, interpretation, and reporting (5,10-13). In order to advance quantification in routine clinical use, a range of image-processing software tools are being developed to extract spatial features from images and to use modeling methods that include both spatial and temporal characteristics. These image-derived quantitative measurements serve as useful aides to radiologists for image interpretation, potentially improving the sensitivity and specificity for both lesion detection and disease characterization.

With the boom of molecular imaging techniques for pre-clinical and biological research, quantitative imaging readouts are potentially of even greater value by providing a noninvasive means for characterizing disease longitudinally and thus, insight into the natural history of disease (14,15). Another substantial benefit is derived from the use of validated methods to study the efficacy of novel therapeutic agents. Investigations involved animal models that can correlate the results obtained by performing invasive tests with those obtained from using noninvasive bioimaging methods will enable translational research with human studies that require imaging findings to augment the clinical observations.

Presently, a gap still exists between the physics-based development of new techniques and the applications used in the study of disease. There is a need for targeted investigations that might establish the usefulness of more quantitative imaging measures for the assessment of disease state (16,17). In order to further advance and promote quantitative imaging and imaging biomarkers to be included in future radiologic practices, there is also a critical need to develop and validate algorithms that can process imaging data to provide clinical information for decision-making, and ideally automatically. At present, some initiatives,

such as the Quantitative Imaging Biomarkers Alliance (QIBA), are being undertaken to address these issues. It has been stated that RSNA is committed to helping transform the discipline of radiology from a qualitative to a more quantitative science, and to help patients benefit from accelerated development and dissemination of new pharmacologic, biologic and interventional diagnosis and treatment approaches.

Quantitative Imaging in Medicine and Surgery (QIMS) will promote research and development of quantitative imaging methods for the measurement of disease progression and prognosis, therapeutic optimization, surgical planning, image-guided intervention, and response to therapies. QIMS will educate practicing radiologists about strategies of augmenting subjective image interpretation with quantitative measures. To achieve these goals, QIMS will strive to engage multidisciplinary teams that involve clinicians, radiologists, as well as imaging scientists who include physicists, engineers, and chemists. QIMS will strive to stay at the forefront of developing and applying robust methods to understand disease and help accelerate the development of better treatments. In light of the advances being made with multimodal imaging, QIMS will focus on publishing research findings from studies using quantitative imaging protocols and methods in various imaging modalities, ranging from anatomical imaging to functional imaging and to molecular imaging.

Acknowledgements

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