



New Dawn Fades: From Imaging to Quantitative Imaging Biomarkers and Beyond

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ABSTRACT

In the modern ages of rapid technological and computational advances, development of numerous novel diagnostic imaging techniques have enabled not only visual detection of disease processes, but also provided the tools to achieve quantified functional, structural, dynamic, metabolic, and molecular information. A pathway toward the quantitative imaging by use of quantitative imaging biomarkers analysis has been widely opened, enabling further development of radiomics, radiogenomics, and radioproteomics analysis in addition, and initiating the dawn of theranostics, eventually bringing the wishful personalised medicine concept closer to reality.

Key words: Radiology, Diagnostic Imaging, Quantitative Imaging, Quantitative Imaging Biomarkers, Radiomics, Personalised Medicine.

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Living in the era of an almost unimaginable technological and computational advances in almost all areas of our lives, we have been witnessing a number of extraordinary newly developed imaging techniques and methods. Since the development of X-rays, ultrasound (US) technique, computerised tomography (CT), and finally magnetic resonance imaging (MRI) emerged, introducing a whole new spectrum of possibilities to produce images and to differentiate between the normal and pathological tissues. However, most of the diagnostic imaging methods and procedures that radiologists are using in a routine practice nowadays were originally developed to detect and diagnose a disease by visualising the signals alterations caused by the underlying disease processes, and hence recognising the pathological pattern, with only a limited attempts to quantify what was seen¹.

Understanding that the role of diagnostic imaging does not comprise the means to depict anatomical and morphologic abnormalities only, a transitional shift from an entirely morphoanatomically oriented imaging methods towards those that incorporate multimodal or multiparametric acquired data, including functional,

structural, dynamic, metabolic, and molecular information² has begun in the last decades and is still and unstopably ongoing, especially intensely in the field of neuroimaging.

Based on the irrefutable statement of Cha in 2006, that to treat patients with brain tumors without the use of neuroimaging is impossible to imagine², we are already aware that current technological capabilities in neuroimaging have evolved to the level that allows us not only to visualise the tumorous processes in the brain, but also to scrutinise cellular and bioarchitectural alterations of tumorous tissue, to characterise and grade brain tumors, as well to observe and follow-up early and late effects of treatment response in the patients^{2,3}.

Recognising and using *ex vivo* biomarkers (eg, genomic, proteomic, etc) in the clinical practice, a necessity to accelerate the information flow in regard to disease prognosis or outcome emerged, resulting in a particular interest to develop reliable *in vivo* biomarkers, in a first place non-invasive imaging biomarkers as rapid as possible³.

Therefore, using both new and emerging techniques, but also some already present in clinical practice, a new concept of quantitative imaging has been introduced, enabling a real metric quantification of pathological processes features. According to Quantitative Imaging Biomarkers Alliance (QIBA) of Radiological Society of North America, quantitative imaging represents 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 develops, standardises and optimises anatomical, functional and molecular imaging acquisition protocols, data analyses, display methods and reporting structures that 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 care⁴.

Quantitative imaging has already become an increasingly used metric tool in current radiology practice, with the application from research trials and investigations to daily use in radiology reading rooms. Imaging methods that quantify imaging features assist in the clinical assessment of many patients, providing a source of reliable biomarkers for a spectrum of diverse diseases, that are used to provide more accurate diagnosis and/or prognosis, to determine the choice of therapy or to monitor therapy response⁵.

Being based whether on hybrid/molecular imaging techniques, such as positron emission tomography (PET), combined with CT or MRI⁶, or in several cases deriving from CT, many of these outstanding techniques, providing the quantitative imaging biomarkers (QIBs), are actually arising from MR imaging, which, even after almost forty years of continuous improvements, does not cease to surprise us with the novel achievements and possibilities. Different MRI derived techniques are actually allowing us both to observe the meticulous morphometric details, and to characterise various tissue structures on different magnetic field strength devices, but also to examine the biochemical tissue composition *in vivo* by use of ¹H MR spectroscopy, to obtain dynamic data on tissue perfusion by use of perfusion MRI with exogenous or endogenous contrast tracer, to obtain functional information

and to map the brain activities by use of functional MRI and to get the insight into the tissue internal bioarchitecture and brain pathways by use of diffusion imaging, including diffusion tensor and/or kurtosis imaging^{5,7}.

In addition, capability to collect important metabolic and molecular information by integration of CT or MRI devices in hybrid systems with positron emission tomography (PET) by use of numerous and different specific radionuclide tracers opened the door to the whole new quantitative imaging biomarker (QIB) molecular data sets assessment^{6,8,9}.

Based on the information provided, QIBs could be generally categorised as morphoanatomical, dynamic, structural/textural, functional, metabolic and/or molecular, whereas each QIB represents the final result of a predefined image acquisition process, resulting in a quantifiable image from the patient under evaluation, reconstructed by the computer processing algorithm by automated or manual identification of the relevant regions of interest (ROI), measured and reported usually by application of another computer algorithm or artificial intelligence¹.

Since a good and qualified biomarker should have three properties, including biological relevance to the disease process under the study, sensitivity to the disease process, and reliability, ie good reproducibility¹⁰, QIBs are strictly assessed to provide full performance under study conditions, in order to enable better *in vivo* features quantitative metric evaluation¹.

Therefore the constant endeavor to develop, validate, and clinically implement both prognostic biologically driven QIBs, that could predict the disease progression probability in the absence of treatment, and predictive QIBs, that may indicate the outcome of the applied therapy is of utmost importance², especially in oncology, and highly valuable in predicting the final disease response, progression-free survival, recurrence and overall survival of the patients^{11,12}.

Permanent and continuous introduction of new, underlying disease processes sensitive and reproducible QIBs, almost certainly continues to fulfil a large number of gaps in our heretofore understanding of physiological and pathological processes in the whole human body, causing in-

evitable shift from quantitative imaging towards radiomics analysis, and finally, personalised medicine^{13,14}.

Understanding that diagnostic images are not only images anymore, but real data bases, containing multi-layered, statistically measurable information, a whole new area of unique radiomics possibilities in radiology has opened¹⁵, firmly directing the future of medicine through the accurate early diagnosis and maximally personalised and individually tailored therapy treatments to the future concept of personalised and precise medicine¹².

In the era of radiomics, but also radiogenomics and radioproteomics data mining out of radiological diagnostic images, relating *in vivo*

quantitative imaging biomarkers to genetic, molecular and biochemical features of the disease or tumour, it is to expect that imaging would become an inevitable and crucial milestone in the patient oriented therapy planning, monitoring and follow-up, by use of non-invasive or minimally invasive treatment options, especially taking into the account the apparent dawn of theranostics^{12,16}.

Moreover, already developed applications and techniques, such as chemical exchange saturation transfer (CEST) imaging¹⁷, or MRI fingerprinting^{18,19} could lead us into the nowadays still hardly imaginable directions in the imminent future, with potentially irreversible impact on radiological profession - toward imaging without images.

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CONFLICT OF INTEREST

None.

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