The Evolution in the MR-Based Biomarker

Neil M. Rofsky, MD, FACR, FISMRM, FSCBTMR
neil.rofsky@utsw.edu

OBJECTIVES:

1) List some examples of potential MR biomarkers
2) To compare and contrast how traditional biomarkers relate to MR biomarkers
3) Understand the challenges in establishing reliable and reproducible MR biomarkers
4) To stimulate activity towards improving the 'manufacturing cycle' of MR biomarkers

DISCUSSION:

Background:

The variety of features that can be extracted from living tissues with the use of magnetic resonance (MR) techniques has provided medicine with valuable diagnostic tools. The early imaging assessments that were formulated from qualitative interpretations of structure and variations in signal intensity on T1- and T2-weighted images are still relevant and powerful diagnostic assets in today's practice of medicine.

Increasingly, there is demand and opportunity to convert strategies with qualitative value to those with more quantitative value. In so doing, the non-invasive nature and robust ability of MR to extract form and function from normal and diseased tissues create opportunities for establishing MR-based biomarkers.

Definition:

The NIH biomarker working group has provided a generic definition of a biomarker as follows: "…a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention."

Some examples of MR determined biomarkers are perfusion - e.g. arterial spin labeling (*tumor, ischemia, dementia*), diffusion - e.g. ADC (*tumor density/activity*, *acute neurodegeneration*), endothelial permeability – e.g. DCE / K^{trans} (*angiogenesis*), tissue composition - e.g. Dixon separation techniques such as fat and iron accumulation (s*teatohepatitis*), biomechanics - e.g. Cine - balanced GRE (*MI*); metabolite assessment - e.g. NAA (*neurodegeneration*), and cartilage properties - e.g. T1-rho and T2 mapping (*osteoarthritis*).

Changing perspectives:

The needs for imaging are expanding towards 1) increased precision in diagnosis, 2) longitudinal assessments of morphology, 3) monitoring response to therapy (immediate and long term) for the purposes of timely therapeutic decision-making, and 4)

enhancing the yield for biopsy and surgical procedures. An accompanying need for predictable quantitation in MR procedures follows.

Imaging can serve as an important surrogate end point to help with implementation of new medical products or strategies by replacing large, long costly studies and clinical outcomes with smaller faster and cheaper studies; when effective, the surrogate end point rather than the clinical outcome is the determinant of success.

Comparative perspective – laboratory medicine:
A plethora of laboratory tests are used daily to determine the status of an organ system a physiologic state or systemic condition and thus to guide management decisions. An extensive history in laboratory medicine precedes the medical imaging efforts towards establishing biomarkers.

The clinical laboratory is a fundamental component of healthcare, driving a majority of health care decisions from the results of laboratory tests. These decisions range from diagnosis through therapy and prognosis. Trust in the fidelity of a given result and knowledge of the range of normal values allows for a reliance on the information to make management decisions.

There are many protections in place to ensure that laboratories produce reliable results. Federal and state government, laboratory professional organizations, as well as individual laboratories themselves have instituted these protections to help maintain standards of quality.

Passed by Congress in 1988, the Clinical Laboratory Improvement Amendments (CLIA) were adopted to ensure the accuracy, reliability, and timeliness of patient test results. CLIA covers testing in all U.S. states, and every clinical laboratory in the country must obtain a certificate that defines the complexity of tests that the particular laboratory can perform. This can be instructive as imaging data evolve.

Challenges for MR evaluations:
Most of the assessments in MR studies are qualitative, subjective and nuanced. While the current state offers meaningful contributions to patient care, better precision, predictability and uniformity in a given result are needed to move forward.

A deeper understanding of the entire acquisition and processing chain of MR information, including protocol design and implementation, pulse sequence standardization and execution, device electronic performance standards, reconstruction algorithms, data transfer mechanisms, post processing strategies, result evaluation strategies and result reporting, is needed to improve the result product. An accompanying commitment towards standardization of the result product across instruments will be needed, challenging the culture and technical prowess of our field.

In obtaining superior detail, reliability and relevance from our results, a path is paved towards the 'MR –based biomarker' evolving into a robust portfolio of strategies that are able to drive an increasing number of healthcare decisions.

CONCLUSION:

Greater impact in healthcare is achievable with a more concentrated effort to develop and standardize MR-based biomarkers.

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