Measuring Response to Novel Therapies: Thinking Differently

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With the advent of newer localized treatments and molecularly targeted systemic therapies in oncology, the imaging manifestations of cancer treatment response have become more varied and subtle. Previously, when cytotoxic chemotherapy agents were the mainstay of systemic cancer therapy, tumor shrinkage had been the imaging hallmark of successful treatment. However, new anti-cancer regimens have arisen that make use of local tumor targeting or cytostatic molecularly targeted agents, alone or in combination with traditional cytotoxic chemotherapies. As such, the appearance of, and in some cases the very definition of, successful anti-tumor therapy has changed. In this new molecular era, the radiologist must be aware of the pitfalls and the opportunities of enhanced imaging techniques in the assessment of the cancer patient undergoing traditional and novel therapies.

Initially, nuclear medicine techniques—in particular FGD-PET—dominated the non-morphologic imaging landscape in the assessment of tumor response to therapy in humans. While FDG (and other PET and SPECT agents) continue to play an important and increasing role in evaluating tumor response to therapy, other imaging techniques have evolved into functional, rather than simply morphologic assays of tumor status in humans. Ultrasound, computed tomography, and optical imaging have all been utilized to assay physiologic aspects of tumors before and after therapy. However, magnetic resonance imaging has perhaps the greatest range of imaging features which may be harnessed to provide both morphologic and functional characterization of tumor status in the oncologic patient.

For the radiologist, understanding the potential of functional imaging assessment of tumor response to therapy begins with an understanding of the current types of molecularly targeted therapy in oncology practice today. In 2013, there are upwards of 40 FDA approved targeted therapies directed against nearly as many cancer types. These agents act by disrupting key signaling pathways halt or reverse cancer growth. Commonly targeted pathways include those involved in angiogenesis, cell proliferation, DNA stabilization, and cellular apoptosis.

MRI offers a range of imaging techniques that may capture the molecular and physiologic effects of these agents on cancer physiology. MRI possesses excellent morphologic detail and contrast, which enables the radiologist to detect, characterize, and stage cancers throughout the body. In addition, the large dynamic range of T1- and T2-weighted imaging allows the radiologist to identify subtle physical changes in cancer tissue content. Most importantly, techniques such as diffusion weighted imaging, perfusional imaging (dynamic contrast-enhanced imaging and arterial spin labeling), and spectroscopic imaging are evolving in body MRI. These newer methods, which can be readily combined with standard imaging techniques in a single patient visit, enable the radiologist to interrogate the physiologic status of tumors in ways not previously achieved. Finally, novel imaging methods such as hyper-polarized MRI are being introduced into early phase human studies, raising the potential for MRI to become a true multi-potent imaging method for cancer evaluation.

The ability of these novel MRI methods to document early treatment responses has been demonstrated in numerous studies of cancer therapeutic monitoring. However, the best method(s) for detecting effective anti-tumor targeting early in therapy may vary based on tumor and treatment type. Novel imaging assessments often require quantitative analytics to determine the degree of tumor response. Standardized qualitative or quantitative thresholds which allow

the radiologist to declare confidently the presence (or absence) of effective anti-tumor targeting are lacking in most instances. Equally important, the prognostic relationship between early physiologic tumor change by functional MR imaging and long-term patient outcomes remains elusive in most clinical scenarios.

Enabling the MRI radiologist to recognize the patterns of effective anti-tumor targeting on standard and novel MR imaging is a critical first step toward helping the radiologic and oncologic community achieve the goal of maximizing the potential of MRI for monitoring the oncologic patient.