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Letter to Cancer Center Directors: Progress in Quantitative Imaging As a Means to Predict and/or Measure Tumor Response in Cancer Therapy Trials

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To the Editor

The purpose of this correspondence is to alert cancer center directors and their associated biomedical imaging programs about recent progress in quantitative imaging as a means to predict and/or measure tumor response to drug or radiation therapy, a development that is critical to (for example) implementing adaptive therapy trial designs. There have been a number of initiatives in this area by the National Cancer Institute (NCI) and the Radiological Society of North America (eg, the Quantitative Imaging Biomarkers Alliance¹) to advance quantitative imaging methods that can be readily adopted by the NCI-funded cancer centers. These efforts can potentially position the NCI-funded cancer centers to collectively share resources to implement quantitative imaging methods into clinical trials. One substantive step cancer centers could take is to implement a formalized and systematic process to collaborate with radiology departments and imaging research centers to integrate advanced imaging into the clinical trial development process. As a result, oncology trial designs would be more likely to include appropriate imaging measures to provide accurate staging, intratherapy assessment, and follow-up evaluations.

By way of background, there is a growing need in both clinical practice and clinical trials for quantitative methods that can sensitively and accurately detect—and even predict—the response of tumors to therapy. Newly developed imaging techniques are showing promise by offering quantitative decision support results with only minimally invasive and user-independent methods. This capability necessarily involves advanced imaging methods that go beyond traditional radiography (eg, computed tomography or anatomic magnetic resonance imaging). Indeed, advanced imaging may provide more clinically relevant information—particularly in the context of targeted molecular therapeutics, the initial activities of which may be cytostatic, rather than cytotoxic. In addition, inflammatory responses to radiation and vascular disruptive agents have also challenged response assessment, with determination of progression versus pseudoprogression being particularly problematic.

The NCI has long recognized the potential of advanced quantitative imaging to provide minimally invasive biomarkers related to the underlying pathophysiological status of cancer, and to monitor the effects of targeted cancer therapies.² Because advanced imaging methods are likely to provide an early indication of therapeutic efficacy, and can be repeated

throughout a course of therapy to provide frequent monitoring of response, they are likely to play a fundamental role in guiding patient management in the future.³ As directors of NCI-designated cancer centers, you are uniquely positioned to initiate the important step of incorporating advanced imaging to improve the quality of clinical trials and, ultimately, patient care.

To expedite the development of advanced imaging biomarkers, the NCI established the Quantitative Imaging Network (QIN) in 2008 with its mission to “improve the role of quantitative imaging for clinical decision making in oncology by the development and validation of data acquisition, analysis methods, and tools to tailor treatment to individual patients and to predict or monitor the response to drug or radiation therapy.”⁴ QIN goals are to provide technical resources to support the incorporation of advanced imaging into clinical trials. For example, technical and methodologic developments in quantitative dynamic positron emission tomography and comprehensive multiparameter magnetic resonance imaging within the QIN have led to the maturation of a number of advanced imaging techniques to the point that they can be readily deployed in clinical trials. Specific examples include data collection methods for positron emission tomography/computed tomography that are minimally dependent on the different commercial imaging platforms, and methods of analysis that minimize operator dependence. In addition, NCI and QIN members are supporting public resources to permit data and tool sharing across the NCI-funded cancer centers to help develop a pipeline for greater adoption of more standardized clinical protocols.

In light of these developments, the Executive Committee of the QIN (Appendix Fig A1, online only) recommends that reinvigorated steps be taken to incorporate quantitative imaging methods into clinical trials whenever appropriate. Within an individual cancer center, we stress the importance of establishing an image analysis and data management laboratory that provides advanced imaging support from trial design to data analysis. Building this infrastructure requires establishing a strong collaboration among the cancer center leadership, the clinical trials office, the department of radiology and biomedical imaging research institute, and oncologists (radiation, medical, and surgical). This often includes expertise in bioinformatics, computer engineering, medical physics, and statistics that are naturally coordinated through the cancer centers. A mature knowledge base now exists (eg, the members of the QIN) to guide those who are interested in establishing such a program, and we encourage you to consider taking the first steps toward establishing a quantitative imaging program for cancer clinical trials at your institution.

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Appendix

Fig A1. Geographic locations of the 19 network centers of the participating institutions in the Quantitative Imaging Network (QIN). The Executive Committee of the QIN primarily consists of principal investigators from the National Cancer Institute (NCI) –funded U01 programs at each of the centers. The QIN grew from the NCI program announcement “Quantitative Imaging for Evaluation of Responses to Cancer Therapies.”⁴ The network is designed to promote research and development of quantitative imaging methods for the measurement of tumor response to therapies in clinical trial settings, with the overall goal of facilitating clinical decision making. Projects include the appropriate development and adaptation/implementation of quantitative imaging methods, imaging protocols, and software solutions/tools (using existing commercial imaging platforms and instrumentation) and application of these methods in current and planned clinical therapy trials. UCLA, University of California, Los Angeles; UCSF, University of California, San Francisco.