IV.   The Quantitative Imaging Network
Robert Nordstrom, PhD

Quantitative imaging is the extraction of quantifiable data from medical images to assess disease status or changes. The goal of the Quantitative Imaging Network (QIN) is to translate quantitative imaging methods and algorithms as clinical decision support tools into clinical utility, so that all imaging scanners serve as measuring instruments.

QIN has established a roadmap with the following milestones:

1. Evaluation of imaging hardware performance
2. Creation of harmonization methods through software or protocols to reduce bias and variance during data collection
3. Creation of robust algorithms to extract quantitative information from images
4. Testing and performance validation of algorithms
5. Introduction of candidate algorithms into clinical workflow

QIN uses U01 cooperative agreements to fund research teams. Because awardees begin their programs at different times, their research programs are in different stages of development. Since its founding 10 years ago, QIN has received 276 applications, issued 35 awards, and currently supports 17 research teams. On average, each research team receives $570,500 per year, which is similar to the typical amount for investigator-initiated grants from the Cancer Imaging Program. In addition to the funded members, QIN has associate members from the United States, India, Bulgaria, Denmark, Germany, Sweden, Ireland, and South Korea who contribute to QIN but do not receive NCI funding.

QIN's research has resulted in more than 450 peer-reviewed reports, many written jointly by more than one QIN team. In addition, the editors of four journals have invited QIN to prepare manuscripts for a dedicated QIN issue. QIN's tool catalog has 67 clinical decision tools that will be benchmarked by the fall of 2018 to determine their stages of development. QIN has created 15 challenges to help qualify tool performance.

Dr. Nordstrom reviewed QIN's performance against its roadmap. Although QIN is working on every item in the roadmap, it is experiencing challenges in testing and validating algorithm performance and introducing candidate algorithms into clinical workflows. Quantitative imaging could be useful for identifying patients who are likely to do well with a precision medicine intervention. However, the tools developed for this purpose are not widely used in clinical research yet, partly because testing for ease of use and compatibility with other clinical data is still being done.

To encourage research teams not yet a part of the QIN lacking experience in quantitative tool development and validation to focus on clinical validation and translation, the QIN award mechanism is changing from U01 to UG3/UH3. The UG3 phase will focus on algorithm software creation and verification, and the UH3 phase will support clinical validation and translation. For research teams that are experienced in quantitative tools development, the U01 program will be converted to an R01 research grant program. This change will transfer more control of the network from NCI to the research teams and help teams compete successfully for other funding sources.

Leaders of QIN and some of its research teams are discussing collaborative opportunities with the NCTN groups. For example, the ECOG-ACRIN Cancer Research Group is providing data that can be

used for QIN challenges, and it is using QIN tools in its clinical trials. Dr. Nordstrom and members of QIN are visiting all the NCTN adult groups to encourage them to incorporate quantitative imaging tools in their trials. Dr. Nordstrom closed by asking CTAC what more can be done to encourage the use of QIN imaging tools in clinical trials.

Questions and Discussion

New QIN Funding Mechanisms. Dr. Mankoff said that QIN is going in the right direction by replacing U01 with other grant mechanisms. The new UG3/UH3 awards recognize that some groups are doing first-class, innovative research but are not ready to translate their research into the clinic. He also praised the decision to offer R01 awards to more experienced groups whose applications will receive appropriate reviews by a Center for Scientific Review panel with clinical emphasis. This change will encourage teams with tools that still need to be implemented to pursue the appropriate pathway. Dr. Dancey also supported the plan to replace the U01 awards with R01 awards for experienced teams.

Barriers to QIN Tool Implementation. Dr. Mankoff said that the QIN tools need to be implemented in multicenter clinical trials. The tool developers, who focus primarily on quantitative issues, need to advocate for the use of their tools in trials by reaching out to the clinical component of their team.

Dr. Curran said that the new grant mechanisms will help with the application of QIN tools in clinical trials. The NCTN NRG Oncology group has asked a QIN expert in each of their disease sites to speak about the available tools at the upcoming NRG meeting. He characterized the reason for the gap between tool development and the use of the tools in clinical trials as a cultural issue. Radiologists at academic medical centers may lack the hardware and software to implement the tools, they might not be engaged in clinical trials that could use the tools, and the requirements of the trials may seem insurmountable.

QIN Support for Pediatric Research. Dr. Langevin asked why the plans that Dr. Nordstrom had described did not include the Children's Oncology Group. Dr. Nordstrom explained that QIN is open to pediatric research; however, the pediatric research applications received to date did not score well enough during study section review to receive funding.

QIN Tool Life Cycle. Dr. Petersen wondered whether the tools might become obsolete before they are used in clinical trials. Dr. Nordstrom said that the tools are likely to remain productive for a long time, although QIN has not determined the life cycle of its tools. The main challenge is ensuring that each tool is reliable, trustworthy, and free of biases and errors.

QIN Reimbursement for Image Acquisition. Dr. Langevin asked whether QIN awards include funding for reimbursement. Dr. Nordstrom replied that QIN awards do offer funding for the imaging studies required for its research, but it does not support clinical trials in general.

Dr. Matrisian asked whether a funding mechanism similar to NCI's Biomarker, Imaging, and Quality of Life Studies Funding Program (BIQSFP) supports implementation of the QIN tools in clinical trials. Dr. Mankoff said that although BIQSFP does cover validation of imaging tools NCI does not have a mechanism like BIQSFP to pay for development of imaging tools. Typically, the images are analyzed at no cost to clinical trials, and QIN can test imaging studies as part of a clinical trial at very low cost. However, QIN does not fund the acquisition of images that are not part of a trial. Dr. Nordstrom added

that the outcome of interest is often prediction of response, which requires a certain amount of time and information.

Dr. Dancey pointed out that when clinical trials incorporate biomarkers, they start with one or a few central laboratories and key investigators to demonstrate their value before these biomarkers can be adopted more widely. She suggested that NCI make funds available from BIQSFP or another mechanism to support the costs of image acquisition. Dr. Nordstrom reported that QIN leaders have considered this idea.

CTAC Recommendations to Promote QIN Tool Use in Clinical Trials. Dr. Mankoff asked Dr. Nordstrom and CTAC to consider ways to encourage oncology investigators to use the QIN tools in their clinical trials on a no-risk basis, given that QIN has already funded these tools. Dr. Nordstrom explained that although QIN does not support clinical trials, it does encourage teams to test the tools they are developing in at least one site.

Dr. Weiner suggested that instead of having QIN investigators create tools and then determine who might use them, the NCTN investigators could identify the tools they need to answer important clinical questions. Clinical trials could then be designed from the start to ask an important question about, for example, the predictive value of a quantitative imaging strategy. Dr. Nordstrom explained that QIN has done this to some extent. Each QIN team has a clinical component, and the clinical team usually generates the research question for the team. The technical team then works with the clinical group to evaluate the tool. QIN is currently evaluating whether this approach is feasible in the broader community.

Dr. Weiner suggested that QIN consider broader tool implementation at an earlier stage and that QIN teams develop partnerships with NCTN groups. Dr. Nordstrom said that this was an excellent idea. Early on, QIN tried to use this approach, but the tools were not ready for implementation in the clinic. Now that a broad range of tools are ready, it is time to try this approach again.

Dr. Dancey recommended that grantees focus on clinical validation and demonstration of their tool's value to the NCTN and clinical trial community. This will require QIN leaders to continue informing NCTN groups and their investigators of the available tools. One way to accomplish this is for QIN leaders to attend NCTN group meetings.

Dr. Loehrer suggested that QIN bring the NCTN group leaders together to identify the provocative questions that could be answered by quantitative imaging. NCI could then issue a request for applications to address these questions. This approach would have built-in commitment from those conducting clinical research.

Mr. Aron reported that NCI recently brought together a group of brain tumor clinical trials leaders with neuroradiology leaders to discuss some of the same issues raised during this CTAC discussion. He suggested that QIN organize a similar intensive small-group meeting to discuss how to optimize QIN because—at least in brain tumors—QIN is invaluable.