The Quantitative Imaging Network (QIN): NCI’s Historical Perspective and Planned Goals


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Abstract

The purpose of this editorial is to provide a brief history of NIH NCI workshops as related to quantitative imaging within the oncology setting. The editorial will then focus on the recently supported NCI initiatives, including the Quantitative Imaging Network (QIN) initiative, its organizational structure, including planned research goals and deliverables. The publications in this issue of Translational Oncology come from many of the current members of this QIN research network.
Discussion

The NCI has been active in supporting Quantitative Imaging (QI) over the last decade, within the context of cancer screening and prediction and measurement of response to therapy. This has included the organization and completion of several targeted workshops over the last decade related to this topic and support for a number of related research initiatives. The workshop topics and recommendations will first be briefly reviewed as they provide the context by how NCI leadership justified the support for the research initiatives. Several of the NCI initiatives and progress made will first be reviewed briefly, followed by a more extensive discussion of the Quantitative Imaging Network (QIN); the topic of this issue of Translational Oncology. The intent of this editorial is thus to clarify historically how NCI has developed initiatives to support QI and the QIN, and to outline our continued commitment to support this important area research.

Several trans-NIH workshops were organized where NCI had an important role. The first such workshop was organized in June 2004 under two NIH wide consortiums, namely the Bioengineering Consortium (BECON) (1) and the Biomedical Information Science and Technology Initiative (BISTI) (2). It was entitled “Biomedical Informatics for Clinical Decision Support: A Vision for the 21st Century”, and highlighted the need for the development of QI methods, within the broader context of clinical data collection strategies, and harmonization of data acquisition and processing across imaging and other biosensors. The primary recommendation made as a result of this workshop was the critical need for improved data integration methods from data collected by these diverse platforms, as required to support the robust implementation of clinical decision support software tools in the clinical trial setting, namely for cancer and other diseases. Recommendations were also made to develop public research resources to promote the development and validation of clinical decision support tools. NIH BISTI has greatly expanded its role over the last decade, particularly in the area of informatics requirements for genomics, as well as modeling and analysis more generally. Now BISTI is collaborating with the newly formed NIH Big Data to Knowledge Initiative (BD2K), which includes data collection by QI (3). Already a new Centers initiative has been announced and there are plans for small grants (R01s) that are to be funded in targeted big data areas as well.

The second complementary workshop was organized in 2006 by National Institute of Standards and Technology (NIST), NCI, and other NIH institutes, in collaboration with the U.S. Food and Drug Administration (FDA), as it became increasingly clear that technical standards for QI were required (4). The intended goal of this trans-federal agency imaging workshop was to engage all stakeholders including academia, the device and pharmaceutical industries, and imaging societies such as the Radiological Society of North America (RSNA), Society of Nuclear Medicine (SNM), the American Association of Physicists in Medicine (AAPM), and International Society of Magnetic Resonance in Medicine (ISMRI) to recognize the need for QI standards and to play key roles in promoting and adopting these standards within the clinical trial setting. The NIST workshop recommendations had an impact on the formulation of national consensus approaches as applied to QI methods for cancer, Alzheimer’s disease, and osteoporosis in particular. One important outcome, in part, was the formation of a unique alliance organized by the RSNA referred to as the “Quantitative Imaging Biomarker Alliance (QIBA) initiated in 2007; and later supported by National Institute of Biomedical Imaging and Bioengineering that focuses on current QI methodology in clinical trials (5). Another outcome, in part, was an increased interest in the formation of Public Private Partnerships with the pharmaceutical industries, namely as important
stakeholders, to promote standardized QI protocols for drug trials by the congressionally mandated Foundation of the NIH, partnering with NCI and other NIH institutes (6).

NCI has organized several other workshops specifically dedicated to the role of QI as applied to the cancer problem. For example, NCI in collaboration with Canadian Institute of Health Research, Institute of Cancer Research (CIHR-ICR) and Cancer Research United Kingdom (CR UK), held a workshop in London (June 2011) entitled “Linking ‘Omics to Patient Care Through Imaging”(7). One of the primary goals of this meeting was to explore the importance of correlation of quantitative imaging methods with the emerging field of genomics for clinical decision support, and to explore leveraging of research resources by the different cancer funding agencies on an international scale. This workshop resulted in expanding the support for QIN teams by CIHR for Canadian investigators, with ongoing discussions with CR UK and other international contacts in India and China to explore further leveraging of research resources including imaging archives. Finally, NCI organized a workshop in June 2013 entitled “Correlating Imaging Phenotypes with Genomic Signatures” where one of the goals was to explore how to scale up research resources and high speed computation methods, including cloud computing, to correlate imaging phenotypes with genomics signatures across large scale studies to predict the response to drug or radiation therapy. The recommendations included the need for further technical standards for QI to implement these proposed correlation studies, including the expansion of research sources, such as The Cancer Imaging Archive (TCIA) (8), designed to permit correlation of imaging phenotypes with genomic data collected by The Cancer Genome Atlas (TCGA) Initiative (9). Thus all the above workshops, have in part, laid the foundation for NCI leadership to not only identify a means to address potential solutions for QI standards as applied to cancer, but more importantly, to assist in justifying support for QI initiatives.

The first NCI QI initiatives were focused on the development of public resources such as annotated image databases for the purpose of permitting the comparison of the relative performance of algorithms for cancer detection or measurement of response to therapy, referred to as the “Lung Image Data Base Consortium (LIDC)” (2002-2007) (10) and the “Reference Image Database to Evaluate Response to Therapy (RIDER)” (2005-2010) (11). Both these databases were originally hosted by the NCI Biomedical Imaging Archive (NBIA), developed in 2006 under the caBIG initiative. More recently they have been hosted on TCIA, starting in 2009, to ensure HIPAA compliance (12). While the LIDC and RIDER databases helped to develop consensus on methods for evaluation of algorithms, and to promote the importance of public research resources in QI, they did not address issues related to implementation of QI protocols within the clinical trial setting. This limitation lead to another NCI initiative in 2007 designed to support “Clinical Centers of Excellence in QI” across several NCI designated cancer centers, referred to as the Imaging Response Assessment Teams (IRAT) (13). This initiative resulted in the formation of several multidisciplinary IRAT programs/cores within NCI designated cancer centers. These cores have succeeded in implementing several improvements in clinical trial design in collaboration with several NCI’s clinical trial networks.

A complementary initiative, referred to as the Centers for Quantitative Imaging Excellence (CQIE), was initiated in 2009, with the goal of certification of NCI designated cancer centers for QI methods, in collaboration with ACRIN (2010-2013) (14). Yet despite the level of success by the IRAT and CQIE initiatives, it became increasingly clear that NCI needed to support the development and evaluation the next generation of advanced image acquisition and analysis methods, while promoting in
parallel, the development of technical imaging standards and expanded research resources. Thus, this sequence of workshops and initiatives played an important role in justifying NCI investment in supporting the QIN, approved in 2007, and published in 2008 (15) and renewed in 2011(16). A reissue of the program announcement has been approved for May 2014 for an additional three years, based on the success of the earlier initiatives, and now includes support for Trans-QIN research resources.

The QIN PAR 11-150 is a cooperative agreement using a U01 funding mechanism. The primary goal of QIN is: (a) the collection of image and meta data from ongoing phase 1-3 clinical trials to generate a research resource of relevant clinical data; (b) development of innovative methods for data collection, and analysis using this research resource, and (c) explore a means to develop a consensus on QI methods, with a long term goal of validating the performance of clinical decision support systems for imaging, within the clinical trial setting. The technical and clinical focus of QIN is to develop robust methods to predict and/or measurement of response to therapy, and encourage their broad dissemination within the imaging, oncology, and device industry communities. These goals are consistent with the increasing interest by NCI in the implementing of adaptive therapy trials and personalized or precision medicine therapy strategies that will require advanced molecular and functional imaging methods. Applications to the QIN initiative thus require multidisciplinary teams of researchers to be developed across both cancer and computer science centers of excellence to address all of the resources necessary to meet these goals. The public announcement (PAR) requires oncologists, radiologists, medical physicists, computer scientists, and informatics to participate in each research team, who traditionally often do not collaborate together on a large scale. NCI now has 17 participating multi-disciplinary teams in the network, comprising over 200 funded investigators, with two additional teams funded in the last quarter of 2013 and will join the network early in 2014. Most of the teams are located within NCI designated comprehensive cancer centers where there is an opportunity to explore common research cores and/or research resources.

The QIN has a unique network management structure as shown in Figure 1. It is specifically designed to encourage research collaboration across cancer center sites and other centers of excellence. The governance consists of: (a) an overarching Executive Committee (EC) that coordinates the research goals within the network and as an outreach effort to interact with other imaging stake holders, and (b) a Coordinating Committee (CC) that manages four cross-team working groups (WG’s) shown in Figure 1. The WG’s are tasked to develop consensus positions on namely on (a) Data Acquisition, (b) Bioinformatics/IT and Data Sharing, (c) Image Analysis and Performance Metrics and (d) Clinical Trial Design and Development. The timetable and growth of the QIN funded teams since 2009 is shown in Figure 2, where the necessary population of WG’s was only met in late 2011; namely to develop consensus approaches across several imaging modalities and organ sites.

This special issue of Translational Oncology contains articles of research progress by several different QIN research teams and working groups. The research efforts by these investigators are to be highly commended as they have enthusiastically accepted the task to meet the goals of this network, as reflected in the wide range of publications in this issue of the journal. For example, significant advances have been made in phantom designs that address the physical measurement uncertainty problem across different sites for a given imaging platform, such as PET CT and DW MRI and DCE. This work has led to exploring a means for harmonizing data collection across these imaging platforms, by modeling and characterization of data collection across platforms, in particular PET CT and DW MRI. Another example
is the development of a range of advanced software tools that have the potential to both operate across different clinical sites for a given imaging platform and minimize operator or imaging site dependence on data collection and analysis. The latter goals are critical to support multi-site, multi-platform clinical trials and acceptance by oncologists involved in cancer therapy trials. Similarly, the informatics and metrology tools required to compare the relative performance of algorithms in an objective manner, commonly referred to as a “Grand Challenges”, have been developed and initiated for CT, DCE and DW MRI; where the latter methods proved to be technically very challenging. A means for sharing annotated data and Meta data has been implemented with patient data de-identification methods meeting HIPAA requirements using the TCIA (17), a critical requirement for a public resource. Initial efforts for software tool sharing, particularity metrology tools, is being explored for example using HUB Zero (18). Plans are in progress to make this data and metrology tools both publically available once the methods are fully validated by the QIN network and to work with RSNA (QIBA), and other interactional groups to seek further optimization of QI methods for cancer and other diseases.

QIN Clinical Trial Design and Development WG have been also actively collaborating over the last year with the EGOG-ACRIN and CALGB-ALLIANCE, both groups involved in the recently formed NCI National Clinical Trial Network (NTRN) (19). These developments are consistent with the long-term goal for QIN to serve as cost-effective technical research resource for oncology trials both nationally and internationally, and to develop highly reproducible QI techniques that provide greater biologic meaning to clinical trial endpoints (20). The above collaboration has also included the use of advanced molecular imaging methods, such as novel QI tracers with (18F) fluorothymidine for PET scanning or QI techniques with conventional imaging modalities utilizing contrast enhanced CT (21).

The NCI long-term strategy for support of QI has been through the use of a series of U01 and R01 program announcements (PAR’s) that permit the enrichment of the NCI imaging portfolio. One aspect of this strategy is the implementation of a HUB and SPOKE model, where the QIN U01 serves as the hub or test bed for evaluation of QI methods. Examples include PAR’s such as the Academic Industry Partnerships (AIP: PAR-13-169, R01) for translation technology development (22), where such 6 R01’s have been supported that are using QIN as a test bed. Another example is a Trans NCI PAR (R01, U01, and U24’s) for informatics that includes imaging, with one U24 funded, again using QIN as a test bed (23). Investigators throughout the imaging research community, both nationally and internationally, are thus highly encouraged to seek support for QI methods through these PAR’s and planned NIH BIG Data Initiatives, and should make contact with NCI program staff for advice on submission of cancer related applications for support.
References


5. RSNA QIBA: http://www.rsna.org/QIBA.aspx


8. http://cancerimagingarchive.net/


17. TCIA HIPAA Compliance: https://wiki.cancerimagingarchive.net/display/Public/De-identification+Knowledge+Base


19. NCTN: https://research.usc.edu/nci-national-clinical-trials-network-nctn-program/


Figure Captions

Figure 1: The QIN administrative structure showing the Executive Committee over the entire technical network, and the Coordinating Committee dealing with working group issues. Each team provides membership to all of the four Working Groups (WG’s), namely (a) Data Acquisition, (b) Bioinformatics/IT and Data Sharing, (C) Image Analysis and Performance metrics and (d) Clinical Trial Design and Development

Figure 2: Growth of QIN from its initiation in 2008 to the present. Bars represent the number of teams accepted into the network each year, and the continuous line shows the growth of the network.
Technical Teams (currently 17)

Coordinating Committee deals with WG issues.

Four Working Groups (WG’s)
Figure 2

QIN Sites

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