# NCI Clinical Trials and Translational Research Advisory Committee (CTAC)

# Quantitative Imaging Network Working Group Report

NIH NATIONAL CANCER INSTITUTE

*Dr. Janet Dancey*

*CTAC: March 12th, 2020*

# Today's Topics

- Quantitative Imaging Network (QIN) Background, Accomplishments & Challenges
- QIN Working Group
- Recommendations

# *QIN Background, Accomplishments, & Challenges*

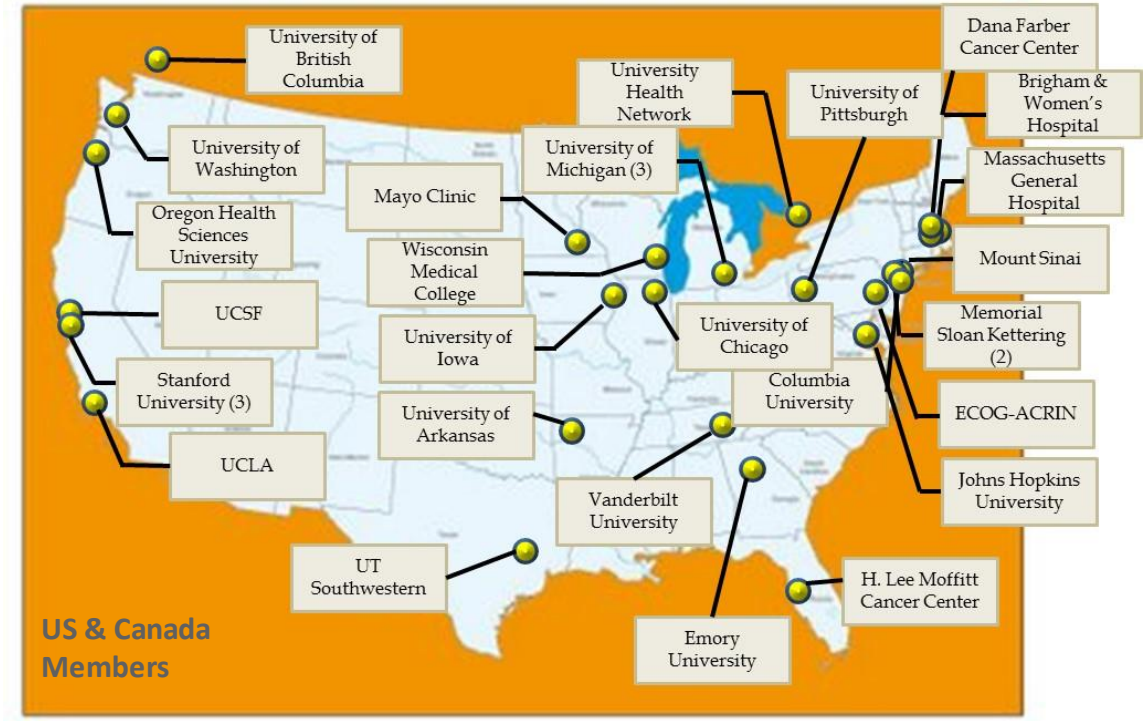
# Quantitative Imaging and Clinical Trials

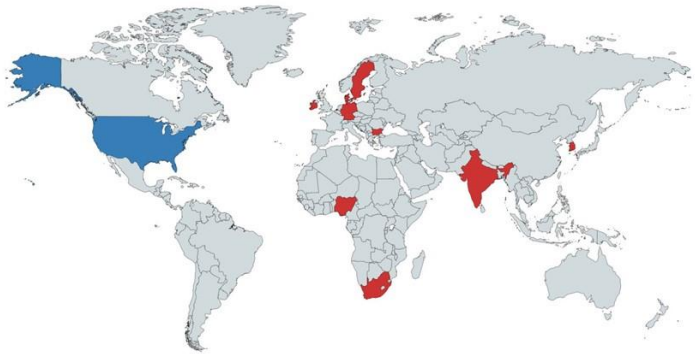
- Quantitative Imaging (in clinical trials): the extraction of measurable information from medical images to assess the status or change in a status of normal and disease
  - Sits at the crossroads of imaging, analytics, and informatics to provide quantitative tools for clinical decision support
  - May offer valuable anatomic, physiologic, metabolic and molecular information, provide important insights into disease location and extent, and reduce the need for multiple biopsies

# The Quantitative Imaging Network

- Currently, a network of 20 supported teams collaborating on the development and validation of tools and methods designed to measure or predict response to cancer therapies in clinical trials
  - Total number of teams over history of network = 43 supported and 29 associate members
  - Total number of institutions = 33 US institutions
  - Total number of states = 17 states and 2 Canadian provinces
  - Total number of countries (non-funded associate members) = 12 countries
- Supported by NCI's Division of Cancer Treatment and Diagnosis (DCTD), Cancer Imaging Program (CIP)
  - Janet Eary, M.D., Associate Director, DCTD/CIP
  - Robert Nordstrom, Ph.D., Director, QIN Program
  - 12 years of support; total funding to date = $103M

# Research Teams (Past and Present) in QIN



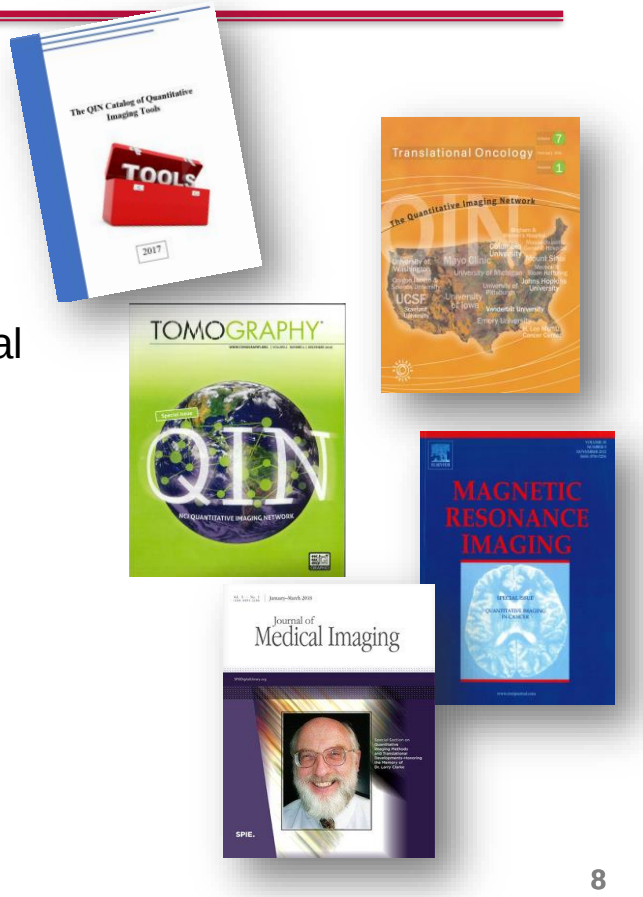



# The Quantitative Imaging Roadmap

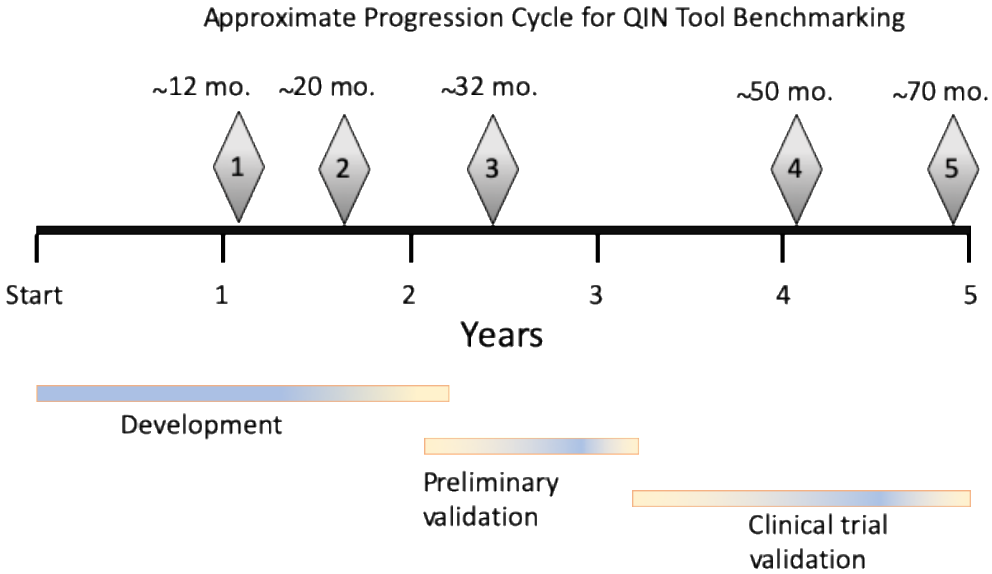
- Evaluation of imaging hardware performance
- Creation of harmonization methods (software and protocol)
  - Reduce bias & variance during data collection
- Creation of robust algorithms to extract quantitative information from images
- Testing and validating performance of algorithms
- Introducing candidate algorithms into clinical workflow
  - FDA and industrial interactions

# Accomplishments to Date

- Over 510 peer-reviewed publications
  - Many are collaborative across the network
- 67 clinical decision tools in the current tool catalog
  - 13 tools have achieved QIN benchmarks for further clinical development
- 5 journal issues dedicated to QIN activities



# QIN Benchmarks – Bench to Bedside




Benchmarks

1. Pre-Benchmark

Peer-reviewed publication describing the tool from phantom or retrospective data.

2. Basic Benchmark

Peer-reviewed publication describing tool performance in a challenge or other group test.

3. Technical Test Benchmark

Peer-reviewed [publication detailing functionality, performance, and limitation of the tool on independent data sets.

4. Clinical Trial Benchmark

Peer-reviewed publication describing tool performance in a clinical use example under developer operation.

5. Clinical Use Benchmark

Peer-reviewed publication demonstrating tool performance in a clinical application under third-party operation.

# Tools Ready for Clinical Validation and Utility

- 3D Slicer
- ePAD
- PyRadiomics
- Automated PET Phantom Analysis & Reporting Tool (APPART)
- PET Tumor Segmentation
- Quantitative DWI QC
- Aegis SER
- AutoPERCIST
- Functional Analysis Platform of imFIAT
- IB Clinic
- MiViewer
- Solid Tumor Segmentation
- Spectroscopic MRI Clinical Interface

# Clinical Trials Utilizing Benchmarked QIN Tools

- SWOG Lung-MAP (NCT03851445): A Master Screening Protocol for Previously-Treated Non-Small Cell Lung Cancer
  - Solid Segmentation tool
- Alliance CALGB-80802 (NCT01015833): Sorafenib Tosylate With or Without Doxorubicin Hydrochloride in Treating Patients With Locally Advanced or Metastatic Liver Cancer
  - Solid Segmentation tool
- Alliance A021602 (NCT03375320): Cabozantinib S-malate in Treating Patients With Neuroendocrine Tumors Previously Treated With Everolimus That Are Locally Advanced, Metastatic, or Cannot Be Removed by Surgery
  - Pet Tumor Segmentation tool
- Alliance CALGB-50604 (NCT01132807): Chemotherapy Based on Positron Emission Tomography Scan in Treating Patients With Stage I or Stage II Hodgkin Lymphoma
  - AutoPERCIST tool
- ECOG-ACRIN 1183: FDG PET to Assess Therapeutic Response in Patients with Bone-Dominant Metastatic Breast Cancer, FEATURE
  - AutoPERCIST tool
- Alliance A021202 (NCT01841736): Prospective randomized phase II trial of pazopanib versus placebo in patients with progressive carcinoid tumors (CARC)
  - ePAD tool

***From Bench to Bedside:***

***Lifecycle of QIN Tools***

- *Solid Tumor Segmentation Tool*
- *AutoPERCIST Tool*

# Development of Solid Tumor Segmentation Tool

- **What**: Semi automated operation to segment solid tumors (e.g., tumors in lung, liver and lymph nodes)
- **Who**: Columbia University
- **When**: 2011 to 2014
- **Why**: To provide computer-aided tools to obtain tumor volume/contours to validate new quantitative imaging biomarkers (e.g., tumor volume, radiomic features)
- **Tool evaluation**: Testing on retrospective data from various sources

# Clinical Evaluation of the Solid Tumor Segmentation Tool

- SWOG Lung-MAP (NCT03851445): A Master Screening Protocol for Previously-Treated Non-Small Cell Lung Cancer
- Alliance CALGB-80802 (NCT01015833): Sorafenib Tosylate With or Without Doxorubicin Hydrochloride in Treating Patients With Locally Advanced or Metastatic Liver Cancer
- SARC 011 (NCT00642941): A phase 2 trial of R1507, a recombinant human monoclonal antibody to the insulin-like growth factor-1 receptor for the treatment of patients with recurrent or refractory Ewing's sarcoma, osteosarcoma, synovial sarcoma, rhabdomyosarcoma

# Solid Tumor Segmentation Tool References


- Tan Y, L Lu, Bonde A, Wang D, Qi J, Schwartz HL, and Zhao B. Lymph node segmentation by dynamic programming and active contours. Med Phys. 2018 May; 45(5):2054-2062. PMID: 29500866
- Yan J, Schwartz LH, and Zhao B. Semi-automatic segmentation of liver metastases on volumetric CT images. Med Phys. 2015 Nov;42(11):6283-6293. PMID: 26520721
- Tan Y, Schwartz LH and Zhao B. Segmentation of lung tumors on CT Scans using Watershed and Active Contours. Med Phys. 2013; 40(4):043502. PMID: 23556926

# Development of the AutoPERCIST Tool

- **What:** Semi-automated analysis of FDG-PET images to provide clinical decision support, image quantitation, image segmentation, image viewer/visualization, and response assessment
- **Who**: Johns Hopkins University and Washington University
- **When**: 2011 to 2014
- **Why**: To provide determination of breast cancer response to therapy
- **Tool evaluation**: Tool was tested during and after development on retrospective data from various sources

# Clinical Evaluation of the AutoPERCIST Tool

- ECOG-ACRIN 1183: FDG PET to Assess Therapeutic Response in Patients with Bone-Dominant Metastatic Breast Cancer, FEATURE
  - Trial has been approved but is not currently activated
- Alliance CALGB-50604 (NCT01132807): Chemotherapy Based on Positron Emission Tomography Scan in Treating Patients With Stage I or Stage II Hodgkin Lymphoma

# AutoPERCIST Tool References


- Nakajo M, Kitajima K, Kaida H, Morita T, Minamimoto R, Ishibashi M, Yoshiura T. The clinical value of PERCIST to predict tumor response and prognosis of patients with oesophageal cancer treated by neoadjuvant chemoradiotherapy. Clin Radiol. 2020 Jan;75(1):79. PMID: 31662200
- Savaikar MA, Whitehead T, Roy S, Strong L, Fettig N, Prmeau T, Luo J, Li S, Wahl RL, Shoghi KI. SUV25 and µPERCIST: Precision Imaging of Response to Therapy in Co-Clinical FDG-PET Imaging of Triple Negative Breast Cancer (TNBC) Patient-Derived Tumor Xenografts (PDX). J Nucl Med. 2019 Nov 22. PMID: 31757841
- Grueneisen J, Schaarschmidt B, Demircioglu A, Chodyla M, Martin O, Bertram S, Wetter A, Bauer S, Fendler WP, Podleska L, Forsting M, Herrmann K, Umutlu L. 18F-FDG PET/MRI for Therapy Response Assessment of Isolated Limb Perfusion in Patients with Soft-Tissue Sarcomas. J Nucl Med. 2019 Nov;60(11):1537-1542. PMID: 30926647
- Pinker K, Riedl C, Weber WA. Evaluating tumor response with FDG PET: updates on PERCIST, comparison with EORTC criteria and clues to future developments. Eur J Nucl Med Mol Imaging. 2017 Aug;44(Suppl 1) 55-66. PMID: 28361188

# The Great Divide Challenge – Validation of QIN tools in Clinical Trials


J Eary 2018

# Clinical Utility Challenges

- Does the QIN tool offer results that are useful to the oncologist?
  - Does it serve a clinical need?
  - Does it provide reliable and repeatable results?
- Does the QIN tool fit into clinical workflow without disruption?
  - Is the tool easy to use?
  - Are the results obtained with the tool compatible with other clinical data?

# *NCI CTAC QIN Working Group*

# Process

- **July 2018:** An overview of the QIN program and the challenges it has encountered with validating and demonstrating QIN tool utility in clinical trials was presented to CTAC
- **November 2018**: CTAC voted to form the QIN Working Group
- **August – November 2019**: The Working Group met via webinar
- **March 2020**: Presentation of Working Group findings to CTAC

# NCI Clinical Trials and Translational Research Advisory Committee
# *Ad hoc* Quantitative Imaging Network Working Group

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Janet E. Dancey, M.D., F.R.C.P.C.
Queen's University
Ontario, Canada

**Members**
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National Brain Tumor Society
Watertown, Massachusetts

John Buatti, M.D.
University of Iowa
Iowa City, Iowa

Susan Chang, M.D.
University of California, San Francisco
San Francisco, California

Walter J. Curran, M.D.
Emory University School of Medicine
Atlanta, Georgia

Michael Knopp, M.D., Ph.D.
The Ohio State University
Columbus, Ohio

Patrick, J. Loehrer, Sr., M.D. Director
Indiana University School of Medicine
Indianapolis, Indiana

David A. Mankoff, M.D., Ph.D.
University of Pennsylvania
Philadelphia, Pennsylvania

Lawrence H. Schwartz, M.D.
Columbia University Medical Center
New York, New York

**Executive Secretary**
Steven A. Reeves, Ph.D.
National Cancer Institute
Bethesda, Maryland

**NCI Cancer Imaging Program**
Janet F. Eary, M.D.
National Cancer Institute
Bethesda, Maryland

Robert J. Nordstrom, Ph.D.
National Cancer Institute
Bethesda, Maryland

# Mission and Deliverable

- Mission
  - Advise on strategies for ***enhancing the integration of quantitative imaging tools into clinical trials.*** Assess the current status, identify barriers, and recommend strategic approaches for integration of quantitative imaging tools into clinical trials.
  - Provide ***recommendations for developing and prioritizing quantitative imaging tools*** that fulfill the needs of clinical trials carried out in the NCI National Clinical Trials Network (NCTN).
- Deliverable
  - A report with recommendations outlining strategic approaches for the development and integration of quantitative imaging tools into NCTN clinical trials.

# *Recommendations*

# Recommendation 1

***Form a pipeline oversight committee with NCTN, IROC, QIN leadership, and NCI program staff to assess advanced QIN tools for NCTN clinical trial validation.***

- Formalize an NCTN-QIN Working Group to guide tool development and assessments.
  - Task members with identifying QIN tools for further development that will have the highest potential for use and greatest impact.
- Develop “Fit-for-Purpose assessment” (FFP) criteria for QIN tools to establish requirements for transition into clinical workflow.
  - FFP is defined as the process through which the operating characteristics and proposed deployment of the specific tools are sufficiently well designed to yield interpretable results that address the specific research question.
  - Examples of FFP criteria include clinical site assessment, image data acquisition and analytics, SOP development, tool training, and QA/QC.
  - FFP would ensure tool regulatory compliance for regulatory filing as needed.

# Recommendation 2

***Provide opportunities for QIN and NCTN scientific leadership engagement.***

- Ensure interaction between QIN and NCTN so that QIN investigators can assess and be aware of NCTN trial opportunities at an early stage of trial development.
- Encourage NCTN imaging committees to include or invite QIN investigators to their meetings.
- NCTN leadership should include or invite *ad hoc* QIN investigators to participate on NCTN group scientific committees.
- QIN should continue presenting at annual NCTN group meetings.

# Recommendation 3

***Promote and incentivize QIN tool development and readiness for NCTN deployment.***

- Encourage appropriate resourcing and utilization of current imaging platforms with a specific focus on IROC to assess the clinical utility and validation of benchmarked QIN tools.
- Leverage current NCTN quantitative imaging expertise in order to increase awareness in the NCTN:
  - ECOG-ACRIN is charged with supporting imaging science, including QI science, across all NCTN groups.
  - Alliance, NRG, and SWOG have well-developed and active imaging committees.
- Provide funding for clinical translation and validation of QIN tools.
- Provide resource assistance with imaging devices, acquisition standardization, and collection.

# Recommendation 4

***Ensure imaging scientists, clinical radiologists, and clinical trialists have clarity about the use of QIN tools in clinical trials and the assessment of realistic endpoints.***

# Recommendation 5

***Ensure that NCTN sites are ready to open trials that include QIN tools.***

- Ensure tools fit into the clinical workflow.
- Provide support and resources to ensure the quality of image data acquisition, tool application, and data transfer for sites.
- Define the plan for the analysis, interpretation, and reporting of data from QIN tools at the time of protocol development.
- IROC and the QIN should provide QA/QC and feedback to the NCTN sites.

# Recommendation 6

***Support image data banking and sharing, with accompanying metadata from NCTN trials, in an archive such as The Cancer Imaging Archive (TCIA).***

- Areas of particular interest include immunotherapy trials with image-based response endpoints, and trials using emerging response measures for PET (e.g., PERCIST) and MRI.
- Existing image repositories in IROC should be catalogued for possible QIN tool testing.

# Summary

- The recommendations address the most important challenges to overcome to enhance the integration of QIN tools into NCTN clinical trials.

- The recommendations lay the groundwork for accelerating the translation and validation of benchmarked tools into clinical trials, and ultimately, to clinical practice.


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