| BY JULIA PUBLICOVER

CENTRALIZED IMAGE MANAGEMENT

for Multi-Centre Clinical Trials

Personalized cancer medicine seeks to identify the right therapy, for the right patient and at the right time. Imaging measurements are a key part of this personalization and need to be performed and analyzed with the highest level of precision and accuracy – this can include stratifying patients for appropriate treatment, designing image-guided treatments and evaluating response.

Clinical trials are used to bring new treatments forward and, increasingly, these are dependent on the growing variety of imaging studies and often include novel, untested imaging techniques. If these expensive trials are to be productive, it is critical that the imaging studies (both proven and novel) be performed with precision and accuracy.

To this end, the Quantitative Imaging for Personalized Cancer Medicine (QIPCM) group was created to help manage the emerging imaging needs of clinical investigators, and ensure they learn as much as possible from the imaging measurements, given the significant personal investment of the patients, the time commitment of the investigators, and the financial support of the funding agency.

QIPCM was established by Dr. David Jaffray, medical physicist and EVP of Technology and Innovation at the University Health Network (UHN) in Toronto. Dr. Jaffray saw the need for quality data collection and management in an area where technology is quickly evolving. With funding from the Ontario Institute of Cancer Research (OICR), Dr. Jaffray built a multidisciplinary team of physicists, oncologists, IT specialists and analysts—all with extensive imaging expertise—to solve the problems faced by clinical investigators.

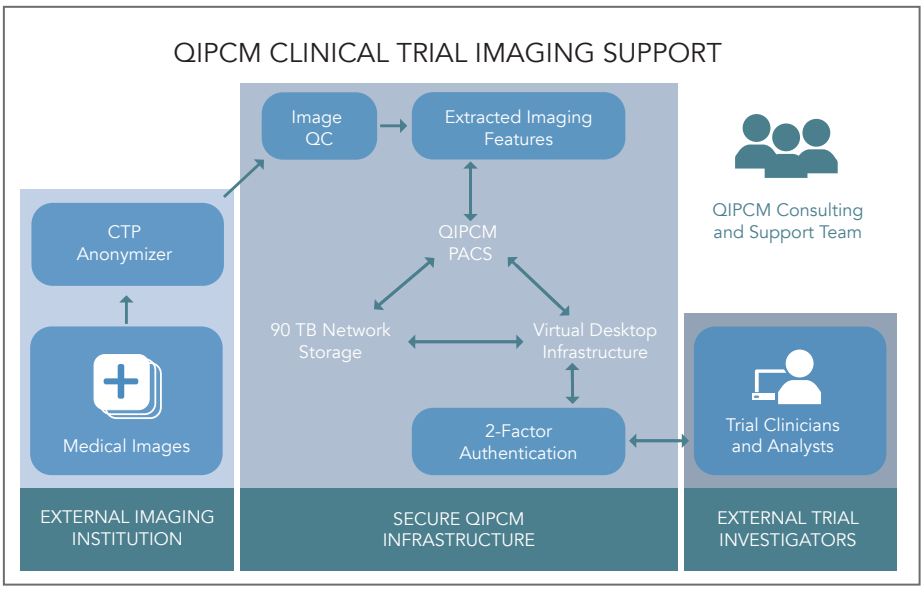
"We have set up the QIPCM service and infrastructure to handle all aspects of the imaging data pipeline for a client," says Dr. Ivan Yeung, medical physicist and physics lead of QIPCM. "Everything is about quality—quality assurance of the scanners and the data, robust anonymization and secure data handling, and expert analysis of the data using transparent, reproducible standards and tools." He adds that QIPCM provides end-to-end quality assurance, workflow, and analysis services for imaging in clinical trials.

A clinical trial needs professional expertise to ensure a well-curated collection of imaging data. This expertise is needed right from trial inception— evaluating the performance of scanners located at multiple participating clinical institutions, and developing imaging protocols to ensure that the trial objectives are met and that the data from all sites is compatible and can be compared. Once data are collected, they must be handled according to government regulations while still being available to investigators at multiple institutions. Standardized image analysis techniques for existing and emerging imaging biomarkers must be applied consistently. In some cases, custom tools need to be developed. The QIPCM team supports this through its internal development team.

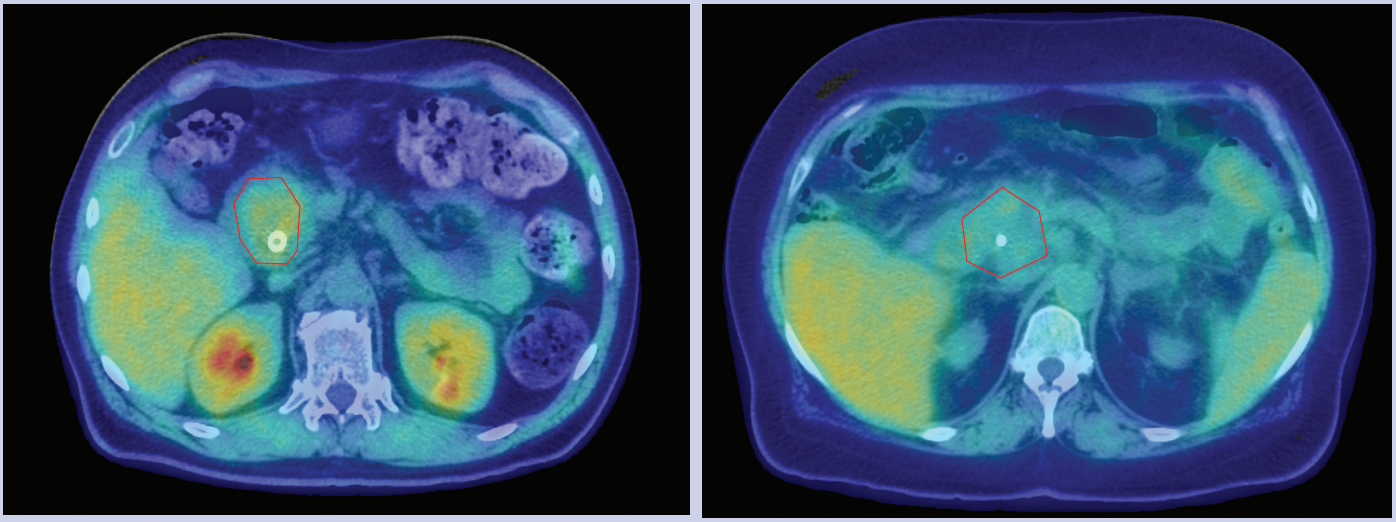
QIPCM is uniquely- and expertly- equipped to provide this expertise and simplify workflow for classical trial structures. With support from CFI and The Princess Margaret Cancer Foundation, QIPCM is armed with a fast, flexible and easy-to-use computing platform for central image review where multiple trial investigators can securely and instantly review images by accessing them from anywhere in the world. This platform uses a central image repository and is built on the VMWareTM infrastructure that allows the specific investigator's software to be globally available.

This management and central review for clinical trials is the technological and functional backbone of QIPCM. However, QIPCM's strength is in their understanding of advanced imaging techniques such as dynamic, functional and molecular imaging. QIPCM's Quality Team, equipped with quality assurance tools, including custom built Dynamic Contrast Enhanced (DCE) phantoms (manufactured by London-based Modus Medical Inc.), visits each institution participating in a trial to do a 'deep dive' into scanner performance.

Modern trials can include many novel endpoints and imaging procedures and QIPCM has the expertise to handle these challenges. For example, the team has developed tools and quality measurements for standardization in PET-based hypoxia imaging (FAZA), including the development of a software tool to quantify the variation of hypoxia measurements in the presence of motion.



CT-PET images of pancreatic cancer patients with high (a) and low (b) FAZA uptake.



The absolute magnitude, even for 'high' FAZA uptake, is much lower than that in conventional FDG PET images. This prompted the QIPCM team to create a new method of analysis to properly quantify FAZA uptake in the pancreatic cancer patient study.

This research was originally published in JNM. Metran-Nascente C, et al. Measurement of tumor hypoxia in patients with advanced pancreatic cancer based on 18F-fluoroazomyin arabinoside (18F-FAZA) uptake. J Nucl Med. In Press. © by the Society of Nuclear Medicine and Molecular Imaging, Inc.

"The partnership with QIPCM is a key element to the success of our recent novel PET-FAZA study in pancreatic cancer patients," says Dr. David Hedley, medical oncologist at the Princess Margaret Cancer Centre and principal investigator of a study of hypoxia measurement in pancreatic cancer patients using PET-FAZA.

QIPCM also works with other unique organizations in Ontario, including the Centre for Probe Development and Commercialization (CPDCTM) in Hamilton and CanProbeTM in Toronto, to bring novel imaging agents to the clinical research community.

"The quality of the molecular imaging agent is a critical part of quantitative imaging studies that is often overlooked", says Dr. John Valliant of the CPDC. "Optimal development and exploitation of novel imaging agents requires that we have eyes on the entire pipeline to ensure we generate the highest quality data to learn as much as possible during a clinical trial."

QIPCM seeks to understand technologies that will impact the field. The team has been involved in studies on both of the recently installed PET/MR scanners in the Province of Ontario. These unique systems combine the superb imaging contrast and resolution in MRI and molecular information provided by PET. This combined scanner gives imaging researchers "the best of both worlds." To bring these on-line as valid instruments in clinical trials, it is critical to validate the performance of the individual MRI and PET components, and to ensure simultaneous image acquisition of the two components will not interfere with each other.

Quantitative imaging promises potential benefits such as reduced trial size, detecting changes in disease or treatment earlier, and reduced bias in analysis. The Quantitative Imaging Network (QIN), which was formed by the National Cancer Institute (NCI) in the U.S., with the mandate to develop quantitative imaging methods and support clinical trials, brings together teams of imaging experts in North America who work with clinical trialists to define the nature of the imaging studies and drill down into the details of the procedure and analysis. The QIPCM is one of the first two Canadian sites to join the network to advance the science and tools of quantitative imaging.

QIPCM steps in to help serve as a rapid translation pipeline for these advanced quantitative imaging methods. Working in close cooperation with experts in the field—some of the people creating the new techniques and tools in the first place—QIPCM can help clinical trials access and make good use of these cutting-edge techniques as soon as they are available. This knowledge-translation-as-a-service approach is a distinguishing feature of QIPCM and cuts out potential years of delay and learning curves between physics innovations and clinical trial implementations.

For example, the emerging field of 'radiomics' applies advanced mathematical algorithms and machine learning techniques to analyze subtle features within images. With these semi-automated approaches hundreds of features can be examined for thousands of patient images in a single study. QIPCM is preparing to support these novel algorithms through active support for trials and curating the clinical trial images for future analyses.

With a mandate to eliminate barriers to the adoption of quantitative imaging, QIPCM has emerged as a novel and highly valuable service that addresses many needs of clinical trials including equipment QA, protocol development, data anonymization, continuous quality control of data during accrual, centralized data storage with remote access, software tools, and image analysis. Currently, investigators from 21 clinical trials have engaged QIPCM and 17 data pipelines have been established with imaging institutions across North America. Ever increasing interest is pushing the program to expand support for clinical trials in all areas of medicine that employ imaging in one form or another.

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