QIN

Quantitative Imaging Network

Volume 1, Issue 2 October 1, 2010

Special points of interest:

- The Qin Wiki Site: https://wiki.nci.nih.gov/display/CIP/QIN.
- Qin Steering Committee teleconference meetings occur on the third Monday of each month at 11:00 AM eastern time.
- Current chair of the QIN Steering Committee is Dr. John Buatti, University of Iowa

Inside this issue:

Quantitative Biomarker Imaging at University of Pittsburgh

The research group at the University of Pittsburgh headed by Dr. James Mountz was the first group to become a part of the Quantitative Imaging Network. They are working to create robust biomarkers of cancer therapy response by adding advanced imaging procedures to existing clinical trials for the treatment of squamous cell carcinoma of the head & neck (SCCHN) and for glioblastoma multiforme (GBM). Standard imaging operating procedures and protocols, including specification of patient preparation, MR pulse sequences, and PET dynamic framing for the conduct of quantitative imaging biomarker cancer therapy trials, have been developed and studies are under way.

The University of Pittsburgh program has been proposed and organized with three specific aims. The first aim is to design systematic imaging methodologies to acquire and quantify, in a reproducible way, image-based biomarkers of 3-D targeted tissue regions that reflect patient oncologic status at serially measured early assessment time points. Next, the team will assimilate these methodologies into ongoing cancer therapy trials at Pittsburgh in order to quantify early imaging biomarker changes as a function of scan timing with a treatment regimen, and establish correlations between biomarker change and patient outcome. Finally, the team will share imaging data with both the imaging development industry and public database resources to advance further software development.

Dr. Mountz explains how the studies are performed. Subjects are scanned before the initiation of therapy to provide the baseline. Then, the patients are again scanned at several therapy time points. MR components include structural T1 images, dynamic contrast enhanced (DCE) imaging, magnetic resonance spectroscopy imaging (MRSI), and single and triple quantum sodium (Na) imaging. All MR studies are being performed on the whole-body 3T Magnetom TIM at the University of Pittsburgh MR Research Center at UPMC/Presbyterian Hospital.

PET scans are being performed dynamically using [F-18] FLT or [F-18] ML-10, an apoptosis tracer developed by Aposense Ltd for the GBM studies, and using [F-18] FDG for the SCCHN studies. Projects were assigned to PET sites based on facilitating protocol compliance, subject convenience, and efficient resource management. Thus, the GBM studies employing the tracers ML-10 or FLT, which benefit from an on-site radiochemistry laboratory, are being conducted on an HR+ Siemens scanner at the main (See page 3)

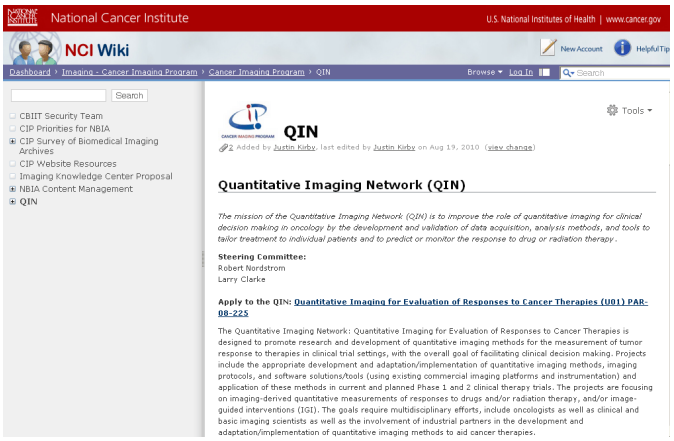
QIN Bioinformatics Working Group Workshop: Nov 15 - 16

November 15 & 16, 2010 have been selected as the dates for a hands-on workshop of the Bioinformatics/IT & Data Sharing working group of the QIN. The purpose of the workshop is to examine caBIG informatics tools and test them against QIN data sets. Organizing the meeting are Larry Clarke and John Freymann from NCI, along with Daniel Rubin from Stanford University and Mia Levy from Vanderbilt University. The purpose of the workshop is to explore the full range of caBIG tools developed for the imaging workspace that may be employed to evaluate the performance of tools for measurement of response to therapy. The scope of tools include Extensible Imaging Platform (XIP), AIM, AVT and the GRID tools that should allow the comparison of the performance of software tools to measure change over time using an array of imaging modalities. One of the aims includes exploring the ability to access databases at separate academic sites through (Continued on page 2)

Dr. Robert Nordstrom, QIN Program Director

QIN Wiki Site

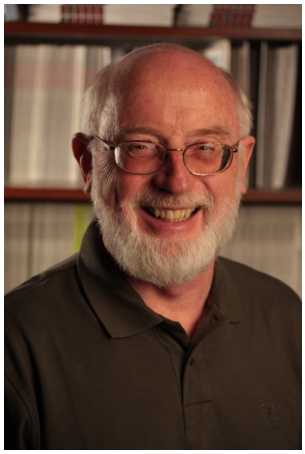
QIN now has a wiki site located at: https://wiki.nci.nih.gov/display/CIP/QIN. It is collaborative and designed to allow you to create new pages and upload documents. To do so, you will need an account. On the top right corner of the wiki page is the "New Account" link. A list of QIN individuals authorized to post to the wiki has been sent to the account manager by the QIN Lead Program Director. All others are free to view and enjoy the site without posting.



The QIN Mission

The QIN Mission Statement in its final form

The mission of the Quantitative Imaging Network (QIN) is 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.



Dr. Larry Clarke to lead bioinformatics workshop

Bioinformatics workshop from page 1

the GRID, and test the validation tools against these databases remotely. The outcome of this workshop should clarify the scope of tools that may be of value to QIN and additional tools needed that caBIG may potentially provide. The workshop is by invitation only and is to be attended by members of the QIN Bioinformatics/IT & Data Sharing Working Group. Other QIN members will be invited as needed. Also, caBIG staff and NCI staff are invited.

Members of the Bioinformatics/IT & Data Sharing Working group include:
Douglas Potter, U. Pittsburgh
Andre Dekker, Maastro, NL
Hugo Aerts, Maastro, NL
Erik Roelofs, Maastro, NL
Steven Eschrich, Moffitt CC
Paula Price, Moffitt CC
Larry Hall, U. South Florida
Tom Casavant, U. Iowa
Justin Otis, U. Iowa
Terry Braun, U. Iowa
Bartley Brown, U. Iowa
Daniel Rubin, Stanford U.
Mia Levy, Vanderbilt U.
Larry Pierce, U. Washington
Andriy Fedorov, Brigham & Women's
John Freymann, NCI
Justin Kirby, NCI
Ed Helton, NCI
Paul Mulhern, Booz Allen

The NCI will be inviting a few members from each QIN team to the workshop. If you have questions, please contact Larry Clarke (lclarke@mail.nih.gov).

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PET research center at UPMC/ Presbyterian Hospital. The SCCHN studies use commercially available FDG for PET/CT imaging, and are performed on a GE-ST PET/CT scanner at UPMC/ Magee Hospital.

Sample Results in the Evaluation of Cellular Proliferation in GMB

The Pittsburgh study is examining the utility of MR-based and FLT PET-based biomarkers for early evaluation of therapy response and for differentiation of progression from pseudo-progression in GBM. Subjects undergo quantitative MR and PET scanning at baseline and 2 - 3 weeks and 72 days after therapy is initiated. Patients are being recruited from existing GBM clinical trials:

1. Stupp regimen (standard dose and fraction external beam radiation therapy with concomitant low dose temozolomide followed by a 1 month rest and then 12 months of adjuvant temozolomide),
2. VEGF trap regimen (standard dose and fraction external beam radiation therapy with concomitant low dose temozolomide followed by a 1 month rest and 12 months of adjuvant temozolomide chemotherapy to which antiangiogenic drug targeting VEGF signaling is added), and
3. An expanded regimen (includes subjects in trials that incorporate bevicizumab and the VEGFR tyrosine kinase inhibitor, cedarinib, during the chemoradiation phase of therapy).

Figure 1 illustrates an example of baseline and 14-day early assessment MRSI results. The 3-D maps of choline (Cho) over creatine (Cr) ratios were generated to reflect cell membrane turnover. The figure shows an overall increase in the degree and extent of the abnormal Cho/Cr ratio at early assessment compared to baseline in a patient with poor outcome.

A major component of the GBM study is the use of PET with FLT. This traces a portion of the pyrimidine salvage pathway and is considered to provide a measure of cellular proliferation. The fact that FLT does not cross the intact blood-brain barrier (BBB) complicates the use of this tracer in brain tumor studies, with the possibility of changes in BBB in response to therapy masking changes in underlying tumor physiology. To address this, as opposed to typical clinical practice in which PET scans are performed at a fixed time point after injection (static imaging), the scans acquired in this QIN project are performed dynamically (i.e. data are acquired as a function of time) for 68 minutes starting at injection.

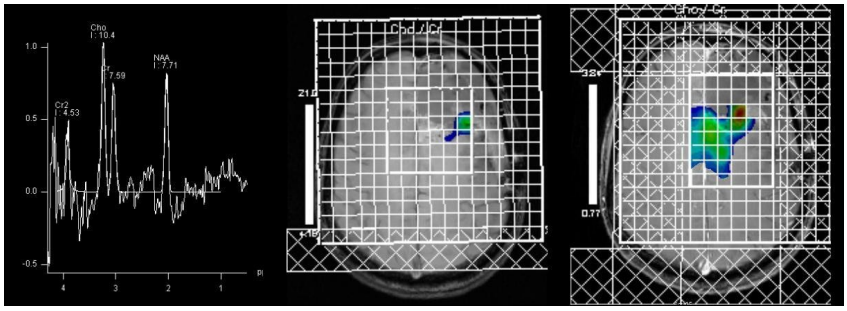

Figure 1: MRI images from a 56-year-old male with left frontal GBM at baseline and at an early therapy assessment point (14 days after therapy initiation). The baseline 1H MR spectrum (left) shows elevated chlorine (Cho), and the 3-D MRSI Cho/Cr map (middle) shows significantly increased Cho/Cr from tumor tissue (colored overlay). There was a significant increase in the degree and extent of Cho/Cr at 14 days (right). The patient did not survive to obtain the 72 day image.

Figure 2 shows the baseline results using MRI, FLT/MR fusion, and FLT PET. Also shown are results recorded with FLT PET (Stupp regimen) on day 21(the early assessment time point). The decrease in SUV between the two scans is evident. Additional information is available from the dynamic data. Figure 3 shows dynamic results from the same subject's baseline scan (blue) and early therapy assessment scan (red). The relative height of the two curves indicates an overall decrease in tracer uptake, presumably in response to therapy. Additionally, faster tracer washout is observed in the early assessment tumor, as indicated by the late-time slopes.

In summary, as proposed in this study, the analysis of image data from ongoing cancer therapy trials is a fundamental step towards the development of an evidence-based scheme for

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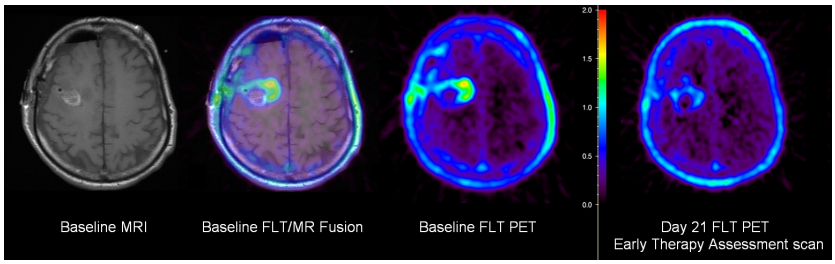

Figure 2: FLT PET images acquired from an 81 year-old male with right frontal lobe GBM at baseline and at early therapy assessment (21 days after therapy initiation). Image color indicates FLT uptake in SUV, which is decreased early in the therapy course.

Dr James Mountz, QIN principal investigator at the University of Pittsburgh

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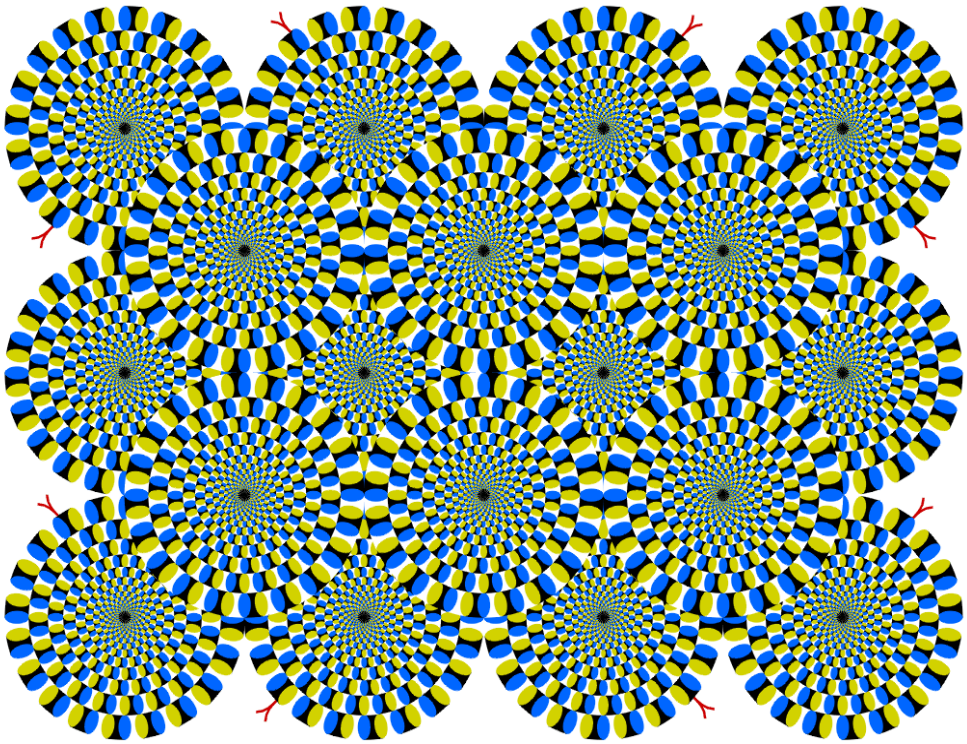
QIN

Too much QIN can make you see things...



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selecting a single, or a few, early therapy assessment time points and quantitative image-based biomarkers to provide the maximum information regarding tumor response. The development of imaging methodologies to acquire and quantify image-based biomarkers reproducibly will, in conjunction with other biomarkers, allow for more accurate and efficient assessment of cancer therapy response, and will thereby forward the standardization of analysis methods to provide robust quantitative imaging tumor-biomarker change measurements over time.

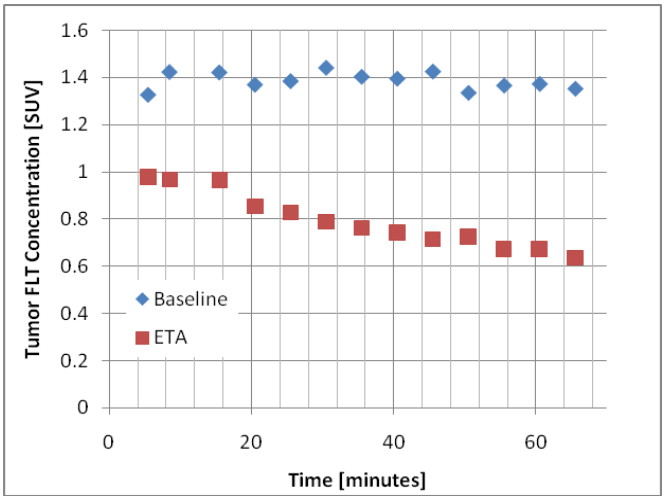

Figure 3: FLT-PET time activity curves (TAC) from the GBM subject in Figure 2. The blue diamonds were obtained from the baseline scan. The red squares were obtained from an early therapy assessment scan acquired 21 days after the therapy. The two PET scans were registered to each other using PMOD software. A tumor region of interest (ROI) was defined on the baseline and also applied to the early assessment scan. Data were rebinned into five minute time frames.