

# Informatics Tools for Protocol Development



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## Disclosures



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COI per FDA 21CFR54.2: None applicable to this lecture



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## Objectives



- To gain knowledge of the range of on-line resources and software available for use in research and clinical trials development to assist in the following:
  - Getting research ideas
  - Obtaining background information on scientific issues and problems
  - Obtaining copies of related clinical trials and methods
  - Scientific tools: image processing, statistical resources
  - Documenting your work with electronic notes, references, and back ups
  - Advertising your protocol (\* with IRB approval). Web sites, social media
  - Funding sources: federal, philanthropies, email notices



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## Acknowledgement



- Daniel Barboriak, MD
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## Getting Research Ideas



- **What research is good to do?**
  - Look at reviews, hypothesis statements, consensus of expert groups
  
- **What research is not good to do?**
  - Been done
  - Not interesting
  - Not feasible



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## Ideas: sharing



- If you have an apple and I have an apple and we exchange these apples then you and I will still each have one apple. But if you have an idea and I have an idea and we exchange these ideas, then each of us will have two ideas.



George Bernard Shaw

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## Ideas: search engines



- Google scholar <http://scholar.google.com>
- Bing <http://www.bing.com>
- PubMed [www.ncbi.nlm.nih.gov/pubmed/](http://www.ncbi.nlm.nih.gov/pubmed/)



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## Ideas: cutting edge meetings



- **RSNA** (Nov 26-30, 2023 Chicago, IL)  
<http://www.rsna.org>
- **SNMMI** (June 24-27, 2023 Chicago IL)  
<https://www.snmmi.org/MeetingsEvents/index.aspx?navItemNumber=504>
- **WMIC** (Sep 5-9, 2023, Prague, Czech Republic)  
<https://www.wmis.org/wmic1/important-dates-2/>



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# Ideas: push technology



- RSS – to keep up to date
- Create personal accounts
- New article search by keyword or journal
  - <https://www.ncbi.nlm.nih.gov/account>
  - <https://support.springernature.com/en/support/solutions/articles/6000083138-manage-springer-alerts-settings>
- New article search that cites classic articles
  - <http://www.scopus.com/home.url>
  - <http://www.webofknowledge.com/>



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# Pub Med detail



The screenshot shows a PubMed article page. The title is "Detection of glioblastoma response to temozolomide combined with bevacizumab based on pMRI and pPET imaging reveals [18F]-fluciclatide as an early and robust predictive marker for treatment efficacy". The authors listed are Gouton-Duroy A, Pagan JB, Fort E, Guillevin S, Verstraeten S, Scahill S, Toubi J, Ouarz, M, Verheijen J, Quenec'h, J, Lacombe M, Larroche M, and Barthelemy M. The abstract text is visible, starting with "The individualized care of glioma patients sought to benefit from imaging biomarkers as precocious predictors of therapeutic efficacy. Contrast-enhanced MRI and [18F]fluorodeoxyglucose (FDG)-PET are routinely used in clinical settings, their ability to forecast the therapeutic response is controversial. The objective of our preclinical study was to analyze sensitive pMRI and pPET imaging biomarkers to predict the efficacy of anti-angiogenic and/or chemotherapeutic regimens. Human U87 and U87v orthotopic glioma models were implanted in nude rats. Temozolomide and/or bevacizumab were administered. pMRI (arteriovenous, diffusion, and microstructural parameters) and pPET [18F]FDG and [18F]fluciclatide (FLT) studies were undertaken soon (1h) after treatment initiation compared with late anatomical pMRI evaluation of tumor volume (TV) and overall survival. In both models, FDG and FLT uptake were attenuated at 1h in response to temozolomide alone or with bevacizumab. The characterization of FLT, reflecting intratumoral heterogeneity, was also modified. FDG was more predictive for treatment efficacy than was FLT (less tightly correlated with outcome, P < .001 for both models). Contrast blood volume was significantly decreased by temozolomide + bevacizumab and was correlated with survival for rats with U87v implants. While FLT was highly predictive of treatment efficacy, a combination of imaging biomarkers was superior to any one alone (P < .0001 in both tumors with outcome). Our results indicate that FLT is a sensitive predictor of treatment efficacy and that predictability is enhanced by a combination of imaging biomarkers. These findings may translate clinically in that individualized glioma treatments could be decided in vivo before after pMRI/pPET examinations.

PMID: 35111502 [PubMed - as appears in publisher]

LinkOut - more resources

Recent activity

- Detected of glioblastoma response to temozolomide combined with bevacizumab
- FLT PET (PET)



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## ISI web of knowledge

ISI Web of Knowledge search results for: Topic=(Estimating kinetic parameters) AND Author=(Tzika)

Results: 2

1. The precise measurement of renal filtration and vascular parameters using a two-compartment model for dynamic contrast-enhanced MRI of the kidney gives realistic normal values  
Author(s): Tzika, Paul S.; Clague, Maria; Moutchouk, and A.; et al.  
Source: EUROPEAN RADIOLOGY Volume 22 Issue 8 Pages 1326-1330 DOI: 10.1007/s00306-012-2365-9 Published JUN 2012  
Times Cited: 9 (from All Databases)

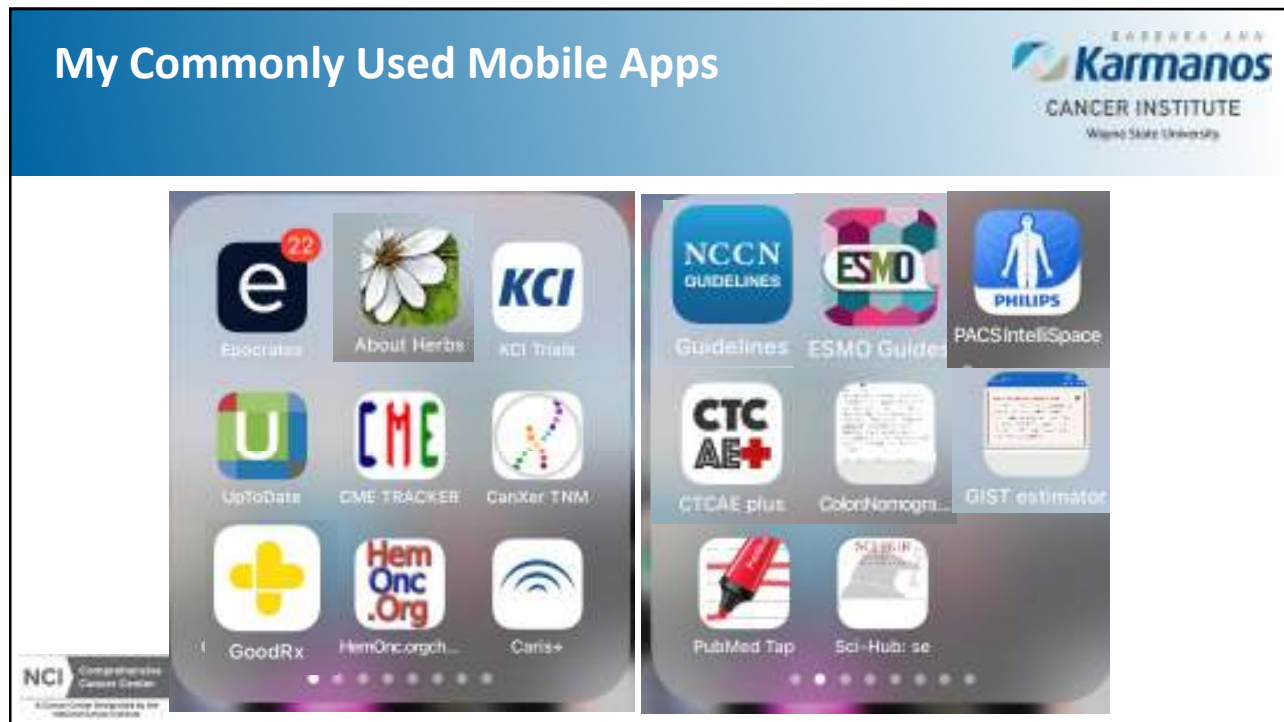
2. The estimating kinetic parameters from dynamic contrast-enhanced T1-weighted MRI of a diffusible tracer: Standardized nomenclature and symbols  
Author(s): Tzika, Paul S.; Clague, Maria; Moutchouk, and A.; et al.  
Source: JOURNAL OF MAGNETIC RESONANCE IMAGING Volume 36 Issue 3 Pages 223-232 DOI: 10.1002/jmri.23208(1888690-3-223)-AID-JMRI23-3-223-2-6 Published SEP 2012  
Times Cited: 274 (from All Databases)

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## Obtaining Background Information on scientific issues and problems

- PubMed <http://www.ncbi.nlm.nih.gov/pubmed>
- RSNA journals <https://pubs.rsna.org/>
- Roentgen Ray Society <http://www.arrs.org>
- Clinical journals (J Clin Oncol, NEJM, ClinCancer Res)
- Science journals (Nature series, Science, CancerRes)
- NCI <http://www.cancer.gov/>
- SEER <http://www.cancer.gov/statistics>
- Cancer Imaging Program <http://imaging.cancer.gov/>

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## Mobile Apps (& Websites)

- Clinical Trials Search [ClinicalTrials.gov](http://ClinicalTrials.gov)
- Drug Information: Epocrates, About Herbs, GoodRx
- Guidelines: NCCN, ESMO
- Cancer Regimens: HemOnc.Org
- Images: PACS system
- Genomics: Caris
- Adverse Events: CTCAE plus
- Medical Information: UpToDate
- Prognostic tables and nomograms
- Meeting information and abstracts
- RSNA journals <http://publications.rsna.org>
- Roentgen Ray Society <http://www.arrs.org>
- Clinical journals (J Clin Oncol, NEJM, ClinCancer Res)
- Science journals (Nature series, Science, CancerRes)
- NCI <http://www.cancer.gov/>
- SEER <http://www.cancer.gov/statistics>
- Cancer Imaging Program <http://imaging.cancer.gov/>

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## Background Information: troubleshoot



- Avoid redundancy
- Look for weaknesses in the literature
- Check existing evidence based knowledge
- National registry of clinical trials
  - <http://clinicaltrials.gov/>
  - <http://cancer.gov/clinicaltrials/search>
- Read related trials- Google search on trial number, name, or properties if you know of such studies



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## Clinical Trials Resources



- NCI CTEP
  - <http://ctep.cancer.gov/>
  - NCI National Clinical Trials Network



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## Methods Standardization



- QIBA – Quantitative Imaging Biomarker Alliance of RSNA
  - Detailed profiles and protocols
  - <https://www.rsna.org/qiba/>



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## Online Training



- Clinical trials certification CITI  
<https://www.citiprogram.org>
- NIH Online Presentations and Summaries  
<https://clinicaltrials.gov/ct2/manage-recs/present>
- Many universities offer training



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## Scientific Tools: Image Processing



- Image J <http://rsbweb.nih.gov/ij/>
- Fiji <http://fiji.sc/wiki/index.php/Fiji>
- Medical Image Processing, Analysis and Visualization <http://mipav.cit.nih.gov>
- 3D Slicer <http://www.slicer.org>
- Horos (free) <https://horosproject.org>
- Osirix <http://www.osirix-viewer.com>
- PMOD <http://www.pmod.com/technologies/index.html>



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## Imaging Processing



- Precision Imaging Metrics (Yunu) <https://www.precisionmetrics.org/>
- Mint Medical <https://mint-medical.com>
- Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) <https://www.nitrc.org/>
- I do imaging (Free) <https://idoimaging.com>



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## Imaging Processing: other tools



- Simulation
  - JSim
- CAD tools
  - Neural networks
    - JavaNNS
  - Support vector machines



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## Scientific Tools: statistical tools



- Web tools
  - [http://en.wikipedia.org/wiki/List\\_of\\_statistical\\_packages](http://en.wikipedia.org/wiki/List_of_statistical_packages)
  - The R project <http://www.r-project.org>
  - Vanderbilt free PS: Power and sample size calculator  
<https://biostat.app.vumc.org/wiki/Main/StatCalc>
  - Collaboration with a real human statistician



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## Scientific tools: other sources



- **Open source data / imaging archives**
  - Available DICOM images to test methods and parameters derived from images
  - The National Biomedical Imaging Archive (NBIA) is a searchable, national repository integrating in vivo cancer images with clinical and genomic data  
<http://cancerimagingarchive.net>



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## Documenting your work: electronic notes, references, and back ups



- The traditional lab notebook no longer works for many of us
- But what is the right answer?
- Choices: proprietary vs. open source, documenting patents, cloud vs. private, individual vs. collaborative
  - Google “electronic lab notebook”
  - Benchling <https://benchling.com/academic>
  - Evernote, Onenote, Google Docs



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## Documenting: tabbed notebooks



- Good for reference info “how I did it and when” and “tasks lists”
- Keynote – NF (Windows)
  - <https://sourceforge.net/projects/keynote-newfeat/>
- The Guide (Windows)
  - <http://theguide.sourceforge.net>
- Dropbox <https://www.dropbox.com>
- Sugar Sync <https://www.sugarsync.com>
- Back Up your data multiple ways and get it automated.
- Security also a concern



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## Keynote detail



**Project Information**

★25 Recommend this on Google

**Project feeds**

**Code license**  
Mozilla Public License 1.1

**Labels**  
To-Do lists, Security, TextEditors, Notebook, Outliner

**Members**  
dore\_@gmail.com

**Featured**

**Downloads**  
Release 1.7.9.1 (Free version) [View](#)  
Release 1.7.9.3 (Beta 3) [View](#)  
[Show all...](#)

**Wiki pages**  
[ChangeLog](#)  
[ChangeLog-Sp](#)  
[LastVersion\\_BETA](#)  
[Show all...](#)

**Links**

**Blogs**  
[Daniel's blog \(archival\)](#)

**External links**  
[KeyNote NF in SourceForge](#)  
[KeyNote NF Forum](#)  
[KeyNote in SourceForge](#)

Tabbed notebook with RichText editor, multi-level notes and strong encryption.

This project is an evolution of Trianglos Keynote (of Marek Jedrnski), with new features like:

- **Checkboxes on children of selected nodes**  
Selecting checkboxes for all nodes (ViewTree Checkboxes – now ViewAll nodes Checkboxes) is still possible. Besides, checkboxes can be shown only on children of selected nodes (Children Checkbox)
- **Hidden nodes**  
Capacity to work with hidden nodes. Nodes can be hidden in two ways:
  - Activating a mode which automatically hides checked nodes (Show or Hide checked nodes)
  - Filtering one node's nodes or all nodes under a searching criterion (Filter Tree Note)
- **Alarms on nodes**
- **Better treatment of tables**
- **Improved treatment of links**
- **Multilanguage support**
- **New kind of virtual nodes: links to other nodes (Mirror nodes)**  
Allow to organize the information in different ways, because nodes can be simultaneously in different notes. It will be possible to sort, rank and structuring in a free tree hierarchy, independent of the hierarchy in which leaf nodes reside.
- **Unicode compliant**
- **New KeyNote file format: compressed**

Original program can be found in <http://www.trianglos.com/trse/keynote.html>

This project in Google Code complements the one located in [SourceForge](#), hosting the source version control (Subversion) and the Issue Tracker.

**Intention**

I'm working in a totally new application, based in .NET and db4o object oriented database. My intention is to add to this new application basically the same functionality of today's KeyNote and all that things that I'm really interested in. I have a very clear idea of what I want and there are many things that are very more difficult to implement in current KeyNote. This new application will be open source too. Soon I will create a new project in Google Code for that new application.

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## Writing Tools



- Importance of outlining
- Word
- OpenOffice <http://www.openoffice.org>
- Notepad (Windows) <http://notepad-plus-plus.org>
- Typesetting for scientific publications?
  - LaTeX <http://www.latex-project.org>
- Version Control- always an issue



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## Bibliography Management



- Endnote <http://endnote.com>
- Papers <https://www.papersapp.com>
- Zotero (free browser, cloud based reference manager) <http://www.zotero.org>
- Mendeley (reference manager, PDF manager with annotation and commentary, a social networking site) <http://www.mendeley.com>



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# EndNote detail



- Sharing libraries with all authors
- Papers can be attached to reference
- Add references from local and web library services



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The screenshot displays the EndNote interface. On the left, a list of references is shown with columns for Author, Title, Journal, and Year. A red arrow points to a specific reference in the list. On the right, a detailed view of the selected reference is shown, including fields for Author, Title, Journal, and Abstract. A red arrow points to the 'Add' button in the reference view.



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## Advertising your protocol



- Getting the word out
- Web sites becoming more important
  - Content management systems
  - Wikis
  - Websites as a collaboration tool
    - Basecamp <http://basecamp.com>
    - iMeet Central <https://imeetcentral.com/>
- Social media – the wave of the present
- All need IRB approval



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## Advertising: e-newsletter



- Monthly Newsletter
  - Lists of trials
  - Articles on specific protocols
- Web search for trials at the cancer center
  - <https://www.karmanos.org/karmanos/find-a-karmanos-clinical-trial>
- Smart Phone App
  - KCI Trials at iPhone App store



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## Selling your protocol



- Leadership is key – use communication effectively
  - Medicine is full of ‘good ideas’ – execution is all that counts
- Present to ALL stakeholders
  - Address their self interest
  - Accrual will be your Achilles heel
- Leverage institutional resources
- Don’t be afraid to get out your message



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## Funding



- Federal sources – NIH DOD NSF
  - <http://grants.gov>
  - Getting ideas and setting priorities  
<http://www.cancer.gov/researchandfunding>
  - <http://report.nih.gov>
  - Grants awarded  
<http://projectreporter.nih.gov/reporter.cfm>
- Philanthropies
  - <https://www.rsna.org/research/funding-opportunities>
  - <http://ww5.komen.org>
  - <http://www.pardeefoundation.org>
- Industries (pharmaceuticals, imaging)
- American Cancer Society
  - <http://www.cancer.org/aboutus/acspolicies/state-fundraising-notices>



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# Questions?

