Letter from the Director: Radiology Research in the 21st Century

For many years, scientists like us who work in radiology departments have been preoccupied with the development of new medical imaging tools or paradigms aimed toward futuristic clinical applications. Such efforts have often been rewarded with the blessings of extramural funding, and publications in prestigious journals and conferences. To that end we, at RAI Labs, have generally done well, with paper publications this past year at a record total. However, it raises questions. Is this what medical imaging research enterprise should be about? Are publications and grants sufficient indicators of quality research? Is anticipated clinical application enough?

In November of last year, the radiology department held its first ever research retreat, where we sought a collective view of imaging research that goes beyond the divisions of basic science and clinical research, and beyond MD-directed and PhD-directed research. At the same time, we are witnessing new emphases on assessing the utility of medical imaging in clinical practice in terms of needed quality, benefit to risk ratio, and comparative effectiveness. Questions raised along these lines include the extent by which radiation dose can be reduced without impacting diagnostic performance; the explicit way by which a new imaging technique can improve clinical practice; how the cost of an advanced imaging procedure can be justified. I believe we have all the expertise and tools needed to answer these questions. Our science, regardless of its recognition in papers and grants, can and ought to be contributing to solutions for these challenges. More than ever, we can no longer pursue our stated goal of clinical relevance in isolation. The research and clinical realms are merging into a unified state where clinical practice is informed and made evident by proven science, and ground-breaking research is energized and made relevant by clinical needs.

Radiology research is changing. The era of basic science and clinical science as two distinct disciplines—the model that worked well for us in the last century—is over. Imaging practice and imaging as a pathway to discovery are merging into a single discipline. Radiology is the most natural home for such a united discipline. As members of the radiology department, we should not be only comfortable with this shift, but rather we should embrace it and lead it. What about papers and grants? Are funding agencies really interested in such hybrid approaches? Are journals taking submissions like this? The answer is a resounding yes. Just look at many recent national collaborative initiatives by NIH and RSNA. And if you have any lingering doubts, remember this: public recognition will follow good science; and this should is as it should be, not be the other way around!

Ehsan Samei, Director

Tomosynthesis Symposium

Joseph Lo and James Dobbins co-chaired a conference held at Duke from April 30 to May 2 entitled “Tomosynthesis Imaging Symposium 2009: Frontiers in Research and Clinical Applications.” It was the first conference of its kind dedicated to tomosynthesis imaging in multiple diagnostic and therapeutic modalities. The conference included a welcoming session sponsored by Siemens Medical Solutions, a poster session sponsored by GE Healthcare, and a lunch sponsored by Hologic. About 80 registrants from 8 different countries gathered to discuss the latest clinical and research trends. It concluded with a White Paper Discussion which will result in a publication that may serve to facilitate communication with funding agencies as well as to influence research and clinical implementations of tomosynthesis in the future.

ACR Accreditation at Duke Hospitals

Recently insurance companies and the US government have required accreditation of clinical imaging facilities as a requirement for reimbursement for imaging services. In 2009, the Clinical Imaging Physics Group (CIPG) took the leadership in seeking accreditation from the American College of Radiology (ACR) for the clinical imaging operation at Duke University Hospital. Duke Hospital is now accredited for four modalities: MRI, CT, Nuclear Medicine, and PET. CIPG organized a team of 25 physicists, radiologists, and technologists to facilitate collection of a large amount of clinical, physics, and credentialing data related to 9 MRI, 12 CT, 9 Nuclear Medicine, and 2 PET scanners in operation at DUH. The accreditation provides Duke with a reputable endorsement, enables improvements in our clinical operation, improves the consistency of equipment performance, and facilitates organized documentation of Duke’s QA procedures. (see page 3 for more about CIPG.)
Quantitative Image Analysis and Modeling

Computer-Aided Diagnosis — Breast Imaging: Georgia Tourassi continues to develop a CADe system to detect masses in mammograms. The newest prototype showed improved sensitivity and specificity with screening mammograms and is showing promise with digital breast tomosynthesis images. See pg 8 to read about how eye-tracking devices will be used.

Computer-Aided Diagnosis — Chest Imaging: Qiang Li, Jiahui Wang, Daniel Sullivan and collaborators at the University of Chicago are developing a CAD to assess patient responses to treatment by calculating a treatment response index using PET and CT images. They are currently testing a lesion segmentation method using a phantom with simulated lesions.

Lung Disease Quantification: Qiang Li, Jiahui Wang, and collaborators Feng Li and Kunio Doi at the University of Chicago, are continuing to quantify interstitial lung diseases in CT images. Papers in *Medical Physics and Physics in Medicine and Biology* describe the automated segmentation of lungs with severe interstitial lung disease, and improvements for detecting and segmenting abnormal tissues.

Lung Disease Quantification — Staging Lung Disease: Qiang Li, Jiahui Wang, Daniel Sullivan, Terence Wong, Edward Coleman, and collaborators from the departments of Surgery and Radiation Oncology are developing a CAD to clinically stage lung cancers with PET/CT images that will help predict survival rates and determine if surgery is viable.

**XCAT Series of Phantoms for Imaging Research**: Paul Segars and collaborators recently updated the anatomy of the XCAT phantom, a computational model of the human body. They developed anatomically-detailed models for the standard adult male and female that contain thousands of parameterized structures so that features (body dimensions, weight, organ volumes, etc.) can be varied to create many different subjects for high-resolution imaging research.

**Multi-scale Model of the Human Heart**: The Segars lab is developing a finite-element (FE) mechanical model of the human heart to be incorporated into the XCAT phantom for cardiac imaging research. Greg Stone developed a 4-chamber mesh for the heart and is now working to simulate the contraction of the heart using the FE package Continuity.

**Breast Phantoms**: Christina Li, James Dobbins, and Paul Segars created a series of detailed 3D breast phantoms from CT data that have the ability to simulate multimodality imaging data (mammography, tomosynthesis, CT, MRI, PET, SPECT, and ultrasound). Li is now working to incorporate finite element techniques to realistically simulate breast compression on the models. NIH funding for this project started in January.

Image Quality Index: Yuan Lin, Ehsan Samei, Jim Dobbins, and Carestream Inc. are pursuing methods to define image quality metrics based on clinical images.

Emerging Quantitative Imaging Techniques

**Neutron Imaging**: Anuj Kapadia, and collaborators demonstrated the ability to measure hepatic iron using portable neutron generators from Adelphi Technologies, Inc. These rugged table-top generators will form the basis of the clinical prototype NSECT devices for in-vivo iron detection.

**Gamma Spectroscopy**: Anuj Kapadia, Calvin Howell, and Triangle Universities Nuclear Laboratory showed that select energy levels in iron could be excited by gamma rays using Duke University’s High-Intensity Gamma-Ray Source (HIGS). This demonstrated that iron concentrations can be accurately measured when mixed with other elements.

**Quantitative CT**: Ehsan Samei, Samuel Richard, and Baiyu Chen are working to systematically assess the impact of CT acquisition parameters on characterizing lung nodule volumes in terms of precision and accuracy.

**Dual Radiography**: Erich Schnell is working on methods to improve DQE of computed radiography (CR) plates by measuring pixel-to-pixel variation for each CR plate.

**Chest Tomosynthesis — Optimization and Quantitation**: Kelly McGrady, Page McAdams and James Dobbins are completing an observer study measuring sensitivity and specificity of lung nodule detection using tomosynthesis.

**Breast Tomosynthesis — Optimization and Quantitation**: Samuel Richard, John Thompson, Joseph Lo and Jay Baker are including clinically relevant measures such as detectability of lesions, and “estimability” of lesion location and size in quantitation of tomosynthesis performance.

Special Points of Interest:
- Mammography and lung cancer CADs
- Customizable whole-body phantoms
- Phantoms that simulate heart contractions
- Measuring iron in vivo
- Lower doses and high image quality
- Bringing tomosynthesis to the clinic
- Making radiology affordable
- Improving radiology training

**Wide Angle Tomosynthesis**: Samuel Richard, John Thompson, Baiyu Chen, and Ehsan Samei completed a simulation study comparing the relative merits of wide-angle tomosynthesis to conventional breast tomosynthesis and CT.

**Multi-Modality Breast Density Analysis**: Christie Shafer, Deep Mehtaji, and Joseph Lo are testing if tomosynthesis can measure breast density quantitatively. Results (Shafer et al. *Med. Phys.* 37:1004-1016) showed excellent linear relationships between reconstructed voxel values and known lesion densities under various imaging conditions. Mehtaji is extending this work to anthropomorphic phantoms, and Shafer is testing if random periareolar fine needle aspiration (RPFNA) data shows that chemoprevention, such as Tamoxifen, reduces density and/or atypia in a high-risk population.

**Performance Metrology and Optimization**: DQE: Ehsan Samei and Nicole Ranger are extending eDQE to mammography. The new metric will incorporate dose to better characterize the balance between image quality and dose.

**Clinical Optimization of CT**: Ehsan Samei, Xiang Li, Samuel Richard, Max Amurao, and Baiyu Chen are developing a comprehensive, phantom-based methodology for determining optimum acquisition and processing protocols in clinical CT. They are focused on evidence-based protocols for reducing dose and improving image quality.
Awards and Honors

- Alexie Riofrio, third year medical student, won the first place for the Association of University Radiologists (AUR), Scientific Trainee Prize for: “Performance of Single-Versus Two-Projection Breast Tomosynthesis for Lesion and Cancer Detection”
- James T. Dobbins, PhD was elected president of the Society of Directors of Academic Medical Physics Programs, Inc. (SDAMPP) and Ehsan Samei, PhD was voted to be SDAMPP’s president-elect. Their terms will run from October 2009 until December 2010.
- Qiang Li, PhD and collaborators at the University of Chicago received an exhibit award (certificate of merit) from RSNA for: “Bone Scan: Temporal Subtraction Enhances Changes over Time.”
- Joseph Lo, PhD was promoted to Associate Professor of Radiology in July.
- Anuj Kapadia, PhD was promoted to Assistant Professor of Radiology in May.
- Georgia Tourassi, PhD was awarded NIH Bridge Funding in August 2009 for her IT-CAD research.
- Ehsan Samei, PhD was commended for “Distinguished Service as Associate Editor of Medical Physics” by the Medical Physics editorial board at RSNA in October; was awarded funding from GE Healthcare for CT protocol optimization; and voted in as president-elect of the southeast chapter of AAPM.
- Ehsan Samei, PhD and James T. Dobbins, PhD received funding from Carestream, Inc. to develop tools to assess image quality.
- Paul Segars, PhD received an NIH R01 grant, starting in January 2010, to develop a multi-modality breast phantom.

Research Updates (continued)


Medical Image Display Assessment Metrology: Ehsan Samei and Travis Greene developed institution-wide procedures to evaluate clinical displays at Duke, and are extending the metrology to include color displays.

Technique Optimization of Digital Mammography: A paper published by Nicole Ranger, Joseph Lo and Ehsan Samei (Med. Phys. 37:962-969) shows that significant dose reductions are achieved when technique is optimized for digital mammography systems.

Emerging Clinical Applications

Low-cost Tomography for Global Health Applications: James Dobbins, Paul Segars, and Jered Wells report promising initial results for the design and construction of a low-cost CT for the developing world. Preliminary studies to evaluate strategies for motion mitigation are underway.

Knowledge-Based Optimization of Radiation Therapy: Vorakarn Chanyavanich, Matt Freeman, Joseph Lo and Shiva Das, funded by the Wallace H. Coulter Translational Partners Grant Program, are optimizing IMRT treatment plans for prostate cancer patients. They showed it is possible to generate new, high-quality treatment plans by matching new cases to ones in their database. Chanyavanich will continue to improve the system’s robust performance with multiple matching cases. Freeman will optimize the mutual information algorithm to incorporate variably weighting of the contributions from different beam projections and different anatomical overlap regions.

Personalized Decision Support in Radiology: The Tourassi lab continues to study the local behavior of decision models in order to develop computational frameworks for case-specific reliability analysis. The initially-proposed computational framework showed tremendous promise in a pilot study where it was applied to a CADx model predicting the malignancy status of masses using BI-RADS descriptors; it dramatically improved the negative predictive value of the CADx system yet maintained 100% sensitivity for malignant masses.

Adaptive Educational Systems in Radiology: Georgia Tourassi and Maciej Mazurowski completed a pilot study testing different models for measuring the error-patterns of radiology residents during mammography interpretation. The study’s initial results were presented at the 2010 SPIE Medical Imaging Conference. Analysis of a more extensive study will be published soon in Medical Physics.

Clinical Trials and Outcome Analysis

Clinical Trial of Breast Tomosynthesis: Joseph Lo, Jay Baker, and Anne Jarvis are conducting a clinical trial of Siemens MAMMOMAT NovationTOMO breast tomosynthesis system with over 320 subjects enrolled to date.

Alexie Riofrio presented results comparing the performance of single- versus two-projection breast tomosynthesis at the Association of University Radiologists Annual Meeting.

Clinical Trial of Chest Biplane Correlated Imaging (BCI): Ehsan Samei, Jin Wooi Tan, Sarah Boyce, and Page McAdams completed an observer study showing that BCI provides better ROC performance than standard chest radiography. A more complete study is planned for early 2010.

Clinical Trial of Chest Tomosynthesis: GE is sponsoring Duke as the lead site of a clinical trial testing the use of VolumeRAD chest tomosynthesis devices for lung nodule detection.

Pediatric CT Dose Optimization: Xiang Li and Ehsan Samei are completing an observer study looking at how reducing noise and dose affects pediatric CT lung nodule detection.

CIPG is Improving Duke Hospital Operations

The Clinical Imaging Physics Group (CIPG) (cipg.duhs.duke.edu) was initiated by RAI Labs in 2009 as a core clinical imaging physics service for Duke University Hospital. Since its inception, the group has taken a leading role to enable ACR accreditation of Duke clinical imaging operation (see pg 1). In 2010, CIPG is focusing on (1) optimizing our imaging protocols in terms of quality/dose; (2) developing a new system for monitoring and documenting radiation dose levels, (3) implementing a new electronic problem reporting system, and (4) improving the consistency of our quality operation across the Duke enterprise through the newly-launched Duke Quality Imaging Standard cooperation (dqis.duhs.duke.edu).
Focus on Research — Chest Tomosynthesis Clinical Trial

James Dobbins's laboratory has been working in tomosynthesis research for over 20 years and has developed its own tomosynthesis algorithm called Matrix Inversion Tomosynthesis (MITS) (see article below). They have shown that chest tomosynthesis using flat-panel detectors can triple the detection sensitivity of subtle pulmonary nodules compared with conventional chest radiography. Based on a multi-year collaboration with the Dobbins' lab, GE has released a commercial tomosynthesis device for worldwide sale.

Currently, the lab is investigating the technique for improving detection of pulmonary nodules in an NIH-funded clinical trial. Initial results have demonstrated strong improvement using tomosynthesis as compared to conventional PA chest radiography.

Images from 97 human subjects have been collected. Interim analysis of 21 subjects showed that digital tomosynthesis significantly improved the detection sensitivity of known small lung nodules in all size groups when compared to PA chest radiography (see table).

Patients undergoing CT to follow up lung nodules were consented and enrolled to receive an additional digital chest radiograph and digital tomosynthesis exam. Tomosynthesis was performed with a commercial CsI/a-Si flat-panel detector and a custom-built tube mover. Seventy-one images were acquired in 11 sec, reconstructed with the MITS algorithm at 5-mm plane spacing, and then averaged (7 plane running average) to reduce noise and low-contrast artifacts. Total exposure for tomosynthesis imaging was equivalent to that of 11 digital PA radiographs (comparable to a typical screen-film lateral radiograph or two digital lateral radiographs). CT scans (1.25-mm section thickness) were reviewed to confirm presence and location of nodules.

Three chest radiologists independently reviewed tomosynthesis images and PA chest radiographs to confirm visualization of nodules identified by CT. Nodules were scored as either “definitely visible”, “uncertain”, or “not visible”. Based on the CT results, 175 nodules with diameters between 3.5 and 25.5 mm were detected, which were then grouped according to size. The criteria for a true positive was defined as a nodule that was scored as “definitely visible.” Using this criteria, the sensitivity determined for all nodules was 70% (±5%) for tomosynthesis as compared to 22% (±4%) for PA radiography (p<0.0001)(see table). These were the first published results in the world showing detection improvement for pulmonary nodules with flat-panel tomosynthesis devices (Medical Physics 35: 2554-2557, 2008).

### Table: Detection Sensitivity

<table>
<thead>
<tr>
<th>Nodule Size</th>
<th># of nodules</th>
<th>Tomosynthesis</th>
<th>PA radiography</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>175</td>
<td>70% (±5%)</td>
<td>22% (±4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3 to 5 mm</td>
<td>40</td>
<td>53% (±8%)</td>
<td>7% (±5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5 to 10 mm</td>
<td>106</td>
<td>71% (±5%)</td>
<td>20% (±3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt; 10 mm</td>
<td>29</td>
<td>90% (±6%)</td>
<td>53% (±7%)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Focus on Research — Deblurring Images

In order to get high quality slice images, it is imperative to use a deblurring algorithm (Fig 1). The algorithm developed by the Dobbins lab called Matrix Inversion Tomosynthesis (MITS) performs very well at this task by using linear algebra to solve for the blur that occurs from anatomy outside of the plane of interest in a tomosynthesis reconstruction.

In order to optimize the image acquisition process for a particular detection task with a given reconstruction algorithm, one must determine the best total tube angle, the optimum number of projection images, and the best plane spacing for reconstructed images. The Dobbins lab constructed the world’s first flat-panel-based tomosynthesis device using a commercial-grade detector and a customized tube-mover (Fig 2); then conducted experiments to determine the optimum acquisition parameters. Simulated impulse response functions, modulated transfer functions (MTFs), and noise power spectra (NPS) were produced to evaluate MITS compared to conventional shift-and-add tomosynthesis for a variety of acquisition parameters.

Based on these optimization experiments, the best acquisition parameters for detection of pulmonary nodules using the MITS algorithm are 71 projection images, 20-degrees of total tube movement, and 5 mm plane spacing. Acquisition parameters optimized for other reconstruction algorithms such as filtered backprojection are slightly different.
Focus on Research — Multi-Modality Breast Phantom

Breast imaging is an important area of research with many new techniques being investigated to further reduce the morbidity and mortality of breast cancer through early detection. Computerized phantoms can provide an essential tool to evaluate and compare new imaging systems and techniques.

Current computerized phantoms used in breast imaging research lack sufficient realism in depicting the complex three-dimensional (3D) anatomy of the breast; are often limited to a single application such as mammography; and cannot be applied to other existing and emerging breast imaging modalities and techniques such as tomosynthesis or CT.

This project will create over a hundred detailed 3D computational breast phantoms capable of realistically simulating a wide range of anatomical variations in health and disease with the flexibility to model different compression states of the breast for various imaging modalities. The models will be incorporated into the four-dimensional extended cardiac-torso (4D XCAT) phantom, a computerized model of the human body, for breast imaging research.

The phantoms will be created based on high-resolution dedicated breast CT datasets obtained from John Boone at the University of California, Davis. The different breast tissues will be segmented from the CT datasets and then modeled using computer graphics tools. Figure 1 shows an early-stage model of the breast phantom. Figure 2 shows comparisons of actual patient data to simulated multi-modality imaging data generated from the phantom.

This project will build the necessary foundation to quantitatively evaluate and compare existing and emerging breast imaging techniques, not just in terms of simplified physical characteristics, but in terms of clinically relevant performance; and thus provide a unique and vital tool for breast imaging research.

Figure 1. 3D renderings of an initial breast model with the breast surface, pectoral muscle, and fibroglandular tissue.

Figure 2. Comparison of simulated images to patient images using: (A) mammography (B) tomosynthesis, and (C) PEM.

Focus on Research — Multi-Modality Breast Density

This collaboration between Joseph Lo, Ehsan Samei, Christy Shafer; Victoria Seewaldt (Director of Duke University Breast Cancer Prevention Clinic); and Jay Baker (Chief of Duke Breast Imaging Clinic) will develop a breast cancer screening technique that combines the advantages of three-dimensional imaging such as MRI, with the faster, cheaper, more-accessible, easier-to-analyze, and less-invasive advantages of tomosynthesis. Since many previous studies have established quantitatively that breast density is well correlated with cancer risk, this new technique will be used to measure breast density. However, it will take it one step further by investigating the correlation between breast density and cytological cancer risk measured by Random Periareolar Fine Needle Aspiration (RPFNA).

A fully-automated breast segmentation and classification paradigm was developed using MRI scans from 118 high-risk screening subjects enrolled in Dr. Seewaldt’s on-going studies. Once the breasts were successfully separated from the image background (figure 1), an iterative, bimodal segmentation technique was employed to distinguish fibroglandular from fat voxels (figure 2) in order to determine breast density.

Breast density measurements from these imaging techniques will be compared directly to cytological ground truth from RPFNA, since RPFNA has been validated as an accurate assessment of short-term breast cancer risk in high-risk patients.

The next step will be to measure density using tomosynthesis and to validate those results against the imaging gold standard from MRI. Breast MRI is considered the imaging “gold standard” for determining breast density because it is three-dimensional (3D) and thus provides good contrast between fat and fibroglandular tissue, whereas mammography does not. MRI, however, has many disadvantages including expense, limited-availability, and long scan times; therefore breast tomosynthesis could be developed as an alternative 3D imaging technique. Initial studies demonstrate an encouraging correlation of density measurements made by tomosynthesis and MRI (Figure 3). This work is currently funded by a Synergistic Idea Award from the DoD Breast Cancer Research Program.

Figure 1. Segmentation of breast from background was performed to locate the breast boundary, sternum and lateral breast corners (X marks).

Figure 2. Breast from segmented MRI slice, with highlighted fibroglandular voxels.

Figure 3. Tomosynthesis slice images (top) are very similar to MRI slice images (bottom).
RAI Labs Publications in 2009

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Arrivals/Departures

Lynne Hurwitz joined RAI Labs faculty in June. She has been a faculty member of the Duke radiology Department since 2003 in the division of cardiothoracic imaging. Her research interests focus on technology assessment and radiation dosimetry for cardiothoracic imaging.

Alexie Riofrio returned to her 4th year of medical school after completing her research, done under the direction of Joseph Lo and Jay Baker, comparing single-projection breast tomosynthesis to two-projection breast tomosynthesis.

Shawn Mendonca left RAI Labs to attend medical school at Michigan State University.

Sushravya Raghunath, a BME master’s student, began an independent study with Georgia Tourassi working on IT-CAD in August.

Alex Modestou graduated from Duke University with his BS in Physics and Mathematics, and is currently pursuing an MT at Duke as a teaching fellow of the Knowles Science Teaching Foundation.

Wei Guo, a visiting scholar from China, will be working with Qiang Li on developing CADs for detecting lung nodules.

Medical Physics master’s student, Olav Christianson, joined the Samei lab to work on dose monitoring.

Simon Murphy is a new member of the Samei lab and will be working on image quality metrology as part of his Medical Physics master’s degree.

Jainil Shah and Dipti Talreja, master’s students in Duke University’s BME program, began working in the Kapadia lab this fall.

Alumni News

Ada Chen, PhD, former student of James Dobbins and assistant professor at Southern Illinois University Carbondale, was awarded her first NIH R01 grant to develop a fast-speed breast tomosynthesis scanner based on multi-beam carbon nanotube X-ray sources with collaborators at UNC Chapel Hill, NCSU, and XinRay Systems.

Amar Chawla, PhD joined Duke University’s Radiation Oncology Department this fall as a post-doctoral fellow.

Other News

Samuel Richard married Hilary Ellis on December 12.

Joseph Lo married Cortney Phelon April 25 at the Washington Duke Inn and their son Remington “Remy” Chang-Tai Lo was born October 8 at Duke hospital.

Aimee and Jered Wells welcomed their daughter, Juniper Grace on July 17.

Society of Directors of Academic Medical Physics Programs, Inc. Held Elections

The Society of Directors of Academic Medical Physics Programs (SDAMPP), co-founded by Ehsan Samei and James Dobbins in 2007, has 73 founding members and held its first election of officers and board members in 2009. Dr. Dobbins is serving as SDAMPP’s first elected president and Dr. Samei is serving as president-elect until December 2010. The organization is optimistic about its future impact on all medical physics educational programs.

Radiology Dept. Held Research Retreat

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