ACP, Florida Chapter

Tampa, September 7, 2018

Our Team focus:
- CCTA versus Stress Tests
- Vulnerable Plaque versus Plaque Burden
- CT-FFR and AI
- Sherlock Program :CTA and CT-FFR Applications
- Cognification
The Transformation of Medicine

- Employment of Physicians by Organizations, Stark Law, Value
- Digitalization of Medical Records & HIPAA
- Codification of Diagnosis and Encounters
- RVUs equivalent of billable hours/ Monitoring Productivity
- Management by those with limited medical experience
- Industrialization, M & A, Doctors and Patients as Commodities
- Substitution of Guidelines for Critical Thinking
- Payers Profound Influence and Interference
- Physician Burnout 40%
- Monitization of all Activities, Bundled payment
- Private Equity Purchases, Management, Growth, and Resales
  • Cognification
Eric E. Harrison MD, FACP
Cardio-Oncology, ICOS
CEO PrivaCors Inc
Cardio-Orthopaedics®
Department of Cardiology,
Professor of Medicine
Morsani School of Medicine,
University of South Florida
Tampa, Florida.
Chief of Medicine,
HCA Memorial Hospital.
eeharrison253@harrisoncardiovascular.com
813-323-5447
Financial Disclosure

- Vital Images Inc., Minnetonka, Minn.
Available/Suggested Techniques for Detection of Vulnerable Plaques

**Invasive**
- Angiography
- IVUS
- MRI
- OCT
- Angioscopy
- Spectroscopy
- Thermography
- Elastography

**Non-Invasive**
- MRA&MRI
- EBCT
- Radioisotope Imaging
- CCTA
Personal Patient Coronary Plaque Management

Management of Coronary CTA Findings

- Normal CTA
- Nonobstructive CAD
- Obstructive CAD (≥ 50% Stenosis)

Stable Outpatient
- Reassurance
- Lifestyle and pharmacological preventive therapies
- Lifestyle modifications, OMT & consider further testing

Acute Chest Pain
- Discharge
- May be one and done, 1%
- CT-FFR
  - for preventive therapy
  - further testing
Our Tampa CCTA Milestones

• 2004: Early Adaptor of CCTA
• 2004: Founding Member SCCT, Vital Images Research/Teaching
• 2004: Converted a clinical practice from SPECT/Cath to CCTA, revenue loss $$$
• 2005: Best selling DVD on CCTA
• 2006: Created our own Cardiac CT/PET/MRI Diagnostic Center
• 2006: USF Cardiac PGY4-6 Training Program
• 2012: Advanced Cardiac Imaging PGY7 Fellow Program
• 2016: Joined IBM Watson Imaging Consortium for AI for CCTA imaging: 1/24
• 2017: HeartFlow Program launched: CT-FFR
• 2018: Working with Enlitic for AI for CCTA Imaging
New Dramatic Change in Testing Results/Outcomes

Scottish Computed Tomography of the HEART Trial

• This is the first time a noninvasive test (CCTA) for CAD has demonstrated a benefit (a 50% decrease in rate of fatal and nonfatal MIs) in hard clinical outcomes
• through better targeted investigations and treatments in patients presenting with suspected angina due to CAD compared to standard treatment!

This study results in a significant cost savings and decrease in mortality and morbidity. The glacial response of health insurers to change and improved technology portends an imminent correction.

50% drop in heart attacks with CCTA instead of stress tests
Adjustment of System to new information

New European Nice Guidelines For Chest Pain 2016

1.3.4.3 Offer 64-slice (or above) CT coronary angiography if:
- clinical assessment (see recommendation 1.3.3.1) indicates typical or atypical angina or clinical assessment indicates non-anginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves. [new 2016]
## Table 4. Correlation Between Abnormal Stress Tests, CCTA, and Invasive Angiography

<table>
<thead>
<tr>
<th></th>
<th>ICA &gt;50% Stenosis (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>False Positive (%)</th>
<th>False Negative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal MPI</td>
<td>174</td>
<td>64.7</td>
<td>29.4</td>
<td>59.2</td>
<td>34.5</td>
<td>40.8</td>
<td>65.5</td>
</tr>
<tr>
<td>Abnormal SE</td>
<td>31</td>
<td>40.8</td>
<td>48.9</td>
<td>57.4</td>
<td>32.8</td>
<td>42.6</td>
<td>67.2</td>
</tr>
<tr>
<td>Abnormal TMET</td>
<td>25</td>
<td>69.4</td>
<td>40.0</td>
<td>62.5</td>
<td>47.6</td>
<td>37.5</td>
<td>52.4</td>
</tr>
<tr>
<td>Abnormal stress test, any</td>
<td>230</td>
<td>60.4</td>
<td>34.2</td>
<td>59.3</td>
<td>35.2</td>
<td>40.7</td>
<td>64.8</td>
</tr>
</tbody>
</table>
Outpatient Care: Cardiology Cookbook
Cardiologist Financial Incentive

“The Cardiology Cascade”

- H&P
- EKG
- Echo
- office SPECT scan $600
- Cath $600
- Coronary FFR
- PTCA $1200 (ad hoc 60%)
- OHS $600

40% up to 88% False +
65% False -
Robust Radiation

MPI SPECT has poor concordance with FFR in patients with multivessel CAD!

if kept in town
IPA Nassau Suffolk
Cardiology
29 cardiologists, 5 practices
Nuclear cardiology committed 29,
3 SPECT, 1 PET, 1 unknown
Some individual MD CCTA training: 4
Research has shown only 4 characteristics:
- Thin cap
- Liquid lipid
- Larger diameter
- Sometimes look like a napkin ring

Only 4? This seems too simple
Current Knowledge of Symptomatic Patient Plaques

Motoyama et al: Opus

- 2015 Plaque Characterization by Coronary Computed Tomography Angiography and the Likelihood of Acute Coronary Events 2015 with 2 correlates for high risk plaque: positive remodeling PR (RI=1.1) and low attenuation plaque LAP (< 30 hu). 4423 patients enrolled over avg. of 3.0 years. 45 pts with high risk plaques developed ACS, 43 without with ACS

- 2007 Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes Correlates were PR and LAP.

- 2009 Computed Tomographic Angiography Characteristics of Atherosclerotic Plaques Subsequently Resulting in Acute Coronary Syndrome
Sherlock Plaque Score: Local Findings

Plaque Parameters: Morphology, Composition, Function, Juxtaposition

- Activated Platelets Y ___ N ___
- Convergent –Divergent double cone Angle 1-5 summation of C/D
- Plaque Ulcer Depth in mms
- Lipid Lake Necrotic Core , “notch” with adventitia base ,% NCS, %NCP, “napkin ring”
- % fibrosis . %FS, %FP, Ca in plaque , distal calcium in proximity for reflective wave
- Distance from Lumen of NCS mms
- % Diameter Stenosis 40%,50%,60%,70%,80%
- Stenotic lesion distance from Origin mms
- Stenotic lesion distance to end of vessel mms
- Amount of Myocardium subtended in gms
- HeartFlow CCTA-FFR _____FMM_____CCTA-MPI_____

- TOTAL__________ Reversibility potential ________ Progression potential_______
  Occlusion potential____
Vulnerable Plaque: The Paradigm That Failed? Thought Leaders:

Valentin Fuster, ACC
Peter Libby, Brigham
Steve Nissen, Cleveland Clinic

“The Vulnerable Plaque”: Transitioning from a Focus on Individual Lesions to Atherosclerotic Disease Burden for Coronary Artery Disease Risk Assessment
Parting Words of wisdom about total plaque burden:
“Many Plaques are vulnerable!
It’s Whaque a Plaque!“
Partnering with HeartFlow for FFR access

Example of Heart Flow, CT-FFR

FFR was low in a patient with only 60% stenosis because of large necrotic core plaques which attenuated vessel dilatation with adenosine CFD.
Artificial Intelligence for the Interpretation of Coronary Computed Tomography Angiography: Can Machine Learning Improve Diagnostic Performance? Daisuke Utsunomiya*, Takeshi Nakaura and Seitaro Oda Diagnostic Radiology, Faculty of Life Sciences, Kumamoto, Japan *Corresponding author: Daisuke Utsunomiya, Diagnostic Radiology, Kumamoto University, 1-1-1, Honjo, Chuo-ku, Kumamoto, Kumamoto, Japan, Tel: 81-96-373-5261; E-mail: utsunomi@kumamoto-u.ac.jp Received date: September 19, 2016; Accepted date: October 17, 2016; Published date: October 25, 2016

Copyright: © 2016 Utsunomiya D, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Recent development of artificial intelligence (AI) and machine learning system has a potential to improve the clinical diagnosis of coronary artery disease. Coronary computed tomography angiography (CCTA) provides important information of coronary arteries: i.e., stenosis severity, lesion length, plaque attenuation, and degree of calcium deposition. However, the comprehensive analysis of these factors may be difficult. We analyzed patient characteristics and CCTA findings of 56 patients. We used AI (a random forest) to identify the ischemia-related lesions, and compare the diagnostic performance of a random forest and a logistic regression analysis. By the analysis of a random forest, the area under the curve was increased from 0.89 (a logistic regression analysis) to 0.95 (a random forest). Machine learning models can be helpful for the interpretation of CCTA for detecting ischemia-related coronary lesions.
Our team has curated a coronary computed tomographic angiography (CCTA) cardiac data base since we started Advanced Cardiac Imaging at Memorial Hospital in Tampa, Florida in 2004, 14 years and 5,000 patients ago. This data base with Bayesian inference generates hypotheses to learn to recognize plaque morphology, composition and function to predict heart attacks: the CCTA Sherlock Program. In addition, CT-FFR can be derived from a supercomputer in Palo Alto to measure blood flow in the coronary arteries from the CT scan data sets (HeartFlow®).
Our Program

This process has been shown to give direct value and effectiveness in recognizing vulnerable plaques that can lead to MACE (Major Adverse Cardiac Events). Our team is involved in the application of the CCTA Sherlock program with the Sherlock Plaque Score in addition to echocardiography, limited carotid U/S, CMR and EKG rhythm recordings creating Tampa Bay Risk Score for evaluating:

• Cardio-SOF: Special Operations Soldiers, SOCOM
• Cardio-First Responders: Police and Firemen, City of Tarpon Springs
• Cardio-Orthopaedics: Preoperative Pelvic floor, Hip, and Knee surgery patients, Cardio-Oncology, Cancer patients, cardiotoxicity, ICOS
• Cardio-Concierge, Patients with concierge doctors,
• Cardio-RISK, People with multiple risk factors
• Cardio-CAD, People with CP or known CAD
LAD Plaque progression proximal to stent: 20 mos.
LAD Plaque progression proximal to stent: 20 mos.
Protocol
Plaque Regression
Hypothesis

24 hours

Plaque: Transcomposition/Morphology/Functionality to Occlusion

4 days

188 days

420 days

>700 days

48 year-old life saved—CCTA Results

Plaque of interest on the right

Position:

Hershey’s Kiss Plaque NC

Early Reticulated NC

Herhey’s Kiss Plaque NC
Long Term Prognosis!

Putting the Program into Action
And Gathering More Data!

Decades: 30s → 40s → mid 40s → 50s → 60s → 70s → 80s
The Tampa Group

Left to Right Plaque Transcomposition/Morphology/Functionality Equation (TMF)

Observations, Risk, and Objectives

DANGER ZONE

Malignant Coronary Calcinosi

Plaque Erosion/fracture

Calcific stenosis

Benign Coronary calcinosi

Safety Zone

Plaque Ulcer + Activated platelets

Microbiota

Macrophages

STATINS ACCELERATE

reversible

Necrotic Core

Fibrofatty

Fibrotic

Calcified

Safety Zone - 4 days to 188 days to 620 days

Decades: 30 s  40 s  mid 40 s  50  60 s  70 s  80 s

CONFIDENTIAL
Long Term Prognosis

COR-RADS Reporting and Data System

1) 15 years, zero events
2) Less than 1% per year risk
3) If totally calcified, low risk

Risk of these depends on LV, and whether vulnerable plaque is present. or calcific plaque is obstructive or erosive

Definition of significant coronary artery disease

Significant coronary artery disease (CAD) found during CT coronary angiography is ≥ 70% diameter stenosis of at least one major epicardial artery segment or ≥ 50% diameter stenosis of at least one intermediate epicardial artery segment.

F = FFR by Vessel Name

• CAD-RADS 0 0%  no CAD
• CAD-RADS 1 1-24%  minimal non-obstructive CAD
• CAD-RADS 2 25-49%  mild stenosis
• CAD-RADS 3 50-69%  moderate stenosis
• CAD-RADS 4 70-99%  severe stenosis
• CAD-RADS 5 100%  total occlusion
• CAD-RADS N  Non-diagnostic: further evaluation?
• / separates two or three modifiers
• Modifiers: S = stent, G = graft, V = vulnerability

JCCT 10 (2016) 269-281
Applications / Cognification Plans

• Cardio-Orthopaedics
• Patient with + FH and low Ca Score
• Calcium Score Examples over time and theory
• An asymptomatic Cardio-Orthopaedic Patient
• An Asymptomatic SOF Patient
Coronary Plaque Dashboard: 110pts

Danger Zone
- Plaque Ulcer
- Activated Platelets
- Fibrofatty

Dangers Zone
- 75% of MIs
- Calcific stenosis
- Plaque Erosion/fracture

Malignant Coronary Calcinosis
- 25% of MIs
- Chronic Total Occlusion
- Minimal Fibrotic Plaques
- Minimal Calcific Focal Nodules
- Dense Sheets of calcium

Benign Coronary Calcinosis
- 10 patients with patent grafts & stents
- 70% after stent

Freedom of Coronary Morbidity
- 70% + FFR
- 60% + FFR

OSCARS: Orthopaedic Surgery Cardiovascular Anatomy Risk Score for outpatient TJA

LOW RISK
INTERMEDIATE
High Risk

30 patients
64 patients

Decades: 30s → 40s → mid 40s → 50 → → 60s → 70s → 80s
Patient: AL

Prognosis

• Calcium Score 33
• Minimal Nonocclusive calcified LAD and RCA Plaque
• Calcium Score may stay the same (one and Done) or gradually increase by ossification
• Continue Current Rx and Life Style
• No compelling need to repeat study in the future.
Patient with Ca2 of 5 and single calcified plaque 12 years ago. Current Assessment

“One and Done”
"An increasing body of evidence suggests that greater calcium density in plaques is associated with decreased CVD risk,"

Calcium score increases over 11 years: 283 to 625.

Two Patho-etiologies of Progressive Coronary Calcification

1) Transcompositional coronary calcification
   • necrotic core → fibrofatty → fibrous → calcification

2) Ossification Plaque Growth
   • Calcium begats calcium
   • Hydroxyapatite added to pre-existing calcified plaque whether visible on CT or sub CT resolution
CASE 1

How can we change this and prevent myocardial infarction and AF?
Example: Patient with risk of both!

- 68 y/o CMM
- remote history of AF 12 years ago and recent recurrence in Sept, AF with HR 84 when preop evaluation for endoscopy.
- No Known Coronary Artery Disease
- Normal EKG and Echo
- Low Risk for Hip Replacement

But he has episodes of atrial fibrillation and could have hidden CAD. Are we underestimating his risk of hip surgery by age and history alone as nonmodifiable risk factors? Why do we do this?
Sherlock program: COMPOSITE OF INFORMATION FROM A SINGLE CCTA SCAN

Putting the Program into Action
Coronary Plaque Dashboard

Danger Zone
Plaque Ulcer 1-5
Convergent-Divergent Double Cone
Angles: 1,2,3,4,5
Lipid Lake: Necrotic Core
1,2,3,4,5
40, 45, 50, 55, 60, 65

75% of MIs
Activated Platelets
Fibrofatty
Calcific stenosis
Main Left Stenosis
Plaque Erosion/fracture
Chronic Total Occlusion
Minimal Fibrotic Plaques
Benign Coronary Calcinsosis
Minimal Calcific Focal Nodules
Dense Sheets of calcium

NORMAL

Malignant Coronary Calcinsosis
DANGER ZONE
25% of Mls

Individual Patient
Male, Age 68

Decades: 30 s → 40s → mid 40s → 50 → → 60s → 70s → 80s

Sherlock Plaque Score
Actions Taken based on plaque MCF (Sherlock Score)

- Called chief of orthopedics of FOI/TGH who was going to replace the hip.
- Change hospitals and surgeon so my RN navigator can watch patient for a heart attack.
- Plan: Prevent PAF with ranolazine/dronedarone pre, op,& post.
- Medicare won’t cover a stent; patient was told he would have an heart attack and would be rescued, surgery on Friday.
- Navigator followed patient and discharged him home with daughter who had Nurse Navigator’s cell phone number. D/C ed home Sat.
- Patient developed Chest Pain during lunch within an hour of arriving home and called and was told to come back to the hospital. Returned to Hospital. Sat.
Acute Coronary Insufficiency with severe CP after hip surgery and stopping Eliquis: PTCA/Stent of LAD

Random probability of predicting an Mi on any one day post op hip is >1/10,000
Ray RA LAD: Stents in proximal LAD
I’m very happy that I had my hip surgery and also grateful that Dr. Harrison and Sharon prevented me from getting atrial fibrillation but also knew I would get a heart attack which they anticipated and prevented damage to my heart and hip.
48 y/o asymptomatic SOF whose father had a heart attack at age 44.

“You are going to have a heart attack next week and we’ve got to do something to prevent it!”
Double half cone

Dome shaped NC

Benign Calcified Plaque giving a calcium score of 7 in the LAD

Hypothesis

LL + CDDC = ACS
4 days later...

• Patient began having left clavicular (prior fractured during parachute jump) discomfort while playing a video game, similar to before, 30 min duration, burning in quality with sweating. Wife noted change in color, Patient had not initiated his recommended medical therapy. He shrugged off his discomfort, but his wife recalled the CTA plaque demonstration online during husband’s visit, and called EMS for further evaluation.
SOF Survivor

Classified:
This never happened
• My associate, our 4th year fellow and I read Echos, CCTAs, CMRs daily.

• My team and I spend about 15 mins per study teaching CCTAs to our fellow.

• It is possible to read a study every 5 mins but this requires a lot of pointing and clicking with the mouse to get through a study.

• The workflow is very active. For 12 per hour, \(100 = x\) per day. I need to accelerate this by a factor of \(10 \times\) for one division of 15 hospitals and for 20 divisions accelerate by \(200 \times\)!
What do we do?

• How to go from n=100 to n=1000?
  • Example of Successful Models:
    • Numerical Computer Interpretation of EKGs.
    • HeartFlow FFR Numerical Supercomputer use.

• Our model with Deep Learning Supercomputer:
  • personal plaque analysis prognosis with learning through a
cognitive computed prognostic data base
  • FFR equivalent calculation,
  • Medicare billing code for heartFlow’s cardiac CT FFR coronary
artery disease numerical supercomputer calculated blood flow
Increased efficiency and productivity with cost saving, decreased
LOS
  • Reference Images
  • Evidence based current bibliography
How to get to 100x?

20,000 CCTAs/daily

1) Partner with IBM Watson Healthcare for cognitive computing for pattern recognition and storage. Join their ecosystem of corporate partners & software developers
2) Study the workflow to reduce clicks and automate
3) Share all images with Watson data base in our network as well as others
4) Assign coordinates to all arterial segments automatically with software for loci fixing and site comparison (address)
5) Every plaque can be reduced to a string of numbers with an “address”
6) Export all data into a report automatically
7) Use Universal Reporting System nomenclature CAD-RADS 1-6 /v/s/g
8) Use hospital sites for alpha development beta testing.
New Partner: Enlitic

Our Mission

Every time a doctor sees a patient, they are solving a complex data problem. The goal of each case is to arrive at an optimal treatment decision based on many forms of clinical information, such as the patient’s history, symptoms, lab tests, and medical images. The quality and quantity of this data is rapidly improving—it’s estimated to grow over 50-fold this decade, to 25,000 petabytes worldwide by 2020. Our world-class team of medical professionals and data scientists has made it our mission to improve patient outcomes by using this data to its maximum potential.

Enlitic uses deep learning to distill actionable insights from billions of clinical cases. We build solutions to help doctors leverage the collective intelligence of the medical community.
Our mission is to improve personal patient cardiovascular health by co-developing and co-evaluating new artificial intelligence technology for cardiac imaging.
Physician Curators

Digested CTA information with images, prognosis, and recommendations imported into EMR for clinical cardiologist review, sign off, and charge, like the GE Muse EKG system.
The Scottish Study Compared outcomes of patients suspected of having angina pectoris randomly assigned to stress testing modalities versus CCTA.

The outcome of this study demonstrated:

1) Patients receiving stress tests had 50% less heart attacks and mortality.
2) Patients receiving CCTAs had 50% less heart attacks and mortality.
3) There was no difference between the two groups.
4) Stress tests resulted in better targeted investigations and treatment.

Answer: 2) Patients receiving CCTAs had 50% less heart attacks and mortality. This was because of the findings resulted in better targeted investigations and treatments.

CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial
The SCOT-HEART investigators††Members listed at end of report
Published: 15 March 2015, Lancet, Volume 385, No. 9985, p2383–2391, 13 June 2015