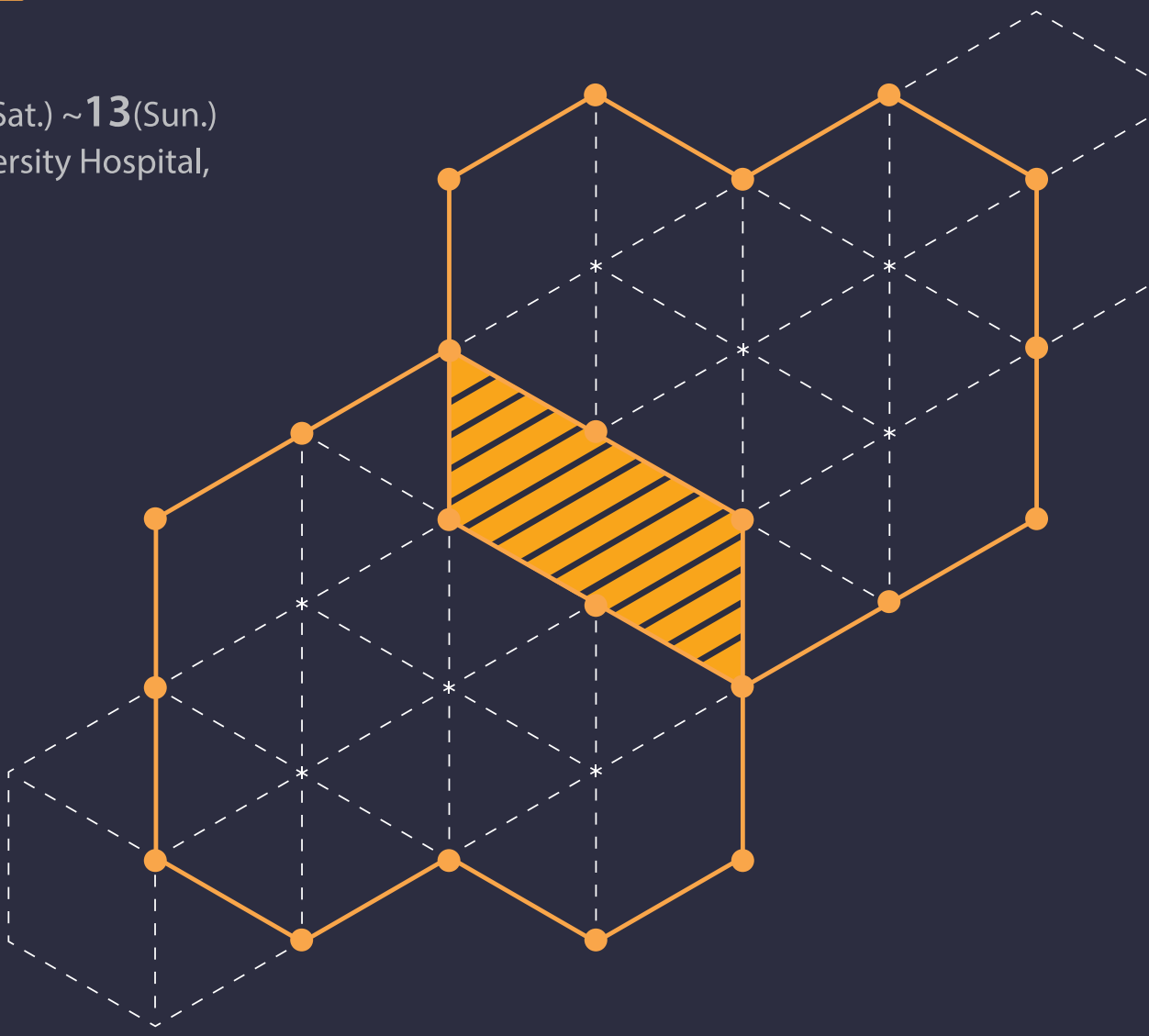
Cardiovascular Imaging in Computed Tomography Summit

2018. 5. 12(Sat.) ~13(Sun.)
Konkuk University Hospital,
Seoul, Korea

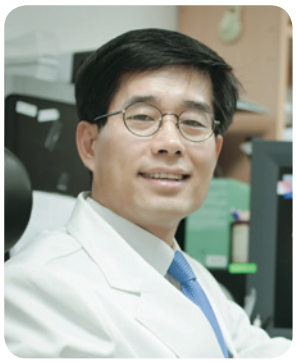


Hosted by CIVICS

Endorsed by SOCIETY OF CARDIOVASCULAR COMPUTED TOMOGRAPHY, SCCT KOREA IRC, ASCI Asian Society of Cardiovascular Imaging, KSCI KOREAN SOCIETY OF CARDIOVASCULAR IMAGING, NASCI North American Society for Cardiovascular Imaging

Contents

Welcome Message



On behalf of the Organizing Committee of the Cardiovascular Imaging in Computed Tomography Summit (CIVICS 2018), it is our great pleasure and honor to invite you to the 3rd meeting of the CIVICS, which will be held from May 12 to 13, 2018 in Seoul, Korea.

The CIVICS 2018 will deal with the up-to-date and practical knowledge and share academic achievements on cardiac CT images. This year, we will include cardiac MRI and echocardiography as well. The organizing committee designs a full two-day program that will cover the educational programs and the latest trends in cardiac imaging field. We invited many distinguished speakers in cardiovascular imaging field from Asia and the United States. Prof. U. Joseph Schoepf will give us the excellent talk in the plenary session.

The 3rd meeting aims at the good relations among all participants and speakers in Asian countries and domestic areas. I am sure that the CIVICS 2018 will be valuable and beneficial to all participants, and will contribute to the improvement of scientific standards and quality in our field. In addition to providing valuable scientific knowledge, the organizing committee will provide opportunities to socialize and communicate with colleagues and friends in Korea and Asian countries.

We believe that this conference will become the basic network and working environment for cardiac CT images in Asia. I sincerely want to invite all of you to join us in the 3rd annual meeting of the CIVICS in Seoul, Korea.

Tae Hoon Kim

President, CIVICS 2018 Organizing Committee

About CIVICS

Our Objectives

We seek to accomplish the following:

- Update our members on the latest research findings in the field of Cardiovascular Imaging and Computed Tomography;
- Facilitate academic exchange;
- Provide training and professional development for our members;
- Develop networking opportunities for our members;
- Promote the growth of our field; and
- Strengthen scientific and mutual benefits by cooperating with other similar associations

History of CIVICS

Over the last decade, rapid technological advancements in Computed Tomography (CT) has made it possible for us to get contrast-enhanced images of coronary arteries in high resolution with just small amounts of radiation. Because so many experts find the use of CT to be highly appropriate and efficient, the rate of CT's usage in Korea, despite its high cost, is now the second highest among OECD. As of October 1, 2012, the Health Insurance Review & Assessment Service (HIRA) recognized the appropriate indications of the CT for coronary artery. In light of these trends, and the everchanging medical world, CIVICS was founded to meet the needs of those medical specialists who focus on the study of cardiovascular imaging in CT. CIVICS endeavors to enhance the effectiveness and clinical usefulness of the cardiovascular imaging of CT. We try to accomplish this by promoting academic activities throughout Asia, for experts from a number of disciplines including cardiology, radiology and other specialists who study in this field.

CIVICS 2018 Organizing Committee

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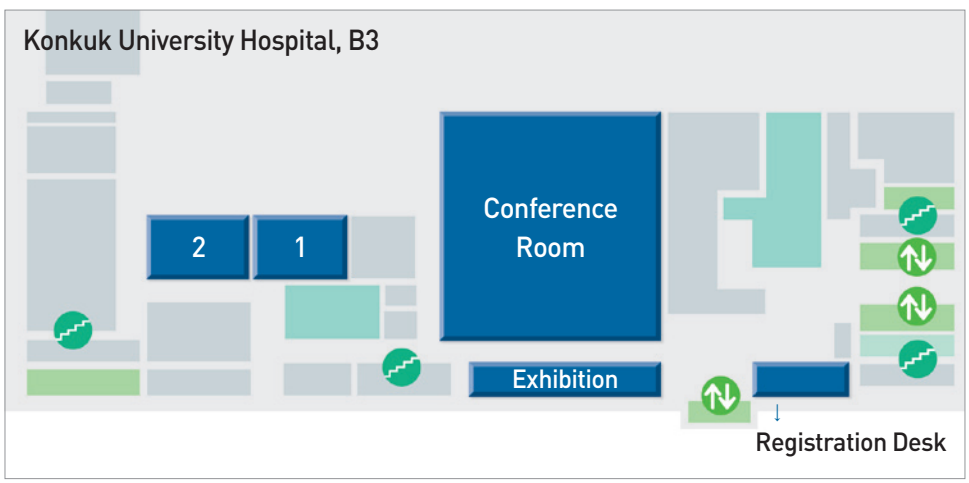
Consultant	Gerald de la Salle	Korea University

Meeting Information

General Information

Title	Cardiovascular Imaging in Computed Tomography Summit
Date	2018. 05. 12(Sat.) ~ 13(Sun.)
Venue	Konkuk University Hospital, Seoul, Korea
Hosted by	CIVICS 2018 Organizing Committee
Endorsed by	North American Society for Cardiovascular Imaging (NASCI) Society of Cardiovascular Computed Tomography (SCCT) Asian Society of Cardiovascular Imaging (ASCI) Korean Society of Cardiovascular Imaging (KOSCI)
Official Language	English

Floor Plan



Conference Room	- CIVICS Main Lecture
Lecture Room 1	- Workstation
Lecture Room 2	- Secretariat - Speaker's Lounge

Industrial Exhibition

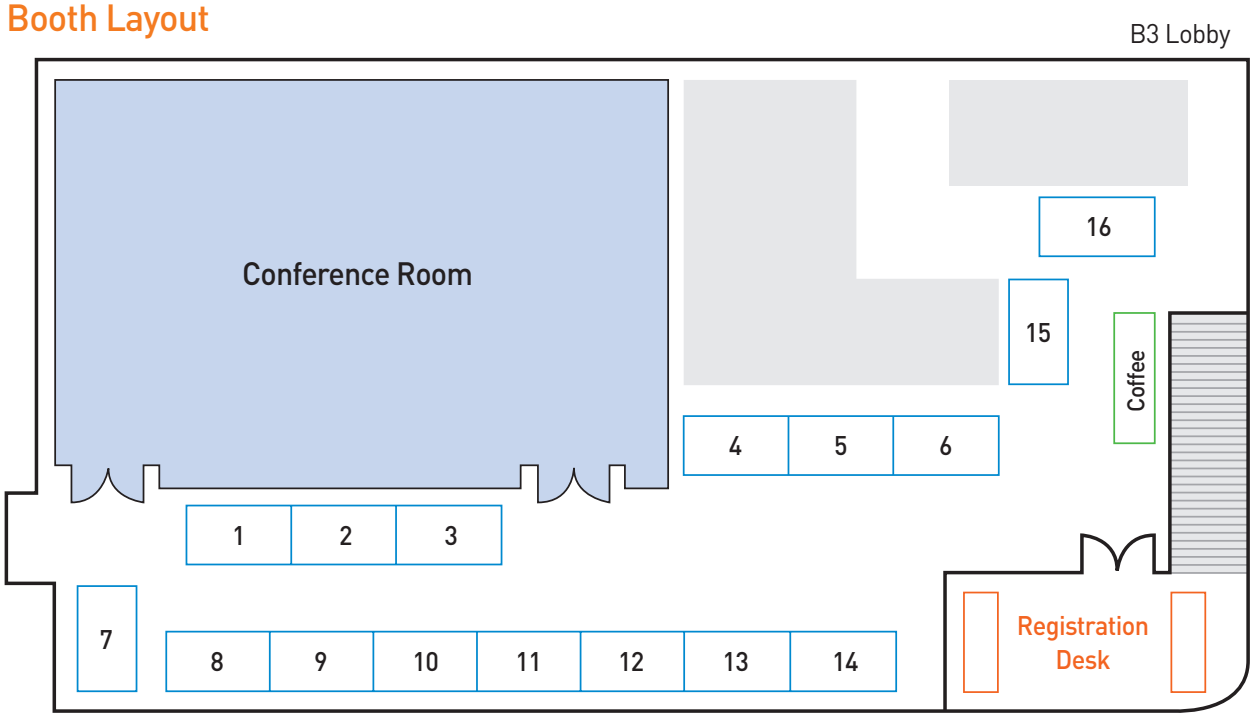
Place

Konkuk University Hospital, B3 Lobby

Date & Time

May 12(Sat.) 08:30 ~ 17:30
May 13(Sun.) 08:30 ~ 17:30

Booth Layout



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Scientific Program

May 12 (Sat.) Day 1

Time	Session & Lecture	Chairperson & Speakers
08:40-10:30	**Session 1. From Request to Image Presentation (Korean Language)**	Bae Young Lee (The Catholic University of Korea, St. Paul's Hospital, Korea) Yun-Hyeon Kim (Chonnam National University Hospital, Korea)
08:40-08:55	CT and CMR in clinical practice	Iksung Cho (Chung-Ang University Hospital, Korea)
08:55-09:10	How to get good cardiovascular CT, particularly in challenging patients	Doo Kyoung Kang (Ajou University Hospital, Korea)
09:10-09:40	CT의 reconstruction 및 해석 - hands on (workstation 이용) - coronary artery, valve, cardiomyopathy	Dong Hyun Yang (Asan Medical Center, Korea)
09:40-09:55	Checklist and preparation of patient before the MR	Sung Ho Hwang (Korea University Anam Hospital, Korea)
09:55-10:10	How to get appropriate protocol of cardiac MR	Cherry Kim (Korea University Ansan Hospital, Korea)
10:10-10:30	Panel Discussion	Hong-Mi Choi (Seoul National University Bundang Hospital, Korea) Kyongmin Beck (The Catholic University of Korea, Seoul St. Mary's Hospital, Korea) Hyun Woong Shin (Daegu Fatima Hospital, Korea), Byeong Ryeol Park (Cheomdan Medical Center, Korea)
10:30-10:45	Intermission	
10:45-10:50	Opening Ceremony	Tae Hoon Kim (Gangnam Severance Hospital, Korea)
10:50-12:00	**Session 2. Present and Future of Cardiac Imaging from Leaders**	Jae Hyung Park (Myongji Hospital, Korea) Jae-kwan Song (Asan Medical Center, Korea)
10:50-11:15	Plenary Session I : Recent update on comprehensive role of cardiac CT	U. Joseph Schoepf (Medical University of South Carolina, USA)
11:15-11:40	Plenary Session II : The future of cardiac imaging: Expectations and concerns - Cardiac Imaging in the era of artificial intelligence: Hopes, hypes, and caveats	Tae-Hwan Lim (University of Ulsan College of Medicine, Korea)
11:40-12:00	Panel Discussion	Jongmin Lee (Kyungpook National University Hospital, Korea) Yong-Jin Kim (Seoul National University Hospital, Korea)
12:00-12:20	Luncheon Symposium I - Simens Healthcare	Tae Hoon Kim (Gangnam Severance Hospital, Korea) U. Joseph Schoepf (Medical University of South Carolina, USA)
12:20-13:20	Lunch	
13:20-15:00	**Session 3. Ischemic Heart Disease**	Hweung-kon Hwang (Konkuk University Hospital, Korea) Yeon Hyeon Choe (Samsung Medical Center, Korea)
13:20-13:40	FFR CT - challenge and limitation	Bon-Kwon Koo (Seoul National University Hospital, Korea)
13:40-14:00	CT-perfusion - challenge and limitation	Akira Kurata (Ehime University, Japan)
14:00-14:20	Clinical impact of plaque characteristics	Eun Ju Chun (Seoul National University Bundang Hospital, Korea)
14:20-14:40	SPECT and PET for ischemia	Sang-Geon Cho (Chonnam National University Hospital, Korea)
14:40-15:00	Panel Discussion	Hyung-Bok Park (Catholic Kwandong University, International St. Mary's Hospital, Korea) Yeonyee E. Yoon (Seoul National University Bundang Hospital, Korea) Kyoung Sook Won (Keimyung University Dongsan Medical Center, Korea), Jin Hur (Severance Hospital, Korea)
15:00-15:20	Intermission	
15:20-17:00	**Session 4. Expanded Role of CT in the Evaluation of Valvular Heart Disease**	Hyun-keun Chee (Konkuk University Hospital, Korea) Kee-Sik Kim (Daegu Catholic University Medical Center, Korea)
15:20-15:40	Echocardiographic evaluation of VHD (TAVI 위주) - possibilities and limitation	Geu-Ru Hong (Severance Hospital, Korea)
15:40-16:00	Expanding role of CT in VHD	Young Jin Kim (Severance Hospital, Korea)
16:00-16:20	Interventionist's expectation of VHD (TAVI 위주) - pre- and postop	Jung-min Ahn (Asan Medical Center, Korea)
16:20-16:40	Surgeon's expectation of VHD - pre- and postop	Byung Chul Chang (CHA University Bundang Medical Center, Korea)
16:40-17:00	Panel Discussion	Young Joo Suh (Severance Hospital, Korea) Jae-Hyeong Park (Chungnam National University Hospital, Korea) Jung-Hee Lee (Yeungnam University Medical Center, Korea), Soonchang Hong (Wonju Severance Christian Hospital, Korea)

Scientific Program

May 13 (Sun.) Day 2

Time	Session & Lecture	Chairperson & Speakers
08:40-10:20	**Session 5. Beyond the ACS in Patients with Acute Chest Pain**	Seung Min Yoo (CHA University Bundang Medical Center, Korea) Akira Kurata (Ehime University, Japan)
08:40-09:00	Update of new cardiac biomarkers	Jang-Whan Bae (Chungbuk National University Hospital, Korea)
09:00-09:20	CT diagnosis of ACS and mimics - focusing the heart	Ji Won Lee (Pusan National University Hospital, Korea)
09:20-09:40	CT diagnosis of acute aortic diseases- significant mimickers of ACS	Takuya Ueda (Tohoku University Hospital, Japan)
09:40-10:00	MR diagnosis of ACS mimics	Sung Mok Kim (Samsung Medical Center, Korea)
10:00-10:20	Panel Discussion	Sung Gyun Ahn (Wonju Severance Christian Hospital, Korea) Sang Min Park (Chuncheon Hallym University Medical Center, Korea) Kwang Nam Jin (SMG - SNU Boramae Medical Center, Korea), Young Jun Cho (Konyang University Hospital, Korea)
10:20-10:35	Intermission	
10:35-12:15	**Session 6. Debate - Hypertrophic Cardiomyopathy**	Sang-Chol Lee (Samsung Medical Center, Korea) Tae-Hwan Lim (University of Ulsan College of Medicine, Korea)
10:35-10:55	How risk stratification and prevent the SCD (overall - family hx, gene, sx, ECG, echo..)	Jun-Bean Park (Seoul National University Hospital, Korea)
10:55-11:15	Surgical treatment of HCM -preop evaluation and follow-up	Joonhwa Hong (Chung-Ang University Hospital, Korea)
11:15-11:35	Role of CMR for risk stratification	Seung-Pyo Lee (Seoul National University Hospital, Korea)
11:35-11:55	Differential diagnosis of HCM mimics using CMR	Chul Hwan Park (Gangnam Severance Hospital, Korea)
11:55-12:15	Panel Discussion	Dong Jin Im (Severance Hospital, Korea) In-cheol Kim (Keimyung University Dongsan Medical Center, Korea) Ki Seok Choo (Pusan National University Yangsan Hospital, Korea), Wook Sung Kim (Samsung Medical Center, Korea)
12:15-12:45	Luncheon Symposium II - Central Medical Service, GE Healthcare Korea	
12:45-13:25	Lunch	
13:25-15:05	**Session 7. Cutting Edge Techniques in Cardiovascular Imaging**	Jung Im Jung (The Catholic University of Korea, Seoul St. Mary's Hospital, Korea) Soon Jun Hong (Korea University Anam Hospital, Korea)
13:25-13:45	Dual and multi-energy CT	U. Joseph Schoepf (Medical University of South Carolina, USA)
13:45-14:05	T1 mapping beyond delayed MR	Xiaohai Ma (Beijing Anzhen Hospital, China)
14:05-14:25	Viability assessment with minimal or non-contrast imaging	Hyuk Jae Chang (Severance Hospital, Korea)
14:25-14:45	Myocardial functional assessment by CMR and echocardiography	Eui-Young Choi (Gangnam Severance Hospital, Korea)
14:45-15:05	Panel Discussion	Gong Yong Jin (Chonbuk National Universtiy Hospital, Korea) Hongseok Ko (National Medical Center, Korea) Heesun Lee (Seoul National University Hospital Healthcare System Gangnam Center, Korea) Hyemoon Chung (Kyung Hee University Medical Center, Korea)
15:05-15:20	Intermission	
15:20-16:50	**Session 8. SCCT - Beyond the Horizon**	Byoung Wook Choi (Severance Hospital, Korea) Takuya Ueda (Tohoku University Hospital, Japan)
15:20-15:35	New contrast agents for spectral CT	U. Joseph Schoepf (Medical University of South Carolina, USA)
15:35-15:50	Myocardial microcirculation	Akira Kurata (Ehime University, Japan)
15:50-16:05	Cardiovascular molecular imaging	Xiaohai Ma (Beijing Anzhen Hospital, China)
16:05-16:20	Onco-cardiology imaging	Yoojin Hong (Severance Hospital, Korea)
16:20-16:35	Research Progress of Cardiac CT on RSNA 2017	Jian Cao (Peking Union Medical College Hospital, China)
16:35-16:50	Panel Discussion	Hwanseok Yong (Korea University Guro Hospital, Korea) Hyun Jung Koo (Asan Medical Center, Korea) Eun-Ju Kang (Dong-A University Hospital, Korea), Jin Young Yoo (Chungbuk National University Hospital, Korea)

Day 1
May 12 (Sat.)

SESSION 1

From Request to Image Presentation (Korean Language)

Chairperson **Bae Young Lee** (The Catholic University of Korea, St. Paul's Hospital, Korea)
Yun-Hyeon Kim (Chonnam National University Hospital, Korea)

Presentation

CT and CMR in clinical practice
Speaker Iksung Cho (Chung-Ang University Hospital, Korea)

How to get good cardiovascular CT, particularly in challenging patients
Speaker Doo Kyoung Kang (Ajou University Hospital, Korea)

CT의 reconstruction 및 해석 - hands on (workstation 이용) - coronary artery, valve, cardiomyopathy
Speaker Dong Hyun Yang (Asan Medical Center, Korea)

Checklist and preparation of patient before the MR
Speaker Sung Ho Hwang (Korea University Anam Hospital, Korea)

How to get appropriate protocol of cardiac MR
Speaker Cherry Kim (Korea University Ansan Hospital, Korea)

Panel Discussion

Panel Hong-Mi Choi (Seoul National University Bundang Hospital, Korea)
Kyongmin Beck (The Catholic University of Korea, Seoul St. Mary's Hospital, Korea)
Hyun Woong Shin (Daegu Fatima Hospital, Korea)
Byeong Ryeol Park (Cheomdan Medical Center, Korea)

CT and CMR in clinical practice

Iksung Cho (Chung-Ang University Hospital, Korea)

MEMO

How to get good cardiovascular CT, particularly in challenging patients

Doo Kyoung Kang (Ajou University Hospital, Korea)

Contents

1. Patient preparation
2. Acquisition parameters
3. Acquisition modes (Scan techniques)
4. Contrast medium injection

Patient preparation

1. Instructions for patients
2. Heart rate control
3. Intravenous access, ECG lead attachment , and patient education
4. Nitroglycerin (NTG)

Instructions for patients

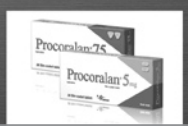
- Avoid solids for 4 hours before the CT examination and caffeine for 12 hours before CT examination.
  - Adequate oral hydration with drinking clear fluids up to 1 hour before the examination.
- Check allergies to contrast agent, renal insufficiency (serum creatinine > 1.5-2.0 mg/dL), pregnancy, severe heart failure and contraindications of b-blocker and NTG.
  - Stop Viagra® (sildenafil), Levitra® (vardenafil) for 24 hrs and Cialis® (tadalafil) for 48 hrs, if patient has a plan to administrate NTG.

Heart rate control

- β-blockers are the first-line treatment agent.
  - Metoprolol and then atenolol: cardio-selective β-blockers
- Effect of β-blockers
  - Reduce the heart rate
  - Helpful in patients with irregular heart rates
  - Prevent the heart rate variation following contrast injection and nitroglycerine administration.

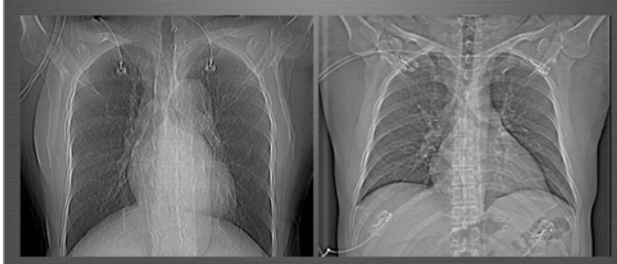
Administration of β-blocker

- Oral administration
  - 50-100 mg of metoprolol administered orally 1 hour prior to CT scanning. After 1 hour, if the heart rate is not in the desired range, additional intravenous β-blocker administration should be considered.
- IV β-blocker administration
  - Initially 2.5 mg dose of metoprolol IV over 1 min
    - a second dose of 2.5 mg of metoprolol
    - up to two additional doses of 5 mg each of metoprolol
- Calcium channel blockers
- Ivabradine



IV access, patient positioning and ECG lead attachment

- Intravenous (IV) access in antecubital vein using 18-G catheter or larger.
- ECG leads placement outside scan range.



- Mid-clavicular line + between 2nd and 4th intercostal space
- Left mid-abdomen + 10cm from the umbilicus
- Mid-clavicular line + directly below the clavicle
- Mid-clavicular line + 6th and 7th intercostal space

Patient education

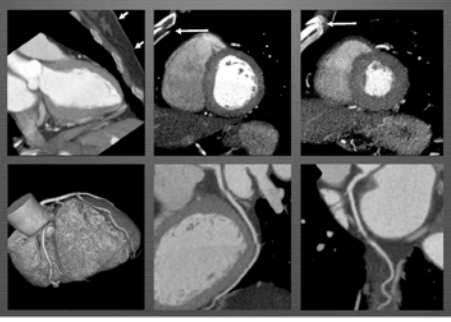
- Redundant breathing instruction and breath-hold exercise
  - Breathe in – breathe out – breathe in – hold your breath
  - Comfortable breath in about 75% of full inspiration

Maximum inspiration and Valsalva maneuvers
↑ intra-thoracic pressure → delay in systemic venous return
→ suboptimal opacification of the coronary arteries

- Increased anatomic coverage
  - High-pitch DSCT in patients with HR < 60bpm
  - Use wide detector CT

Respiratory motion artifact

- Patient's breathing during scanning
- Blurring, gaps, overlap (double contour) and also stair-step artifacts.
  - Shown as across the scan field
  - Stair-step (misregistration) artifacts of sternum or chest wall



Nitroglycerin (NTG)

- Nitroglycerin is a potent vasodilator, which dilates both normal and abnormal coronary arteries by relaxing vascular smooth muscle.
  - actually improved diagnostic accuracy of coronary CTA

- Administration of NTG
  - Single tablet of nitroglycerin (0.4-0.6mg) sublingually 1-2 minute before CT scanning
  - 2 puffs (400-800mcg) of sublingual spray 5 minutes before initiation of scanning

Acquisition parameters

1. Tube voltage & Tube current
2. Gantry rotation time (speed)
3. Table increment (feed) and pitch
4. Field of view (FOV) and scan range

Optimal tube voltage and tube current

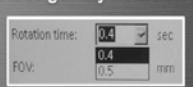
- Balance between sufficient image quality and low radiation dose

- SCCT guideline
  - 100 kV: ≤90 kg or BMI ≤30 kg/m^2
  - 120 kV: > 90 kg and BMI > 30 kg/m^2

- Tube current (mA) may be manually selected or protocolized based on the patient's BMI and chest circumference.
  - Range: 300 ~ 800 mA.
  - Higher tube current
    - heavily calcification / Intracoronary stent / obese patients

Gantry rotation time (speed)

- For cardiac CT examination, the fastest gantry rotation time is typically selected.



- The gantry rotation times of the most recent scanners range from 270 to 350 msec.

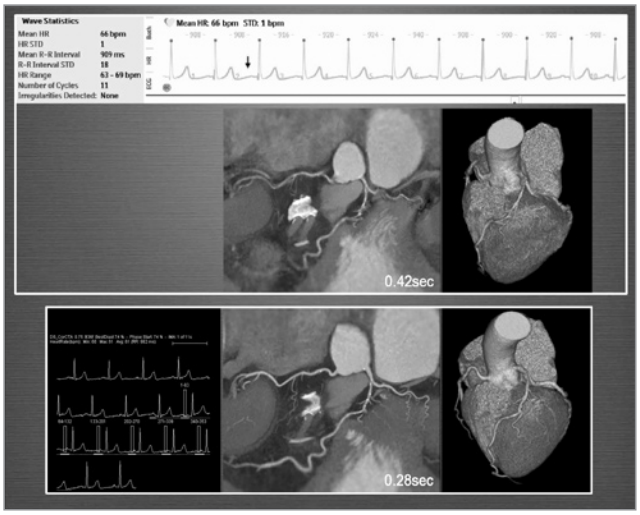
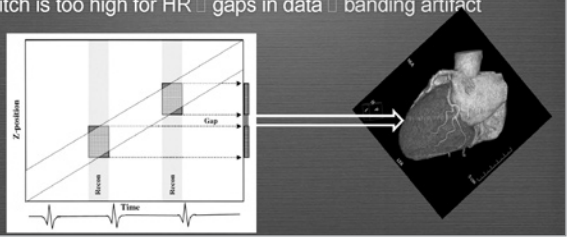
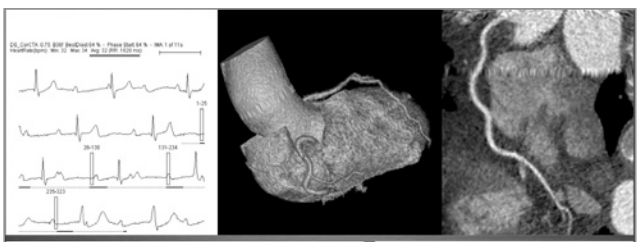


Table increment (feed) and pitch

- Pitch is defined as the longitudinal (z-axis) table increment during one gantry rotation (360°) to total x-ray beam width.
- In retrospective ECG gated CT, typical pitch factors for cardiac MDCT range from 0.2 to 0.4.
- If pitch is too high for HR → gaps in data → banding artifact





Concept of minimal heart rate for each pitch value to avoid interpolation artifact when using dual-source CT: a phantom study

Joon-Won Kang · Kyung-Hyun Do · Jae-Yeon Chang · Hyun Jung Cho · Joon Beom Seo · Tae-Hwan Lim

Int J Cardiovasc Imaging (2010) 26:103–109

Table 1 Adaptive pitch values according to the estimated heart rate

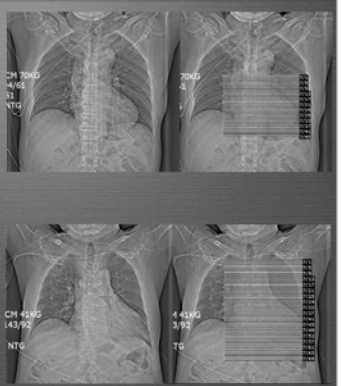
Heart rate (bpm)	Pitch value
>40	0.2
>50	0.22
>60	0.28
>70	0.33
>80	0.39
>90	0.44
>100	0.5

MinHR for the pitch value 0.2 was 37 bpm
MinHR for the pitch value 0.5 was 91 bpm

If the heart rate of the patient drops below 37 bpm → prospective method

Field of view (FOV) and scan range

- The field of view (FOV)
  - FOV of 200 – 250 mm or less is suitable for cardiac CT.
- Scan range
  - For coronary CTA: from the carina to the bottom of the heart (approximately 10–12 cm long)
  - In patients who underwent bypass grafts: extended upper range to the middle of the clavicle (18-25cm)



Acquisition modes (Scan techniques)

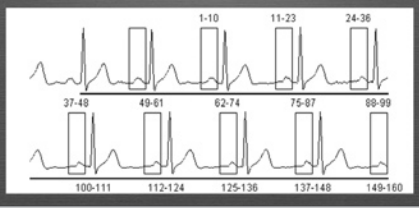
1. Prospective ECG-triggering (step-and-shoot or sequential mode)
2. Retrospective ECG-gating
3. Volume CT technique using 256 or 320 slice wide detector
4. High pitch technique

Prospective ECG-triggering (step-and-shoot or sequential mode)

- The x-ray tube is turned on only during a certain previously defined phase of the R-R interval, but no radiation is delivered during the remainder of the R-R interval.
  - Maximum heart rate threshold
    : 60-65 bmp of single-source CT and < 75bpm for dual-source CT
  - Functional information is not available.

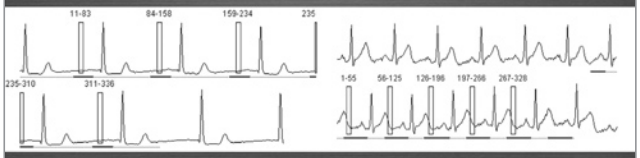
Retrospective ECG-gating

- Images are acquired throughout the entire cardiac cycle during simultaneous ECG recording.
- Image reconstruction is performed in specific periods of the cardiac cycle retrospectively referencing to the ECG signal.
- A low pitch (0.2-0.4) is needed to avoid gaps in anatomic coverage.



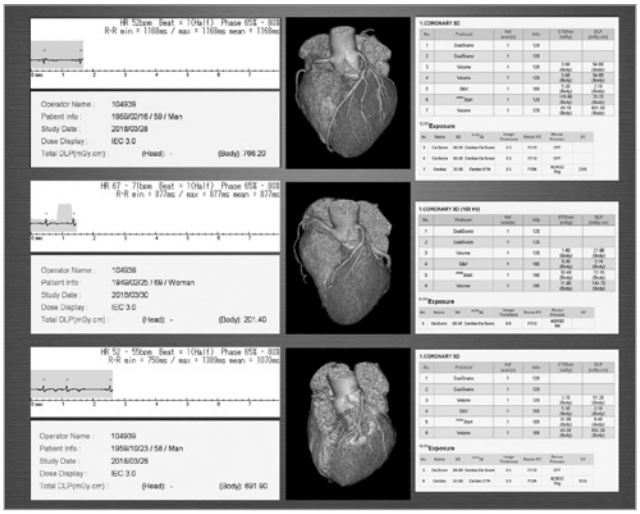
Retrospective ECG-gating

- Less dependent on heart rate, and allow ECG editing retrospectively.
- Evaluate cardiac function
- Higher radiation exposure of between 12 and 20mSv.
- ECG based tube current modulation (ECG pulsing) technique
  - Low heart rate < 65bpm pulsing window of 65-75% of R-R interval.
  - Higher heart rate > 65bpm pulsing widow of 30-70% of R-R interval to cover both systolic and diastolic phase.



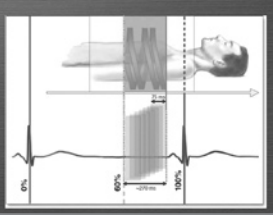
Volume CT technique
using 256 or 320 slice wide detector

- Acquire images of the whole heart in a single heart beat.
- No table movement during data acquisition is able to eliminate the stair-step artifacts.
- The lack of slice overlap leads to low radiation exposure.



High pitch technique

- Prospective ECG-triggered helical scan (Flash mode or high-pitch technique) with dual-source CT system
  - Rotation time of 280–330 msec temporal resolution of 75–83 msec.
  - Gapless z-sampling with a high pitch (up to 3.4) enables complete coverage of the heart in a single heart beat.
- Radiation dose can be reduced to 1mSv and below.
- Requires heart rates of less than 60 – 65 bpm.

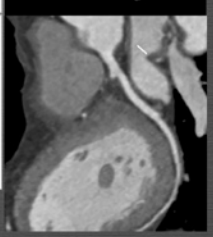


High pitch technique

Physician: 100271
Operator.

Total mAs 941 Total DLP 145 mGycm

	Scan	kV	mAs / ref.	CTDIvol mGy	DLP mGycm	TI s	cSL mm
Patient Position F-SP							
Topogram	1	120	35 mA			3.6	0.6
DS_CaScSeq	2D	120	56 / 80	2.18	30	0.17	1.2
PreMonitoring	6	120	20	1.00	1	0.28	10.0
Contrast Monitoring	7	120	20	4.98	5	0.28	10.0
FI_CorCTA	12D	120	323 / 370	5.27	109	0.28	0.6



Selection of optimal CT scan protocol

- Prospective ECG-triggered techniques
  - in patients who have stable sinus rhythm and low heart rates
  - If the cardiac anatomy or coronary artery disease is the main concern
- Retrospective ECG-gated techniques
  - in patients with irregular heart rhythm or high heart rates or both
  - If cardiac functional information is the main concern
- Large (wide) detector array of 256-or 320-slice or dual-source CT system prospective ECG-triggering
  - in patients who cannot breath hold
  - low radiation exposure

Contrast medium injection

1. Optimum level of coronary artery enhancement
2. Contrast concentration, volume, and injection rate
3. Saline chasing technique and injection protocol
4. Contrast timing methods

Optimum coronary artery enhancement

- The optimal vascular attenuation for stenosis detection in coronary CTA ranges from 250HU to 350HU.
  - Higher attenuation > 500HU significant underestimation of stenosis in smaller vessels.
  - Lower attenuation < 200HU poor coronary 3-D image.

TABLE 2: Summary of Detectability Rates for Vessel Attenuation Groups

Degree of Stenosis (%)	200 H	300 H	350 H	500 H
3-mm vessel diameter				
25	83.3	91.1	100	0*
50	100	100	100	66.7*
75	100	100	100	100
5-mm vessel diameter				
25	100	100	100	100
50	100	100	100	100
75	100	100	100	100

TABLE 4: Summary of Measured Accuracy of Percentage Stenosis

Degree of Stenosis (%)	200 H	300 H	350 H	500 H
5-mm vessel diameter				
25	36.1 ± 14.3*	26.8 ± 5.0	25.2 ± 3.4	21.5 ± 2.5
50	61.7 ± 16.3	56.9 ± 4.3	55.6 ± 4.0	49.8 ± 3.1
75	80.4 ± 10.8	80.6 ± 7.0	75.2 ± 7.1	75.8 ± 2.7
2-mm vessel diameter				
25	29.3 ± 6.8	25.1 ± 3.4	24.5 ± 6.2	NA
50	56.9 ± 15.4	52.8 ± 10.1	47.2 ± 7.1	21.3 ± 9.7*
75	79.3 ± 13.2	73.7 ± 9.5	73.4 ± 10.5	39.5 ± 13.4*

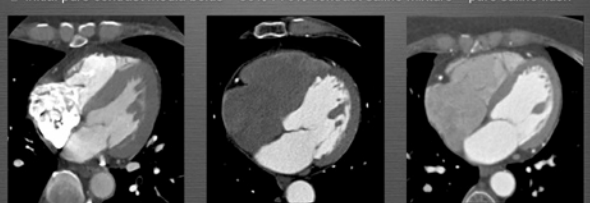
Fei et al. AJR 2008; 191:43–49

Contrast agent

- Concentration of contrast medium
  - High iodine concentrations (e.g. 350, 370, or 400mgI/mL)
- Contrast volume
  - As the speed of CT data acquisition increase, smaller amount of contrast media is required.
  - With 64-slice scanners, the required contrast volume is as low as 50–70ml.
- Injection rate
  - Injection rates of up to 4-6mL/s via an antecubital vein are commonly used for coronary CTA.

Injection protocol

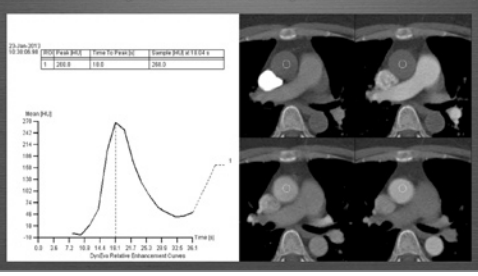
- Uniphasic (monophasic) injection protocol
  - Streak and beam-hardening artifacts.
- Biphasic injection protocols
  - Pure (or undiluted) contrast media + Saline bolus of 15-20mL
  - Biphasic concentration protocol: Initial undiluted contrast bolus + diluted contrast bolus
- Triphasic injection protocols
  - Initial pure contrast media bolus + 30% : 70% contrast-saline mixture + pure saline flush



Pure contrast only | Pure saline flush | 40% contrast flush

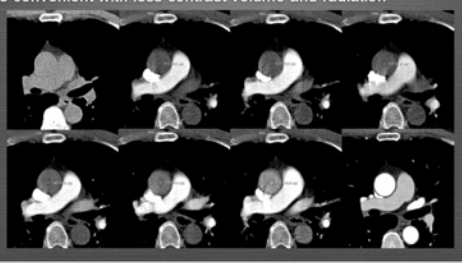
Contrast timing methods

- The test-bolus (timing-bolus) method
  - Based on test-bolus IV injection of 10-20ml of contrast media, followed by a 30-50ml saline flush during dynamic low-dose monitoring scans.
  - Scan start delay: time to peak + additional 3–4sec delay
  - Practice breath-holding / experience contrast agent / test IV access patency

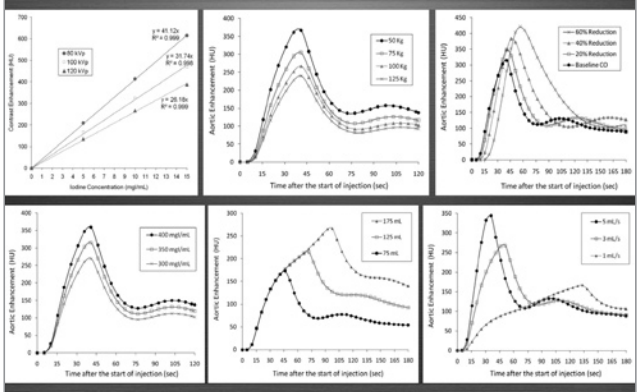


Contrast timing methods

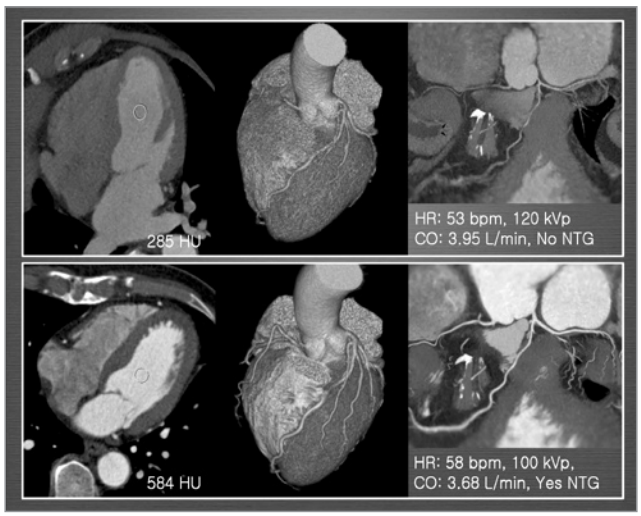
- Automated bolus tracking (bolus triggering) technique
  - Acquisition of a series of dynamic low-dose (e.g. 120 kVp, 20 mAs)
    - certain trigger threshold > 100-200HU
    - diagnostic scanning after 4-8sec trigger delay
  - More convenient with less contrast volume and radiation



Simulated contrast enhancement curves



Bae KT. Radiology. 2010;256:32-61



Thank you for your attention

CT의 reconstruction 및 해석 - hands on (workstation 이용) - coronary artery, valve, cardiomyopathy

Dong Hyun Yang (Asan Medical Center, Korea)

Contents

- Coronary artery disease
  - Coronary plaque, CT perfusion
- Coronary stents
  - Metallic stents, BVS
- Native valvular heart disease
  - Aortic valve, mitral valve
- Prosthetic valvular heart disease
- Hypertrophic cardiomyopathy

Coronary Artery Disease: Live Demo

- High risk plaque morphology
  - Low attenuation, Napkin ring sign, Positive remodel
- Plaque regression after medical treatment
- Coronary artery dissection
- Recanalized organizing thrombus
- CT perfusion
- Comparison between CT and OCT

Coronary Stent: Live Demo

- In-stent restenosis
- Stent neoatherosclerosis
- Mechanical deformity of the stent
- Bioresorbable Vascular Scaffolds
- Comparison between CT and OCT

Valvular Heart Disease: Live Demo

- Aortic stenosis
- Aortic regurgitation
- Mitral regurgitation
- Infective endocarditis

Prosthetic Valve: Live Demo

- Subvalvular pannus
- Valvular thrombus
- Paravalvular leakage

Hypertrophic Cardiomyopathy

- Left ventricular geometry using CT
- Systolic anterior motion of the mitral valve
- Papillary muscle abnormality

MEMO

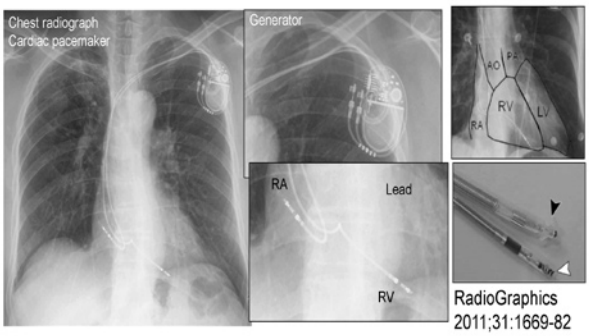
Checklist and preparation of patient before the MR

Sung Ho Hwang (Korea University Anam Hospital, Korea)

Keywords & Key Questions

- Cardiac Pacemaker & MRI
- Can patients with pacemaker perform MRI?
- Can patients with pacemaker perform cardiac MRI?

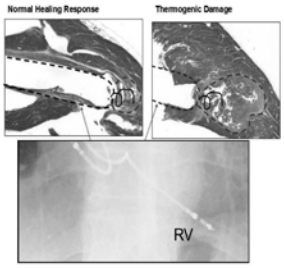
Cardiac Pacemaker-Arrhythmia



RadioGraphics 2011;31:1669-82

Under MRI Environment

- Cardiac pacemaker (ferromagnetic material)
  - Tissue heating, pacing leads
  - Movement and vibration
  - Inappropriate pacing, reset
- Contraindication to MRI (?)



Patients with Pacemaker

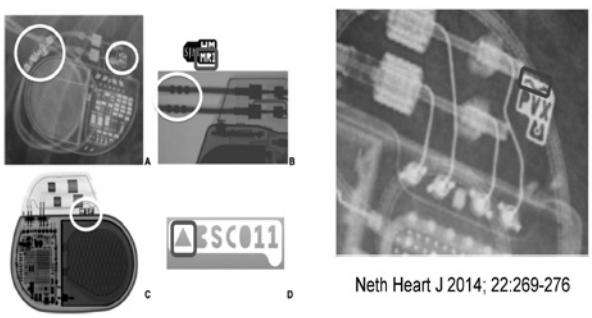
- MRI need ↑, over the lifetime
- MR safe: no hazards in all MRI environments
- MR conditional: no hazards in specific MRI environments

PACE 2005;28:2878-91

MR-conditional Pacemaker

Company	Device	Model	Approved Range
Biotronik	pacemaker	EVIA DR-T	3.0T
	pacemaker	EVIA SR-T	3.0T
	pacemaker	SAFIO S	3.0T
	pacemaker	SOLIA S, T, JT	3.0T
	ICD	IFORIA 7 DR-T	1.5T
	ICD	IFORIA 7 VR-T	1.5T
Boston Scientific	pacemaker	Accolade MRI SR	3.0T
	pacemaker	Accolade MRI DR	3.0T
	pacemaker	Ingevity MRI lead	3.0T
	pacemaker	Fineline Lead	1.5T
	ICD	Autogen MRI SR	1.5T

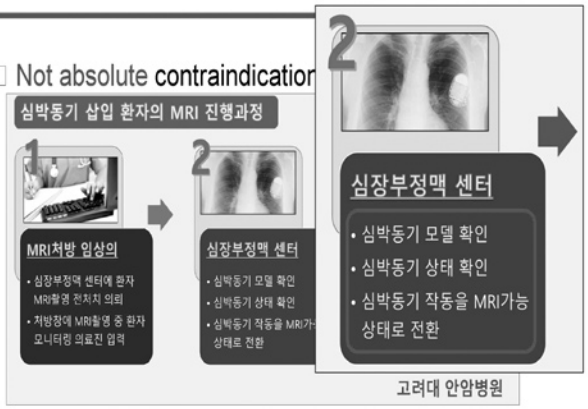
Marker of MR-conditional Pacemaker



Neth Heart J 2014; 22:269-276

MRI for Patients with Pacemaker

- Not absolute contraindication



Roles of Arrhythmia Center

- MR conditional pacemaker
- At least 6 weeks after implantation
- No device damage (fracture of lead)
- Pacemaker VVI mode, fixed rate pacing

Roles of Radiologist

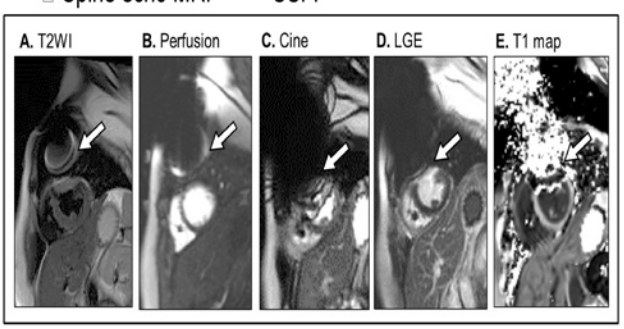
- MR system magnetic field strength (1.5T vs. 3T)
- RF energy, SAR (specific absorption rate) ≤ 2W/kg
- Design MR protocol
  - MR scan time ≤ 30 min
  - Cardiac MR image quality

Artifact by Pacemaker

- Magnetic susceptibility
  - leads and generator of pacemaker
- MR sequence with long TE, remarkable artifact
  - Steady-state free pression (SSFP), cine MRI
  - Inversion recovery sequence

Cardiac MR Sequence & Artifact

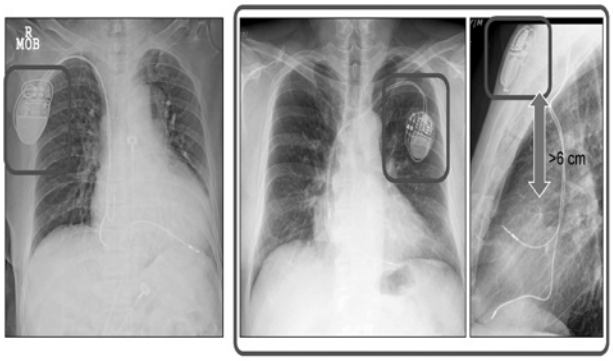
- Spine echo MRI <<<< SSFP



Cardiac MR Sequence & Artifact

- Anterior LV wall (generator), Right ventricle (lead)
- Four chamber view <<< Short-axis, Two-chamber view

Location of Pacemaker, Generator



In Summary

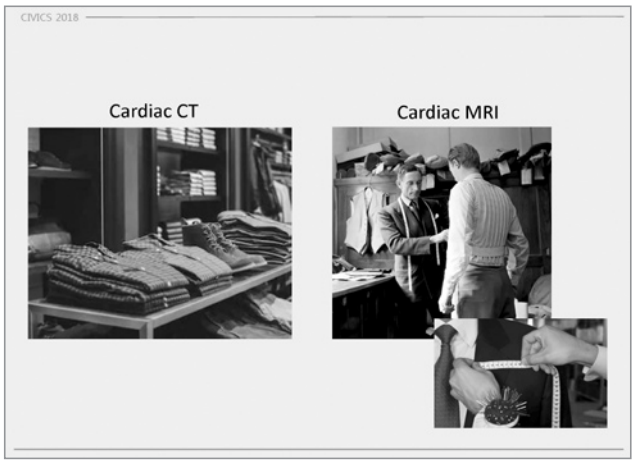
- Cardiac pacemaker is not absolute contraindication to MRI.
- With appropriate screening and application of a safety protocol, MRI can be safely performed in patients with pacemaker.
- Cardiac MRI can offer diagnostic information in most cases of pacemaker.

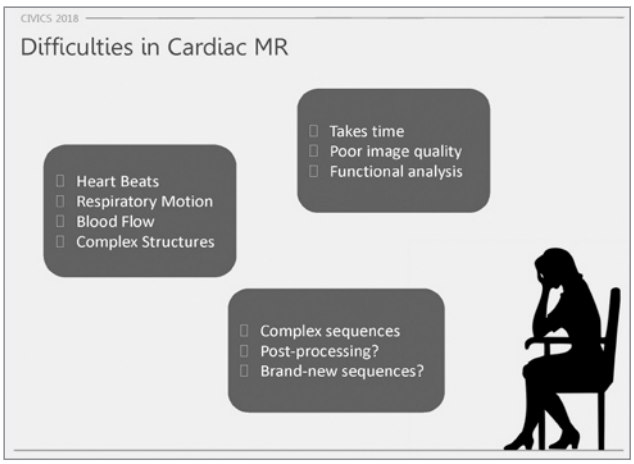
- Thank you for your attention.

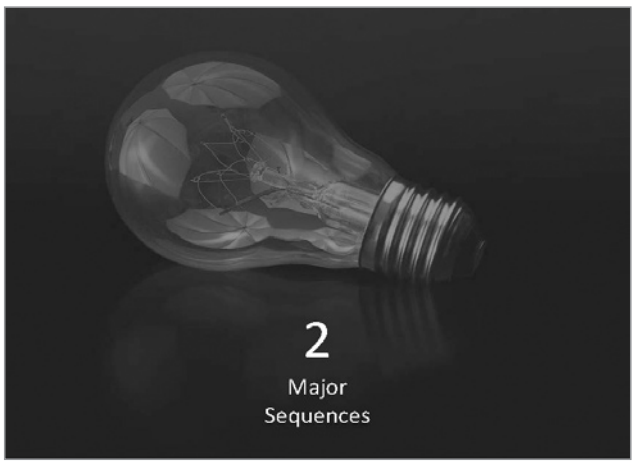
MEMO

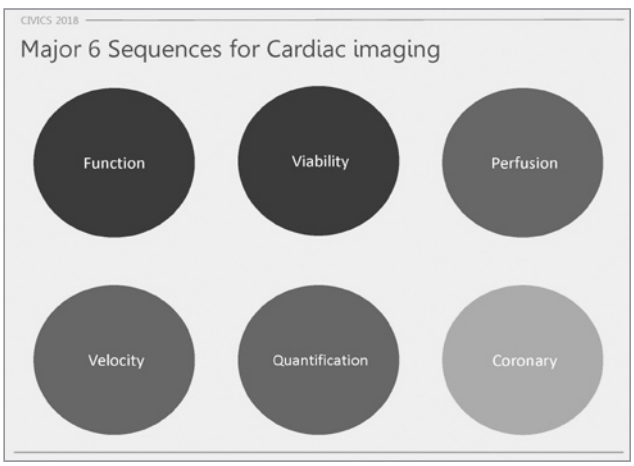
How to get appropriate protocol of cardiac MR

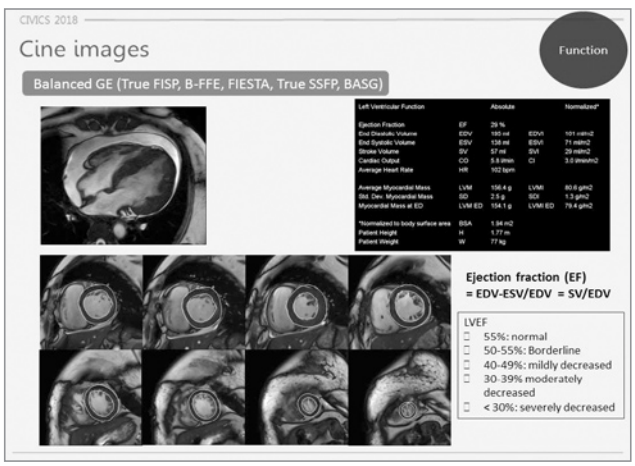
Cherry Kim (Korea University Ansan Hospital, Korea)











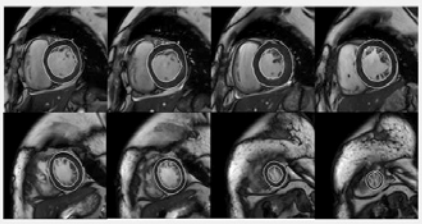
CMCS 2018

Cine images

Function

- **Regional assessment**
  - Wall thickening = average thickness ES – average thickness ED/average thickness ES

- **Regional wall motion abnormality**
  - Normal: Systolic wall thickening > 40 %
  - Hypokinesia: Systolic wall thickening 10-40%
  - Akinesia: Systolic wall thickening < 10 %
  - Dyskinesia: Segment moving outward during systole
  - Aneurysm: Fixed defect



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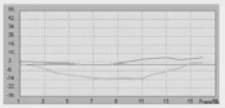
Myocardial Tagging Imaging

Function

- Variant of cine imaging
- Cine image + tagging pulse
- To measure regional myocardial strain
- Can identify scars or regions in the myocardium which are not contracting



http://www.vhlab.umn.edu/atlas/cardiac-mri-tutorial/functional-assessment.shtml

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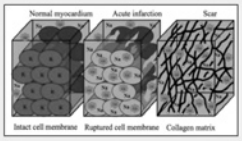
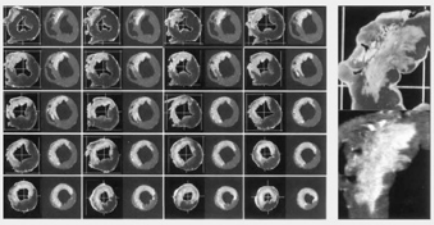
Delayed enhancement_LGE

Viability



- Retained contrast in regions of fibrosis or infarction
  - Increased in the interstitial spaces by cell damage
  - Washout time of contrast agent was prolonged
- No contrast in normal myocardium



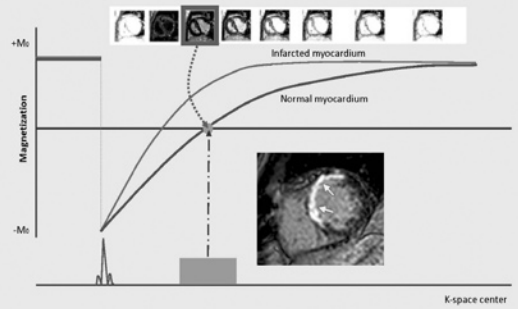
Kim RJ, et al. Circulation 1999

CMCS 2018

Delayed enhancement_LGE

Viability

T1-weighted ultrafast GE or SSFP with 180 inversion pulse



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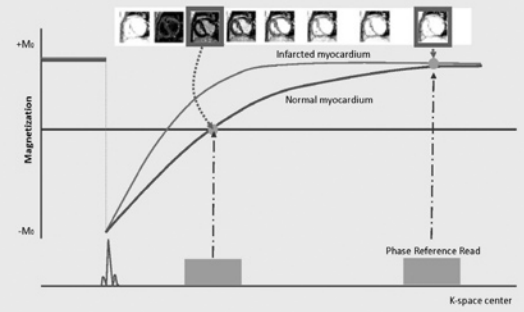
Phase-sensitized Inversion Recovery (PSIR)

Viability



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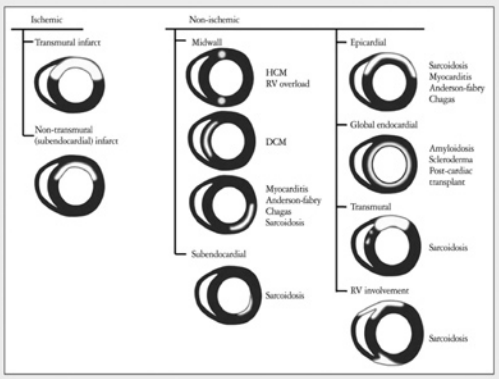
Delayed enhancement_LGE



J cardiovasc Ultrasound 2013

CIVICS 2018

T2 weighted image

Viability

- Determining age of infarction
- Edema in acute MI or cardiomyopathy
- Consistently larger than the area of irreversible necrosis shown on LGE image

*** Area at risk**
- Hypoperfused during coronary occlusion
- T2 High SI

Figure 1: Diagram shows that an image of the area at risk (black) and infarct size (white) can be used to determine the amount of myocardial salvage (blue). Red circle represents short axis of left ventricle, and gray circle represents blood within the cavity. (Adapted and reprinted, with permission, from reference 1.)

Arai AE, Radiology 2012

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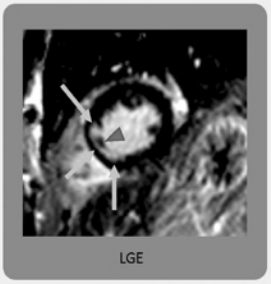
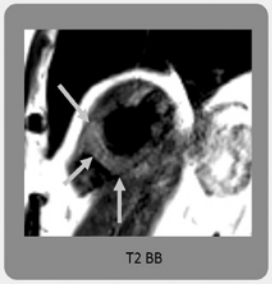
Delayed enhancement_LGE

Viability

T1-weighted ultrafast GE or SSFP with 180 inversion pulse



LGE



T2 BB

- Microvascular obstruction: Dark enhancing area within the enhancing scar
- Severe microcirculatory damage

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LGE and T2WI

Viability

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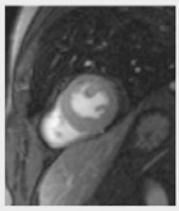
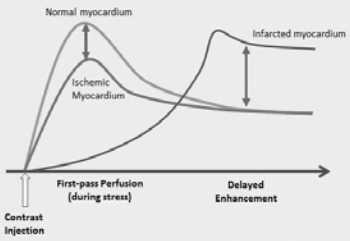
Perfusion

Perfusion

Spoiled GE (TurboFLASH, turbo fast-field echo, GRASS)

Steady-state free precession (TrueFISP, balanced turbo field echo, turboFIESTA)





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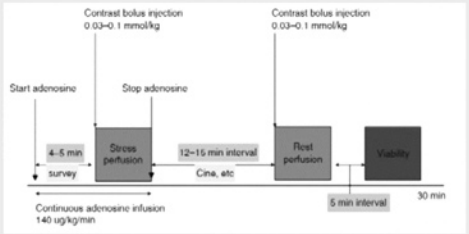
Perfusion

Perfusion



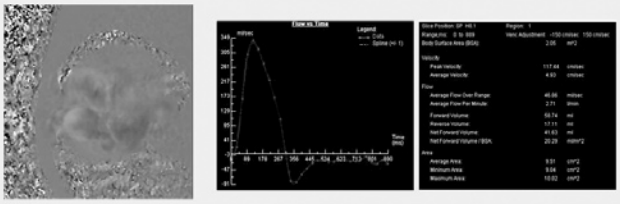
Practical textbook of Cardiac CT and MR

CIVICS 2018

VENC Cine MRI

Velocity

Spoiled GE (FLASH, T1-FFE, SPGR, RF-spoiled FE, RSSG)



- **Valvular post-stenotic and regurgitant flow**

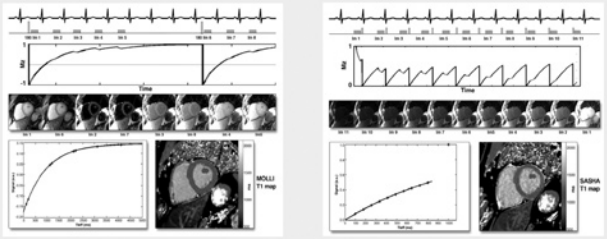
  Regurgitant fraction (%) = Retrograde volume/antegrade volume x 100
- Pulmonary artery and vein blood flow
- Qp/Qs

CMCS 2018

T1, T2, T2* mapping

Quantification

Preparation Pulse



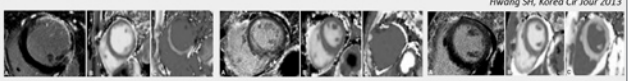
CMCS 2018

T1, T2, T2* mapping

Quantification

- Absolute value (time)
- Quantification of tissue value
  - **T1 mapping**
    - Pre-contrast enhancement
    - Post-contrast enhancement
    - Extracellular volume fracture (ECV)
  - **T2 mapping**
    - Sensitive than T2WI in edema
  - **T2* mapping**
    - Susceptibility
    - Hemochromatosis, iron overload

Hwang SH, Korea Cir Jour 2013



Infarcted myocardium | Amyloidosis | Eosinophilic myocarditis

CMCS 2018

EXPERT CONSENSUS DOCUMENT

ACCF/ACR/AHA/NASCI/S
2010 Expert Consensus
Cardiovascular Magnetic

A Report of the American College of Ca
Expert Consensus Documents

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Int J Cardiovasc Imaging (2010) 26:187–202
DOI 10.1007/s10554-010-9708-y

ORIGINAL PAPER

ASCI 2010 standardized practice protocol for cardiac magnetic resonance imaging: a report of the Asian society of cardiovascular imaging cardiac computed tomography and cardiac magnetic resonance imaging guideline working

Review Article | Cardiovascular Imaging

http://dx.doi.org/10.3348/kjr.2014.15.6.659
pISSN 1229-6929 eISSN 2005-8330
Korean J Radiol 2014;15(6):659-688

Korean Journal of Radiology

KJR

2014 Korean Guidelines for Appropriate Utilization of Cardiovascular Magnetic Resonance Imaging: A Joint Report of the Korean Society of Cardiology and the Korean Society of Radiology

Yeonyee E. Yoon, MD[1*], Yoo Jin Hong, MD[2*], Hyung-Kwan Kim, MD[3], Jeong A Kim, MD[4], Jin Oh Na, MD[5], Dong Hyun Yang, MD[6], Young Jin Kim, MD, PhD[2], Eui-Young Choi, MD, PhD[7]

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CMCS 2018

Ischemic heart Disease

Acute myocardial infarction	Chronic ischemic heart disease
LV function and structure	LV function and structure
LGE	LGE
T2 WI	Stress perfusion
Repeat perfusion study and/or early post-contrast GRE with long TI (400-600ms) for MVO	

CMCS 2018

Arrythmogenic right ventricular cardiomyopathy (ARVD)

- LV & RV function and structure
- LGE
- T1WI (with/without fat suppression)
- T2WI
- Transaxial cine images including RVOT/RV & vertical long axis RV with tricuspid inflow

CIVICS 2018

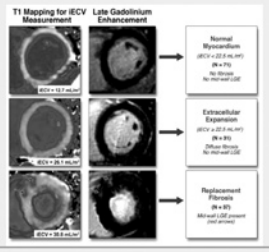
Non-ischemic cardiomyopathy

- LV & RV function and structure
- LGE
- Stress perfusion
- T2WI (Triple IR if acute edema/necrosis is suspected)
- T2* for myocardial iron in Thalassemia
- VENC (outflow obstruction)

CIVICS 2018

Valvular heart disease

- LV & RV function and structure
- LGE
- VENC (according to the valvular lesion of interest)



- Myocardial extracellular expansion and replacement fibrosis in AS

Chin C, JACC img 2017

CIVICS 2018

Cardiac masses

- LV function and structure
- LGE
- T2WI (with/without fat suppression across the mass & surrounding structure)
- T1WI FSE and turbo SE with fat suppression
- First pass perfusion through the mass

*심장질환 : 심장초음파 검사 상 아래의 질환이 의심되어 2차적으로 시행한 경우
가) 심근병증 (심장 이식 후 상태 포함)
나) 복잡 선천성 심기형 또는 심장과 연결된 대혈관기형을 동반한 선천성심질환

Thank you

MEMO

SESSION 2

Present and Future of Cardiac Imaging from Leaders

Chairperson **Jae Hyung Park** (Myongji Hospital, Korea)
Jae-kwan Song (Asan Medical Center, Korea)

Presentation

Plenary Session I :
Recent update on comprehensive role of cardiac CT
Speaker U. Joseph Schoepf (Medical University of South Carolina, USA)

Plenary Session II :
The future of cardiac imaging: Expectations and concerns
- Cardiac Imaging in the era of artificial intelligence: Hopes, hypes, and caveats
Speaker Tae-Hwan Lim (University of Ulsan College of Medicine, Korea)

Panel Discussion

Panel Jongmin Lee (Kyungpook National University Hospital, Korea)
Yong-Jin Kim (Seoul National University Hospital, Korea)

Plenary Session I : Recent update on comprehensive role of cardiac CT

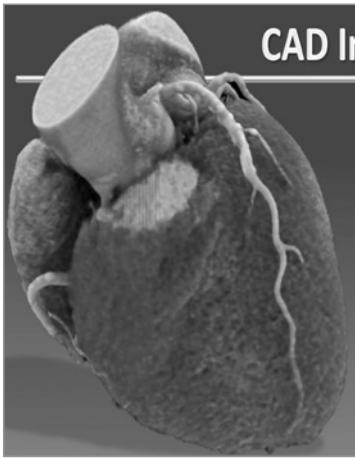
U. Joseph Schoepf (Medical University of South Carolina, USA)

Disclosures

Consultant for / research support from

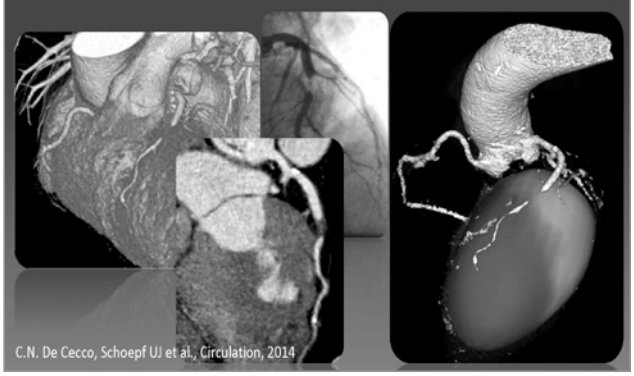
- Astellas
- Bayer
- GE Healthcare
- Guerbet
- HeartFlow Inc.
- Siemens Healthineers

CAD Imaging with CT



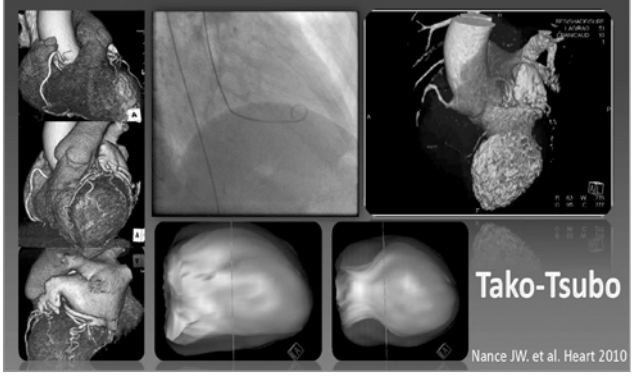
- Structure
- Function
- Innovations

Structure – We Have It Down



C.N. De Cecco, Schoepf UJ et al., Circulation, 2014

Function – We Have It Down



Tako-Tsubo

Nance JW. et al. Heart 2010

Where we are coming from

Classic efficacy trials to establish baseline CCTA accuracy compared to catheter angiography

Standard Dose CCTA - Accuracy

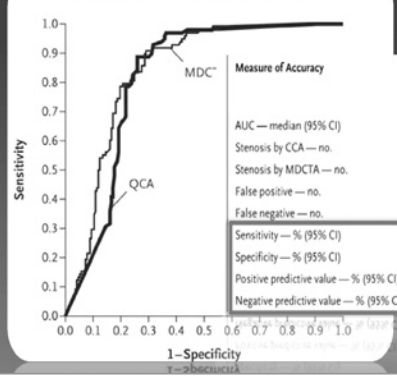
Table 2 Patient-Based Analysis **Single Vendor Multicenter Trial – n=230**

	Estimate, %	95% CI, %	Subjects in Group, n	Subjects Correct by CCTA, n
≥50% stenosis				
Sensitivity	95	85–99	55	52
Specificity	83	76–88	172	142
PPV	64	53–75	81	52
NPV	99	96–100	143	142
≥70% stenosis				
Sensitivity	94	79–99	31	29
Specificity	83	77–88	196	162
PPV	48	35–62	60	29
NPV	99	96–100	164	162

Budoff MJ et al., JACC 2008

Core 64

Patient-Based Analysis for Predicting Revascularization



Measure of Accuracy	Patient-Based Detection: Quantitative MDCTA (N=291)	Visual MDCTA (N=291)
AUC — median (95% CI)	0.93 (0.90–0.96)	0.93 (0.89–0.95)
Stenosis by CCA — no.	163	163
Stenosis by MDCTA — no.	152	146
False positive — no.	13	11
False negative — no.	24	28
Sensitivity — % (95% CI)	85 (79–90)	83 (76–88)
Specificity — % (95% CI)	90 (83–94)	91 (85–96)
Positive predictive value — % (95% CI)	91 (86–95)	92 (87–96)
Negative predictive value — % (95% CI)	83 (75–89)	81 (73–87)

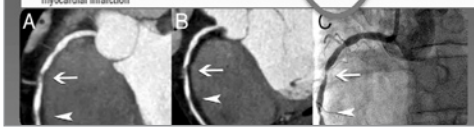
Single Vendor
Multicenter Trial n=291

Miller JM et al., NEJM 2008

Standard Dose CCTA - Meijboom

Multivendor, Multicenter 64 Slice CT Trial – n=360

	Prevalence of Disease, %	n	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Patient-based analysis	68	360	99 (98-100)	64 (55-73)	86 (82-90)	97 (94-100)
Stable angina pectoris	63	233	99 (98-100)	64 (53-74)	82 (76-88)	98 (95-100)
Non-ST-segment elevation acute coronary syndrome	79	127	99 (97-100)	63 (45-81)	91 (85-96)	94 (84-100)
Men	76	245	99 (97-100)	66 (53-78)	90 (86-94)	95 (88-100)
Women	51	115	100 (100-100)	63 (50-75)	74 (64-83)	100 (100-100)
Typical angina pectoris	70	151	99 (97-100)	67 (54-81)	87 (81-93)	97 (91-100)
Atypical angina pectoris	50	82	100 (100-100)	61 (46-76)	72 (60-84)	100 (100-100)
Unstable angina pectoris	75	77	98 (95-100)	68 (48-89)	90 (83-98)	93 (79-100)
Non-ST-segment elevated myocardial infarction	84	50	100 (100-100)	50 (15-85)	91 (83-99)	100 (100-100)



Meijboom EB et al., JACC 2008

Accuracy

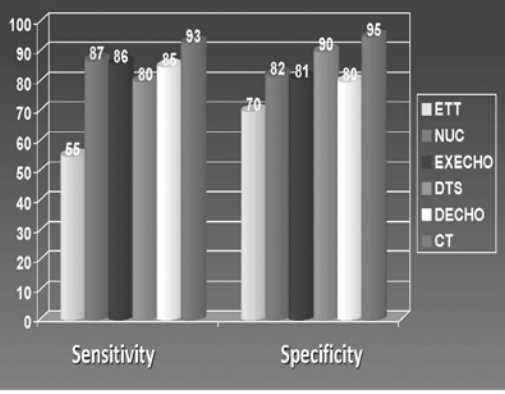
Meta-Analyses

Table 1 Patient-Based Evaluation of Significant (>50% or ≥50%) Stenosis

First Author (Reference)	Number of Patients	Sensitivity n/N	(%)	Specificity n/N	(%)
Tier 1					
Raff[9]	70	38/40	(95)	27/30	(90)
Mollett[6]	51	38/38	(100)	12/13	(92)
Puglisee[7]	35	25/25	(100)	9/10	(90)
Ehara[8]	67	59/60	(98)	6/7	(86)
Herzog[9]	55	19/19	(100)	30/36	(83)
Nikolaou[17]	68	38/39	(97)	23/29	(79)
Leber[10]	65	22/25	(88)	17/20	(85)
Total	391	239/246	(97)	124/145	(86)
Tier 2					
Ropers[22]	81	25/26	(96)	50/55	(91)
Meijboom[23]	104	88/88	(100)	12/16	(75)
Meijboom[27]	402	251/253	(99)	125/149	(84)
Hacker[28]	30	11/13	(85)	10/17	(59)
Oncel[25]	80	62/62	(100)	18/18	(100)
Pundziute[32]	100	53/54	(98)	42/46	(91)
Shabestari[29]	138	104/108	(96)	20/30	(67)
Schuijf[27]	60	29/31	(94)	28/29	(97)
Leschka[79]	74	35/36	(97)	33/38	(87)
Xiao[40]	216	112/115	(97)	91/101	(90)
Leschka[43]	67	47/47	(100)	20/20	(100)
Fine[44]	66	62/66	(94)	0/0	
Total	1418	879/899	(98)	449/519	(87)
Tier 3					
Ghostine[45]	66	28/29	(97)	35/37	(95)
Meijboom[46]	70	18/18	(100)	48/52	(92)
Scheffel[47]	50	13/13	(100)	37/37	(100)
Plass[48]	50	40/40	(100)	9/10	(90)
Total	236	99/100	(99)	129/136	(95)
All Tiers	2045	1217/1245	(98)	702/800	(88)

Mowatt G et al., Health Technol Assess. 2008

Accuracy - CT vs Other Non-Invasive Tests for CAD Dx

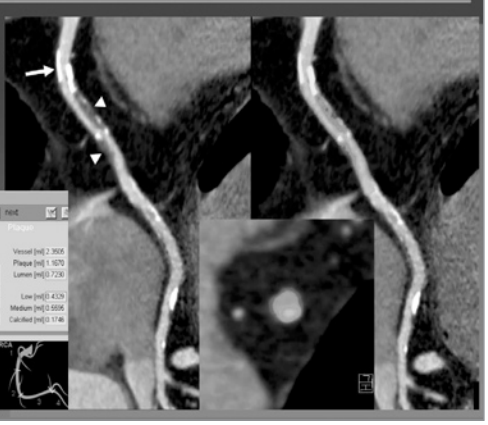


Where we are we going

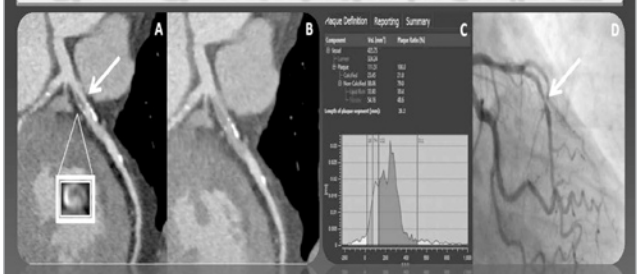
Efficiency trials to establish the clinical utility of CCTA beyond accuracy comparisons with catheter angiography

Prognostic Value

Atherosclerotic Plaque Burden Quantification



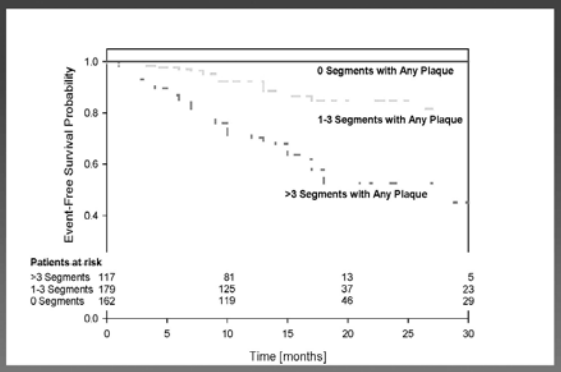
Plaque Characterization by Cardiac CT



CT provides information on plaque composition and allows for identification of vulnerable plaques, which currently do not cause stenosis but have the potential to rupture

Tesche et al., JCCT 2016

Prognosis: MUSC Outcomes in 458 Patients



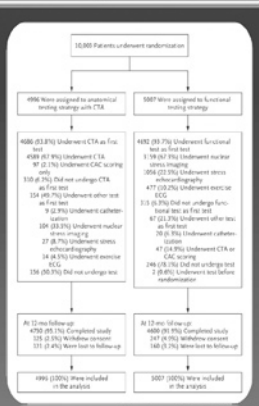
Nance et al. Radiology 2012

Anatomical vs. Functional Testing: PROMISE

Anatomical (CCTA) vs Functional

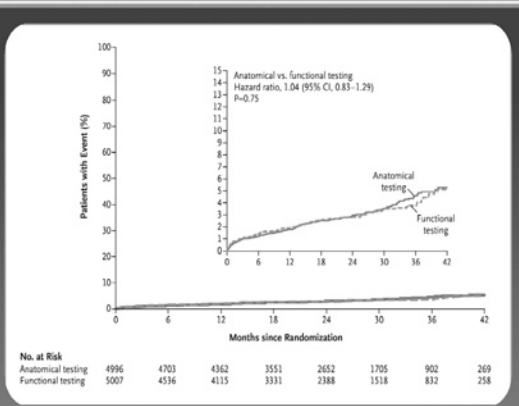
- exercise electrocardiography
- nuclear stress testing
- stress echocardiography

For initial evaluation of symptomatic patients with suspected CAD



Douglas et al., NEJM 2015

Anatomical vs. Functional Testing: PROMISE



Douglas et al., NEJM 2015

Impact on Patient Care

SCOT-HEART

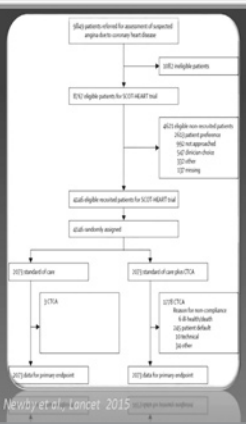
	Standard care and CTCA		Standard care	
	Cancellation	New	Cancellation	New
Investigations				
Stress imaging	121	5	0	6
Invasive coronary angiography	29	94	1	8
Total	150	99	1	14
Medical treatments				
Preventive treatment	77	293	8	84
Antianginal treatment	112	82	6	11
Total	189	375	14	95

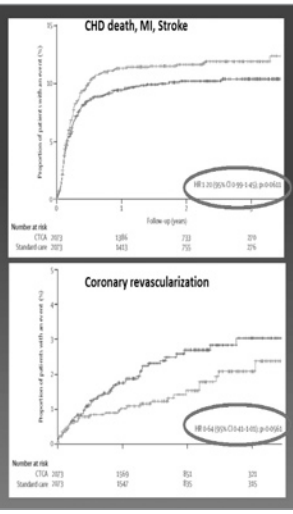
CTCA=CT coronary angiography.

- Confirmation of diagnosis and reclassification of the severity of CHD
- Modification of the therapy regimen (less diagnostics, targeted drug therapy and coronary revascularization)
- Reduction of MACE in follow-up

D. Newby et al., Lancet 2015

SCOT-Heart





D. Newby et al., Lancet 2015

UK - NICE

NICE National Institute for Health and Care Excellence

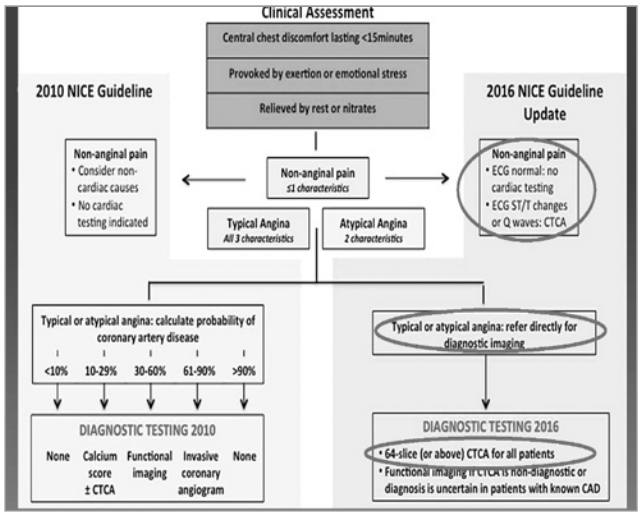
1.3.4.3 Offer 64-slice (or above) CT coronary angiography if:

NICE guideline

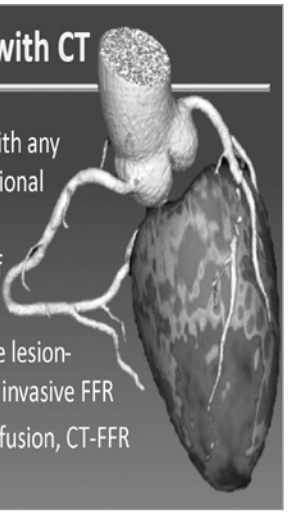
- clinical assessment (see recommendation 1.3.3.1) indicates typical or atypical angina or
- clinical assessment indicates non-anginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves. [new 2016]

1.3.5.1 Offer non-invasive functional imaging (see section 1.3.6) for myocardial ischaemia if 64-slice (or above) CT coronary angiography has shown CAD of uncertain functional significance or is non-diagnostic. [2016]

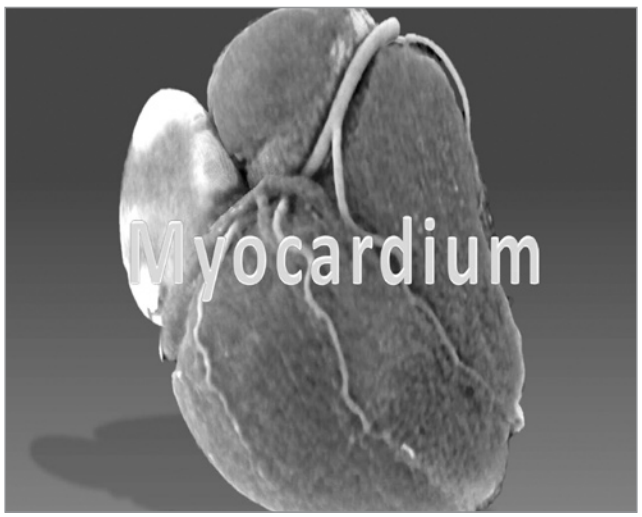
1.3.5.2 Offer invasive coronary angiography as a third-line investigation when the results of non-invasive functional imaging are inconclusive. [2016]



Lesion-Specific Ischemia with CT

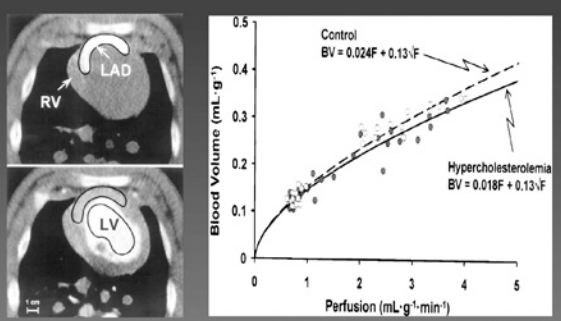


- Anatomical, structural imaging with any modality cannot determine functional significance of lesions
- Patient outcomes are improved if only relevant lesions are treated
- Traditional methods to determine lesion-specific ischemia: Nuc-perfusion, invasive FFR
- CT-based methods: CT-based perfusion, CT-FFR



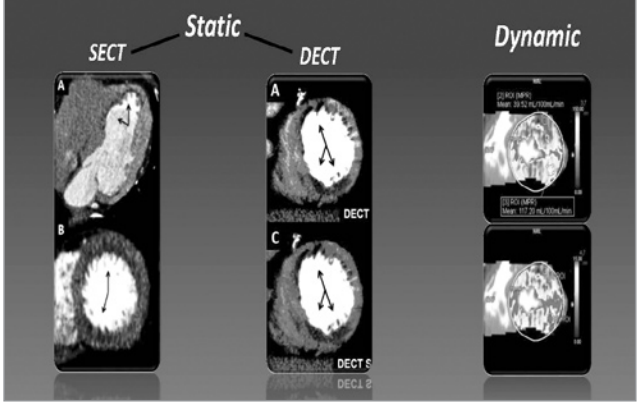
Perfusion CT: An Old Idea...

EBCT: Porcine Model of Myocardial Perfusion



Mohlenkamp, S. et al. Circulation 2000

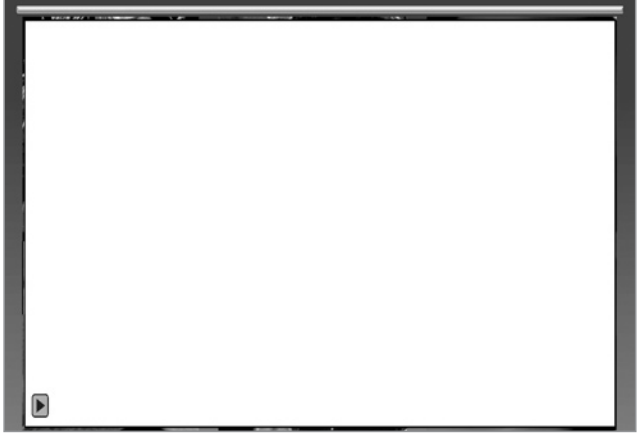
CT Myocardial Perfusion: Approaches



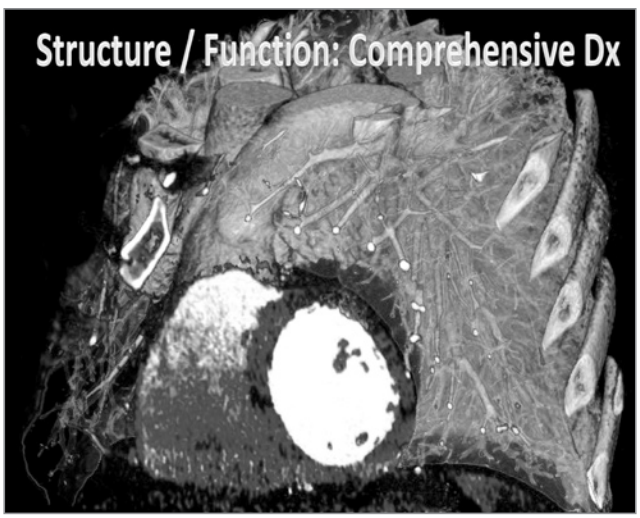
CT Modalities for MPI

- **Dual Energy CT**
  - Layer Detector
  - Rapid KV Switching
  - Dual-Source CT-Based
- **Static Single Heart-Beat Acquisition Techniques**
  - Wide Detector CT Techniques
  - Dual-Source CT Ultra-High Pitch Acquisition
- **Dynamic Myocardial CT Perfusion**

Structure / Function: Comprehensive Dx

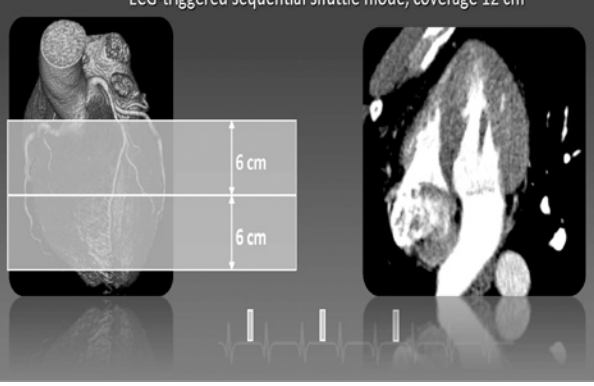


Structure / Function: Comprehensive Dx

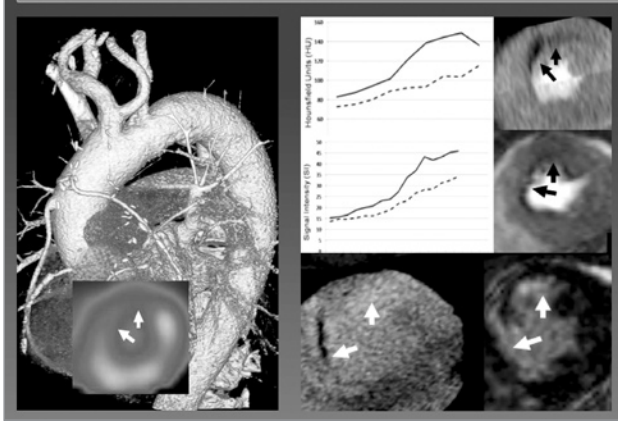


Dynamic Time Resolved Perfusion

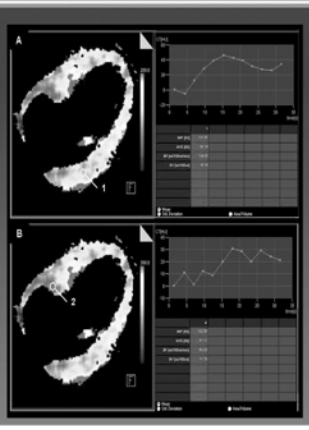
ECG-triggered sequential shuttle mode, coverage 12 cm



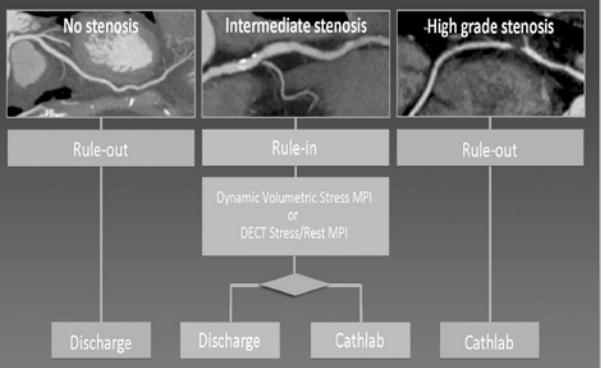
Structure / Function: Comprehensive Dx



Absolute MBF Quantification



Solving Clinical Dilemmas...



Monitoring Therapeutic Effects...

Blood flow in defect:
65 cc/ 100 cc/ min

Blood flow in healthy myocardium:
112 cc/ 100 cc/ min

Ho et al., JCCT 2011

Monitoring Therapeutic Effects...

Blood flow in former defect:
118 cc/ 100 cc/ min

Blood flow in healthy myocardium:
112 cc/ 100 cc/ min

Ho et al., JCCT 2011

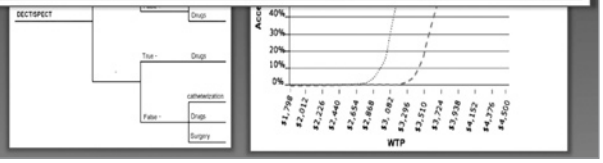
CT Perfusion vs SPECT – Cost Effectiveness

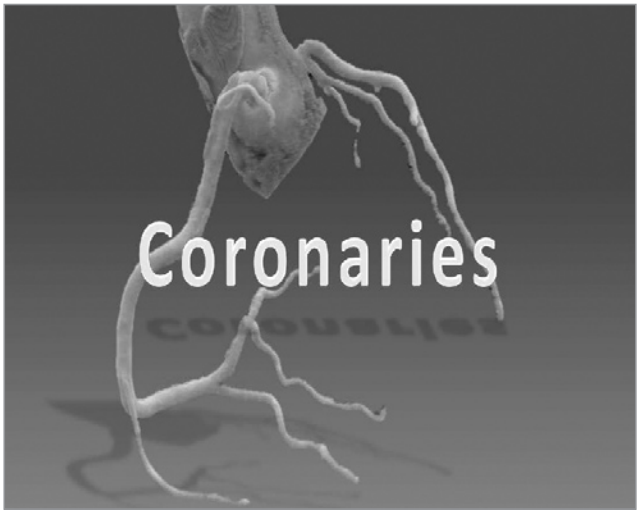
Cost-effectiveness of substituting dual-energy CT for SPECT in the assessment of myocardial perfusion for the workup of coronary artery disease

Mathias Meyer[a,c], John W. Nance Jr.[a], U. Joseph Schoepf[a,b,*], Antonio Moscariello[a,d], Markus Weininger[a], Garrett W. Rowe[a], Balazs Ruzsics[a], Doo Kyoung Kang[a,e], Salvatore A. Chiaramida[a], Stefan O. Schoenberg[c], Christian Fink[c], Thomas Henzler[a,c]

Table 4
Mean costs, health outcomes, and cost-effectiveness for patients with CAD at different pre-test likelihoods.

Pre-test likelihood	Cost (US$) per patient	QALY 80%	ICER per QALY	ICER/correct diagnose 80%	ICER/QALYs 40%	ICER/QALYs 60%
SPECT	$2938	13.49	$3557	$3625	$5922	$5183
DECT	$2631	14.13	$3191	$2938	$3248	$2988
p-Value	0.0002		0.0004	0.0001	0.0001	0.0001



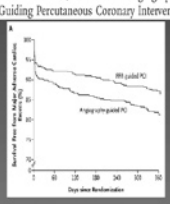


Coronary Fractional Flow Reserve

FAME

The NEW ENGLAND JOURNAL of MEDICINE

Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

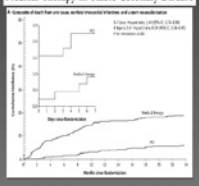


Conclusion:
no intervention for stenoses with FFR > 0.80

FAME II

The NEW ENGLAND JOURNAL of MEDICINE

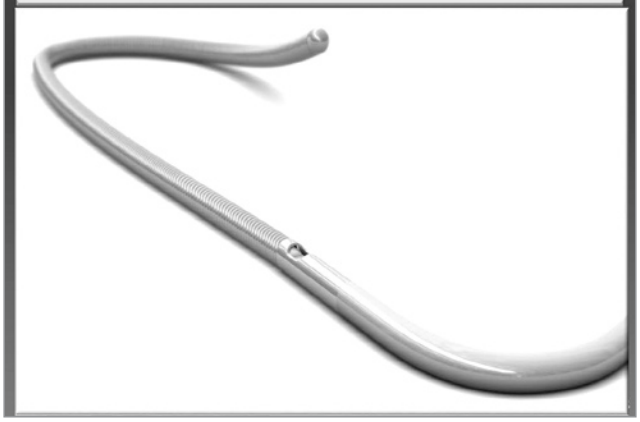
Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease



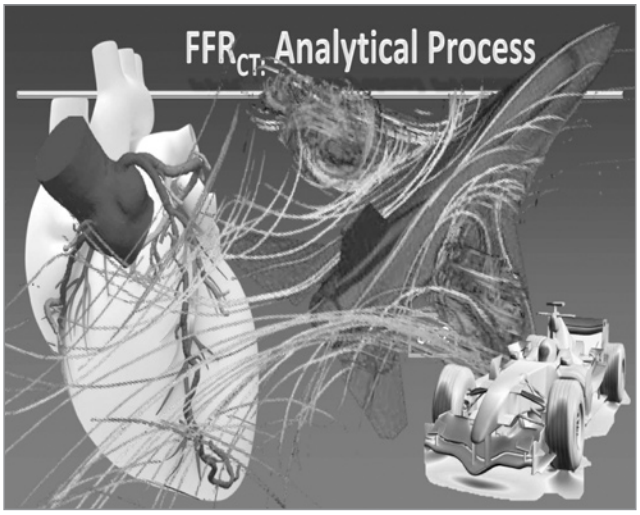
Conclusion:
intervention for stenoses with FFR ≤ 0.80

De Bruy et al, NEJM 2012 - Tonino et al, NEJM 2009.

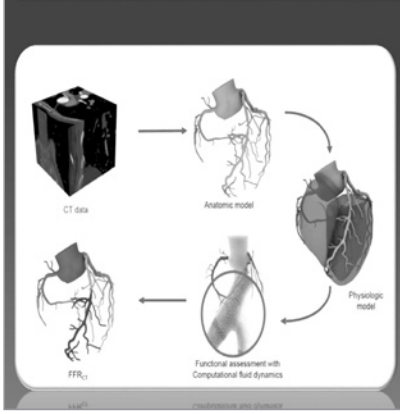
Heart Vessel Fractional Flow Reserve



FFR_{CT}: Analytical Process

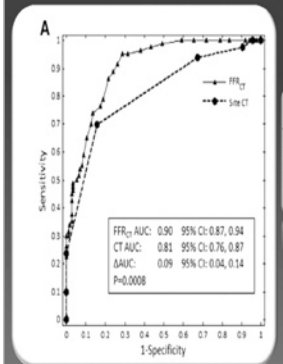


FFR_{CT}: Analytical Process



Taylor C, et al.
J Am Coll Cardiol 2013
61(22):2233-41.

CT-FFR: NXT-Trial



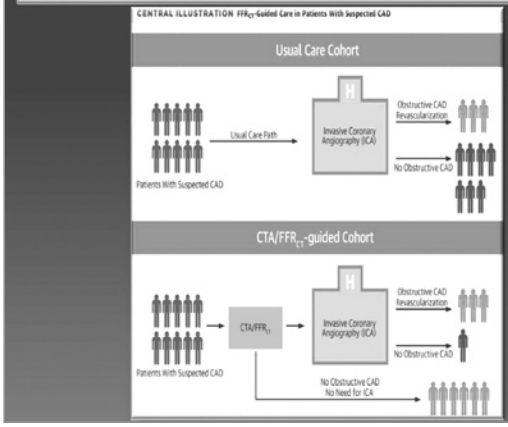
Prospective multicenter trial *n* = 254

	Coronary CTA Stenosis >50%	p Value	FFR_{CT} ≤0.80	p Value	ICA Stenosis >50%
Accuracy	53 (47-57)	<0.001	81 (76-85)	0.09	77 (71-82)
Sensitivity	94 (86-97)	0.088	86 (77-92)	<0.001	64 (53-74)
Specificity	34 (27-41)	<0.001	79 (72-84)	0.29	83 (77-88)
PPV	40 (33-47)	<0.001	65 (56-74)	0.34	63 (52-73)
NPV	92 (83-97)	0.48	93 (87-96)	<0.001	83 (77-89)

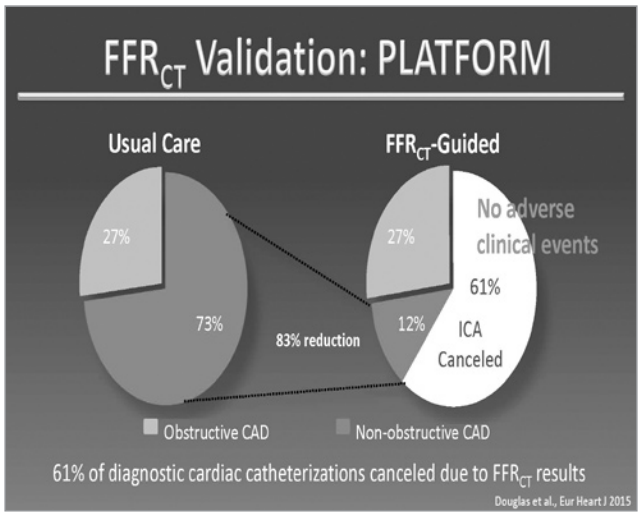
Coronary CTA Stenosis >50%	p Value	FFR_{CT} ≤0.80	p Value	ICA Stenosis >50%
65 (61-69)	<0.001	86 (83-89)	0.032	82 (79-86)
83 (74-89)	0.91	84 (75-89)	<0.001	55 (45-65)
60 (56-65)	<0.001	86 (82-89)	0.18	90 (86-93)
33 (27-39)	<0.001	61 (53-69)	0.18	56 (48-66)
92 (88-95)	0.068	95 (93-97)	<0.001	88 (85-92)

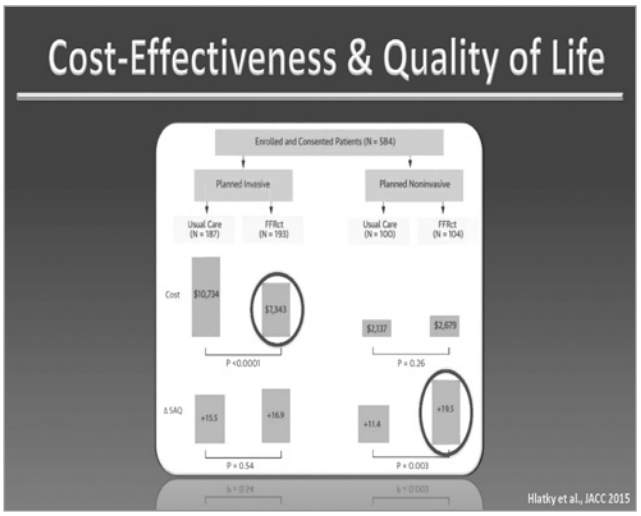
Norgaard et al., JACC 2014

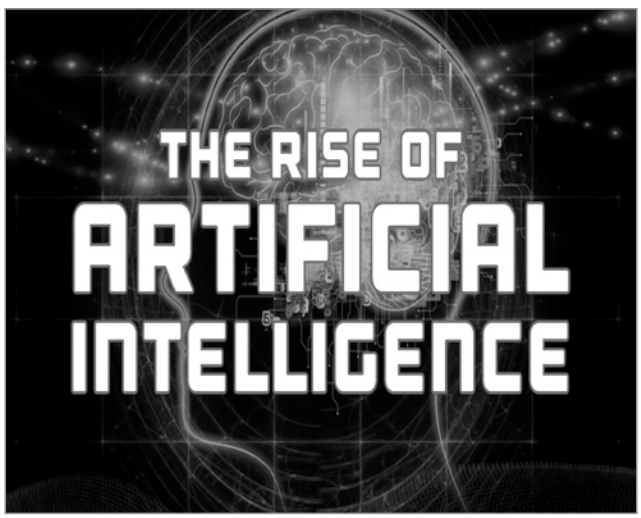
FFR_{CT} Validation: PLATFORM

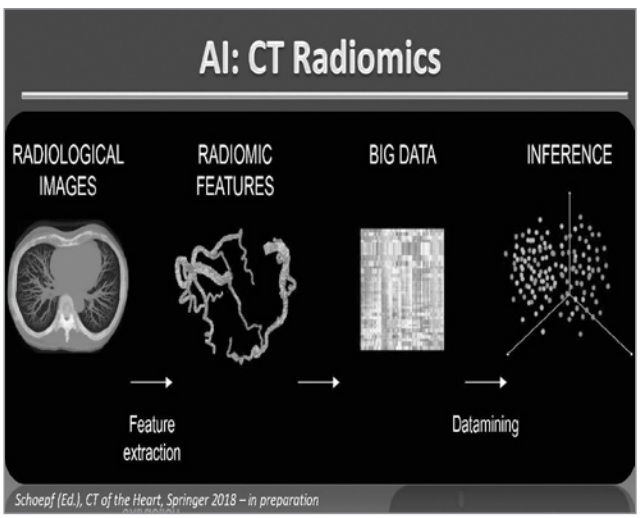


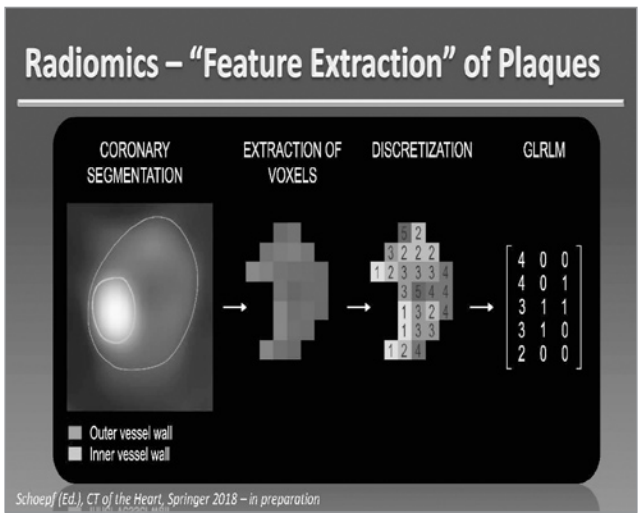
Douglas et al., JACC 2016

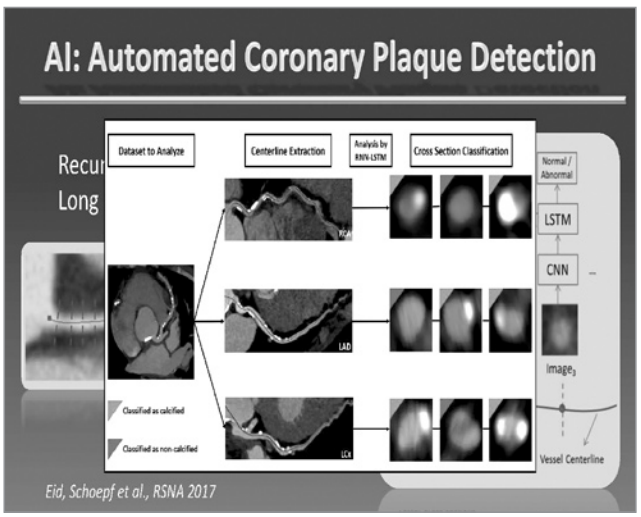

FFR$_{CT}$ Validation: PLATFORM
Usual Care
FFR$_{CT}$-Guided
27%
73%
27%
12%
No adverse clinical events
61%
ICA Canceled
83% reduction
Obstructive CAD
Non-obstructive CAD
61% of diagnostic cardiac catheterizations canceled due to FFR$_{CT}$ results
Douglas et al., Eur Heart J 2015


Cost-Effectiveness & Quality of Life
Enrolled and Consented Patients (N = 584)
Planned Invasive
Planned Noninvasive
Usual Care (N = 187)
FFRct (N = 193)
Usual Care (N = 100)
FFRct (N = 104)
Cost
$10,734
$7,343
$2,137
$2,679
P <0.0001
P = 0.26
Δ SAQ
+15.5
+16.9
+11.4
+19.5
P = 0.54
P = 0.003
Hlatky et al., JACC 2015


THE RISE OF
ARTIFICIAL
INTELLIGENCE


AI: CT Radiomics
RADIOLOGICAL IMAGES
RADIOMIC FEATURES
BIG DATA
INFERENCE
Feature extraction
Datamining
Schoepf (Ed.), CT of the Heart, Springer 2018 – in preparation


Radiomics – "Feature Extraction" of Plaques
CORONARY SEGMENTATION
EXTRACTION OF VOXELS
DISCRETIZATION
GLRLM
Outer vessel wall
Inner vessel wall
Schoepf (Ed.), CT of the Heart, Springer 2018 – in preparation


AI: Automated Coronary Plaque Detection
Dataset to Analyze
Centerline Extraction
Analysis by RNN-LSTM
Cross Section Classification
Normal / Abnormal
LSTM
CNN
Image$_3$
Classified as calcified
Classified as non-calcified
Vessel Centerline
Eid, Schoepf et al., RSNA 2017

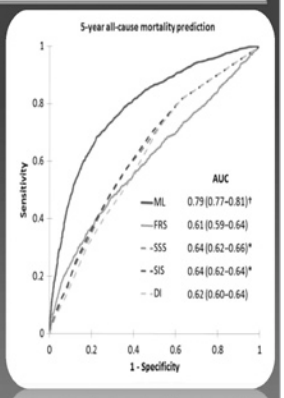
Machine Learning – Prognosis

CLINICAL RESEARCH
Coronary artery disease

Machine learning for prediction of all-cause mortality in patients with suspected coronary artery disease: a 5-year multicentre prospective registry analysis

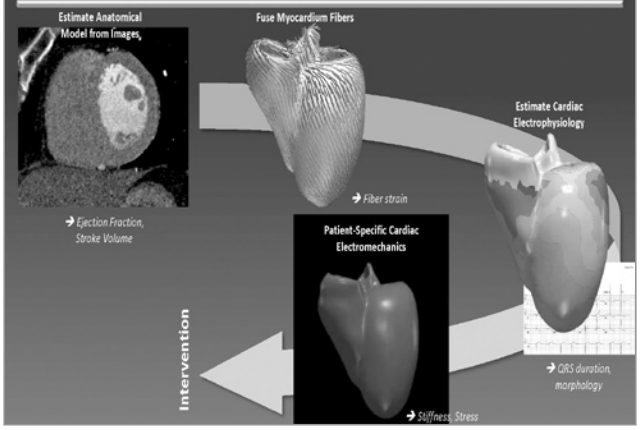
Combined clinical and CCTA features with ML performed better than the FRS or CCTA features alone in the prediction of 5-year all cause mortality

ML can analyze a bigger number of more complex data (clinical, radiological, lab...) to detect previously unknown predictors and improve clinically used prognostic scores

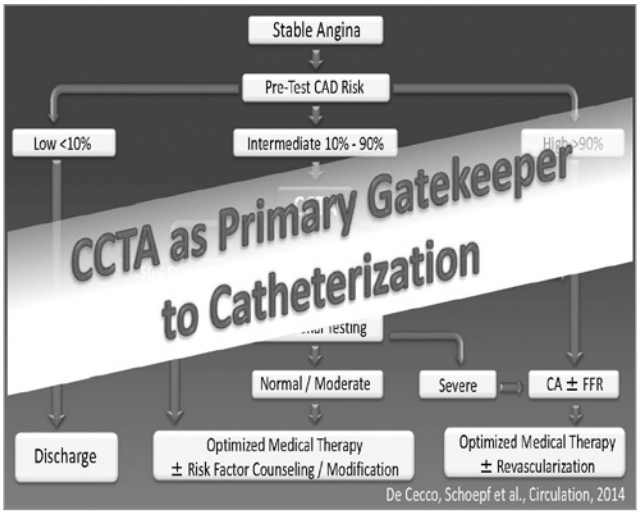


Motwani et al., *European Heart Journal* 2017

AI – Creating a Digital Heart Twin



CCTA as Primary Gatekeeper to Catheterization



De Cecco, Schoepf et al., Circulation, 2014

Summary

- Coronary CT Angiography – We Have It Down!
  - Efficacy established
  - Gentler techniques without losing efficacy
  - Efficiency evidence is reaching critical mass
- Structure and Function – Getting There!
  - Lesion specific ischemia imaging with CT-MPI or CT-FFR enhances cCTA specificity and decreases unnecessary invasive diagnostic work-up
  - Will increasingly guide patient management and inform appropriate revascularization

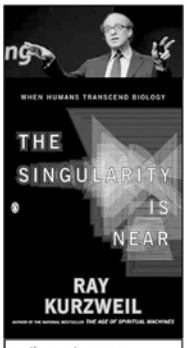
MEMO

Plenary Session II : The future of cardiac imaging : Expectations and concerns - Cardiac imaging in the era of artificial intelligence : Hopes, hypes, and caveats

Tae-Hwan Lim (University of Ulsan College of Medicine, Korea)

Artificial Intelligence: Brief History

- In 1950, Alan Turing asked in his paper
  "Can machines think?"
  Computing Machinery and Intelligence
- In 1956, Terminology first came out
  "Artificial Intelligence"



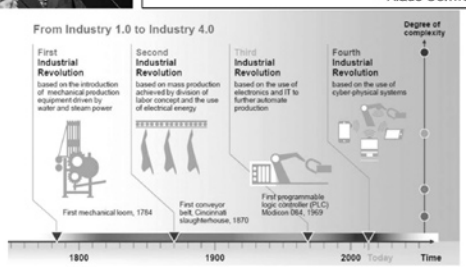
author, entrepreneur, futurist, and inventor
Alma mater: MIT (B.S.)
Employer: Google Inc.

"Singularity"

Once the "singularity" has been reached, Kurzweil says, machine intelligence will be infinitely more powerful than all human intelligence combined.
The Singularity is also the point at which machines intelligence and humans would merge. (2005)

4th Industrial Revolution

Characterized by new technologies fusing the physical, digital and biological worlds, the fourth industrial revolution will impact all disciplines, economies and industries
–Klaus Schwab



Klaus Schwab. The Fourth Industrial Revolution. PortfolioPenguin 2017.

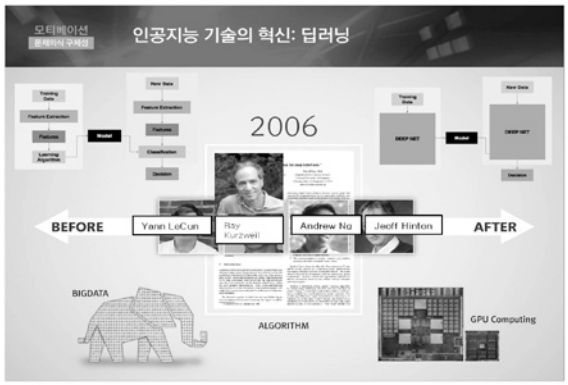
Elon Musk: CEO of Tesla and SpaceX

Artificial Intelligence

- Weak artificial intelligence
  - Narrow AI, applied AI
  - AI focused on narrow task
    - Go, Chess, Spam filtering, shopping assistance, autonomous car
- Strong artificial intelligence
  - Artificial general intelligence (AGI)
  - with consciousness, sentience and mind
  - ability to apply intelligence to any problem

Innovations with AI

Revolution in AI: Deep Learning



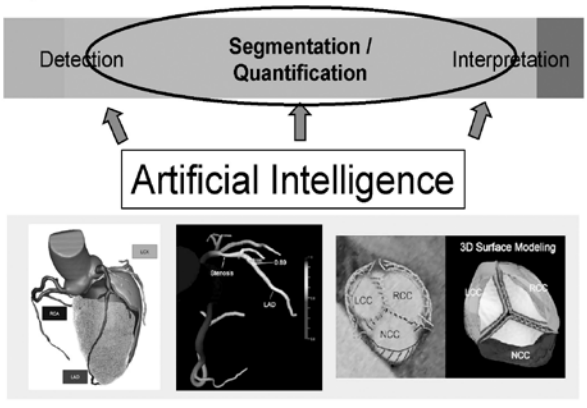
Role of
Artificial Intelligence
in Cardiac Imaging

Hopes

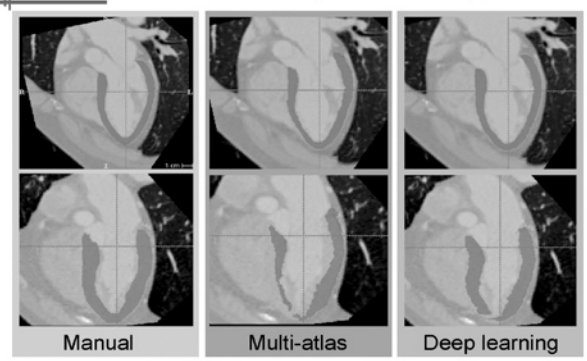
AI Application in Medical Imaging

- Almost all aspects
  - Image conversion, denoising
  - Isolation of lesion, measurement
  - Detection of abnormality
  - Classification of disease
  - Retrieval of similar case

AI in Imaging Diagnosis

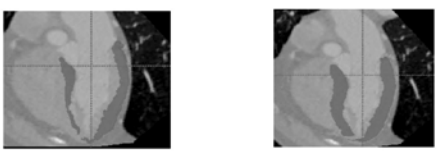


Left Ventricular Myocardium– Multi-atlas vs. Deep Learning



Lee JG, Yang DH et al. Unpublished Data

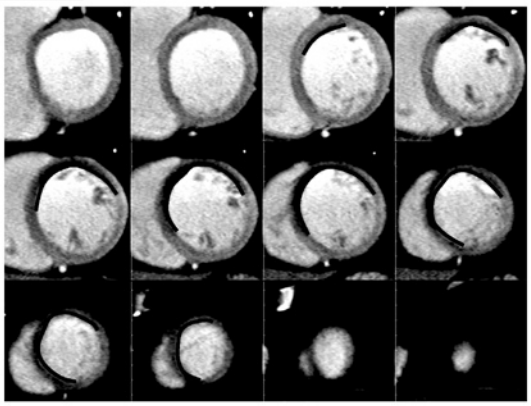
Left Ventricular Myocardium– Multi-atlas vs. Deep Learning



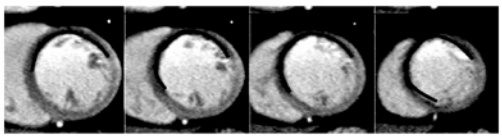
Multi-atlas	Deep learning
• 150 patients - Train 50 pts - Test 100 pts	• 150 patients - Train 50 pts (17,135 images) - Test 100 pts (32,276 images)
• Test running time: - 70 – 80 min/case	• Training time: 20 hours • Test running time: - 1 – 2 min/case
• Dice similarity coefficient - 0.65 – 0.93 (mean 0.87)	• Dice similarity coefficient - 0.84 – 0.95 (mean 0.90)

Lee JG, Yang DH et al. Unpublished Data

CT Perfusion



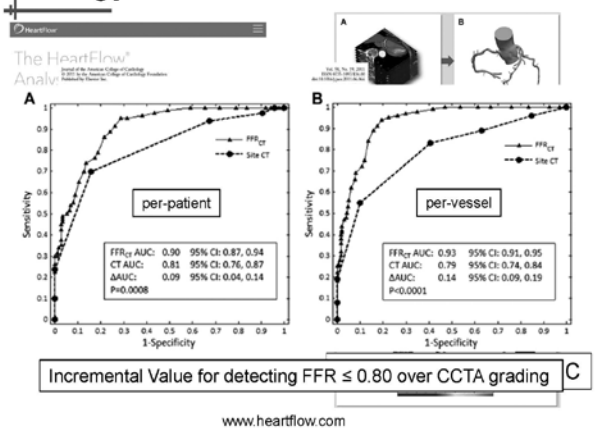
CT Perfusion



Summed Stress Score
→ 14

% Ischemic Burden
–> 35.8% of LV myocardium

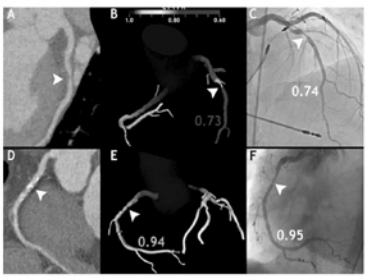
FFR_{CT}: Heart Flow

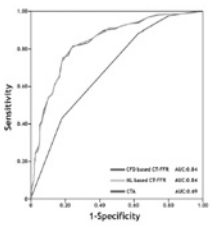


Incremental Value for detecting FFR ≤ 0.80 over CCTA grading

www.heartflow.com

Machine Learning based CT-FFR

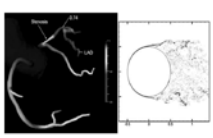




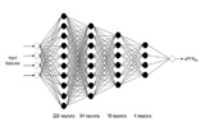
From the MACHINE consortium
Erasmus University Medical Center, The Netherlands
Asan Medical Center, Korea
Medical University of South Carolina, USA
Linkoping University, Sweden
Institute of Cardiology Warsaw, Poland

Coenen A et al. In submission

CT-FFR, CFD vs. ML



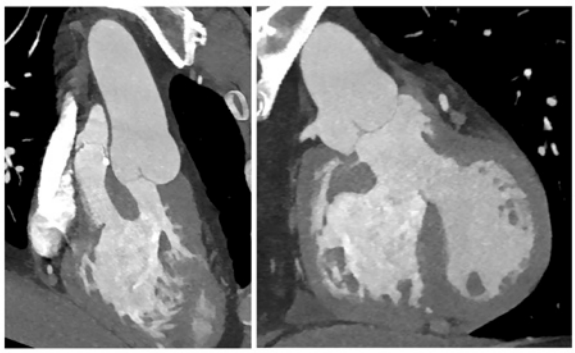
Computational Fluid Dynamics (CFD)
- 10 min (1D)
- ~ hours (3D)



Machine Learning (ML)
- 1~2 seconds

3D Printing Technology:

From Virtual to Reality



- 59 / M
- DORV with remote VSD
- L-malposition of great artery.

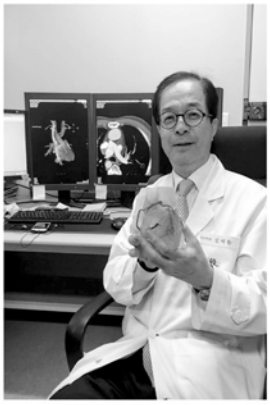
Want to See the Reality !

- 59 / M
- DORV with remote VSD
- L-malposition of great artery.

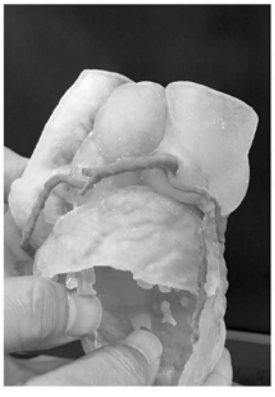
Segmentation

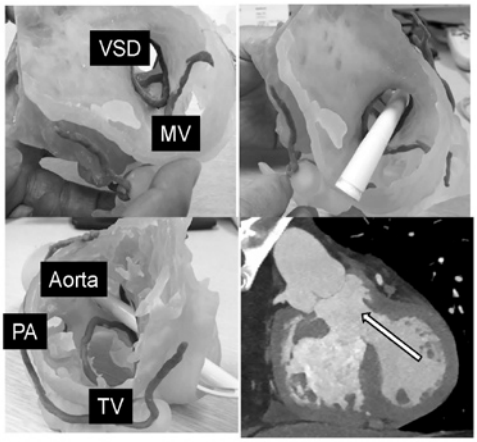
STereoLithography (STL) File

The Reality in My Hands



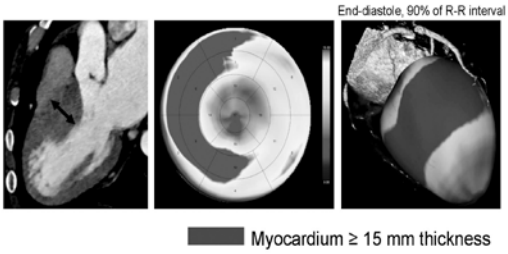
3D Printing for Structural Heart Disease





Cardiac CT: myocardium

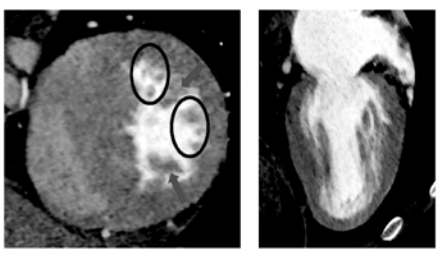
- Asymmetrical septal hypertrophy
- Extent of hypertrophied myocardium



Yang DH et al. Circulation 2015; 132:300-301

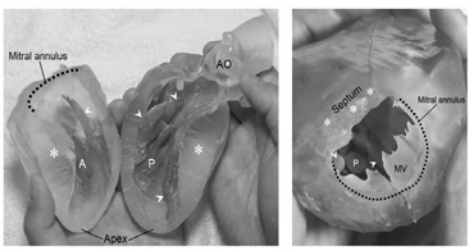
Cardiac CT: papillary muscle

- Accessory papillary muscles
- Prominent muscle bands around PM



Yang DH et al. Circulation 2015; 132:300-301

Myocardial 3D Printing



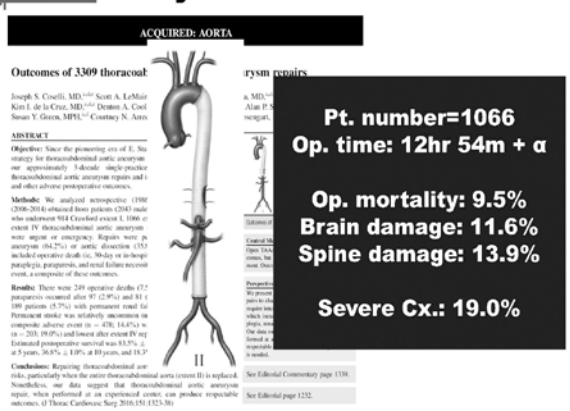
Yang DH et al. Circulation 2015; 132:300-301

Myocardial 3D Printing

The surgeon could handle and disassemble the myocardial 3D model.

Yang DH et al. Circulation 2015; 132:300-301

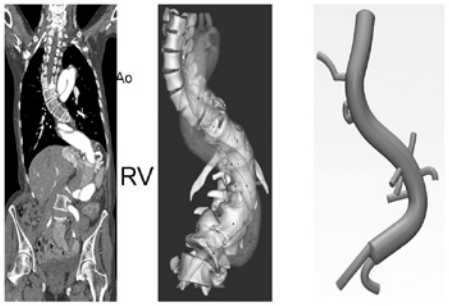
Operative treatment Of TAA Aneurysm



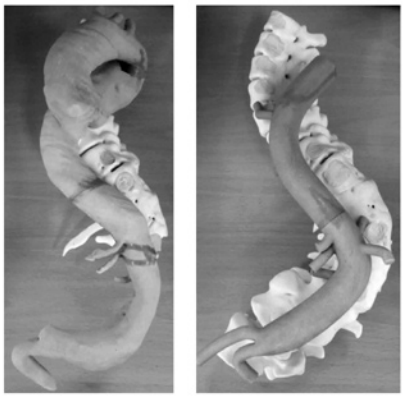
Another Challenge

3D Printing for TAAA

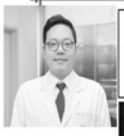
DICOM → Segmentation → Modeling



3D Printing for TAAA

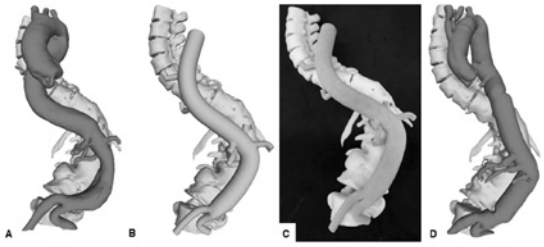


3D Printing Guided Graft Design



J. B. Kim, MD
Cardiac Surgeon
Asan Medical Center

3D Printing Guided Graft Design



Pre-op. Post-op.

Op. time: 6hr 50m
No complication

Role of

Artificial Intelligence

in Radiology

Hypes

Predicting the Future — Big Data, Machine Learning, and Clinical Medicine

Ziad Obermeyer, M.D., and Ezekiel J. Emanuel, M.D., Ph.D.

N ENGL J MED 375:13 SEPTEMBER 29, 2016

"Radiologists focus largely on interpreting digitized images, which can easily be fed directly to algorithms instead."

"Massive imaging data sets, combined with recent advances in computer vision,

"Machine learning will displace much of the work of radiologists"

Emergency Medicine
Brigham & Women's Hospital
Healthcare Policy
Harvard Medical School

Oncologist and Bioethicist
Architect of the "Affordable Care Act"
University of Pennsylvania
Harvard Medical School

Emergency Medicine
Brigham & Women's Hospital
Healthcare Policy
Harvard Medical School

But I think if you look at all of the enthusiasm and hype all around how machine learning will contribute to medicine, I think it's quite striking how little machine learning has contributed to medicine already.

"one of the things that I am most excited about it and most urgent so far exactly is to:
- finding models that can leverage those technologies
- validating them in randomized trials.

"Watson AI will change everything in Healthcare: Radiologists will lose jobs soon"

- "People are going to be overloaded by flood of information. Radiologist will be liable to make fatigue errors."
- "I think it is inevitable that things that are repetitive and can be automated, here, you will have a job impact."
  - "The goal is help make better decision. You will be aided by this sort of technology."

Ginni Rometty, IBM CEO
CNN Interview

Jeoff, Hinton
Univ. of Toronto
Cognitive psychologist
Computer Scientist
Artificial neuralnetwork
"Godfather of AI "
2015 Join Google

Let me start by just saying a few things that seem obvious.

I think if you work as radiologists you're like the coyote that's already over the edge of the cliff but hasn't yet looked down so it doesn't realize there's no ground underneath him.

People should top training radiologists now. It's just completely obvious that within 5 years deep learning is going to do better than radiologists.

Now

Big Data Bust: MD Anderson-Watson Project Dies

Top Cancer Center Spent $62M

Nick McKelly
February 22, 2017

"IBM has made it clear that the Oncology Expert Advisor should not be used with patients." -- Medscape

What Went Wrong?
The answer lies in a 48-page audit the UT made on the project

1. Data from incompatible systems: it's comparable to sticking a pie and a 20-pound turkey in the same oven, and expecting them both to come out perfect at the same time.
2. Wanting to believe in miracle cures: as the same mistake as for human intelligence itself.
3. Exaggerated early tests results. The system was used to limited forms of cancer that may have been easier to diagnose and treat. For instance, the early version of OEA targeted just one group of cancer patients–those with a lower-risk form of leukemia, called myelodysplastic syndrome.

Jim Giuliano, May 3, 2017

FULL TEXT ARTICLE

Artificial intelligence in health care: within touching distance

The Lancet
Lancet, The, 2017-12-23, Volume 390, Issue 10114, Pages 2739-2739,
Copyright © 2017 Elsevier Ltd

Lancet, The

- **There is no doubt that AI in health care remains overhyped and at risk of commercial exploitation.**
- **Despite the excitement around these sophisticated AI technologies, very few are in clinical use.**
- **AI requires thorough and systematic evaluation prior to integration in routine clinical care.**
- **Translating technical success to meaningful clinical impact is the next great challenge.**

Medicine: Science-based Art

Science	Art
Latin: *scire* (to know) - Purely theoretical - Contemplative	Latin: *ars* (craftsmanship) Greek: τέχνη (*téchne)* *"Ars Medica"* *= téchne iatriké* *= the art of medicine*
"analytical"	"accountable"

18/26

ELSI

Ethical,
Legal,
Social,
Implications

Software as a Medical Device (SAMD): Clinical Evaluation

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 8, 2017.

The draft of this document was issued on October 14, 2016.

For questions about this document, contact the Office of the Center Director at 301-796-6900 or the Digital Health Program at digitalhealth@fda.hhs.gov.

Re-Claiming the Heart of Medicine

- **Patient care becomes fragmented and sluggish:** due to multi-sector involvement: health economics, biotechnology, medicolegal, protocols, and programs:
- **Patients are tired of being treated as a commodity**:
- **Reclaiming the heart of medicine:**
  - not a scientific concept,
  - but all **humanitarian mission!**

"Medicine is a Science-based Art"

[69] Levi E. http://ericlevi.com/2015/12/28/biggest-challenge-facing-medicine/

Luncheon Symposium I

SIEMENS Healthineers

Simens Healthcare

Chairperson **Tae Hoon Kim** (Gangnam Severance Hospital, Korea)

Speaker **U. Joseph Schoepf** (Medical University of South Carolina, USA)

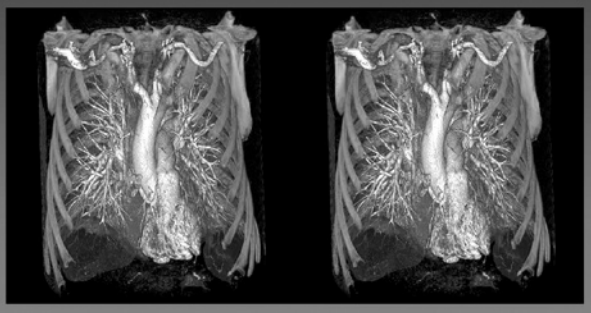
The Cutting-Edge: Cardiac CT Imaging with Dual-Source

The Cutting-Edge: Cardiac CT Imaging with Dual-Source

U. Joseph Schoepf (Medical University of South Carolina, USA)

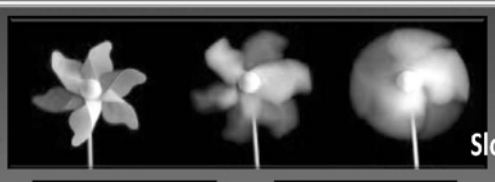
At the Forefront of Innovation...

The Cutting Edge: Scanning Speed

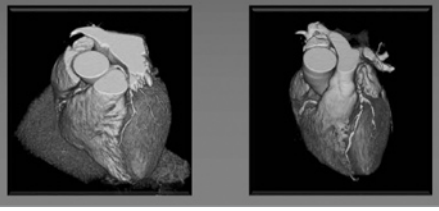


Conventional Technology Dual-Source CT Technology

The Cutting Edge: Scanning Speed

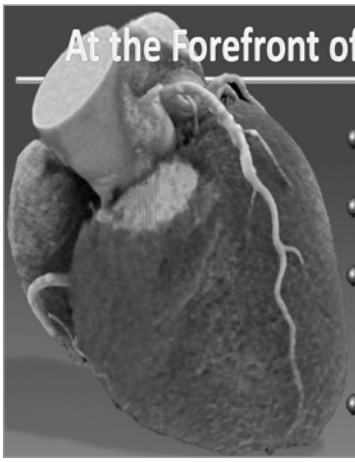


Fast Slow



We Others

At the Forefront of Innovation...



- Image Gently
- Challenging Scenarios
- From Structure to Function
- New Horizons

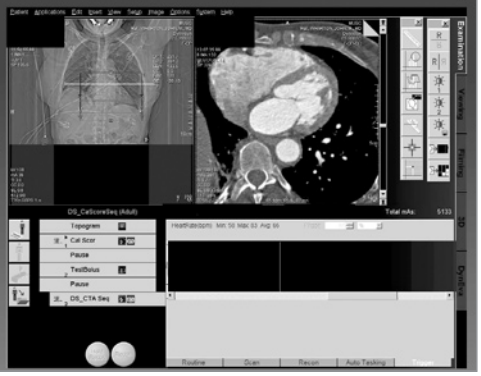
Image Gently

- Validating new imaging standards
  - Prospectively ECG-triggered acquisition
  - Single heart beat acquisitions – ultrahigh pitch applications
  - Iterative reconstruction techniques
- Reducing invasiveness without losing efficacy
  - Lower tube voltage and tube current modulation
  - Reduced contrast media volumes

Reduced Dose - Prospective ECG Triggering

Traditionally for slow (<80bpm), regular heart rates

1.5-3 mSv Effective Dose



Radiation Protection - Low kV

54 yo Woman,

Equivocal SPECT,

100kV Scan,

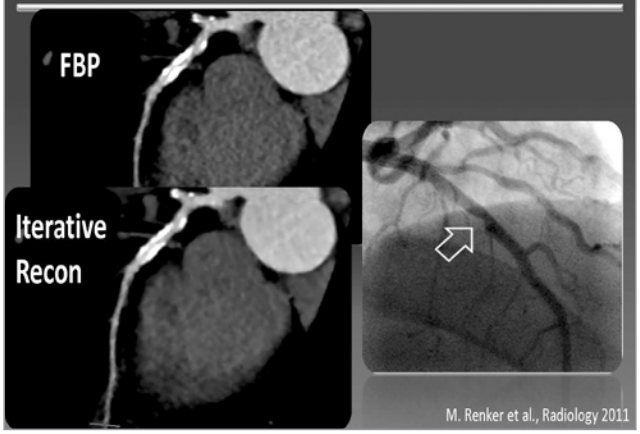
4.6 mSv

Iterative Image Reconstruction

- Improved signal / noise ratio
- Lower radiation dose (e.g. pediatric CT)
- Improved image quality (e.g. obese patients)
- Decreased artifacts (e.g. stents, implanted devices)

G Bastarrika et al., Radiology 2009 – LL Geyer et al., Radiology 2015

Reduced Calcium Blooming Artifacts



M. Renker et al., Radiology 2011

Improved Specificity for Stenosis

n = 55 Patients with Agatston Score >400

Table 3

Specificity (%)		91.2 (46.7, 82.0)		95.8 (69.5, 90.8)
Negative predictive value (%)*		99.2 (69.2, 99.7)		99.4 (73.1, 99.7)
PPV (%)*		61.1 (62.2, 89.9)		76.9 (69.0, 94.6)
Sensitivity (%)*	95.2 (83.8, 99.4)	96.2 (83.8, 99.4)		
Specificity (%)	91.2 (46.7, 82.0)	95.8 (59.5, 90.8)		
Negative predictive value (%)*	99.2 (69.2, 99.7)	99.4 (73.1, 99.7)		
PPV (%)*	61.1 (62.2, 89.9)	76.9 (69.0, 94.6)		
No. of true-positive findings	99	100	66.7 (49.0, 93.1)	79.2 (64.1, 97.1)
No. of false-positive findings	63	30	94.1 (98.1, 99.7)	95 (98.4, 99.8)
No. of true-negative findings	658	691	78.9 (63.1, 68.6)	85.7 (68.6, 83.7)
No. of false-negative findings	5	4	NS	NS

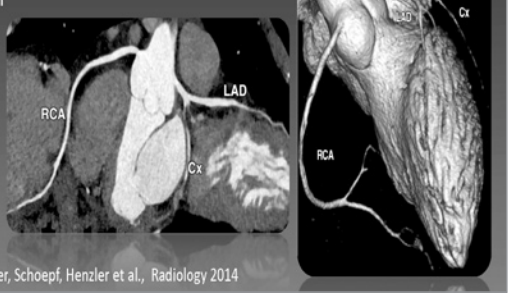
Note.—NS = not significant.

* Data in parentheses are 95% confidence intervals.

M. Renker et al., Radiology 2011

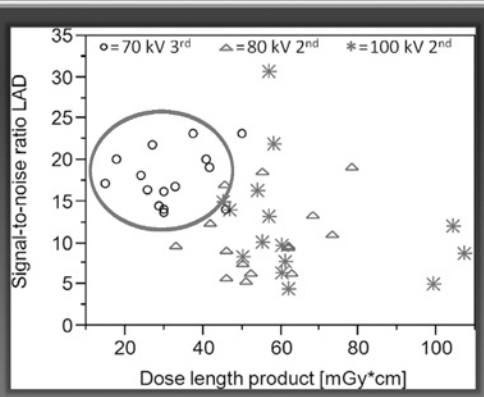
Low kV Scanning in Adults

- 45 years, male
- Chest pain
- HR: 64 BPM
- 70kV
- 0.21mSV

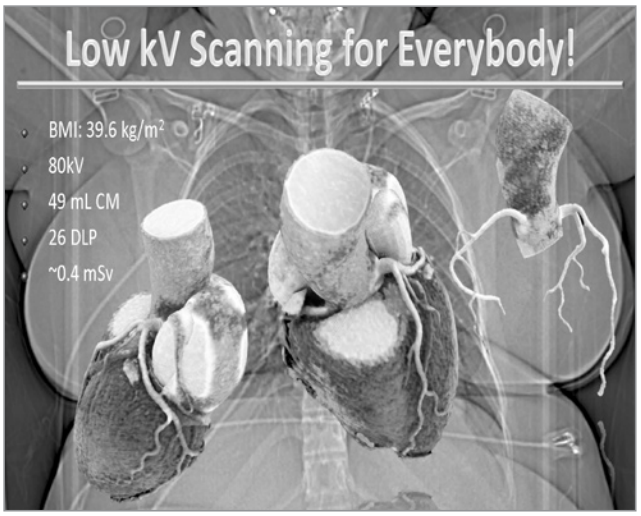


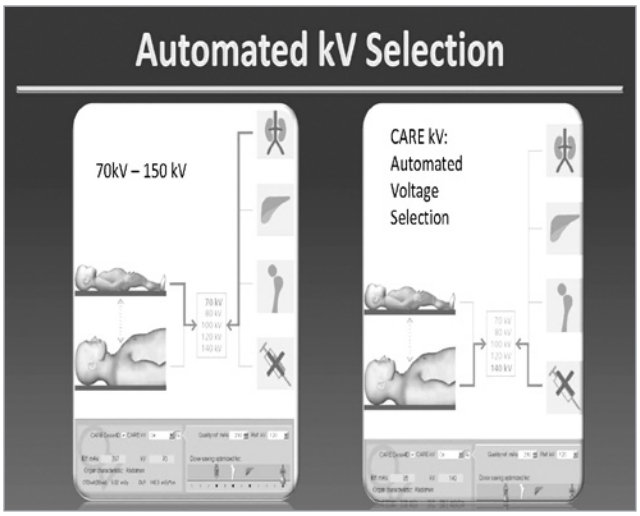
Meyer, Haubenreisser, Schoepf, Henzler et al., Radiology 2014

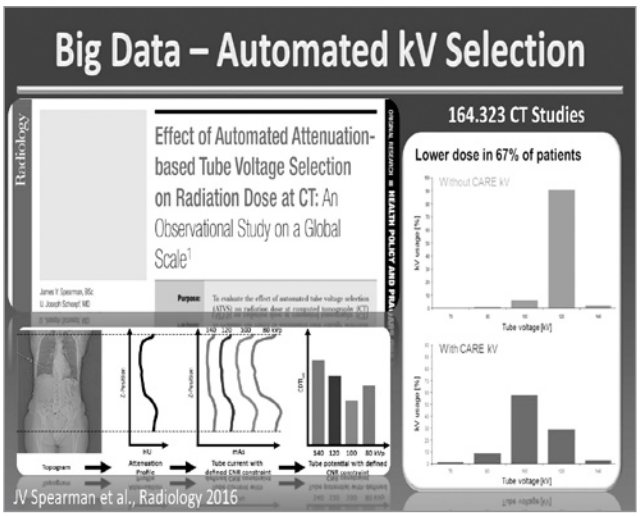
Routine cCTA at < 0.5 mSv is a Reality

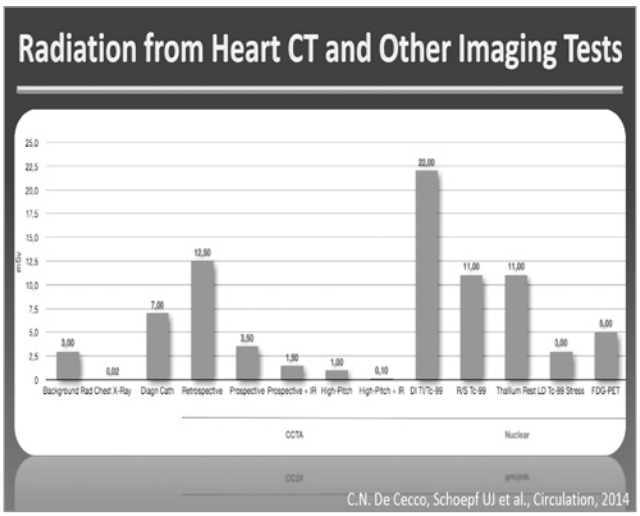


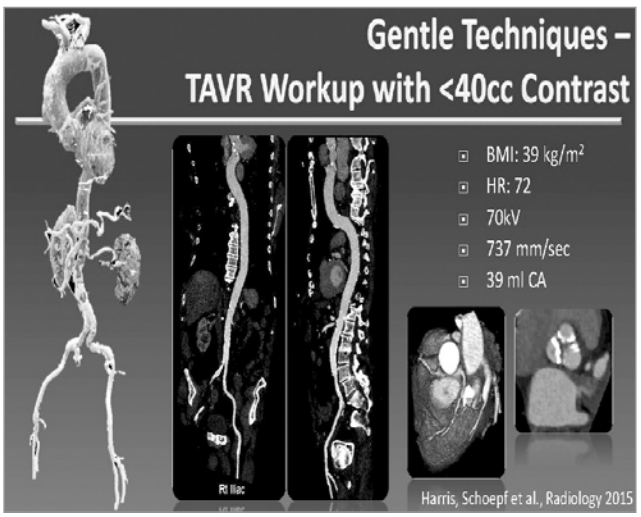
Meyer, Haubenreisser, Schoepf, Henzler et al., Radiology 2014


Low kV Scanning for Everybody!
BMI: 39.6 kg/m²
80kV
49 mL CM
26 DLP
~0.4 mSv


Automated kV Selection
70kV – 150 kV
CARE kV:
Automated
Voltage
Selection


Big Data – Automated kV Selection
Radiology
Effect of Automated Attenuation-based Tube Voltage Selection on Radiation Dose at CT: An Observational Study on a Global Scale[1]
164.323 CT Studies
Lower dose in 67% of patients
Without CARE kV
With CARE kV
Tube voltage [kV]
JV Spearman et al., Radiology 2016


Radiation from Heart CT and Other Imaging Tests
mSv
3,00
0,02
7,00
12,50
3,50
1,50
1,00
0,10
22,00
11,00
11,00
3,00
5,00
Background Rad Chest X-Ray
Diagn Cath
Retrospective
Prospective
Prospective + IR
High-Pitch
High-Pitch + IR
DI T/Tc-99
R/S Tc-99
Thallium Rest LD Tc-99 Stress
FDG-PET
CCTA
Nuclear
C.N. De Cecco, Schoepf UJ et al., Circulation, 2014

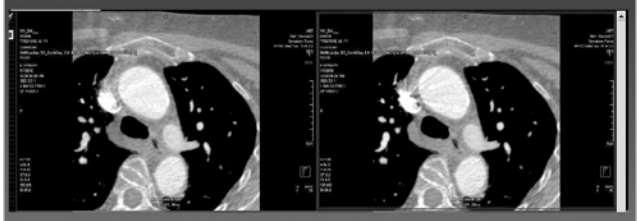

Gentle Techniques –
TAVR Workup with <40cc Contrast
BMI: 39 kg/m²
HR: 72
70kV
737 mm/sec
39 ml CA
Harris, Schoepf et al., Radiology 2015


The Future of
Contrast Media Administration?

Challenging Scenarios: Metal Artifacts

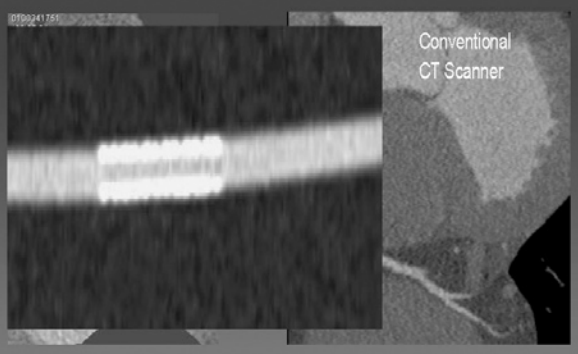
iMAR

High Attenuation Artifacts

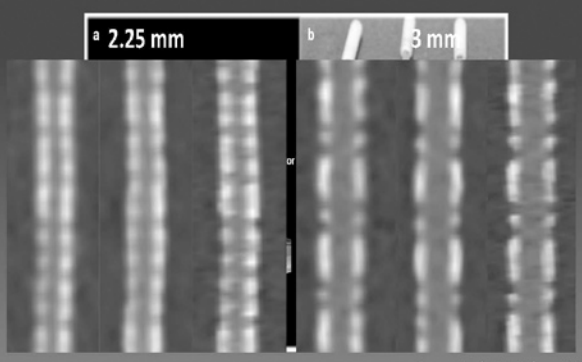


iMAR WFBP

Challenging Scenarios: STENTS

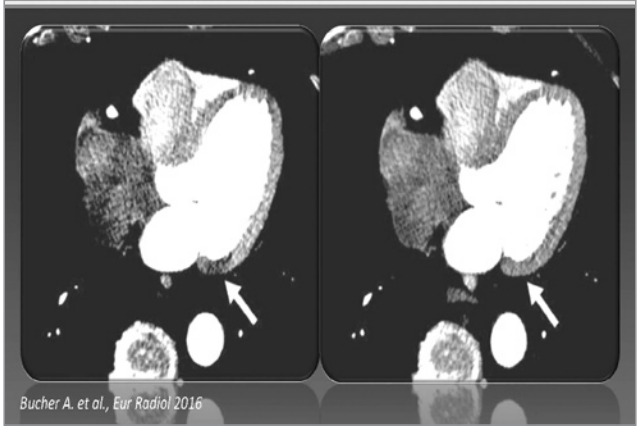


STENTS – INTEGRATED CIRCUIT DETECTOR

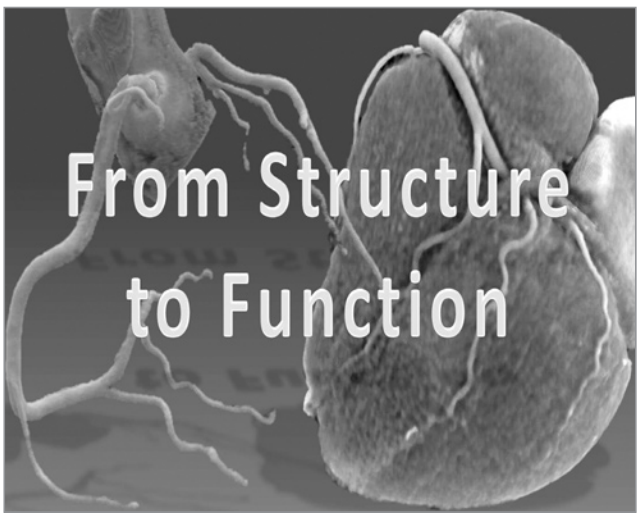


Geyer et al., Radiology, 2015

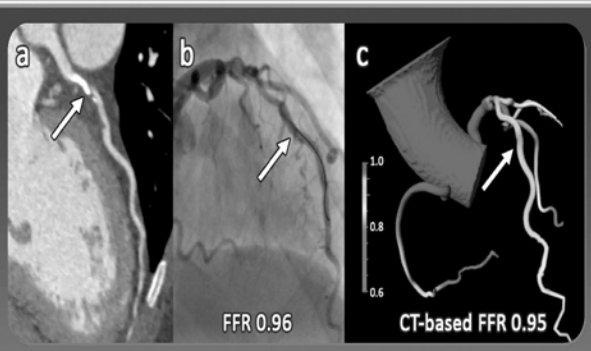
Challenging Scenarios: Beam Hardening



Bucher A. et al., Eur Radiol 2016



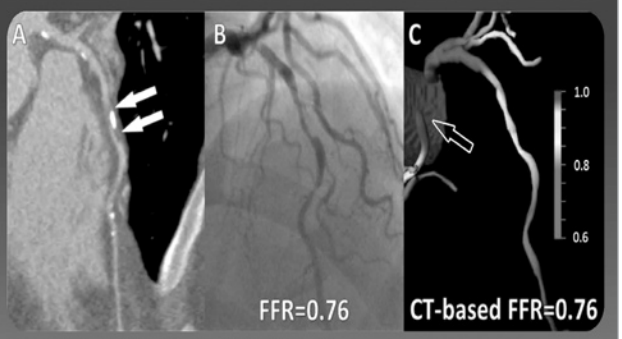
On Site – CT FFR



Novel Algorithm for On-Site Evaluation
CT-FFR, fluid dynamic modeling

Renker et al., Am J Cardiol 2015

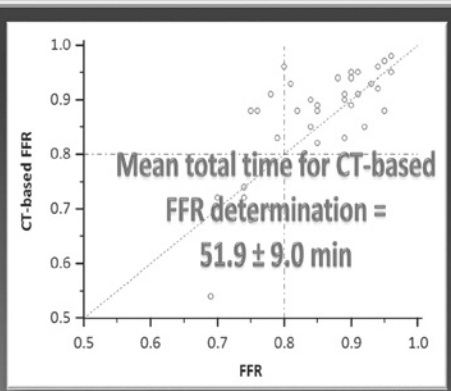
On Site – CT FFR



Novel Algorithm for On-Site Evaluation
CT-FFR, fluid dynamic modeling

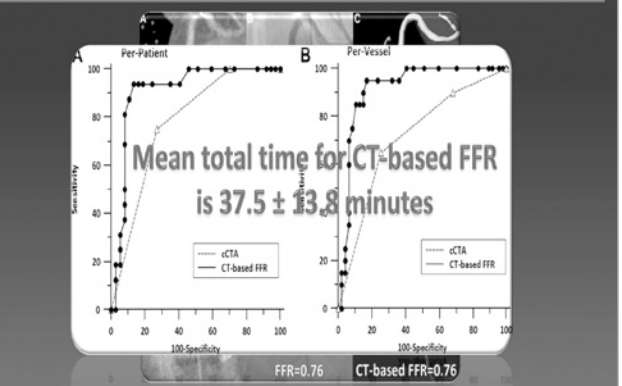
Baumann et al., Eur Radiol 2015

Constrained CFD Model-On-Site-CT-FFR



Baumann, Schoepf et al., Eur Radiol 2015

Constrained CFD Model-On-Site-CT-FFR

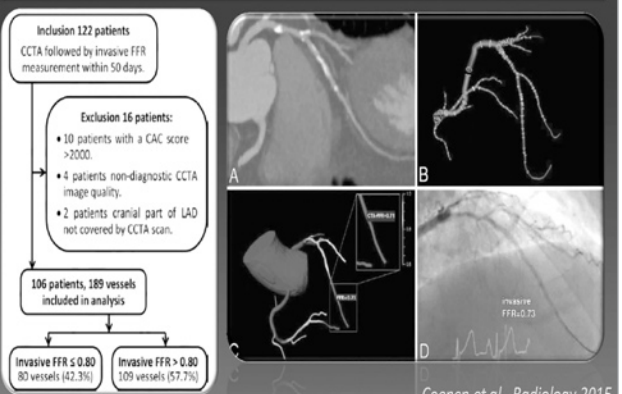


Renker, Schoepf et al., Am J Cardiol 2014

Technical Validation of On-site CT-FFR

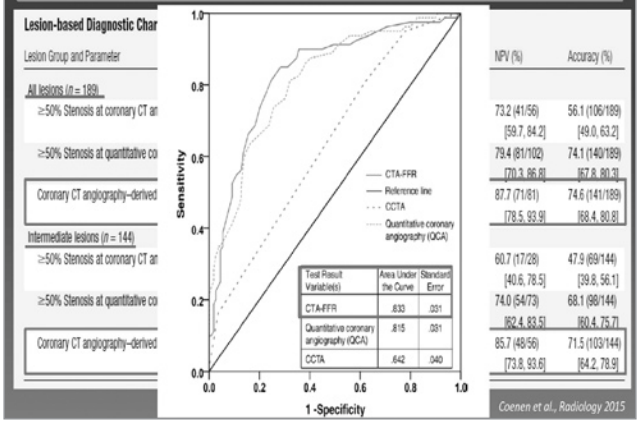
	N (V)	Ref	CAD	CCS	CT	Se	Sp	PPV	NPV	Acc	AUC	BA
Renker AIC 2014	53 (67)	FFR 0.80	30	778	DSCT G1/2	85	85	71	93	NR	0.92 (0.72)	-0.02
Coenen Radiology 2014	106 (189)	FFR 0.80	42	545	DSCT G1/2	88	65	65	88	75	0.83 (0.64)	-0.04 ±0.13
De Geer Acta Rad 2015	21 (23)	FFR 0.80	26	NR	DSCT G2	83	76	56	93	78	NR	-0.03 ±0.15
Kruk JACCimg 2016	90 (96)	FFR 0.80	43	154	DSCT G2	76	72	67	80	74	0.84 (0.66)	-0.01 ±0.19
Yang EHJimg (in press) 2016	72 (138)	FFR 0.80	39	293	DSCT G2	87	77	71	90	81	0.89 (0.85)	-0.06 ±0.27

On-Site CT-FFR



Coenen et al., Radiology 2015

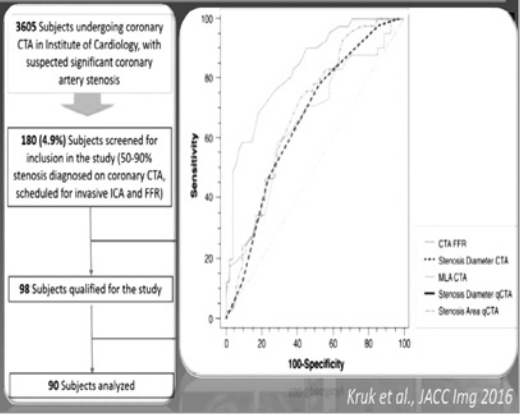
On Site – CT FFR



Coenen et al., Radiology 2015

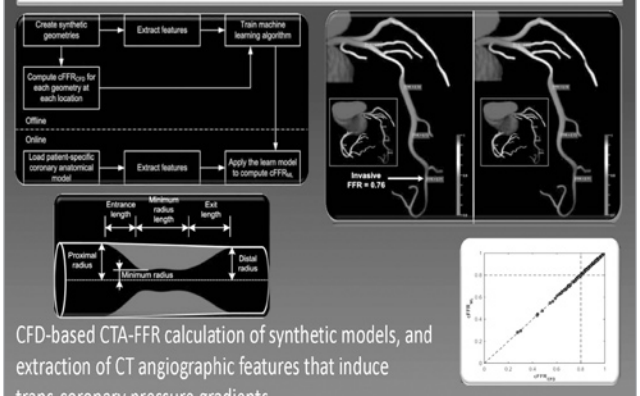
On-Site CT-FFR – Intermediate Lesions

Prospective single-center study *n* = 98 "Intermediate stenosis" (50-90%)



Kruk et al., JACC Img 2016

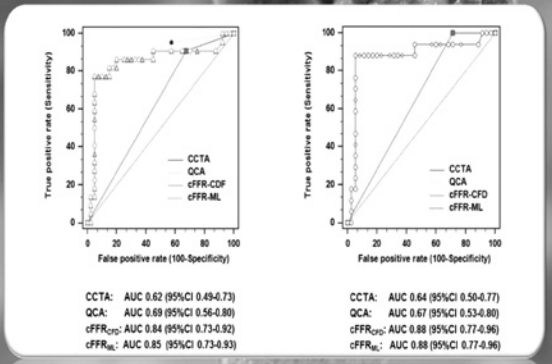
AI – Deep Machine-Learning CT-FFR



CFD-based CTA-FFR calculation of synthetic models, and extraction of CT angiographic features that induce trans-coronary pressure gradients

Itu et al., J Appl Physiol 2016

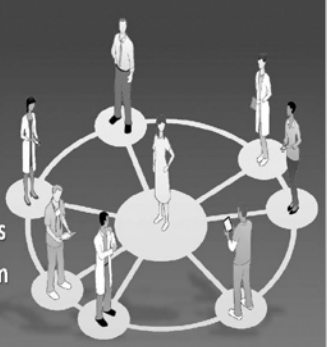
CT-FFR: AI – Deep Machine Learning



Tesche C. Radiology 2018

Patient-Centered Precision Medicine

- Unparalleled acquisition speed
- Powerful x-ray tubes
- Lowest radiation in class
- Minimal contrast media
- Maximal control
- Success in challenging scenarios
- Structure – function conundrum solved
- Exciting new developments



Thank you!

SESSION 3

Ischemic Heart Disease

Chairperson **Hweung-kon Hwang** (Konkuk University Hospital, Korea)
Yeon Hyeon Choe (Samsung Medical Center, Korea)

Presentation

FFR CT - challenge and limitation
Speaker Bon-Kwon Koo (Seoul National University Hospital, Korea)

CT-perfusion - challenge and limitation
Speaker Akira Kurata (Ehime University, Japan)

Clinical impact of plaque characteristics
Speaker Eun Ju Chun (Seoul National University Bundang Hospital, Korea)

SPECT and PET for ischemia
Speaker Sang-Geon Cho (Chonnam National University Hospital, Korea)

Panel Discussion

Panel Hyung-Bok Park (Catholic Kwandong University, International St. Mary's Hospital, Korea)
Yeonyee E. Yoon (Seoul National University Bundang Hospital, Korea)
Kyoung Sook Won (Keimyung University Dongsan Medical Center, Korea)
Jin Hur (Severance Hospital, Korea)

FFR CT - challenge and limitation

Bon-Kwon Koo (Seoul National University Hospital, Korea)

MEMO

CT-perfusion - challenge and limitation

Akira Kurata (Ehime University, Japan)

Disclosure of conflict of interest

I have nothing to declare for this presentation.

CIVICS 2018

Kurata A, Ehime University

CT perfusion (CTP)

- Stress CTP
- Rest CTP
- Dual-energy CTP

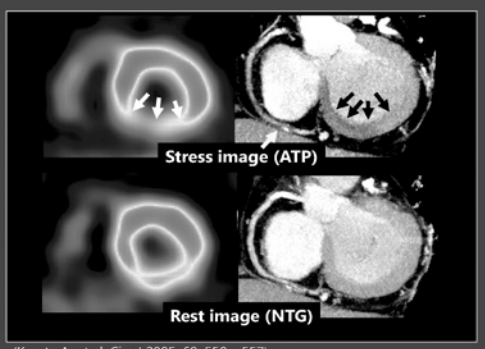
Kurata A, Ehime University

Role of CT Perfusion: diagnostic test

1. Preliminary test
2. Establishment of methodology (scan protocol)
3. Clinical safety and efficacy assessment (radiation, contrast)
4. Diagnostic performance (lesions, vessels, and patients)
5. Impact on diagnostic thinking (incremental value?)
6. Assessment of its extent and severity
7. Impact on patient management, clinical outcome, and prognosis
8. Clinical indications (patient selection)
9. Definition of standard of truth
10. Benefit/risk balance (of CTP) compared to widely accepted comparators (SPECT, MRI, and echo)
11. Multicenter trials

Kurata A, Ehime University

Stress static CTP (16MDCT)

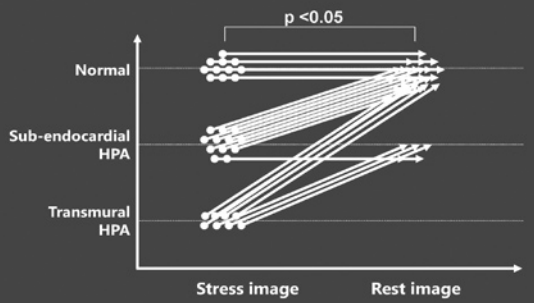


(Kurata A, et al. Circ J 2005; 69: 550 – 557)

Kurata A, Ehime University

Stress dynamic CTP (64MDCT)

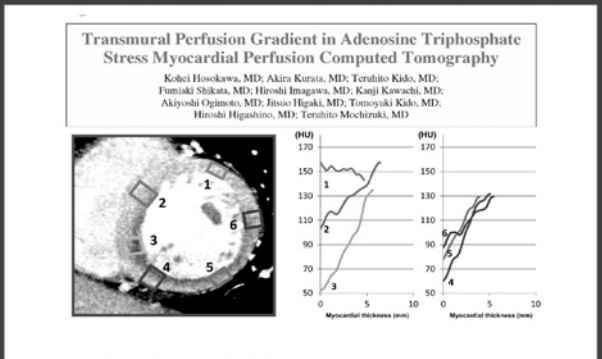
Severity of the hypo-perfusion area at stress and rest



(Kurata A, et al. Circ J 2005; 69: 550 – 557)

Kurata A, Ehime University

Stress static CTP (64MDCT)



Transmural Perfusion Gradient in Adenosine Triphosphate Stress Myocardial Perfusion Computed Tomography

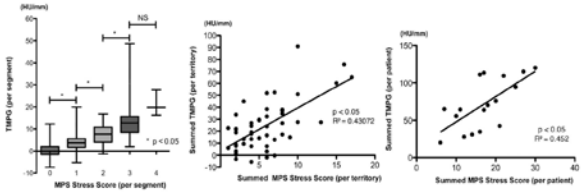
Kohei Hosokawa, MD; Akira Kurata, MD; Teruhito Kido, MD; Fumiaki Shikata, MD; Hiroshi Imagawa, MD; Kanji Kawachi, MD; Akiyoshi Ogimoto, MD; Jitsuo Higaki, MD; Tomoyuki Kido, MD; Hiroshi Higashino, MD; Teruhito Mochizuki, MD

(Hosokawa et al. Circ J 2011; 75: 1905-1912)

Kurata A, Ehime University

ATP stress static CTP (64MDCT)

Transmural perfusion gradient in ATP stress static CTP



- Transmural extent of perfusion defect in ATP stress static CTP image correlated to SPECT score.

(Hosokawa et al. Circ J 2011; 75: 1905-1912)

Kurata A, Ehime University

Wider and faster MDCT

Brilliance 64

- 0.42 s/rotation
- 40 mm Coverage (64-slice)

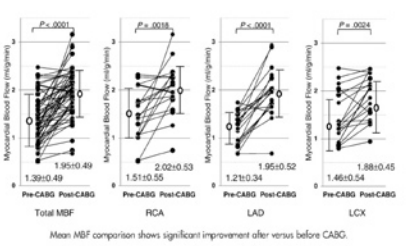
Brilliance iCT

- 0.27 s/rotation
- 80 mm Coverage (256-slice)

Kurata A, Ehime University

ATP stress dynamic CTP (64MDCT)

Regional CT-MBF before and after CABG



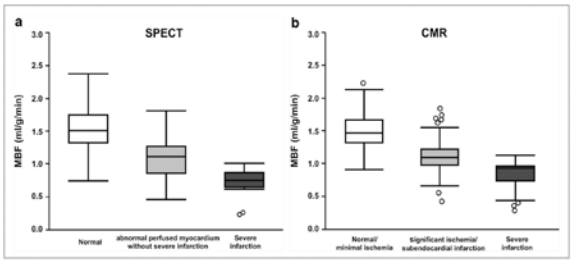
- CT-MBF quantified the post-treatment effect by CABG

(Shikata et al. Am Heart J 2010; 160: 528-553)

Kurata A, Ehime University

ATP stress dynamic CTP (256-sliceCT)

Differentiation of myocardial ischemia and infarction assessed by CT-MBF

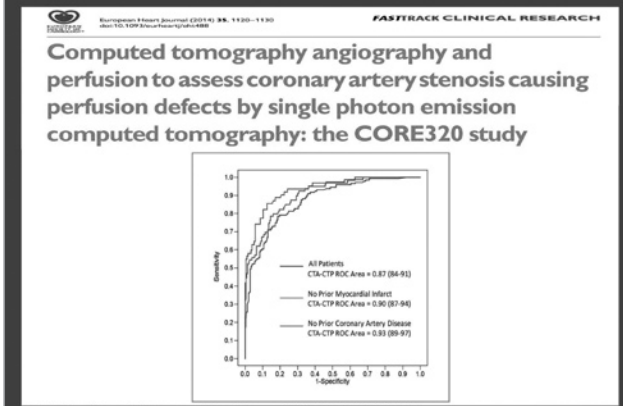


- CT-MBF has a potential to detect abnormal perfused myocardium and severe infarction assessed by SPECT/CMR

(Tanabe Y et al. Eur Radiol. 2016; 26: 3790-3801)

Kurata A, Ehime University

Stress static CTP



European Heart Journal (2014) 35, 1120–1130
doi:10.1093/eurheartj/ehu080

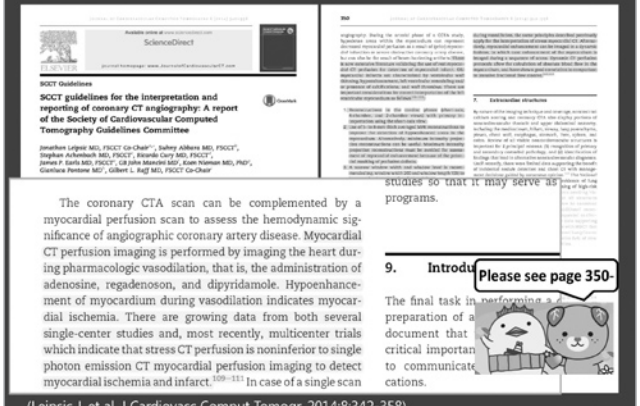
FASTTRACK CLINICAL RESEARCH

Computed tomography angiography and perfusion to assess coronary artery stenosis causing perfusion defects by single photon emission computed tomography: the CORE320 study

(Rochitte CE, et al. European Heart Journal 2014; 35: 1120–1130)

Kurata A, Ehime University

2014 SCCT guidelines



ScienceDirect

SCCT Guidelines

SCCT guidelines for the interpretation and reporting of coronary CT angiography: A report of the Society of Cardiovascular Computed Tomography Guidelines Committee

The coronary CTA scan can be complemented by a myocardial perfusion scan to assess the hemodynamic significance of angiographic coronary artery disease. Myocardial CT perfusion imaging is performed by imaging the heart during pharmacologic vasodilation, that is, the administration of adenosine, regadenoson, and dipyridamole. Hypoenhancement of myocardium during vasodilation indicates myocardial ischemia. There are growing data from both several single-center studies and, most recently, multicenter trials which indicate that stress CT perfusion is noninferior to single photon emission CT myocardial perfusion imaging to detect myocardial ischemia and infarct.[109–111] In case of a single scan

studies so that it may serve as programs.

9. Introdu

The final task in performing a preparation of a document that critical importan to communicate cations.

(Leipsic J, et al. J Cardiovasc Comput Tomogr. 2014;8:342-358)

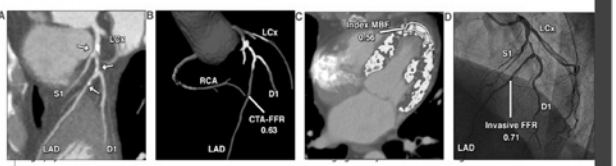
Kurata A, Ehime University

Stress dynamic CTP

JACC: CARDIOVASCULAR IMAGING, VOL. 10, NO. 7, 2017
JULY 2017:760–70

Integrating CT Myocardial Perfusion and CT-FFR in the Work-Up of Coronary Artery Disease

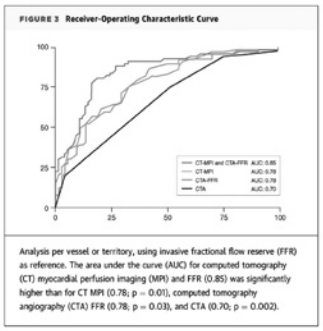
Adriaan Coenen, MD,[a,b] Alexia Rossi, MD, PhD,[b,c] Marisa M. Lubbers, MD,[a,b] Akira Kurata, MD, PhD,[b] Atsushi K. Kono, MD, PhD,[b] Raluca G. Chelu, MD,[b] Sabrina Segreto, MD,[c] Marcel L. Dijkshoorn, RT,[b] Andrew Wragg, PhD,[c] Robert-Jan M. van Geuns, MD, PhD,[a,b] Francesca Pugliese, MD, PhD,[c] Koen Nieman, MD, PhD[a,b]



(Coenen A, et al. J Am Coll Cardiol Img 2017;10:760–70)

Stress dynamic CTP

Integrating CT Myocardial Perfusion and CT-FFR in the Work-Up of Coronary Artery Disease



Analysis per vessel or territory, using invasive fractional flow reserve (FFR) as reference. The area under the curve (AUC) for computed tomography (CT) myocardial perfusion imaging (MPI) and FFR (0.85) was significantly higher than for CT MPI (0.78; $p = 0.01$), computed tomography angiography (CTA) FFR (0.78; $p = 0.03$), and CTA (0.70; $p = 0.002$).

(Coenen A, et al. J Am Coll Cardiol Img 2017;10:760–70)

Stress static CTP

ARTICLE IN PRESS

JACC: CARDIOVASCULAR IMAGING
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ISSN 1936-878X/$36.00
https://doi.org/10.1016/j.jcmg.2017.10.025

Incremental Diagnostic Value of Stress Computed Tomography Myocardial Perfusion With Whole-Heart Coverage CT Scanner in Intermediate- to High-Risk Symptomatic Patients Suspected of Coronary Artery Disease

Gianluca Pontone, MD, PhD,[a] Daniele Andreini, MD, PhD,[a,b] Andrea I. Guaricci, MD,[a,c] Andrea Baggiano, MD,[a] Fabio Fazzari, MD,[a] Marco Guglielmo, MD,[a] Giuseppe Muscogiuri, MD,[a] Claudio Maria Berzovini, MD,[a] Annalisa Pasquini, MD,[a] Saima Mushtaq, MD,[a] Edoardo Conte, MD,[a] Giuseppe Calligaris, MD,[a] Stefano De Martini, MD,[a] Cristina Ferrari, MD,[a] Stefano Galli, MD,[a] Luca Grancini, MD,[a] Paolo Ravagnani, MD,[a] Giovanni Teruzzi, MD,[a] Daniela Trabattoni, MD,[a] Franco Fabbiocchi, MD,[a] Alessandro Lualdi, MD,[a] Piero Montorsi, MD,[a,b] Mark G. Rabbat, MD,[b,c] Antonio L. Bartorelli, MD,[a,c] Mauro Pepi, MD[a]

(Pontone G, et al. JACC Cardiovasc Imaging. 2018 Feb 9. PMID: 29454774)

Stress static CTP

Incremental diagnostic value of stress CTP with whole-heart coverage CT scanner in intermediate- to high-risk symptomatic patients suspected of CAD

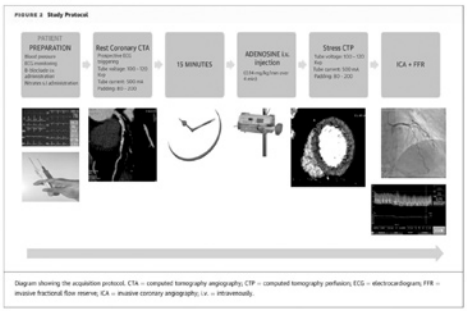


Diagram showing the acquisition protocol. CTA = computed tomography angiography; CTP = computed tomography perfusion; ECG = electrocardiogram; FFR = invasive fractional flow reserve; ICA = invasive coronary angiography; i.v. = intravenously.

(Pontone G, et al. JACC Cardiovasc Imaging. 2018 Feb 9. PMID: 29454774)

Stress static CTP

TABLE 2 Image Quality and Overall Evaluability of Rest Coronary CTA in a Segment-based Model

	N	Overall Artifacts	Breath Artifacts	Blooming Effects	Motion Artifacts	Impaired Signal-to-Noise Ratio	Likert Score	Non-evaluable segments
Rest coronary CTA								
LM	99	31	0	26	0	0	3.6 ± 0.7	1
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0	3.1 ± 0.9	3
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
All segments	**1,526**	**323 (24)**	**12 (1)**	**327 (21)**	**19 (1)**	**15 (1)**	**3.4±0.9**	**39 (2)**

Values are n, mean ± SD, or n (%).
CTA = computed tomography angiography; D1 = first diagonal branch; D2 = second diagonal branch; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LM = left main coronary artery; M1 = first marginal branch; M2 = second marginal branch; PDA = posterior descending coronary artery; PLA = posterolateral coronary artery; RCA = right coronary artery.

TABLE 3 Image Quality of Stress CPT in a Segment-based Model

	N	Score 1	Score 2	Score 3	Score 4	Score
Stress CTP						
1. Basal anterior	98	2	17	29	50	3.30
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
All myocardial segments	**1,274**	**9 (0.7)**	**153 (12)**	**326 (26)**	**786 (62)**	**3.4±0.9**

Values are n, n (%), or mean ± SD.
CTP = computed tomography myocardial perfusion; Score 1 = very uncertain; Score 2 = uncertain; Score 3 = rather certain; Score 4 = very certain.

(Pontone G, et al. JACC Cardiovasc Imaging. 2018 Feb 9. PMID: 29454774)

Stress static CTP

TABLE 4 Diagnostic Accuracy in a Vessel-Based and Patient-Based Model Between Rest Coronary CTA and Rest Coronary CTA Plus Stress CTP Compared With Functionally Significant CAD

	Rest Coronary CTA	Rest Coronary CTA + Stress CTP	p Value
Vessel-based analysis			
True positive	86	80	–
True negative	162	193	–
False positive	50	13	–
False negative	2	8	–
Sensitivity	98 (95-100)	91 (85-97)	0.06
Specificity	76 (71-82)	94 (90-97)	<0.001
Negative predictive value	99 (97-100)	96 (93-99)	0.11
Positive predictive value	63 (55-71)	86 (79-93)	<0.001
Accuracy	83 (78-87)	93 (90-96)	0.002
Patient-based analysis			
True positive	49	49	–
True negative	27	40	–
False positive	23	8	–
False negative	1	1	–
Sensitivity	98 (94-100)	98 (94-100)	1
Specificity	54 (40-68)	83 (73-94)	<0.001
Negative predictive value	96 (90-100)	98 (93-100)	0.7
Positive predictive value	68 (57-79)	86 (77-95)	0.02
Accuracy	76 (68-84)	91 (85-97)	0.004

Values are n or % (95% CI). Functionally significant CAD was defined as stenosis >80% or fractional flow reserve <0.8 in intermediate stenosis 30% to 80%.
CI = confidence interval; other abbreviations as in Tables 1 to 3.

RADIATION EXPOSURE.

- **Coronary CTA: 2.8 ± 1.4 mSv**
- **Stress CTP: 2.5 ± 1.1 mSv**
- **Cumulative mean: 5.3 mSv**
- **Invasive CAG: 10.3 ± 2.5 mSv**

(Pontone G, et al. JACC Cardiovasc Imaging. 2018 Feb 9. PMID: 29454774)

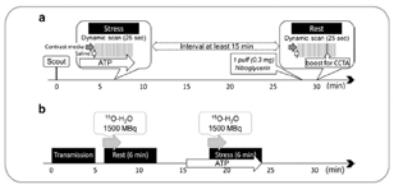
Stress dynamic CTP

Eur Radiol (2014) 24:1547–1556
DOI 10.1007/s00330-014-3164-3

CARDIAC

Quantification of myocardial blood flow using dynamic 320-row multi-detector CT as compared with ^{15}O-H_2O PET

Yasuka Kikuchi · Noriko Oyama-Manabe · Masanao Naya · Osamu Manabe · Yuuki Tomiyama · Tsukasa Sasaki · Chietsugu Katoh · Kohsuke Kudo · Nagara Tamaki · Hiroki Shirato



(Kikuchi Y, et al. Eur Radiol 2014; 24:1547–1556)

Stress dynamic CTP

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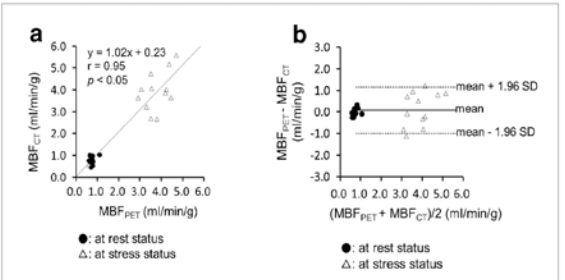

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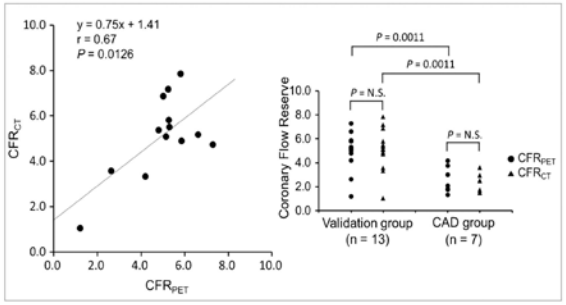
Stress dynamic CTP

Quantification of myocardial blood flow using dynamic 320-row multi-detector CT as compared with 15O-H2O PET

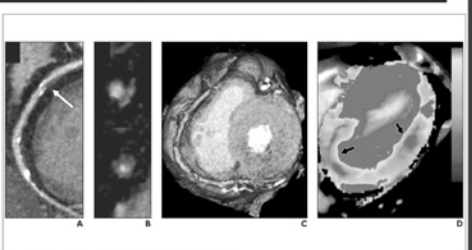


(Kikuchi Y, et al. Eur Radiol 2014; 24:1547–1556)

Stress dynamic CTP

Prognostic Value of Stress Dynamic Myocardial Perfusion CT in a Multicenter Population With Known or Suspected Coronary Artery Disease

Felix G. Meinel[1,2]
Francesca Pugliese[3]
U. Joseph Schoepf[1,4]
Ullrich Ebersberger[1,5]
Julian L. Wichmann[1,6]
Gladys G. Lo[7]
Yeon Hyeon Choe[8]
Yining Wang[9]
Sabrina Segreto[3,10]
Fabian Bamberg[11]
Carlo N. De Cecco[1]



(Meinel FG, et al. AJR Am J Roentgenol. 2017; 208: 761-769)

Stress dynamic CTP

Prognostic value of stress dynamic CTP in a multicenter population with known or suspected CAD

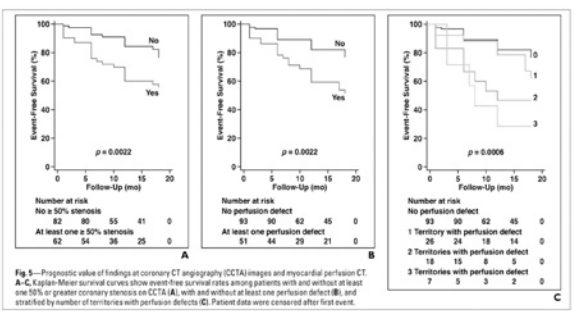


Fig. 5—Prognostic value of findings at coronary CT angiography (CCTA) images and myocardial perfusion CT. **A–C**, Kaplan-Meier survival curves show event-free survival rates among patients with and without at least one 50% or greater coronary stenosis on CCTA (**A**), with and without at least one perfusion defect (**B**), and stratified by number of territories with perfusion defects (**C**). Patient data were censored after first event.

(Meinel FG, et al. AJR Am J Roentgenol. 2017; 208: 761-769)

Systemic review papers

- **Stress CTP**
  - Techasith T, et al. JACC CV Imaging. 2011; 4: 905-16.
  - So A, et al. JCCT 2011; 5: 467-481.
  - Ko SM, et al. Int J CV Imaging. 2015; 31: 1-21.
  - Gonzalez JA, et al. Am J Cardiol. 2015; 116: 1469-1478.
  - Danad I, et al. EHJ CV Imaging. 2016; 17: 836-44.
  - Caruso D, et al. Eur J Radiol. 2016; 85: 1893-1899.
  - Sørgaard MH, et al. JCCT 2016; 10: 450-457.
  - Koo HJ, et al. Int J Cardiovasc Imaging. 2016; 32 Suppl 1: 1-19.
  - Cademartiri F et al. Cardiovasc Diagn Ther. 2017; 7: 129-150.
  - Schuijf JD, et al. Eur Heart J Cardiovasc Imaging. 2018; 19: 127-135.
  - Lu M, et al. Int J Cardiol. 2018; 258: 325-331.
- **Dual-energy imaging**
  - Kang DK, et al. Semin Ultrasound CT MR. 2010; 31: 276-91
  - Schwarz F, et al. Eur J Radiol. 2008; 68: 423-33
  - Danad I, et al. JACC CV Imaging. 2015; 8: 710-723.
  - Jin KN, et al. Eur J Radiol. 2016; 85: 1914-1921.
  - Rodriguez-Granillo GA. Cardiovasc Diagn Ther. 2017; 7:159-170.

Role of CT Perfusion: diagnostic test

1. Preliminary test
2. Establishment of methodology (scan protocol)
3. Clinical safety and efficacy assessment (radiation, contrast)
4. Diagnostic performance (lesions, vessels, and patients)
5. Impact on diagnostic thinking (incremental value?)
6. Assessment of its extent and severity
7. Impact on patient management, clinical outcome, and prognosis
8. Clinical indications (patient selection)
9. Definition of standard of truth
10. Benefit/risk balance (of CTP) compared to widely accepted comparators (SPECT, MRI, and echo)
11. Multicenter trials

Kurata A, Ehime University

Take-home message

- Recent studies showed that
  - Stress CTP is non-inferior to SPECT and MR to detect myocardial ischemia and significant CAD
  - Incremental value of CTP to coronary CTA
- Clinical value of CTP is expanding for not only diagnostic performance, but also the severity and post-treatment assessment, and prognosis.

Kurata A, Ehime University

Thank you very much for your attention

akurata@m.ehime-u.ac.jp

Kurata A, Ehime University

MEMO

Clinical impact of plaque characteristics

Eun Ju Chun (Seoul National University Bundang Hospital, Korea)

Contents

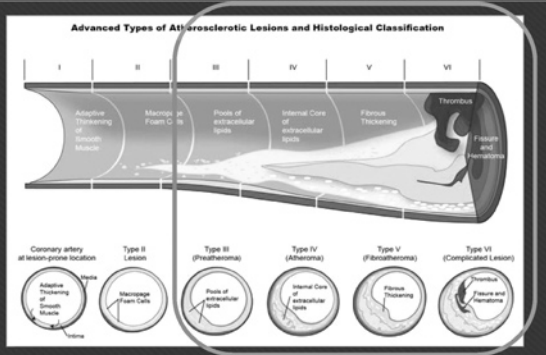
- Atherosclerosis: Pathophysiology
- Plaque imaging with CT
- Plaque characteristics in Stable angina vs. ACS
- Vulnerable plaque
- Plaque imaging using DECT/MECT

SNUBH

Atherosclerosis

SNUBH

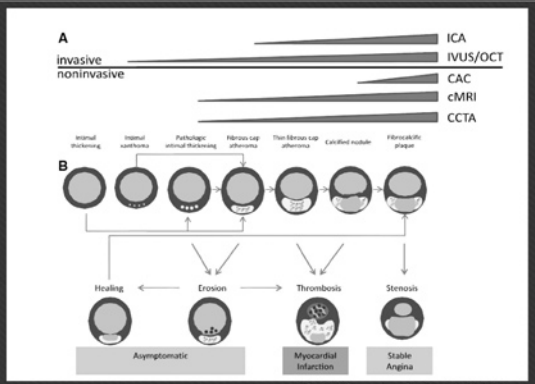
Atherosclerosis



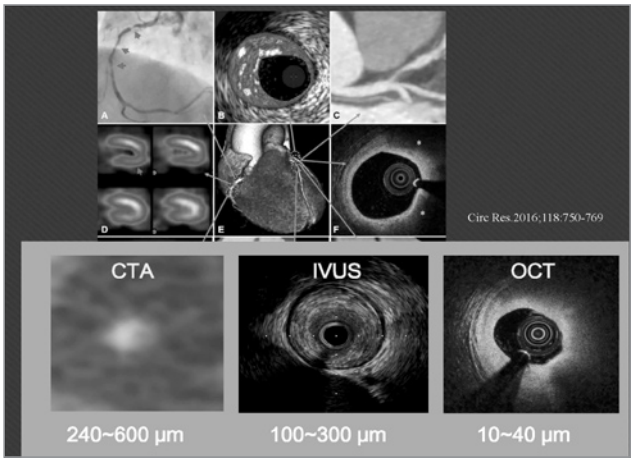
Modified by Stary H.et al. Circulation 1995; 92(5):1335-1374

SNUBH

Atherosclerosis



Circ Cardiovasc Imaging 2015;8:e003316



Plaque on Coronary CT Angiography

SNUBH

CT for evaluation of plaque

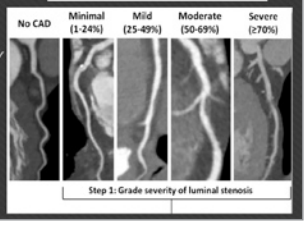
Interpretation of CCTA for lesion

- Stenosis
- Plaque composition
- Remodeling

Degree of Stenosis

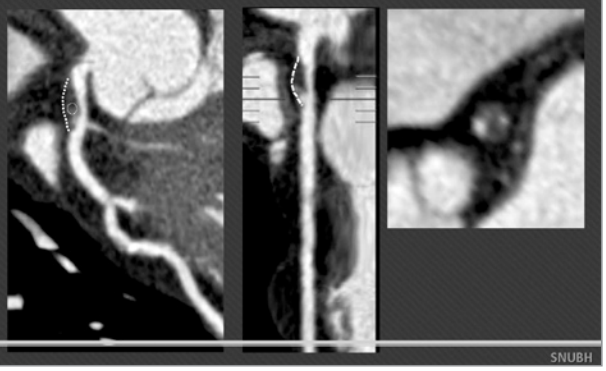
$$= [\,1 - \{\,\frac{C}{(A+B)/2}\,\}\,] \times 100\ (\%)$$

- *Cardiac function, perfusion, viability*



Definition of plaque in CT

- Plaques ; structures >1 mm² within and/or adjacent to the vessel lumen, which could be clearly distinguished from the lumen & surrounding pericardial tissue.



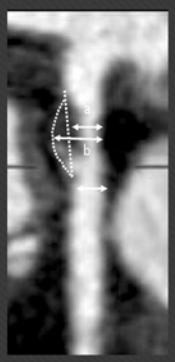
SNUBH

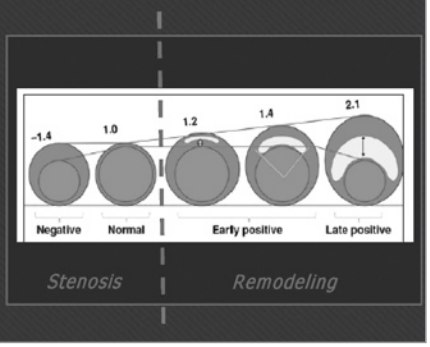
Visual analysis of the plaque type

Plaque type	According to density (HU)
calcified plaque	≥ 130 HU
Mixed (partially calcified)	50% non-calcified plaque
Spotty calcification	Calcified lesion with plaque area < 5 mm²
Non-calcified (soft) plaque	No calcium
Lipid-rich vs. fibrous	50 HU vs. 100 HU
Thrombus	20 HU
Napkin-ring sign	

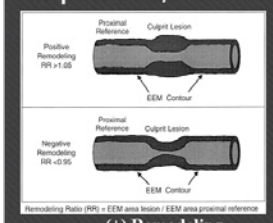
Positive remodeling

- Remodeling Index (RI):
  = EEM area lesion/EEM area reference
  = b/a



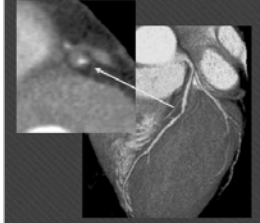


Plaque Area/remodeling



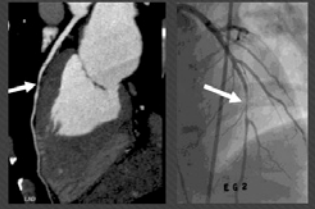
- Positive remodeling: vulnerable plaque…
- Negative Remodeling: fibrous plaque, spasm…

(+) Remodeling



Kim JA, Chun EJ et al. AJR 2011; 197:125-130

(-) Remodeling

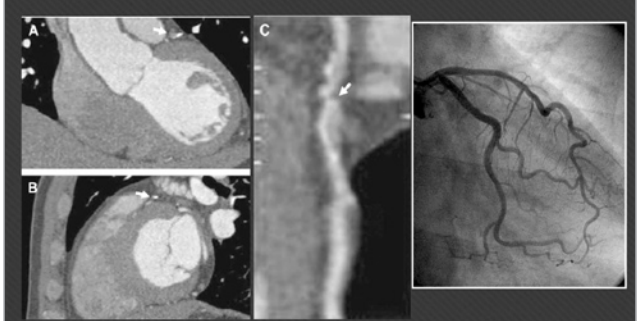


Kang KM, Choi SI et al. KJR 2011

Imaging parameters & plaque detectability

Temporal resolution

- Motion artifact

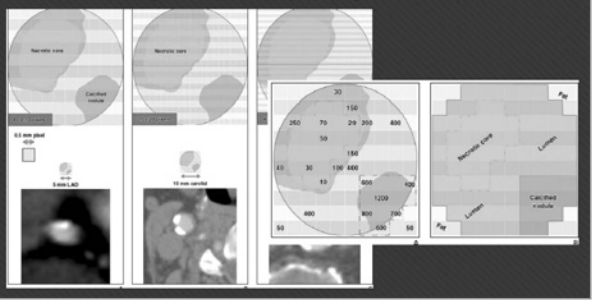


Lesser J et al. J CCT 2009; 3: 4-15

Imaging parameters & plaque detectability

Spatial resolution

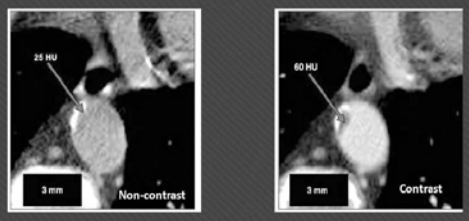
- With large voxel volume in relation to the vessel size averaging artifacts
- Averaging with adjacent pixels causes overestimation of the calcified plaque (blooming artifact)
- Averaging causes underestimate for low-density lesions, especially if the plaque is surrounded by high-density luminal contrast agent



Imaging parameters & plaque detectability

Contrast agent-related factors

- volume of contrast agent, iodine concentration, injection rate,
- heart rate, cardiac output,
- exposure parameters, slice thickness, and reconstruction algorithm



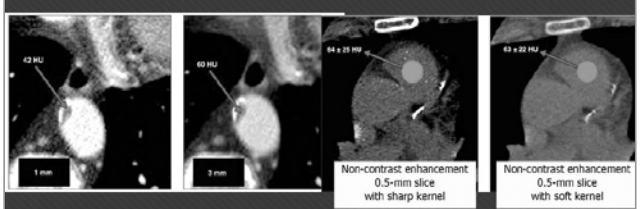
Effect of contrast enhancement on average noncalcified plaque attenuation values.

Saremi F, Achenbach S. AJR 2015;204:W249-W260

Imaging parameters & plaque detectability

Contrast agent-related factors

- volume of contrast agent, iodine concentration, injection rate,
- heart rate, cardiac output,
- exposure parameters, slice thickness, and reconstruction algorithm



Effect of slice thickness on average noncalcified plaque attenuation values.

Effects of reconstruction kernel on small calcified plaques.

Saremi F, Achenbach S. AJR 2015;204:W249-W260

Imaging parameters & plaque detectability

Image resolution

- Improved **temporal resolution;**
  - large z-axis coverage
  - scanner rotation speed
  - faster scan technique; high pitch technique
  - use beta-blocker
- Improved **spatial resolution**
  - thinner collimation
  - smaller detector size (small FOV)
  - special reconstruction algorithm

- control; quantum noise (statistical fluctuation in the number of x-ray photons), patient size, quality of detector & reconstruction algorithm

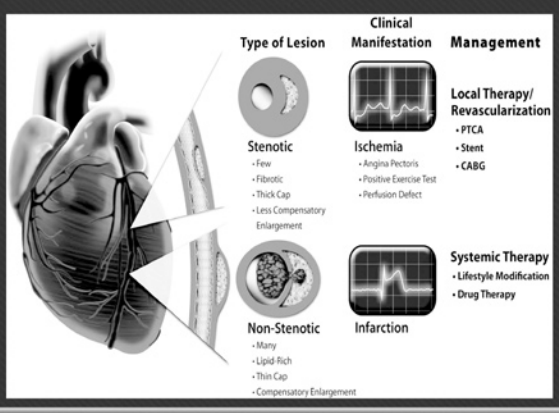
SNUBH

Vulnerable plaque

1. low-attenuated plaque
2. Positive remodeling
3. Napkin-ring sign
4. Spotty calcification
5. Plaque burden
6. Plaque burden

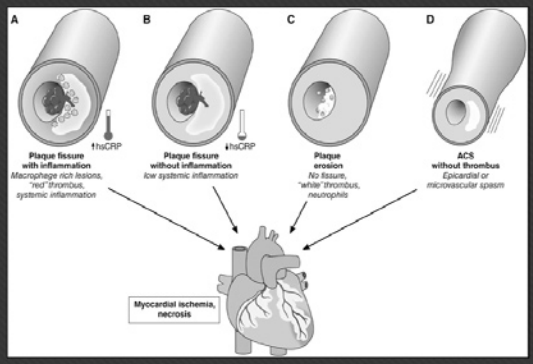
SNUBH

Vulnerable plaque



SNUBH

Four diverse mechanisms cause ACS



Circulation. 2017;136:1155–1166.

Vulnerable plaque

Criteria for Defining Vulnerable Plaques

Major

- Active inflammation: monocyte and macrophage and sometimes T-cell infiltration
- Thin cap with large lipid-necrotic core
- Endothelial denudation with superficial platelet aggregation
- Fissured plaque
- Stenosis 90%

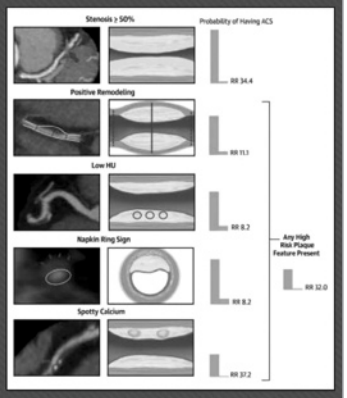
Minor

- Superficial calcified nodule
- Glistening yellow plaque seen at angioscopy
- Intraplaque hemorrhage
- Endothelial dysfunction
- Outward (positive) remodeling

Naghavi, M. et al. Circulation 2003;108:1664-1672

Vulnerable plaque

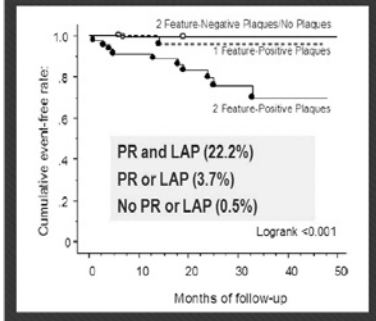
1. Low HU
2. Positive Remodeling
3. Napkin Ring sign
4. Spotty calcification
5. Large plaque burden

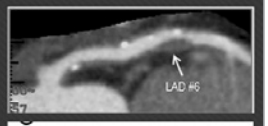


ROMICAT trial II - Puchner et al. JACC 2014

Vulnerable plaque

I. Low attenuation plaques





LAP; < 30 HU **135 kVp**
PR; > 1.1

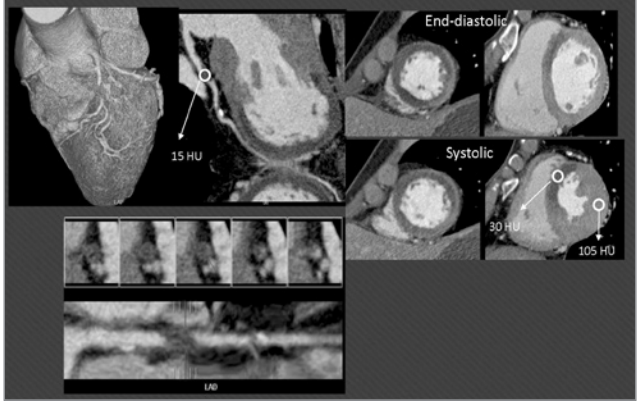
Motoyama et al. JACC 2009; 54:49-57

Vulnerable plaque

- 49Y/M, Acute chest pain (D;3h) with elevated cardiac enzyme

Culprit plaque

- 55Y/M, Acute chest pain (1HA), normal range -- >elevated cardiac enzyme



Vulnerable plaque vs. Culprit lesion (occlusion)

I. Low attenuation plaques

Contents lists available at ScienceDirect

Journal of Cardiovascular Computed Tomography

journal homepage: www.elsevier.com

Research paper

Differences in the CT findings between vulnerable plaque and culprit lesions in acute coronary syndrome

Eun Ju Chun[a, 1], Jin Hee Han[b, 1], Seung Min Yoo[b, *], Hwa Yeon Lee[c], In Sup Song[d], Charles S. White[e]

	Culprit lesion (n=15)	Vulnerable plaque (n=10)	P value
Positive remodeling	13/15(86.7)	5/10(50)	>.05
Positive remodeling index	1.6±0.3	1.3±0.3	>.05
LAP (<30 HU)	11/15(73.3)	6/10(60)	>.05
Napkin ring sign	13/15(86.7)	6/10(60)	>.05
MPA	103. 5±29.2	93.2±30.4	>.05
Degree of stenosis			
Normal	0/15(0)	4/10(40)	
<50%	0/15 (0)	4/10(40)	
50%- <99%	8/15(53.3)	2/10(20)	
Occlusion	7/15(46.7)	0/10(0)	.037
Myocardial hypoperfusion	7/15(46.7)	0/10(0)	.037

Vulnerable plaque

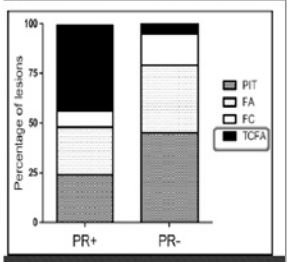
2. Positive remodeling

- Remodeling index (PR ≥1.0) is correlated with higher plaque burden, a larger amount of necrotic core and a higher prevalence of TCFA assessed by VH-IVUS

Table 2
Virtual histologic intravascular ultrasound characteristics between lesions with and without positive remodeling on computed tomographic angiogram

Plaque Characteristics on VH IVUS Image	Presence of Positive Remodeling on CTA	Absence of Positive Remodeling on CTA	p Value
Minimal lumen area (mm^2)	8 ± 4	9 ± 5	0.38
Vessel area (mm^2)*	16 ± 6	15 ± 6	0.24
Plaque burden (%)	51 ± 10	41 ± 16	<0.001
Fibrotic (%)	55 ± 9	51 ± 19	0.18
Fibrofatty (%)	20 ± 11	18 ± 13	0.58
Necrotic core (%)	16 ± 8	10 ± 7	0.001
Dense calcium (%)	9 ± 6	7 ± 11	0.25

Data presented as mean ± SD.
* At minimal lumen area.

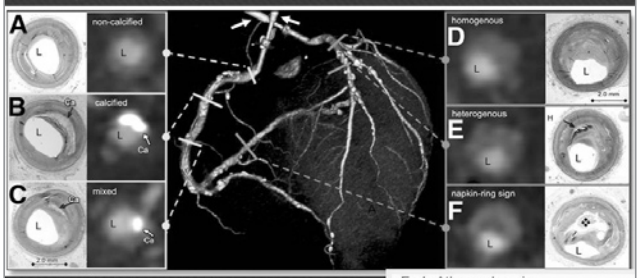


Kroner, ES et al. AJC 2011;107:1725-29

Vulnerable plaque

3. Napkin-Ring sign

Attenuation Pattern-based Classification



(A) Non-calcified plaque / PIT
(B) Mixed plaque / FP with sheet calcification
(C) Mixed plaque / PIT with spotty calcification
(D) Homogeneous / FP
(E) Heterogeneous / EFA with intraplaque hemorrhage
(F) Napkin-ring sign / LFA with large necrotic core

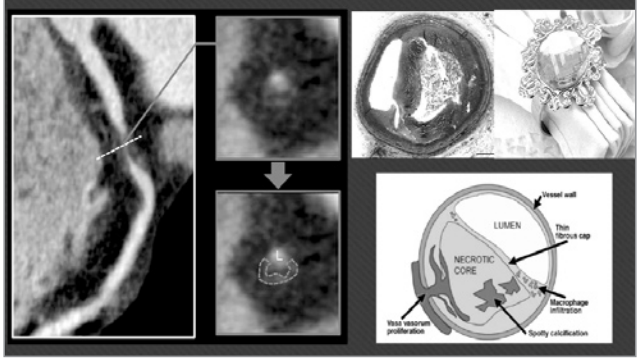
- Early Atherosclerosis:
  - AIT (adaptive intimal thickening)
  - PIT (pathological intimal thickening)
  - Fib (fibrous plaque)
- Advanced atherosclerosis
  - EFA (Early fibroatheroma)
  - LFA (Late fibroatheroma)
  - TCFA (Thin cap fibroatheroma)

Maurovich-Horvat P. et al. JACC Cardiovasc Imaging. 2012 Dec;5(12):1243-52

Vulnerable plaque

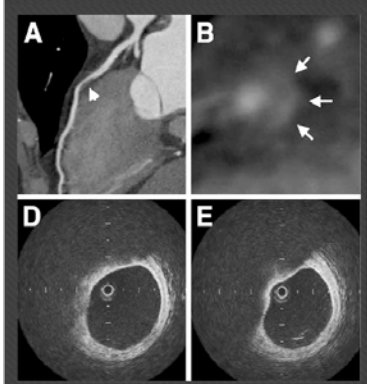
3. Napkin-Ring sign

- Defined by a low attenuation plaque core surrounded by a circumferential area of higher attenuation.



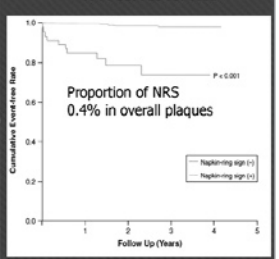
Vulnerable plaque

3 .Napkin-Ring sign; thin cap Fibroatheroma



Kashiwagi et al. JACC Cardiovasc Imaging 2009

K-M curves for ACS

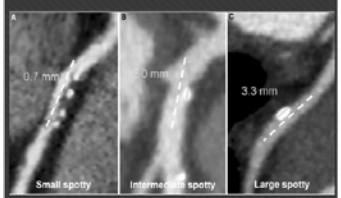


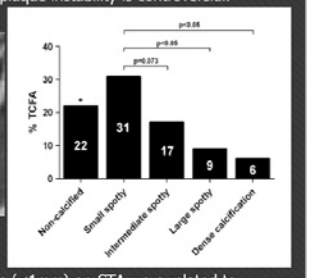
Kashiwagi M. et al. J Cardiol. 2013 ;61(6):399-403

Vulnerable plaque

4. Spotty calcification

- Coronary calcification assessed by CT is highly associated with plaque burden and related to poor clinical prognosis.
- However, the effect of calcification on plaque instability is controversial.



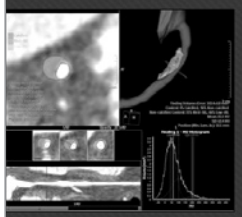


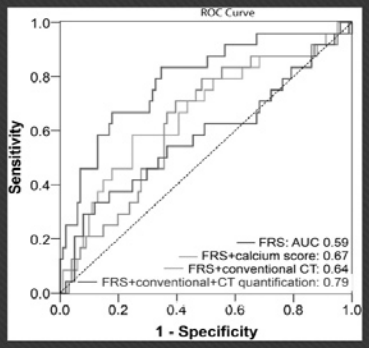
- Plaques with small spotty calcifications (<1mm) on CTA were related to TFCA on IVUS-VH

Van Velzen JE et al. JNC 2011;18:893-903

Vulnerable plaque

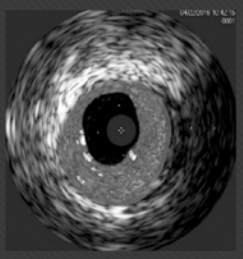
5. Plaque burden

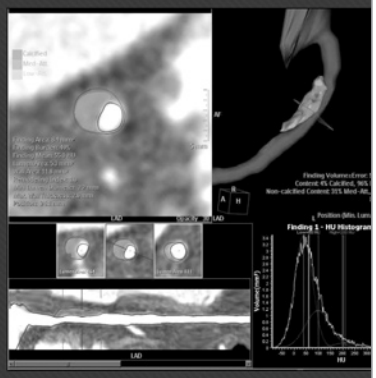




Versteylen et al. JACC 61(22) 2013; 2013:2296–305

Plaque component; complex





VH-IVUS
- Green; fibrous
- Red; necrotic core
- Yellow; fibrofatty
- White; calcification

Vulnerable plaque on CCTA; Challenging point

- Low-attenuation plaque;
  -- What is cut-off value?
  -- 30 HU (135 kVp? 120 kVp? 100 kVp?)
- Measurement method;
  -- mean value of total plaque ?
  -- Lowest pixel value?
  -- Mean 5 pixel value?
- *How many component of high risk plaque feature increased sensitivity?*
- Positive remodeling of calcified plaque
  -- blooming artifact?
  -- True positive remodeling?
- Napkin-ring sign; What is the cut-off value of density between low central portion and peripheral high attenuation?

Plaque characteristics Using by DECT/Multi-energy CT

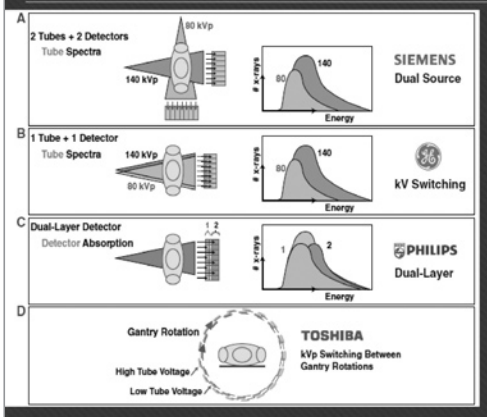
SNUBH

Why need the Dual Energy or Multi-energy?

- Tissues of different chemical composition but the same X-ray attenuation have the same Hounsfield Unit (HU) values, therefore making it challenging to differentiate between tissue types.
- Different elements absorb x-rays with different frequency signature due to their individual electron configurations.
- Between uric acid, hydroxyapatite & calcium in renal calculi or gout
- Calcium-containing plaque, hemorrhagic plaque & iodinated blood in cardiac imaging
- Advantage
  - Reduction of iodinated contrast dose,
  - less beam hardening artifact
  - specific lesion characterization

SNUBH

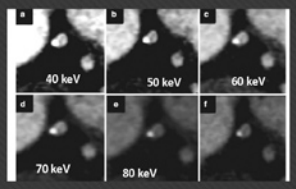
Dual energy and Multi-energy

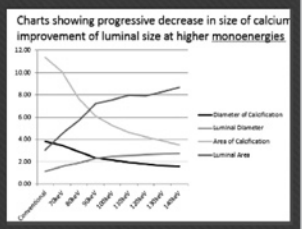


SNUBH

Monochromatic imaging

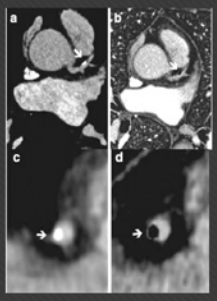
- On the basis of the mass attenuation coefficient properties of the materials, a linear combination of the iodine-water material images is used to create monochromatic CT images at any energy level ranging from 40 to 140 keV.
- Lower energy levels ;
  - higher intraluminal enhancement
  - noise is higher.
  - blooming artifact aggravate

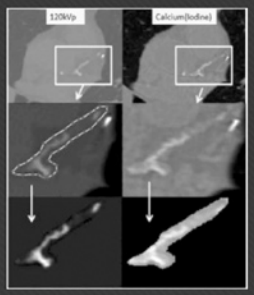




Material decomposition

- *Iodine-calcium;*
  calcium removed
- *Calcium-Iodine;*
  iodine removed (virtual noncontrat)





Thank you very much
for your attention!

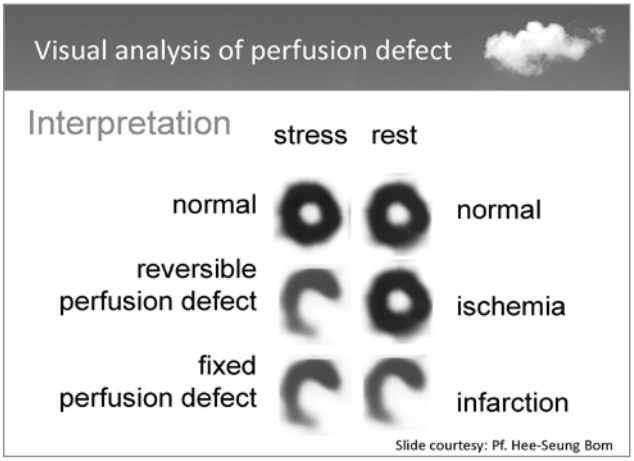
MEMO

SPECT and PET for ischemia

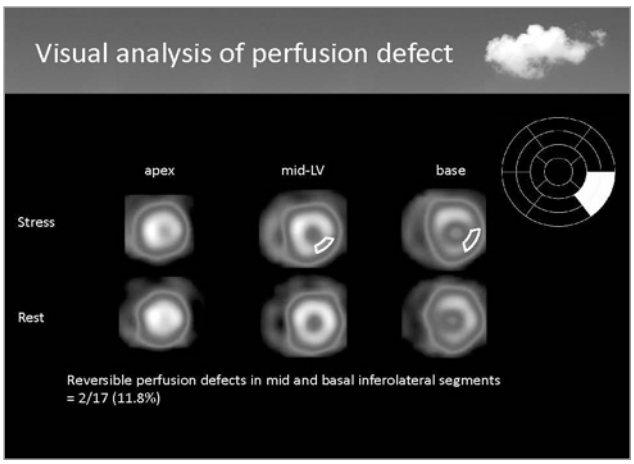
Sang-Geon Cho (Chonnam National University Hospital, Korea)

Visual and
semiquantitative analysis

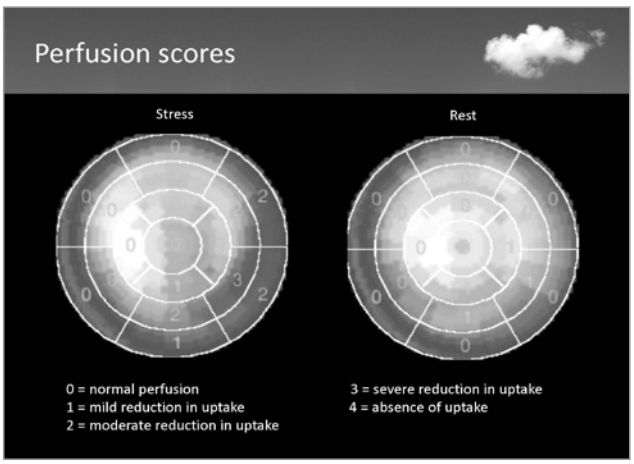
Visual analysis of perfusion defect



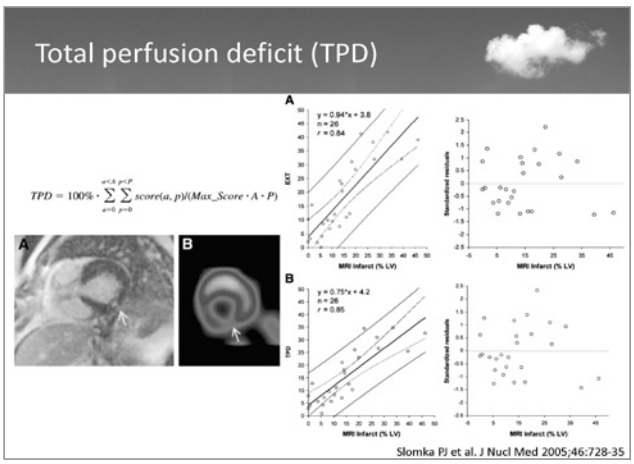
Visual analysis of perfusion defect



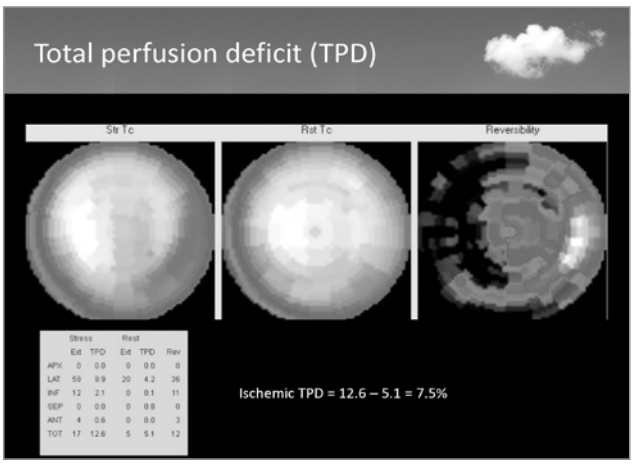
Perfusion scores



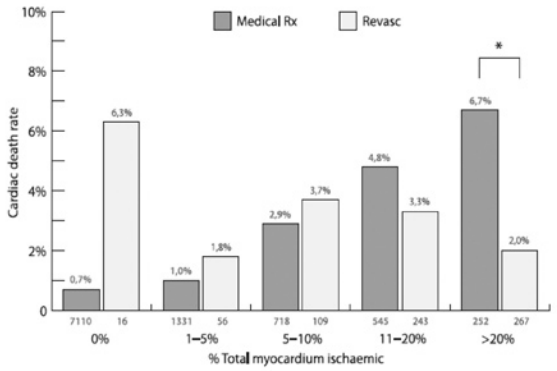
Total perfusion deficit (TPD)



Total perfusion deficit (TPD)

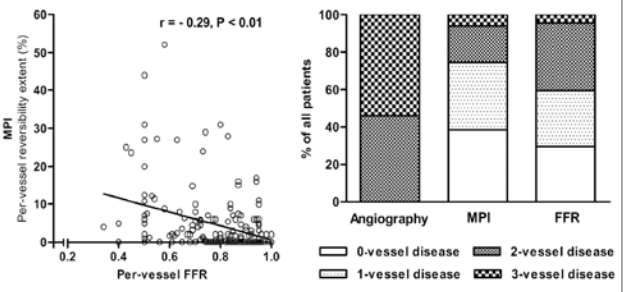


Visual/semiquantitative analysis
Treatment decision



Hachamovitch et al. Circulation 2003;107:2900-7

Limitations



Melikian N et al. JACC Interv 2010;3:307-14

Limitations

Visual and semiquantitative evaluation of SPECT images is not effective for:

1) multivessel disease with balanced ischemia

2) left main disease

3) pure microvascular dysfunction

Quantitative analysis

Why quantification?

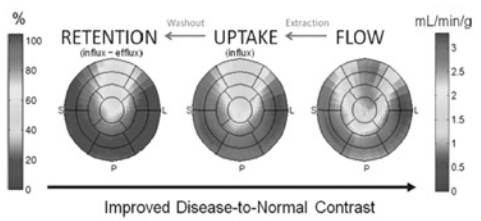
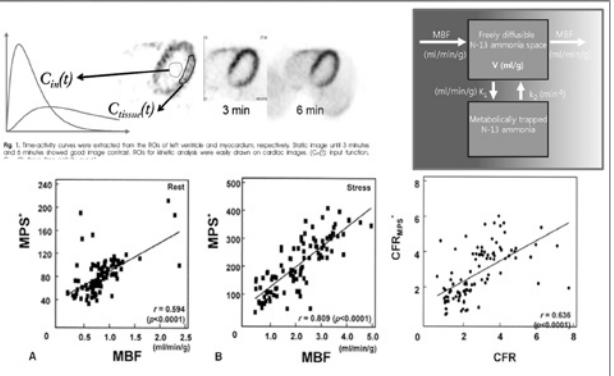


Fig. 12.4 Polar-maps of MBF (flow), ^{82}Rb uptake (K1 influx rate), and retention (net influx – efflux) demonstrating the effects of nonlinear tracer extraction and washout. MBF estimation restores the true disease-to-normal tissue contrast and increases the sensitivity to detect focal disease relative to areas of maximal flow

deKemp RA & Beanlands RSB, 2016

MBF measurement
Compartment method



Lee BI, ... Bom HS. Nucl Med Mol Imaging 2007;41:194-200

CZT cardiac dedicated SPECT
MBF quantification

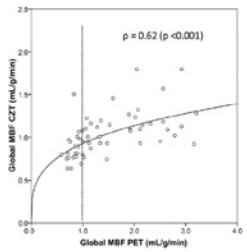


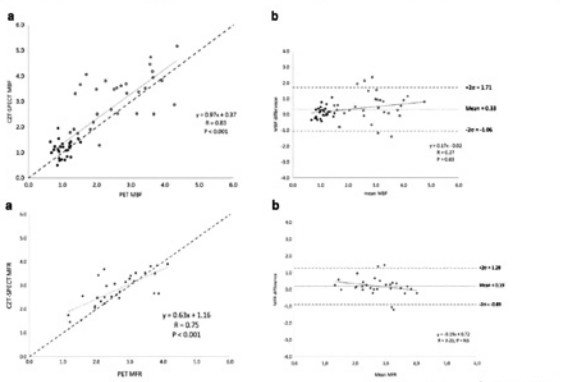
Table 2 Myocardial blood flow values at rest and stress in patients with correctly identified and misidentified PET myocardial flow rate index when using SPECT CZT.

PET MFR	CZT MFR	n	PET MBF stress	PET MBF rest	CZT MBFi stress	CZT MBFi rest
high	high	14	2.32 ± 0.45	0.91 ± 0.17	1.20 ± 0.23	0.87 ± 0.15
high	low	4	2.39 ± 0.78	0.85 ± 0.22	1.14 ± 0.45	1.03 ± 0.32
low	low	7	1.57 ± 0.65	1.06 ± 0.27	1.04 ± 0.14	0.96 ± 0.17
low	high	3	1.19 ± 0.43	0.90 ± 0.17	1.18 ± 0.17	0.82 ± 0.22

High PET MFR: myocardial flow rate ≥ 2 as assessed by PET (13N-ammonia); Low PET MFR: myocardial flow rate < 2 as assessed by PET; High CZT MFRi: myocardial flow rate ≥ 1.26 as assessed by SPECT CZT (99mTc-tetrofosmin); Low CZT MFRi: myocardial flow rate < 1.26 as assessed by SPECT CZT. Values given are ml/g/min ± standard deviation.

Nkoulou et al. J Nucl Med 2016

CZT cardiac dedicated SPECT
MBF quantification



Agostini D et al. EJNMMI 2018

CZT cardiac dedicated SPECT
MBF quantification

Table 4 Concordance between FFR and MFR by PET and CZT in 90 artery territories in 30 patients

$N = 90$	FFR ≤ 0.8	FFR > 0.8
CZT-SPECT MFR < 2.1	7	12
CZT-SPECT MFR ≥ 2.1	5	66
PET MFR < 2	8	9
PET MFR ≥ 2	4	69
MFR vs. FFR	PET MFR < 2	CZT-SPECT < 2.1
Accuracy	86.7%	81.1%
Sensitivity (%)	66.7%	58.3%
Specificity (%)	88.5%	84.6%
Positive predictive value (%)	47.1%	36.8%
Negative predictive value (%)	94.5%	93%

Agostini D et al. EJNMMI 2018

MBF parameters
Hyperemic MBF vs CFR vs RFR

1. Hyperemic MBF:
   MBF measured during stress

2. CFR (≒MFR):

$$\frac{\text{hyperemic MBF}}{\text{resting MBF}}$$

3. RFR:

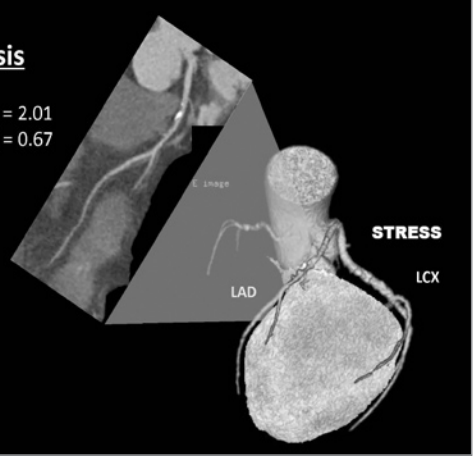
$$\frac{\text{hyperemic MBF in region of interest}}{\text{hyperemic MBF of reference area without stenosis}}$$

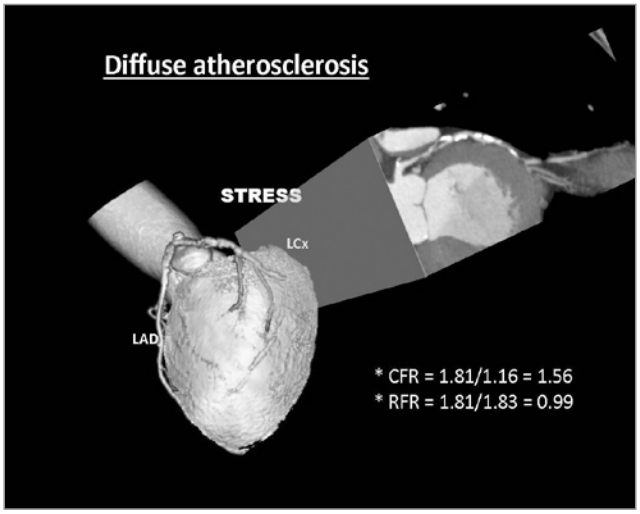
* CFR, coronary flow reserve
MFR, myocardial flow reserve
RFR, relative flow reserve

Characterization of CAD

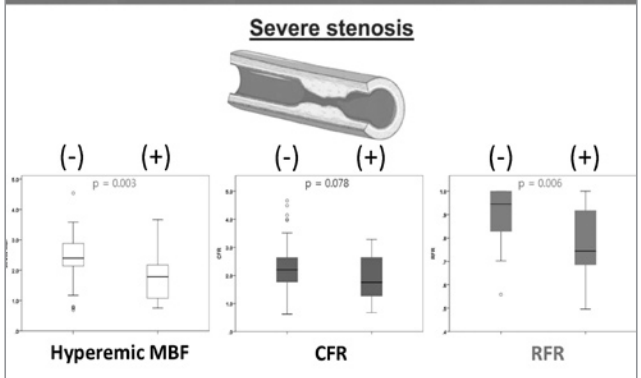
Focal stenosis

* CFR = 1.92/0.95 = 2.01
* RFR = 1.92/2.84 = 0.67



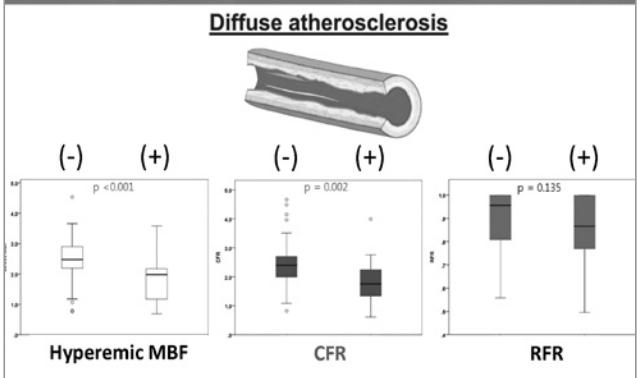


Characterization of CAD



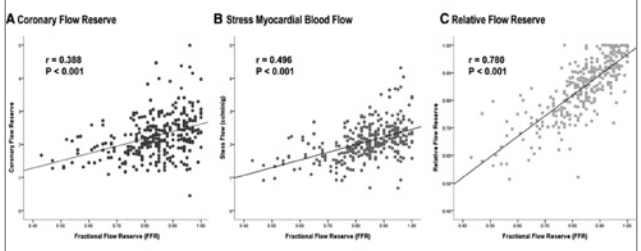
Cho SG et al. Ann Nucl Med 2017;31:144-52

Characterization of CAD



Cho SG et al. Ann Nucl Med 2017;31:144-52

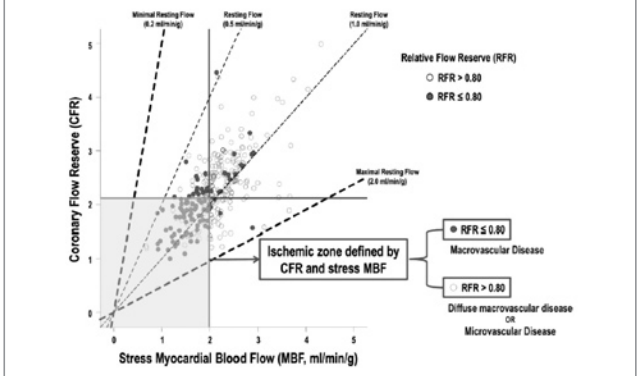
Characterization of CAD



RFR - the best correlation with FFR!

Lee JM et al. Circ Cardiovasc Imaging 2016;9:e004768

Characterization of CAD



Lee JM et al. Circ Cardiovasc Imaging 2016;9:e004768

Resting MBF variability

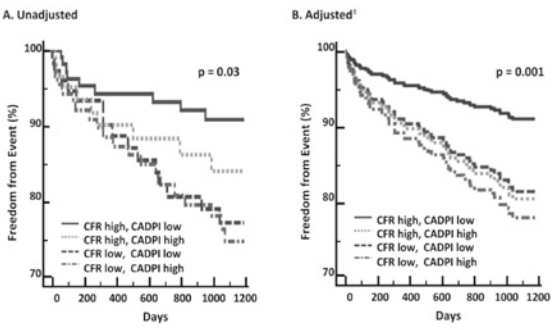
Table 2 Number of patients according to coronary flow reserve and myocardial blood flow

	Resting MBF (ml/min/g)			
	CFR < 2.0 (n = 36)		CFR ≥ 2.0 (n = 34)	
	≥ 1.0	< 1.0	≥ 1.0	< 1.0
Stress MBF (ml/min/g)				
≥ 2.0	16	0	17	12
< 2.0	13	7	0	5

CFR, coronary flow reserve; MBF, myocardial blood flow.

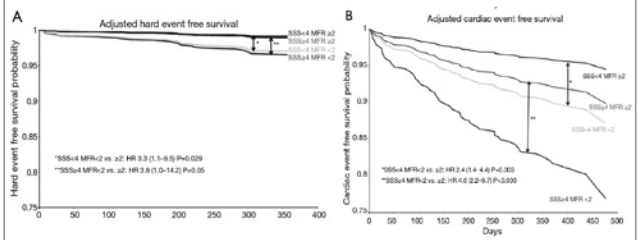
Cho SG et al. Nucl Med Commun 2015;36:619-24

CFR: strong prognostic marker!



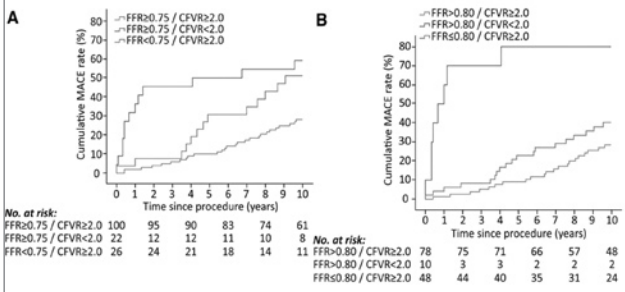
Taqueti et al. Circulation 2015;131:19-27

CFR: strong prognostic marker!



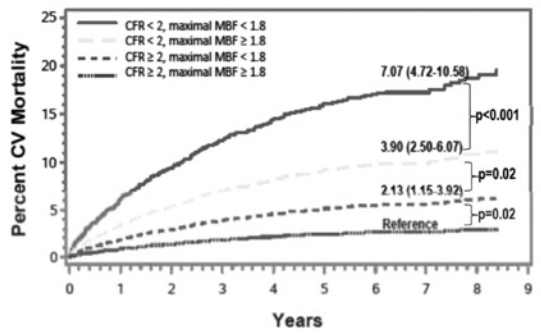
Farhad H et al. Eur Heart J Cardiovasc Imaging 2013;14:1203-10

CFR: strong prognostic marker!



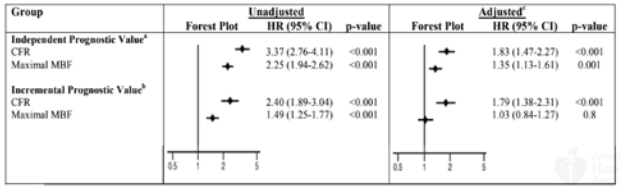
van de Hoef TP et al. Circ Interv 2014;7:301-11

CFR: strong prognostic marker!



Gupta A et al. Circulation 2017;136:2325-36

CFR: strong prognostic marker!



CFR = stronger prognostic marker, even as compared to hMBF!

Gupta A et al. Circulation 2017;136:2325-36

MBF parameters
Characteristics and applications

	Characteristic features	Clinical applications
MBF (hyperemic)	Reflects both focal stenosis and diffuse atherosclerosis Superior to CFR in the diagnosis of significant coronary stenosis Affected by both epicardial CAD and microvascular disease The most sensitive MBF parameter	Screening for multivessel CAD
CFR	Stronger prognostic prediction than any other MBF parameters Reflects both epicardial CAD and microvascular disease Mainly reflects diffuse atherosclerosis Superior diagnostic accuracy to relative uptake analysis May indicate diffuse atherosclerosis in need of bypass surgery	Prognostic stratification Marker of diffuse atherosclerosis Evaluation of microvascular function
RFR	Specifically reflects epicardial, focal CAD Best correlation with FFR	Differential diagnosis of epicardial CA D and microvascular disease Decision of revascluarization

Future perspectives
Flow vs. Pressure

	MBF (flow)	FFR (pressure)
Invasiveness	Non-invasive	Invasive
Stability by hemodynamic/metabolic changes	Variable (esp., at rest)	Stable
Assessment	Absolute	Relative
Normal value	Variable	1.0
Cutoff for PCI	Variable	0.8 (0.75)
Anatomical information (lesion-specificity)	None	Yes
Treatment decision	+	+++
Independent from microvascular disease	No	Yes?

Cho SG et al. Ann Nucl Cardiol 2016;2:99-105

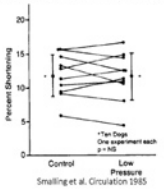
FFR is not perfect

Invasive procedure

Maximal hyperemia is not always achievable.

van de Hoef et al. Eur Heart J 2015

Flow determines function, not pressure.

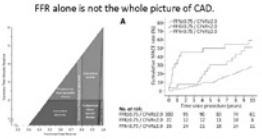


Smalling et al. Circulation 1985

Underestimates the hemodynamic significance of stenosis in a low-flow setting

$$\Delta P = fQ + sQ^2$$

FFR alone is not the whole picture of CAD.



Johnson et al. JACC Cardiovasc Imaging 2012;5:193-202
van de Hoef et al. Circ Cardiovasc Interv 2014;7:301-11

A need for noninvasive, flow-based, lesion-specific physiologic assessment of CAD by PET

Summary

Evaluation of myocardial ischemia using SPECT and PET

1) Visual/semiquantitative analysis: perfusion defect, perfusion scores, TPD
2) Quantitative analysis: hyperemic MBF, CFR, RFR (also available for CZT SPECT)
3) MBF parameters: different characteristics and clinical applications

thank you!

SESSION 4

Expanded Role of CT in the Evaluation of Valvular Heart Disease

Chairperson **Hyun-keun Chee** (Konkuk University Hospital, Korea)
Kee-Sik Kim (Daegu Catholic University Medical Center, Korea)

Presentation

Echocardiographic evaluation of VHD (TAVI 위주) - possibilities and limitation
Speaker Geu-Ru Hong (Severance Hospital, Korea)

Expanding role of CT in VHD
Speaker Young Jin Kim (Severance Hospital, Korea)

Interventionist's expectation of VHD (TAVI 위주) - pre- and postop
Speaker Jung-min Ahn (Asan Medical Center, Korea)

Surgeon's expectation of VHD - pre- and postop
Speaker Byung Chul Chang (CHA University Bundang Medical Center, Korea)

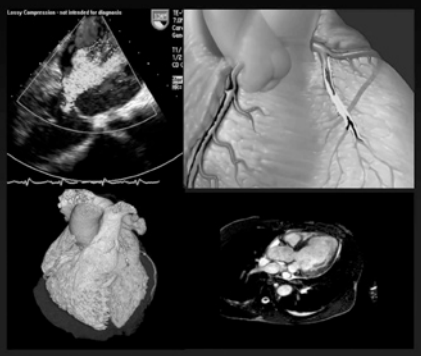
Panel Discussion

Speaker Young Joo Suh (Severance Hospital, Korea)
Jae-Hyeong Park (Chungnam National University Hospital, Korea)
Jung-Hee Lee (Yeungnam University Medical Center, Korea)
Soonchang Hong (Wonju Severance Christian Hospital, Korea)

Echocardiographic evaluation of VHD (TAVI 위주) - possibilities and limitation

Geu-Ru Hong (Severance Hospital, Korea)

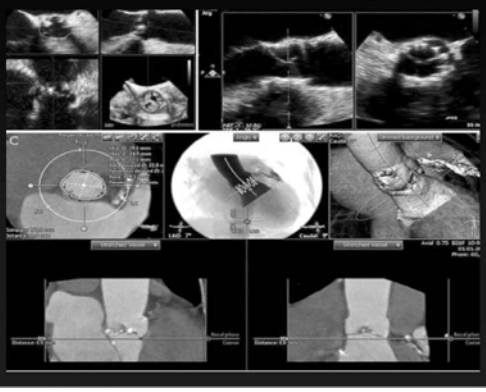
Image Guided Diagnosis & Intervention



Tools in Interventional Imaging

- **Echo**
  - TTE, TEE
  - Contrast, 3D Echo
  - ICE
- **CT**
- **Angiography**
- **CMR**

Multimodality Imaging



Echocardiography & Cardiac Intervention

3D TEE in Cath Lab

Advantages	*Disadvantages*
Shortening of procedure time	Requires experience
Less radiation	More equipment in the room
Improves visualization of structures	Needs team work (more people in the room)
Improves operator confidence	Anesthesia
	Image probe in the angio screen

Imaging is a fundamental component for performing TAVI procedure

Specific Roles of Cardiac Imaging in TAVI

- **Pre-TAVI**
  - Assessment of valvular & LV function (Echo)
  - Iiofemoral evaluation (CT)
  - Aortic size (CT/Echo)
  - Annular sizing (CT/Echo)
  - AV morphological assessment (CT/Echo)
  - Annular/LVOT calcium (CT)
- **During TAVI**
  - Angle of intra-procedural fluoroscopic projection (CT)
  - Monitoring of complications (Echo)
  - Assessment of valvular function-PV leak (Echo)
- **Post TAVI**
  - Follow-up of valvular function (Echo)
  - Long term evaluation: migration/stent fracture (CT)

Echo in TAVI

- Determining severity
- Assessing etiology
- Excluding other cause of LV outflow tract obstruction
- Device selection
  - Annular sizing
  - Aortic root and STJ sizing
  - Position of the coronary arteries

Echo Guidance

- **Echocardiographic guidance has evolved from relatively intensive to limited role.**
- **There may be significant inter-institutional variability**
- **Still very important when new devices are introduced.**

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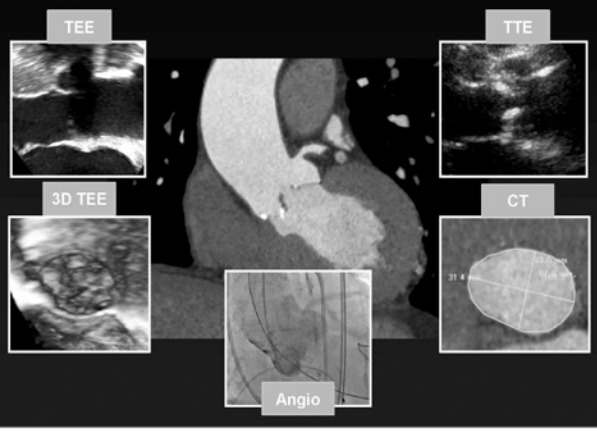
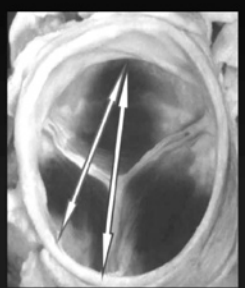
Annulus Sizing is Crucial

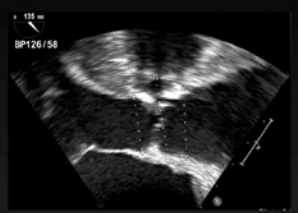
- **Undersizing**
  - Paravalvular regurgitation
  - Valve embolization
- **Oversizing**
  - Reduce valve durability
  - Conduction disturbance
  - Annular rupture

TAVI-Annulus measurement



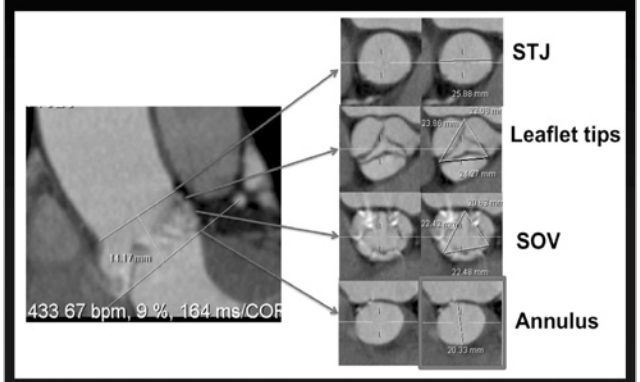
Annulus





Easy to underestimate the annulus diameter

CT: Axial cuts at multiple levels



New Imagings for TAVI

Improving TAVI outcomes

Reducing the risk of complications

Pursuit of Perfection

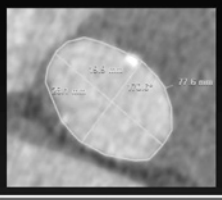
3D Quantatative Automated

Real-time

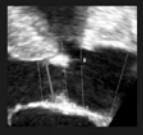
3D measurement

3D TEE vs. CT

Perimeter: 78 (24.8π) mm
Area: 440 mm² (23.7 mm)

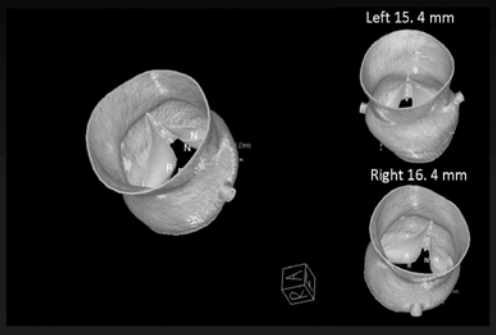


Perimeter: 77.6 (24.7π) mm
Area: 443 mm² (23.8 mm)



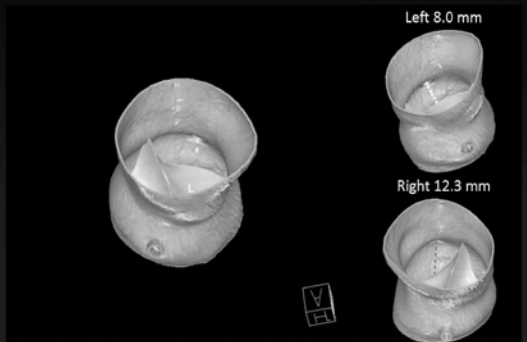
Annulus	21 mm

Automated Quantitative Modeling
Annulus-Commissure Distance- AS



Calleja A, Paaladinesh Thavendiranathan et al., Circ Cardiovasc Imaging 2013:6;99-108

Automated Quantitative Modeling
Annulus-Coronary Ostia Distance- AS



Calleja A, Paaladinesh Thavendiranathan et al., Circ Cardiovasc Imaging 2013:6;99-108

TEE for TAVR Guidance

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Evidence for Intraprocedural TEE

Outcomes and Predictors of Mortality After Transcatheter Aortic Valve Implantation: Results of the Brazilian Registry

Fabio S. de Brito Jr,[1*] MD, Luiz A. Carvalho,[2] MD, Rogério Sarmento-Leite,[3] MD, José A. Mangione,[4] MD, Pedro Lemos,[5] MD, Alexandre Siciliano,[6] MD, Paulo Caramori,[7] MD, Luiz Sao Thiago,[8] MD, Eberhard Grube,[9] MD, and Alexandre Abizaid,[1,10] MD, on behalf of the Brazilian TAVI Registry investigators

Objective: The study sought to evaluate outcomes and predictors of mortality after transcatheter aortic valve implantation (TAVI). Background: TAVI registries can reliably address outcomes and issues that adversely affect results in real-life. Methods: All endpoints and complications were analyzed according to Valve Academic Research Consortium-2 criteria. Results: Between January 2008 and January 2013, 418 patients underwent TAVI in 18 centers and were included in the Brazilian registry. The transfemoral approach was used in 96.2% of the procedures. The CoreValve and Sapien XT prosthesis were used in 360 (86.1%) and 58 (13.9%) cases, respectively. All-cause mortality at 30 days and 1 year were 9.1 and 21.5%. Chronic obstructive pulmonary disease (COPD) (HR: 3.50), acute kidney injury (AKI) (HR: 3.07), stroke (HR: 2.71) and moderate/severe paravalvular regurgitation (PVR) (HR: 2.76) emerged as independent predictors of overall mortality. COPD (OR: 3.00), major vascular complications (OR: 7.99) and device malpositioning (OR: 6.97) were predictors of early (<30 days) mortality, while COPD (HR: 2.68), NYHA class III/IV (HR: 3.04), stroke (HR: 4.15), AKI (HR: 2.44) and moderate/severe PVR (HR: 3.20) impacted late (>30 days) mortality. The use of transesophageal echocardiogram (TEE) to monitor the procedure was found to be a protective factor against overall (HR: 0.57) and late (HR: 0.47) mortality. Conclusion: This multicenter registry reflected a real-life national TAVI experience. Comorbidities, perprocedural complications and moderate/severe PVR were associated with increased mortality and the use of TEE to monitor the procedure acted as a protective factor. © 2014 Wiley Periodicals, Inc.

Key words: transcatheter valve implantation; aortic valve disease; percutaneous intervention; aortic valve disease; percutaneous valve therapy

Brito FS et al. Cath and Cardiovasc Int 85:153-162, 2015

	418 patients (18 centers)
STS score	14.2 ± 11.5
General anesthesia	84%
TEE guidance	70.6%
Access TF	96.2%
Moderate/Severe PVR	9.2%
Tamponade	4%
LV perforation	2%

Brazilian TAVR Registry

2008-2013

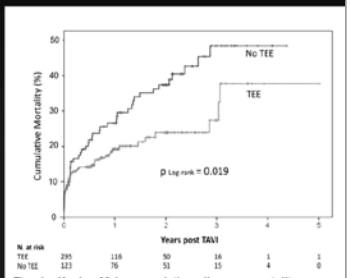

Fig. 4. Kaplan-Meier cumulative all-cause mortality curves for TEE guided and non-TEE guided procedures.

Brito FS et al. Cath and Cardiovasc Int 85:153-162, 2015

CLINICAL INVESTIGATIONS
VALVULAR DISEASE

Paravalvular Regurgitation after Transcatheter Aortic Valve Replacement: Comparing Transthoracic versus Transesophageal Echocardiographic Guidance

Salim S. Hayek, MD, Frank E. Corrigan III, MD, Jose F. Condado, MD, Shuang Lin, MD, Sharon Howell, RDCS, James P. MacNamara, MD, Shuai Zheng, PhD, Patricia Keegan, DNP, Vinod Thourani, MD, Vasilis C. Babaliaros, MD, and Stamatios Lerakis, MD, *Atlanta, Georgia*

- Retrospectively reviewed 454 consecutive patients transfemoral TAVR (balloon expandable) at Emory Healthcare from 2007 to 2014.
- TTE guidance (TTE-TAVR, n=234, mean STS score 10%)
- TEE guidance (TEE-TAVR, n=220, mean STS score 11%)

Hayek SS et al. J Am Coll Cardiol 2017;30:533-40.

	TTE-TAVR	TEE-TAVR	P-value
Second Valve	7 %	2 %	0.026
Balloon post-dilatation	38%	17%	<0.001
PVR at discharge Mild/Moderate/Severe	29/2/1 (%)	35/3/0 (%)	0.120
Malposition	2	2	
Severe Central AR	2	0	

- Minimalist TTE-guided TAVR is increasingly performed in cardiac catheterization laboratories
- Patients undergoing TTE-TAVR were more likely to receive balloon postdilation and second valve implantation
- Paravalvular regurgitation at discharge was not increased with TTE-guided TAVR.

Hayek SS et al. J Am Coll Cardiol 2017;30:533-40.

Valve Assessment during TAVR

- Valve position and orientation
- Leaflet motion
- Transvalvular and paravalvular AR
- Integrity of the ascending aorta
- Mitral regurgitation
- Ventricular wall motion abnormalities

Mechanisms of Aortic Regurgitation

- Malposition of prosthesis
- Undersizing prosthesis
- Underexpansion of prosthesis
- Malapposition of prosthesis
- Aggressive pre-dilatation during BAV
- Guidewire or pigtail catheter interfering with leaflet coaptation

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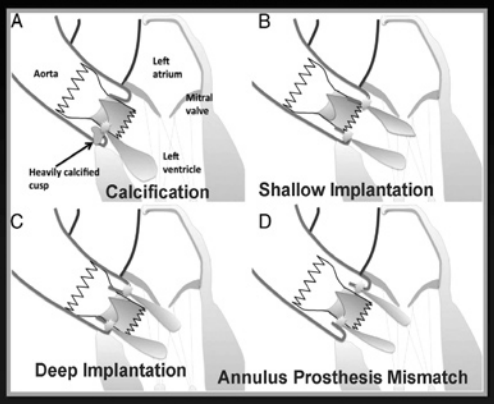
Paravalvular AR After TAVI

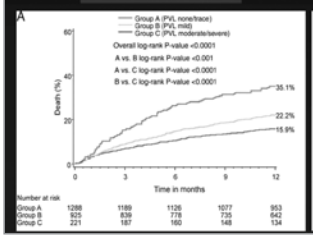


Sinning et al: JACC 59:1134, 2012

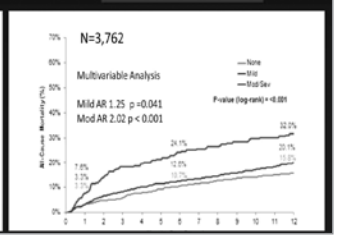
Clinical Impact of PVR

- Moderate/severe PVR
  3-fold increase in 30 day mortality
- Mild PVR
  Conflicting

PARTNER



CoreValve US Pivotal Trial



PVR Grading

A Proposal of Unifying Grading Scheme

Philippe Pibarot, DVM, PhD,* Rebecca T. Hahn, MD,† Neil J. Weissman, MD,‡ Mark J. Monaghan, PhD§

3 class	Trace	Mild	Mild	Moderate	Moderate	Severe
4 class	1	1	2	2	3	4
5 class	Trace	Mild	Mild-Mod	Moderate	Mod-severe	Severe

J Am Coll Cardiol Img 2015;8:340–60

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Characteristics of PVR jets

- Multiple, eccentric, irregular shape
- Confined along LVOT
- Masked by calcification of native valve or stent
- Irregular vena cava contracta

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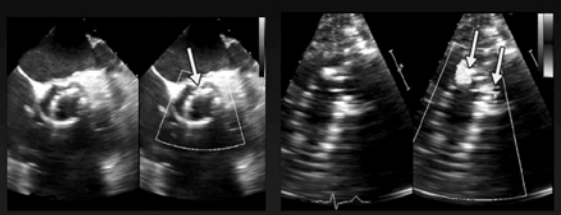
Color Doppler Parameters

- TEE



Mid-esophageal SA Deep transgastric view

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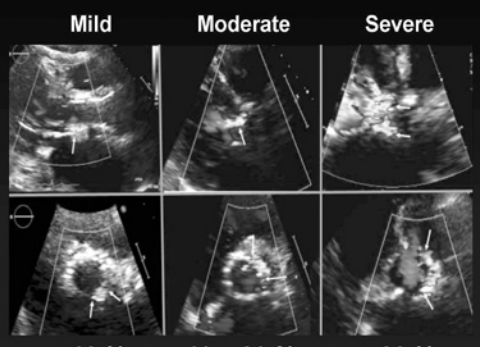
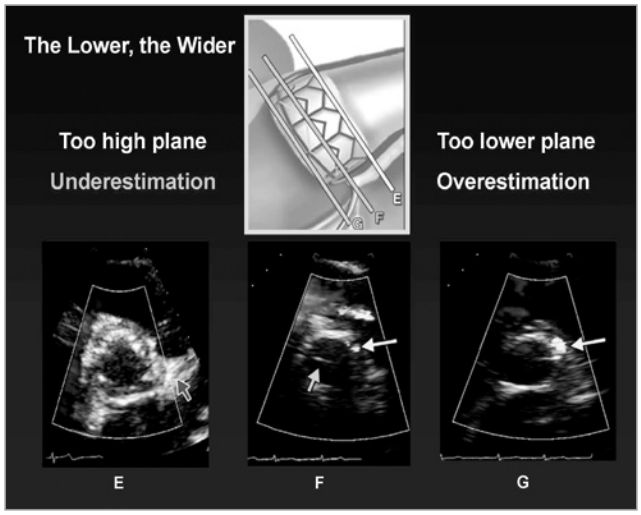
Determination of PVL Severity
Circumferential Extent

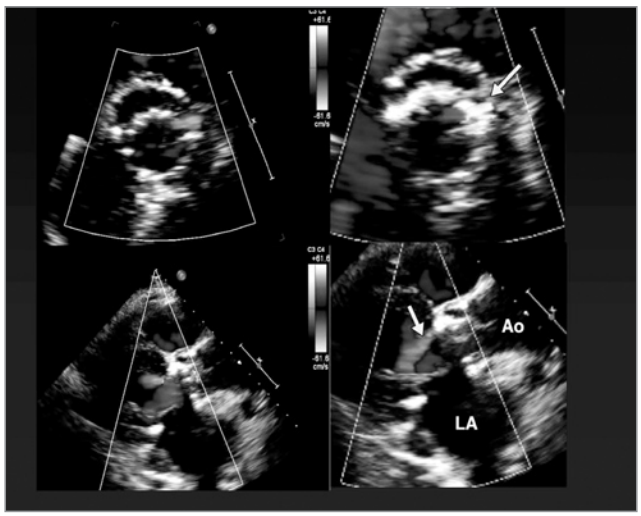


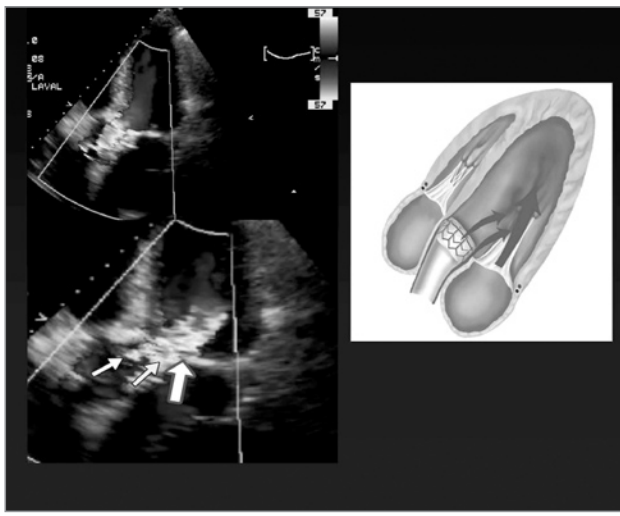


Pitfalls in TTE measurement of PVL

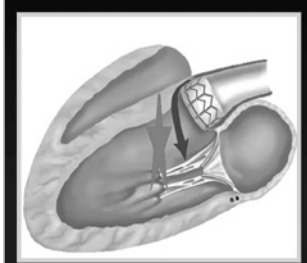
- The posterior jet is not well visualized and largely underestimated in the parasternal views!
- The posterior jet tend to merge with the mitral inflow.

SEVERANCE CARDIOVASCULAR HOSPITAL YONSEI UNIVERSITY COLLEGE OF MEDICINE





Pitfalls in TTE measurement of PVL



The anterior jets are often eccentric because when they enter into the LVOT, they are deviated posteriorly by the prominent septal bulge

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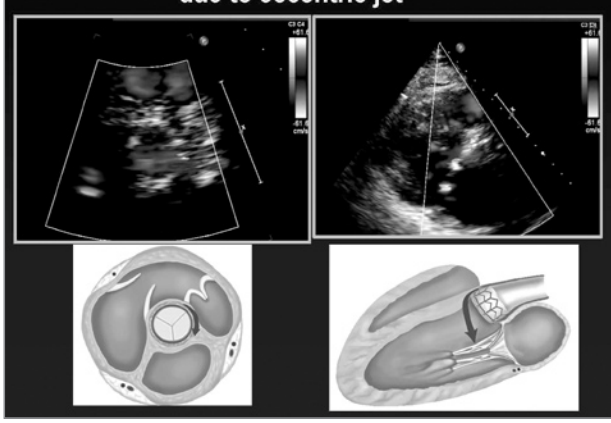
Over-estimation of circumferential extent due to eccentric jet



Regression of Paravalvular Aortic Regurgitation and Remodeling of Self-Expanding Transcatheter Aortic Valve

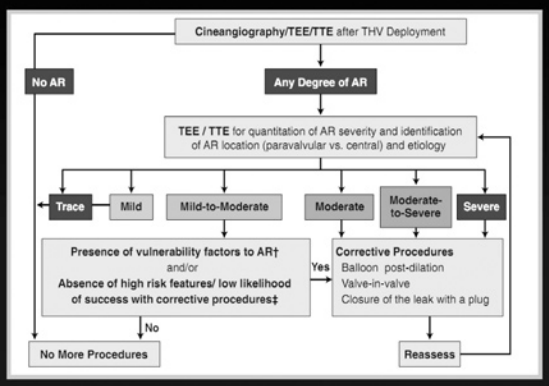
An Observation From the CoreValve U.S. Pivotal Trial

Jae K. Oh, MD,* Stephen H. Little, MD,† Sahar S. Abdelmoneim, MD, MSc,* Michael J. Reardon, MD,‡ Neal S. Kleiman, MD,§ Grace Lin, MD,* David Bach, MD,§ Linda Gillam, MD,‖ Biswajit Kar, MD,‖ Joseph Coselli, MD,‖ Partho P. Sengupta, MD,¶ Kanny Grewal, MD,# James Chang, MD,** Yanping Chang, MS,†† Mike Boulware, PhD,†† David H. Adams, MD,¶ Jeffrey J. Popma, MD,†† for the CoreValve U.S. Pivotal Trial Clinical Investigators

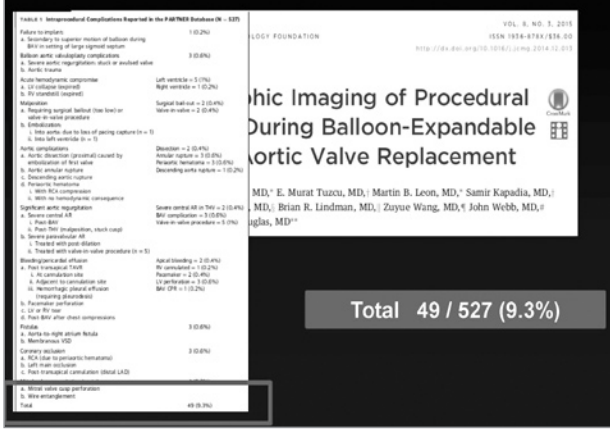
- Of 137 mild PVR patients at discharge,
  89 (65%) had none/trivial at 1 year
- Of 36 moderate PVAR at discharge,
  30 (83%) had < moderate at 1 year

Oh et al. JACC CV Imaging 2016

Echo in Management of PVR



Intraprocedural Complications from Partner Trial



...hic Imaging of Procedural
...During Balloon-Expandable
...ortic Valve Replacement

Total 49 / 527 (9.3%)

Hypotension during TAVI

- Cardiac tamponade
- Aortic dissection
- Myocardial ischemia
- Major bleeding
- Etc….(arrythmia, MR, AR……)

Aortic Dissection

- Aortic dissection can occur following valve deployment or delivery
- Use caution with
  - Severely obliterated sinuses of Valsalva
  - Significant valve oversizing (≥ 4mm)
  - Atheroma in aortic arch

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Cardiac Tamponade

- Pressure rapidly recovers after pericardiocentesis
- Tamponade can occur at each step of the procedure
  - Pacing wires
  - LV wires
  - Annular disruption/ LV perforation
  - Aortic dissection

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TEE-Guided TAVI

Q1. Is there Pericardial Effusion?

(After stiff wire passing into LV)

Q2. How much AR?

(After predilation)

Q3. How about the Valve Position?

(After valve deployment for deciding retrieve the valve)

Q4. Is there Paravalvular AR?

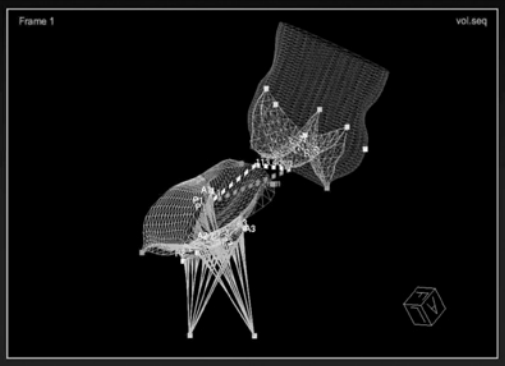
(Before deciding post-dilatation)

Q5. Is there MR?

Q6. Something wrong…… What Happened?

Automated Quantitative Modeling

Aorto-Mitral Relationship



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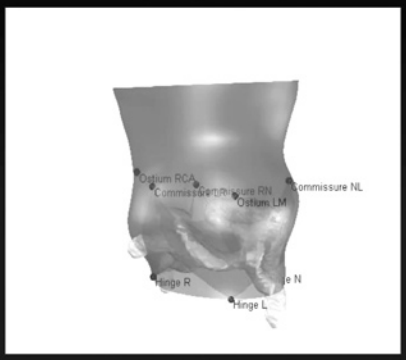
Automated Quantitative Modeling

Aortic Root Calcification



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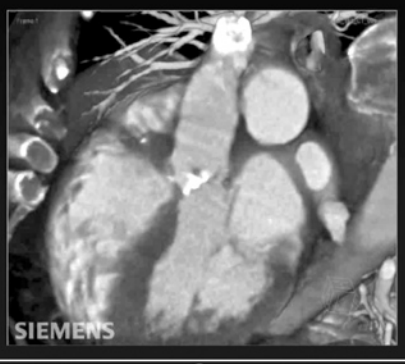
Automated 3-D Modeling (3-D TEE/CT)

Simulation of Valve Deployment



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Cardiac Imaging for SHD

The Future is here

- **Team work**
- **Multiple modalities**
- **Interventional imaging cardiologist**

Take Home Message

- Cardiac imaging has an essential role in the planning and provision of valve intervention
- The imaging specialist must possess procedural knowledge, and precision in quantification, and communication in order to be part of a team that delivers good outcomes

SHD Intervention = Art, Science

Expanding role of CT in VHD

Young Jin Kim (Severance Hospital, Korea)

Recently the role of CT is being expanded according to development of CT technology especially in the field of structural heart disease.

Although echocardiography is the primary and essential modality for the evaluation of patients with valvular heart disease, cardiac CT has distinct advantage in the evaluation of anatomical features of the cardiac valves, including the extent of calcification, the geometry of the annulus and the evaluation of biological and mechanical prostheses.

CT provides abundant anatomic and functional information that complements the information from echocardiography, making it possible to characterize the etiology of the valve disease and its repercussions on the heart and aorta, as well as to quantify the severity of disease.

It is important for cardiologists, radiologists and other cardiac imaging specialists to recognize the features of normal and abnormal valves in patients and potential role of CT.

MEMO

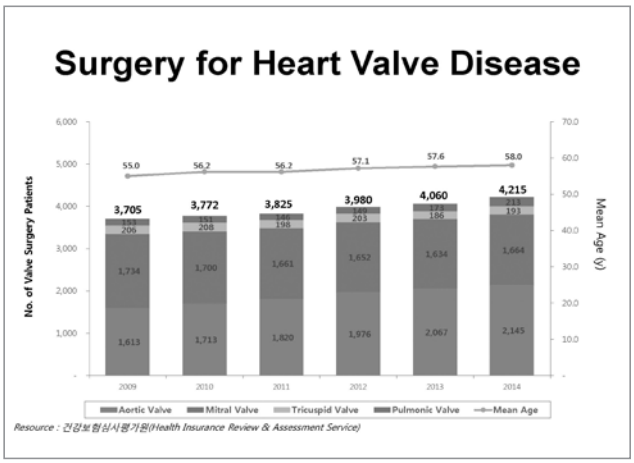
Interventionist's expectation of VHD (TAVI 위주) - pre - and postop

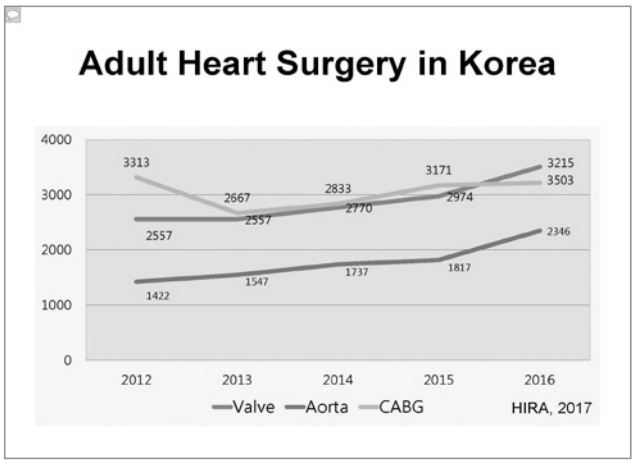
Jung-min Ahn (Asan Medical Center, Korea)

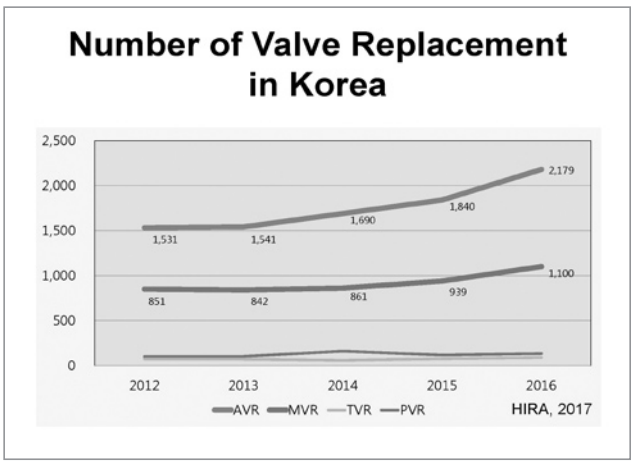
MEMO

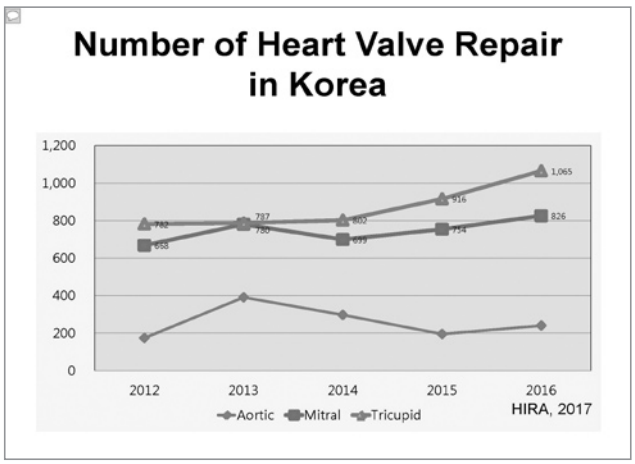
Surgeon's expectation of VHD - pre - and postop

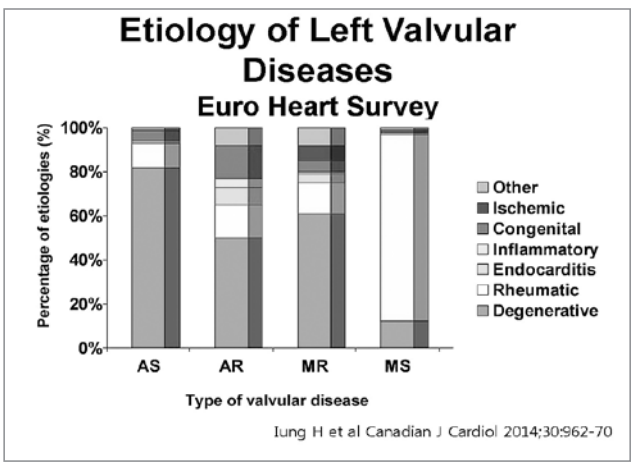
Byung Chul Chang (CHA University Bundang Medical Center, Korea)

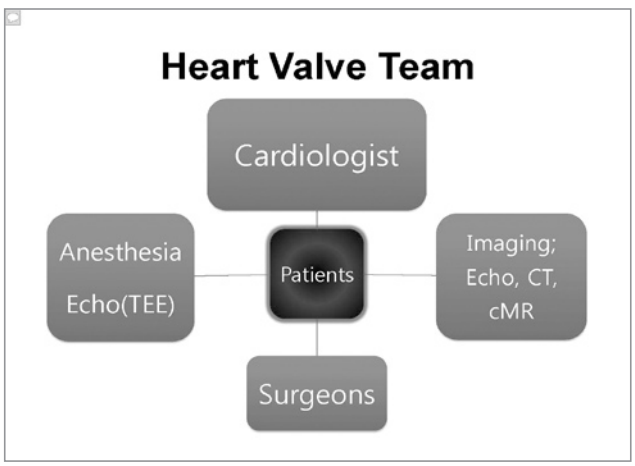












What do Surgeons want to know before surgery?

- Anatomical abnormalities
- Functional abnormalities
  - Functional regurgitation; AV, MR, TR
  - PPM
  - Tethering of mitral leaflets

Role of CT for HVD

- ✓ CT for coronary and/or aorta evaluation
  - Aorta; aneurysm, calcification
  - Arterial branches for atherosclerosis
- ✓ Anatomical abnormalities
  - Systole/diastole; valve, ventricle and atrium
  - Prosthesis (prosthetic valve or annuloplasty ring)
  - Adhesion for redo
- ✓ Functional abnormalities
  - Native valve function; AV, MR, TR
  - Prosthetic valve; pannus, pavavalvular leak, PPM
  - Tethering of AV valve

Preoperative Coronary CT

- Screening for ages more than 40 y-o
- Evaluation of sternal adhesion
- Evaluation of bypass graft in redo
  - Patency
  - LIMA, RIMA course

Preoperative CT for Aorta

- Dilation of ascending aorta
  - requiring aorta surgery; 40%
- Aortic arch and branches
  - connective diseases(Marfan, Ehlers-Danros)
  - Dissection; acute or chronic
- Aortic root, annulus and aorta
- Inflammation

Role of CT for HVD

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  - Arterial branches for atherosclerosis
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  - Prosthesis (prosthetic valve or annuloplasty ring)
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- ✓ Functional abnormalities
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  - Prosthetic valve; pannus, pavavalvular leak, PPM
  - Tethering of AV valve

Choo PJ, 77/F, 10622733

2018-4-18

CC: Chest pain and palpitation

D: 1 day

s/p AVR with Epic 21mm, 2011-3-2

Echo(2018-2-7);

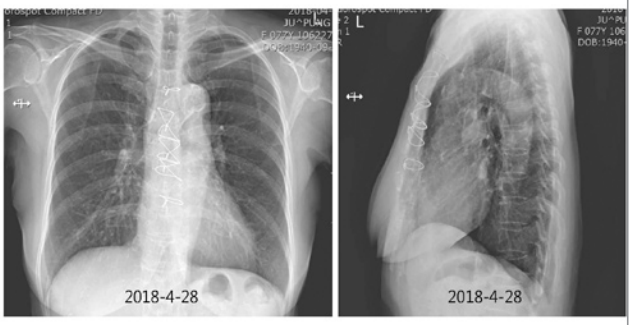
- mild AR with good LV systolic function
- LVEF; 75%(38/21), AVPG: 31/15mmHg

Echo(2018-4-25);

- mild to moderate AR with good LV systolic function
- LVEF; 74%(39/23), AVPG: 33/14mmHg

Aorta Calcification

Choo PJ, F/77, 10622733
s/p AVR with Epic 21mm 2011-3-2



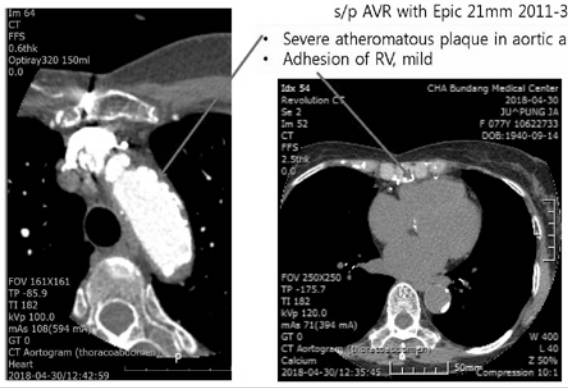
Aorta Calcification

Choo PJ, F/77, 10622733
s/p AVR with Epic 21mm 2011-3-2,

Aorta & Iliac A. Calcification

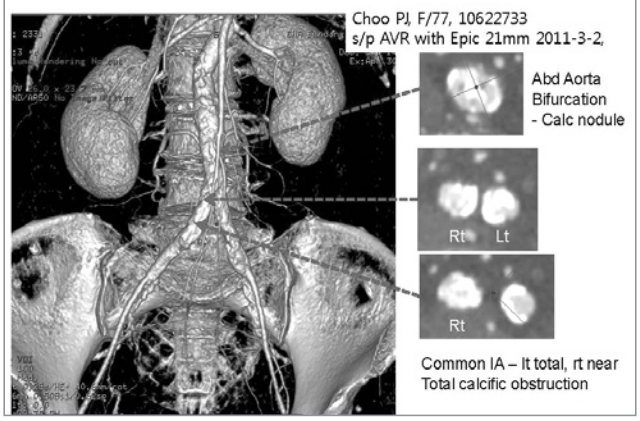
Choo PJ, F/77, 10622733
s/p AVR with Epic 21mm 2011-3-2,

- Severe atheromatous plaque in aortic arch
- Adhesion of RV, mild



Aorta & Iliac A. Calcification

Choo PJ, F/77, 10622733
s/p AVR with Epic 21mm 2011-3-2,



Aorta & Iliac A. Calcification

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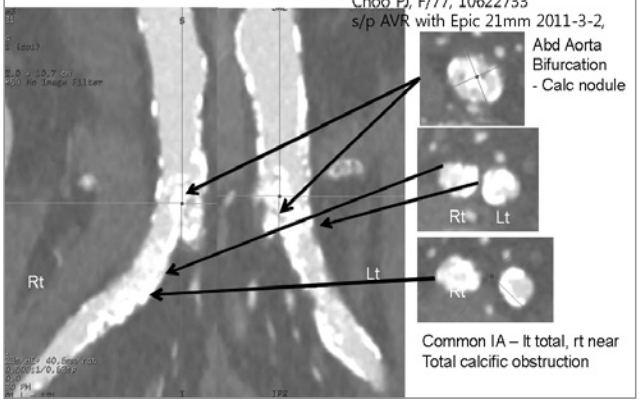


Joo PJ, 77/F, 10622733

2018-4-18

Problems:

- s/p AVR with primary valve failure (AR)
- Severe aorta calcification
- Atheromatous plaques in the aortic arch
- Moderate adhesion of pericardium on RV
- Severe abdominal aorta and iliac artery calcification and narrowing
- Poor femoral and iliac artery for TAVR

Choice of procedure for redo?

Aortic Valve

- AS for evaluation
  - Aorta
  - TAVI, Sutureless AVR, sAVR
- AR
  - Aorta
  - Causes, other valve lesions
  - Endocarditis; extent, abscess
- Annuloaortic ectasia
  - for root replacement with/without prosthesis

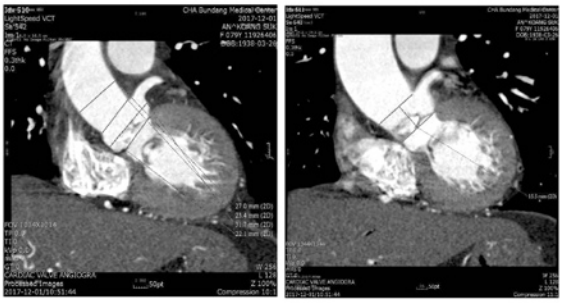
AGS 79/F, 11926406

- CC: Chest tightness
- D: 1 month
- PI: known aortic stenosis for 5 years
  - Recent echo at femur fracture surgery

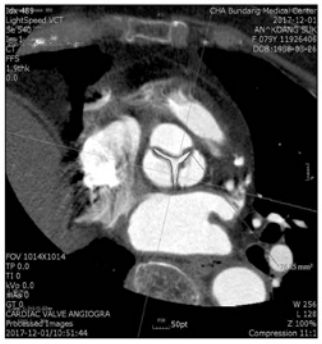
  2017-11-1

  Sever AS with good LV systolic function
    - LVEF-86%, AVPG: 110/74mmHg
    - STS score: 2.58%

AGS 79/F, 11926406



AGS 79/F, 11926406



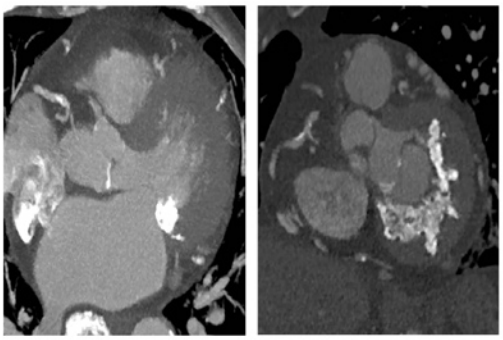
AS Evaluation for Suture-less AVR

Ahn GS, F/78, 11926406
AS s/p AVR with Perceval 2017-12-4,

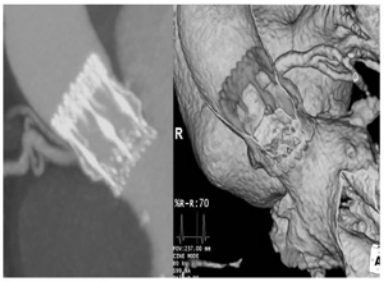
REF/SIZE	AORTIC ANNULUS DIAMETER (mm) = A	AORTIC ROOT HEIGHT (mm)	SINOTUBULAR JUNCTION DIAMETER (mm)
PVS23 /M	21≤ A <23	<22.5	≤27.3-29.9

YHS 84/F, 8452024

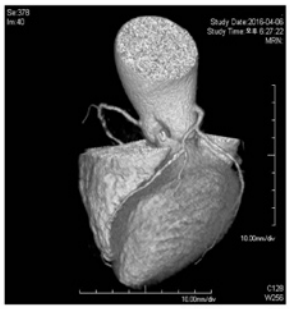
2014.10.28 CT: Severe AS, Severe MAC



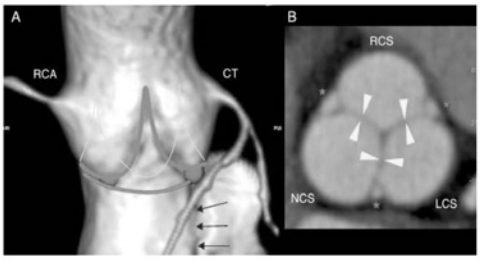
8452024 YHS, 84/F
2017.6.30 post op CT



Aortic Root, Valve and Aorta



Aortic Root, Valve and Aorta



Cuellar H, Radiologia 2013;55:24-36

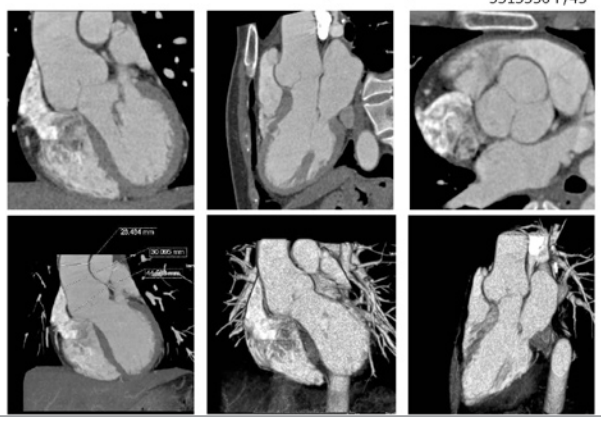
3313336 F/43

Marfan Syndrome, Annuloaortic ectasia

Aortic root replacement with aortic valve preservation

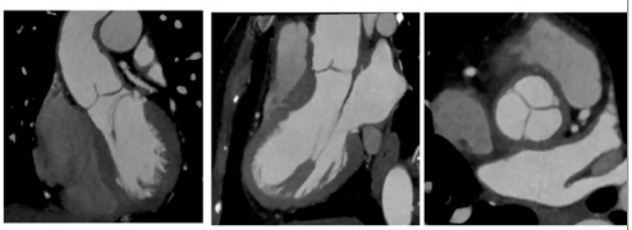
2004-03-26 preop CT

3313336 F/43



2015-02-11 postop CT

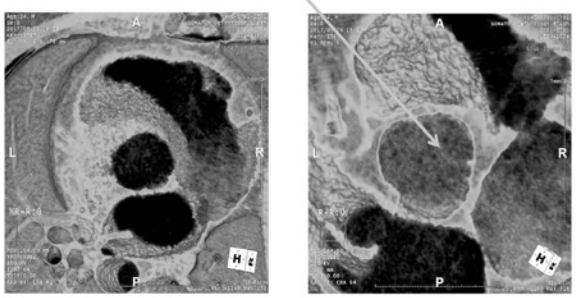
3313336 F/43



Park GY, M/33, 8264363

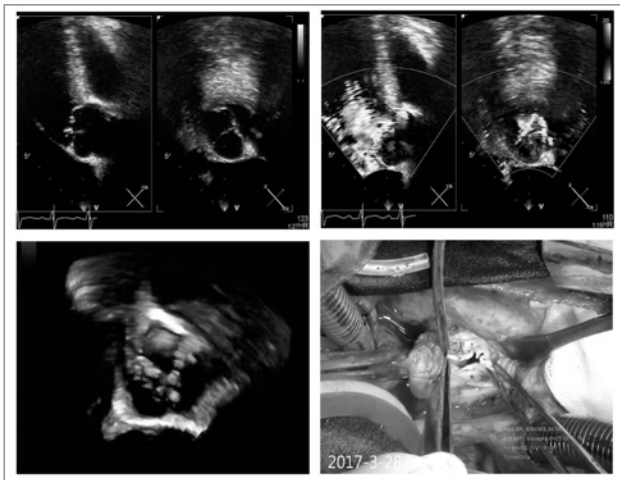
- Park GY, M/33, 8264363
- S/P BAV repair – raphe division and adjust coaptation margin using interruptted Prolene suture 2016-7-19

Park GY, M/33, 8264363 박광열
S/P BAV repair – raphe division and adjust coaptation margin using interruptted prolene suture 2016-7-19



Park GY, M/33, 8264363

- Park GY, M/33, 8264363 박광열
  S/P BAV repair – raphe division and adjust coaptation margin using interruptted Prolene suture 2016-7-19
- Redo AVR due to DOE with AR 2017-3-28



Role of CT for HVD

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  - Arterial branches for atherosclerosis
- ✓ Anatomical abnormalities
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  - Prosthesis (prosthetic valve or annuloplasty ring)
  - Adhesion for redo
- ✓ Functional abnormalities
  - Native valve function; AV, MR, TR
  - Prosthetic valve; pannus, pavavalvular leak, PPM
  - Tethering of AV valve

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Korean J Radiol 2015;16(5):1012-1023

Korean Journal of Radiology
KJR

Measurement of Opening and Closing Angles of Aortic Valve Prostheses *In Vivo* Using Dual-Source Computed Tomography: Comparison with Those of Manufacturers' in 10 Different Types

Young Joo Suh, MD, Young Jin Kim, MD, PhD, Yoo Jin Hong, MD, Hye-Jeong Lee, MD, PhD, Jin Hur, MD, PhD, Dong Jin Im, MD, Yun Jung Kim, MD, Byoung Wook Choi, MD, PhD
All authors: Department of Radiology, Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, Seoul 03722, Korea

Normally Functioning Valves

Table 3. CT Measurement for Opening and Closing Angles in Normally Functioning Valves According to Valve Type

	CT Measurement	Manufacturers' Value	P
Opening angle (degree)	75.1 (76.5–83.3, n = 86)		
SJR (n = 23)	84.1 ± 0.9	85	< 0.001
Carbomedics (n = 15)	77.1 ± 2.1	78	0.121
ATS (n = 12)	69.5 ± 2.8	85	< 0.001
On-X (n = 10)	79.0 ± 2.1	90	< 0.001
Sorin (n = 8)	79.3 ± 1.5	80	0.225
MIRA (n = 8)	78.5 ± 0.6	80	< 0.001
Duromedics (n = 5)	77.0 (76.0–77.1)	78	0.063
SJM (n = 4)	83.4 (83.1–83.8)	85	0.125
MH (n = 1)	59.8	60	N/A
Closing angle (degree)	24.5 (23.0–29.8, n = 84)		
SJR (n = 23)	28.5 ± 2.6	30	0.016
Carbomedics (n = 16)	24.3 ± 1.3	25	0.038
ATS (n = 11)	24.7 ± 1.3	25	0.407
On-X (n = 10)	40.3 ± 0.5	40	0.108
Sorin (n = 8)	21.7 ± 1.1	20	0.004
MIRA (n = 8)	21.9 ± 1.2	20	0.003
Duromedics (n = 4)	19.3 (17.9–20.4)	20	0.625
SJM (n = 3)	29.5 (28.7–30.2)	30	0.219
MH (n = 1)	0	0	N/A

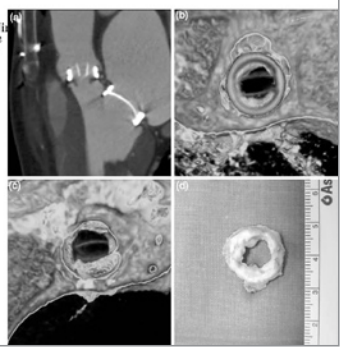
CT = computed tomography, MH = Medtronic-Hall, SJM = St. Jude Medical, SJR = St. Jude Medical Regent

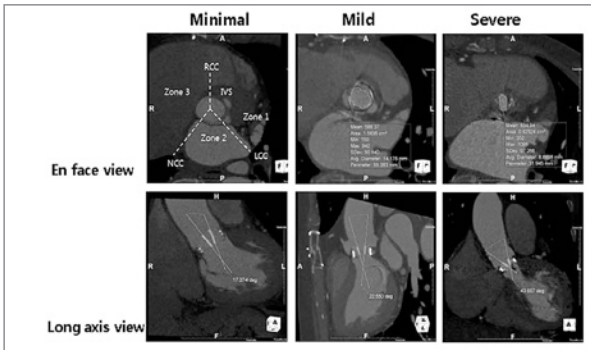
Int J Cardiovasc Imaging (2015) 31:1271–1280
DOI 10.1007/s10554-015-0683-1

ORIGINAL PAPER

Utility of cardiac computed tomography for evaluation of pannus in mechanical aortic valve

Young Joo Suh[1] · Young Jin Kim[1] · Sak Lee[2] · Yoo Jin Hong[1] · Jin Hur[1] · Byoung Wook Choi[1] · Byung-Chul Chang[2]





Valve type	On-X	Sorin	Carbomedics
Valve size (mm)	23	19	19
Mean PG (mmHg)	12	27	84
GOA (cm²)	1.91	1.58	0.623
LOM	absent	absent	present
Opening angle (°)	82	78	68
Etiology	bicuspid	rheumatic	rheumatic
Age at AVR (years)	50.3	51.3	44.5

FU CT Evaluation

Aortic prosthetic valve

International Journal of Cardiology 214 (2016) 454–460

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Added value of cardiac computed tomography for evaluation of mechanical aortic valve: Emphasis on evaluation of pannus with surgical findings as standard reference

Young Joo Suh [a,1], Sak Lee [b,1], Dong Jin Im [a,1], Suyon Chang [a,1], Yoo Jin Hong [a,1], Hye-Jeong Lee [a,1], Jin Hur [a,1], Byoung Wook Choi [a,1], Byung-Chul Chang [b,1], Chi Young Shim [c,1], Geu-Ru Hong [c,*,1], Young Jin Kim [a,**,1]

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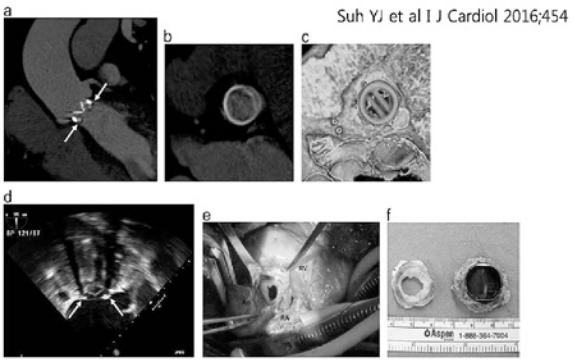
FU CT Evaluation for AV



Role of CT for HVD

- ✓ CT for coronary and/or aorta evaluation
  - Aorta; aneurysm, calcification
  - Arterial branches for atherosclerosis
- ✓ Anatomical abnormalities
  - Systole/diastole; valve, ventricle and atrium
  - Prosthesis (prosthetic valve or annuloplasty ring)
  - Adhesion for redo
- ✓ Functional abnormalities
  - Native valve function; AV, MR, TR
  - Prosthetic valve; pannus, pavavalvular leak, PPM
  - Tethering of AV valve

HOCM and Mitral Valve

- Anatomical abnormalities
  - LV shape
  - Morphology of mitral valve
  - Subvalvular structure
- Functional abnormalities
  - Native valve function; AV, MV, TV
  - SAM

Kim TY, M/46, 8031902

- C.C. : Presyncope and intermittent dizziness
- D. : 2 weeks
- Associated factors: Exercise
  (Running across a crosswalk)
- P.Hx.:

  HTN/ DM (- /-)

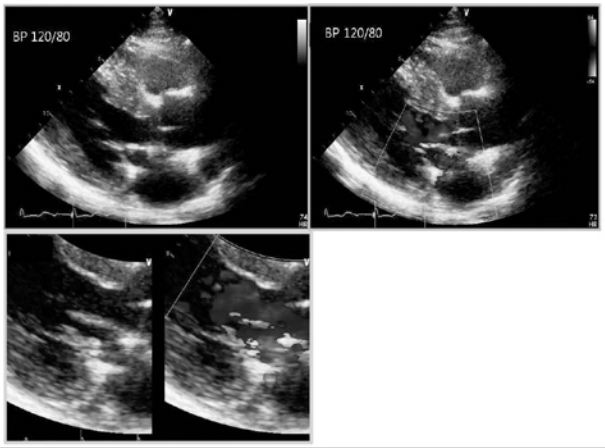
  Severe MR due to Flail PML Dx. (Outside Hosp.)

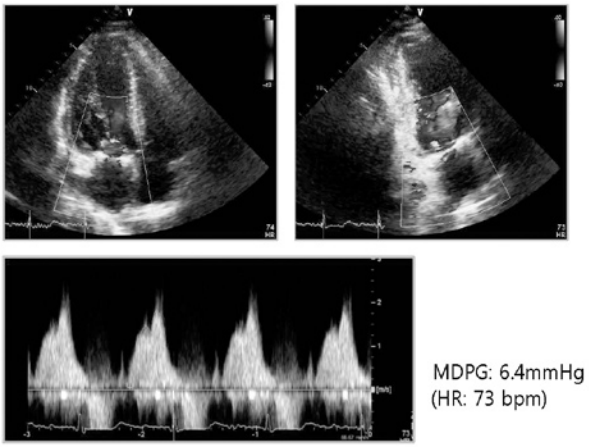
  ➔ Referred to CS Dept.

  ➔ MV repair with C-ring #30 (4 months ago)
  under lower sternotomy

* Post-CPB TEE; mild SAM was noted

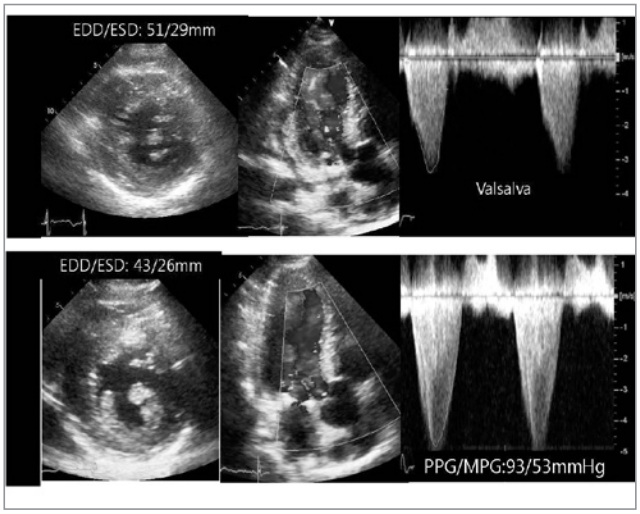
TTE





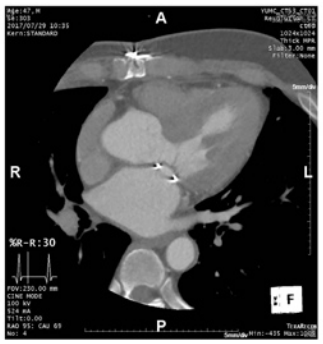
MDPG: 6.4mmHg
(HR: 73 bpm)

What happened?



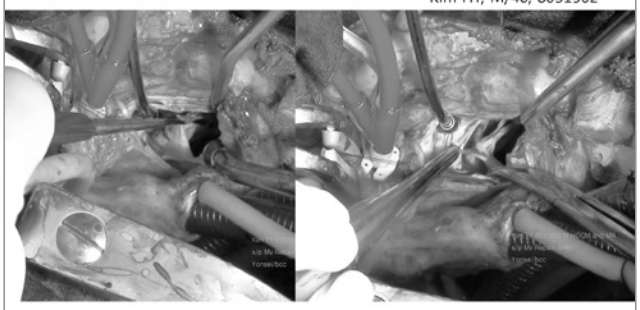
MR with SAM

Kim TY, M/46, 8031902



MR with SAM

Kim HT, M/46, 8031902



LA Appendage

- Morphology
- Size
- Thrombus; small or large

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Correspondence

Significance of left atrial appendage filling defects on cardiac CT prior to pulmonary vein isolation for atrial fibrillation

Arushi Madan [a], Warren Yan [a], Peter Byrne [b], Michael Ward [a,c], Peter Hansen [a], David Whalley [a], Logan Kanagaratnam [d], Gemma A. Figtree [a,c,*]

[a] Department of Cardiology, Royal North Shore Hospital, Sydney, Australia
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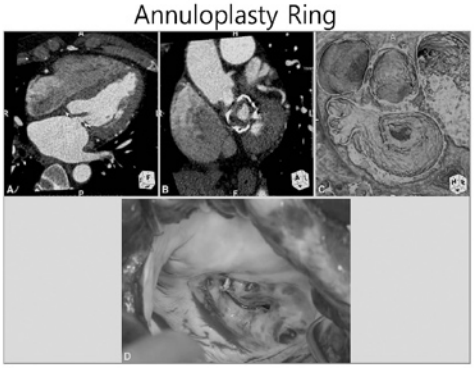
Mitral Valve

Annuloplasty Ring



Suh Y, J Thorac Cardiovasc Surg 2015;150:1082-90

RV and Tricuspid valve

- Functional evaluation of RV
- Tricuspid valve
  - Morphology
  - Annular shape and diameter

CT for HVD

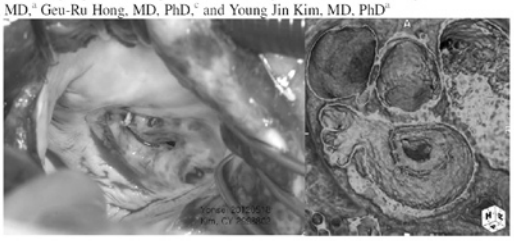
- Progression of valve diseases
- Paravalvular leakage
- Pannus formation

Mitral Valve

Acquired Cardiovascular Disease: Mitral Valve

Assessment of mitral annuloplasty ring by cardiac computed tomography: Correlation with echocardiographic parameters and comparison between two different ring types

Young Joo Suh, MD,[a] Byung-Chul Chang, MD, PhD,[b] Dong Jin Im, MD,[a] Yun Jung Kim, MD,[a] Yoo Jin Hong, MD,[a] Geu-Ru Hong, MD, PhD,[c] and Young Jin Kim, MD, PhD[a]



Valvular Heart Disease

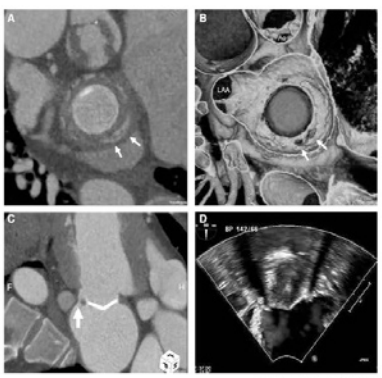
Assessment of Mitral Paravalvular Leakage After Mitral Valve Replacement Using Cardiac Computed Tomography

Comparison With Surgical Findings

Young Joo Suh, MD; Geu-Ru Hong, MD, PhD; Kyunghwa Han, PhD; Dong Jin Im, MD; Suyon Chang, MD; Yoo Jin Hong, MD, PhD; Hye-Jeong Lee, MD, PhD; Jin Hur, MD, PhD; Byoung Wook Choi, MD, PhD; Byung-Chul Chang, MD, PhD; Chi Young Shim, MD, PhD; Young Jin Kim, MD, PhD

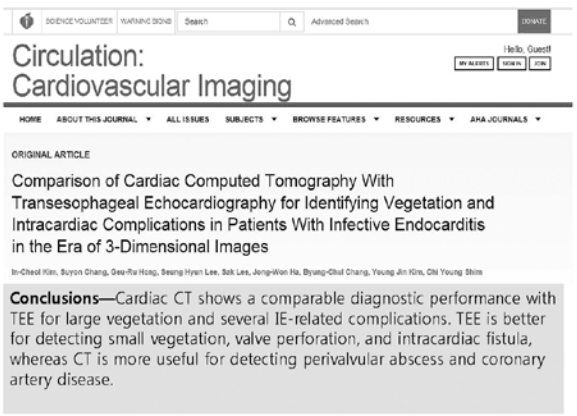
Background—The diagnostic performance of cardiac computed tomography (CT) for detection of paravalvular leakage (PVL) after mitral valve replacement has not been investigated in a large population. We aimed to investigate the diagnostic accuracy of CT for diagnosis of mitral PVL using surgical findings as the standard reference and to compare the diagnostic performance of CT with those of transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE).

Mitral Paravalvular Leakage



Suh YJ Circ CVI 2016;9:e004153

CT in Heart Valve Disease



Circulation: Cardiovascular Imaging

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ORIGINAL ARTICLE

Comparison of Cardiac Computed Tomography With Transesophageal Echocardiography for Identifying Vegetation and Intracardiac Complications in Patients With Infective Endocarditis in the Era of 3-Dimensional Images

In-Cheol Kim, Suyon Chang, Geu-Ru Hong, Seung Hyun Lee, Sak Lee, Jong-Won Ha, Byung-Chul Chang, Young Jin Kim, Chi Young Shim

Conclusions—Cardiac CT shows a comparable diagnostic performance with TEE for large vegetation and several IE-related complications. TEE is better for detecting small vegetation, valve perforation, and intracardiac fistula, whereas CT is more useful for detecting perivalvular abscess and coronary artery disease.

What do surgeons want to know after surgery?

- **Anatomical abnormalities**
  - Progression of native valve disease
- **Functional abnormalities**

➢ Stenosis
  - PPM; prosthesis and/or pannus

➢ Regurgitation; valvular and paravalvular
  - Endocarditis with/without abscess
  - Tethering of mitral and tricuspid valve

➢ Ventricular function

Thank you very much for your attention!

MEMO

SESSION 5

Beyond the ACS in Patients with Acute Chest Pain

Chairperson **Seung Min Yoo** (CHA University Bundang Medical Center, Korea)
Akira Kurata (Ehime University, Japan)

Presentation

Update of new cardiac biomarkers
Speaker Jang-Whan Bae (Chungbuk National University Hospital, Korea)

CT diagnosis of ACS and mimics - focusing the heart
Speaker Ji Won Lee (Pusan National University Hospital, Korea)

CT diagnosis of acute aortic diseases- significant mimickers of ACS
Speaker Takuya Ueda (Tohoku University Hospital, Japan)

MR diagnosis of ACS mimics
Speaker Sung Mok Kim (Samsung Medical Center, Korea)

Panel Discussion

Panel Sung Gyun Ahn (Wonju Severance Christian Hospital, Korea)
Sang Min Park (Chuncheon Hallym University Medical Center, Korea)
Kwang Nam Jin (SMG - SNU Boramae Medical Center, Korea)
Young Jun Cho (Konyang University Hospital, Korea)

Update of new cardiac biomarkers

Jang-Whan Bae (Chungbuk National University Hospital, Korea)

Conditions to be good biomarkers

Austin Bradford Hill's guidelines that increase the likelihood that an association is causative

Guidelines	Characteristics of useful biomarkers
Strength	A strong association between marker and outcome, or between the effects of a treatment on each
Consistency	The association persists in different individuals, in different places, in different circumstances, and at different times.
Specificity	The marker is associated with a specific disease
Temporality	The time-courses of changes in the marker and outcome occur in parallel
Biological gradient (dose-responsiveness)	Increasing exposure to an intervention produces increasing effects on the marker and the disease
Plausibility	Credible mechanisms connect the marker, the pathogenesis of the disease, and the mode of action of the intervention
Coherence	The association is consistent with the natural history of the disease and the marker
Experimental evidence	An intervention gives results consistent with the association
Analogy	There is a similar result to which we can adduce a relationship

New biomarker should be superior than older one, or at least addictive.

New biomarkers in cardiovascular diseases

microRNA

Omentin-1

Galectin-3

sST2

microRNA: overview

microRNA (miR)

- Short (17-25 nucleotides) non-coding RNAs
- Main function: regulate gene expression by hindering the translation of specific mRNAs at the post transcription level
  - Nuclear RNA polymerase II: transcription of the primary microRNA (pri-miR) from the genome
  - Enzyme complex of Drosha-Dgcr8: pri-miR into an 60~70 hairpin structured precursor miR (pre-miR)
  - RanGTP-dependent nuclear export factor, exportin-5: export pre-miR into cytoplasm
  - RNAse III complex: cleaves pre-miR into the mature duplex miR
    - One strand: incorporated into the miR-induced silencing complex (miRISC)
    - The other strand: degraded
  - Prevent target RNA translation or degradation
- Non-canonical pathways for miR biogenesis
  - Drosha-independent pathway, Dicer-independent pathway
- Fine RT-PCR: not easy in the House-lab setting

microRNA: biogenesis

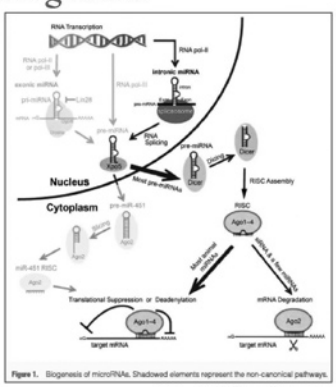


Figure 1. Biogenesis of microRNAs. Shadowed elements represent the non-canonical pathways.

DeRosa S, Indolfi C et al. Circ J. 2014;78:567-75.

microRNA: vulnerable plaque detection

Transcoronary miR gradient and OCT

- Aortic bulb and coronary sinus level of diverse miR
  - Vasculo- and Atheroprotective: miR-126-3p, miR-126-5p, miR-145-5p
  - Anti-angiogenic, proatherosclerotic: miR-92a-3p
  - Proinflammatory, proatherosclerotic: miR-155-5p, miR-29b-3p
- OCT
  - Plaque characters: fibrotic plaque, atheroma, fibroatheroma, calcific fibroatheroma
  - Thin-cap fibroatheroma (TCFA)
  - Rupture plaque

Leistner DM, Zeiher AM et al. Eur Heart J. 2016;37:1738-49.

microRNA: vulnerable plaque detection

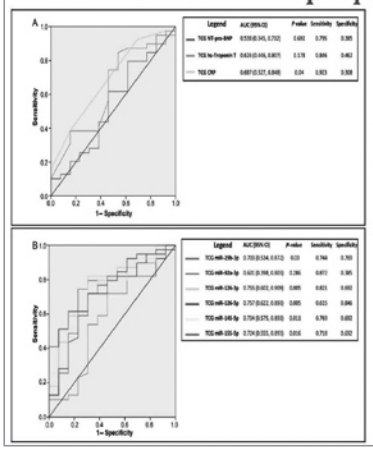
Table 5 Correlations between transcoronary concentration gradients of vessel-wall-associated miRs (TCG) and OCT-derived overall coronary plaque load and distinct plaque characteristics

	Transcoronary concentrations (CVS-AO) of														
	miR-29b-3p	miR-92a-3p	miR-126-3p	miR-126-5p	miR-145-5p	miR-155-5p	miR-486-5p	miR-550a-3p	miR-550a-5p	miR-574-5p	miR-3480-3p	Cel-miR-39-3p	hsTnT	NT-pro-BNP	C-reactive protein
Plaque burden	**0.331**	0.08	**0.29**	**0.378**	**0.356**	**0.349**	−0.05	0.061	0.237	0.097	−0.012	0.148	−0.184	0.048	0.055
P-value	**0.017**	0.572	**0.037**	**0.046**	**0.01**	**0.007**	0.727	0.667	0.091	0.495	0.934	0.296	0.191	0.735	0.697
Fibrotic plaques	−0.11	−0.017	−0.043	−0.088	−0.129	−0.015	0.059	−0.142	−0.183	0.225	0.202	0.042	0.045	−0.209	0.063
P-value	0.437	0.905	0.762	0.536	0.361	0.914	0.676	0.316	0.193	0.108	0.151	0.770	0.75	0.137	0.658
Atheroma	0.031	−0.083	0.147	0.185	0.068	0.255	−0.149	−0.186	0.228	0.217	0.137	0.078	0.006	−0.079	−0.134
P-value	0.828	0.561	0.298	0.190	0.631	0.069	0.293	0.187	0.103	0.123	0.334	0.583	0.966	0.577	0.344
Fibro atheroma	**0.354**	−0.032	0.215	0.194	0.213	0.171	−0.057	0.015	0.077	−0.093	0.084	0.111	0.052	0.217	−0.093
P-value	**0.01**	0.819	0.125	0.168	0.129	0.226	0.691	0.914	0.585	0.51	0.556	0.434	0.712	0.122	0.513
Calcific fibroatheroma	0.106	0.064	0.222	0.240	0.242	**0.323**	−0.155	−0.025	0.189	0.204	0.054	0.222	−0.141	0.058	0.117
P-value	0.456	0.654	0.114	0.087	0.084	**0.019**	0.273	0.861	0.18	0.146	0.704	0.113	0.32	0.681	0.409
Macrophage plaque	0.268	0.029	−0.038	−0.001	0.055	−0.043	0.046	0.025	0.117	−0.113	−0.127	0.049	−0.133	−0.078	−0.191
P-value	0.055	0.783	0.791	0.996	0.697	0.655	0.745	0.859	0.408	0.426	0.371	0.728	0.347	0.58	0.174
TCFA	**0.364**	0.232	**0.383**	**0.341**	**0.387**	**0.333**	0.141	0.097	0.082	0.061	−0.122	0.111	−0.252	−0.14	0.115
P-value	**0.008**	0.097	**0.005**	**0.013**	**0.005**	**0.016**	0.32	0.496	0.562	0.667	0.389	0.431	0.072	0.321	0.418
Ruptured plaque	0.071	−0.03	0.07	0.070	−0.098	−0.038	0.012	−0.007	−0.126	−0.097	0.105	−0.116	0.02	−0.003	0.245
P-value	0.619	0.834	0.622	0.623	0.487	0.787	0.934	0.962	0.374	0.493	0.46	0.415	0.889	0.984	0.058

Significant parameters are in bold.
Spearman's correlations were calculated using SPSS 21. miR, microRNA; hsTnT, high-sensitive troponin T; NT-pro-BNP, N-terminal natriuretic peptide; TCFA, thin-cap fibroatheroma; CVS, coronary venous sinus.

Leistner DM, Zeiher AM et al. Eur Heart J. 2016;37:1738-49.

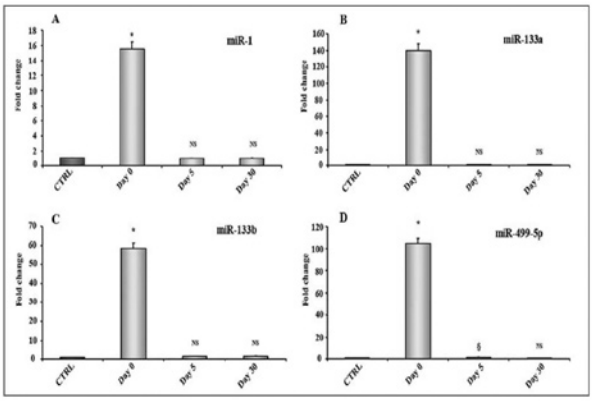
microRNA: vulnerable plaque detection



- Relation to existence of TCFA
  - miR-29b-3p
  - miR-126-3p
  - miR-126-5p
  - miR-145-5p
  - miR-155-5p
- CRP

Leistner DM, Zeiher AM et al. Eur Heart J. 2016;37:1738-49.

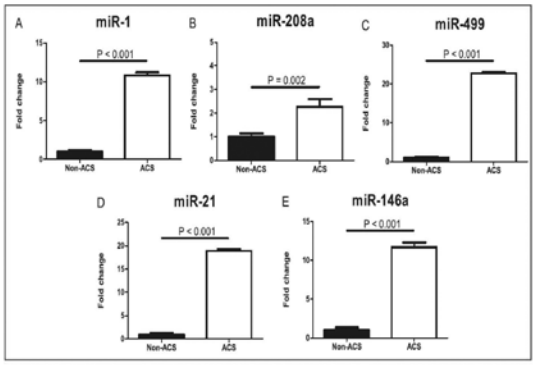
microRNA: STEMI



D'Alessandra Y, Capogrossi MC et al. Eur Heart J. 2010;31:2765-73.

Combination of multiple miR in ACS diagnosis

332 ACS suspected patients (symptom onset to door time: 3.2 hours)



Oerlemans MIFJ, Sluijter JPG et al. EMBO Mol Med. 2012;4:1176-85.

Combination of multiple miR in ACS diagnosis

miR showed earlier elevation in ACS even negative of hs-troponin.

Table 2. Relative expression of circulating miRNAs in serum of suspected ACS patients with a negative hs-troponin ($n = 194$) or with onset of symptoms <3 h ($n = 152$) compared to non-ACS patients ($n = 226$)

MicroRNA	Non-ACS	ACS patients with negative hs-troponin	*p*-value	ACS patients with symptom onset <3 h	*p*-value
miR-1	1.0 ± 0.2	14.9 ± 0.8	0.00	6.0 ± 0.6	0.00
miR-208a	1.0 ± 0.2	2.8 ± 0.7	0.03	2.4 ± 0.5	0.01
miR-499	1.0 ± 0.3	34.2 ± 0.7	0.00	24.0 ± 0.5	0.00
miR-21	1.0 ± 0.3	15.5 ± 0.8	0.00	11.0 ± 0.5	0.00
miR-146a	1.0 ± 0.4	6.2 ± 1.3	0.04	11.9 ± 0.8	0.00

Data are presented as mean ± SEM. *p*-value *versus* non-ACS patients.

Oerlemans MIFJ, Sluijter JPG et al. EMBO Mol Med. 2012;4:1176-85.

Combination of multiple miR in ACS diagnosis

Combination of miR increased AUC upto 0.96 even at the time of negative hs-troponin.

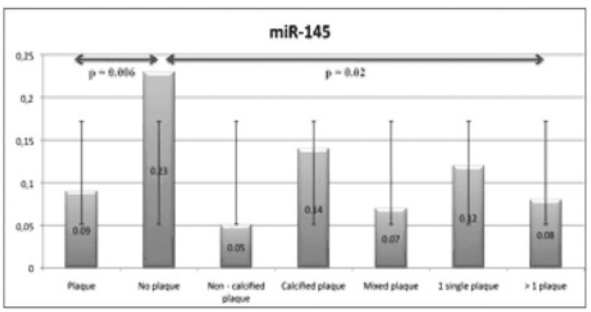
Table 5. AUCs and Odds ratios of miRNAs in suspected ACS patients with a negative hs-troponin in a clinical model ($n = 194$)

Marker	AUC	95% CI	OR[b]	95% CI
Clinical model (CM)	0.84	0.76–0.93	NA	NA
CM + cardiac troponin	0.85	0.77–0.94	NA	NA
CM + cardiac hs-troponin T	0.86	0.79–0.93	NA	NA
CM + cardiac hs-troponin T with				
miR-1	0.92[a]	0.87–0.96	1.44	1.19–1.73
miR-208a	0.87	0.78–0.95	1.12	0.95–1.35
miR-499	0.93[a]	0.87–0.99	1.38	1.19–1.61
miR-21	0.92[a]	0.88–0.97	1.34	1.15–1.55
miR-146a	0.86	0.78–0.93	1.06	0.97–1.15
miR-1 + miR-499 + miR-21	0.96[a]	0.93–0.99	NA	NA

Oerlemans MIFJ, Sluijter JPG et al. EMBO Mol Med. 2012;4:1176-85.

miR-145: inverse relation with atheroma burden

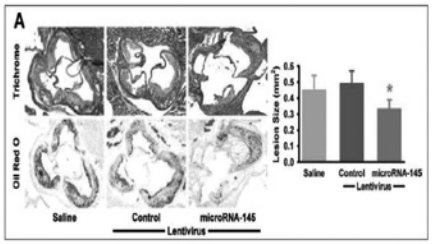
Serum miR-145 and coronary atheroma burden in CCTA.



Rixe J, Dimmeler S et al. Circulation. 2011;124:A15162.

miR-145 suppression & coronary plaque burden

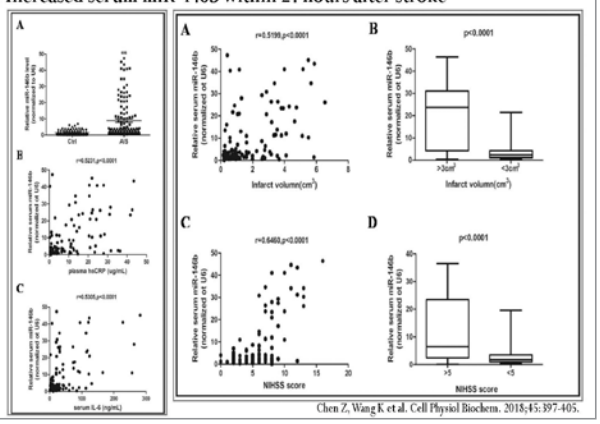
miR-145 overexpression reduced aortic root atherosclerosis in ApoE$^{-/-}$ mouse



Luvren F, Verma S et al. Circulation. 2012;126[suppl 1]:S81-90.

miR-146b in acute human stroke

Increased serum miR-146b within 24 hours after stroke



Chen Z, Wang K et al. Cell Physiol Biochem. 2015;45:397-405.

Candidate miR in cardiovascular diseases

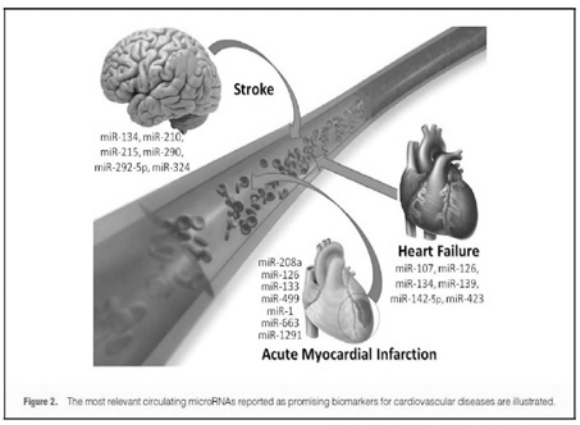
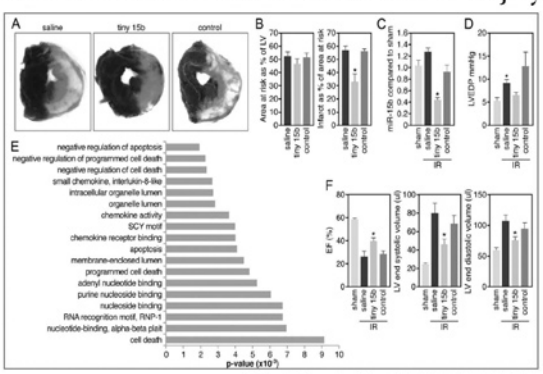


Figure 2. The most relevant circulating microRNAs reported as promising biomarkers for cardiovascular diseases are illustrated.

DeRosa S, Indolfi C et al. Circ J. 2014;78:567-75.

microRNA therapeutics

LNA-modified Anti-miR15 reduced ischemic cardiac injury



Hullinger TG, van Rooij E et al. Circ Res. 2012;110:71-81.

Omentin-1: overview

Omentin-1

Adipokines from adipose tissue

Leptin, adiponectin, TNF-A, IL-1, IL-6, PAI-1, angiotensin, endothelin, resistin

Omentin-1

From adipocytes in lung, intestine, and heart tissue

Anti-inflammatory action

Improve insulin sensitivity via autocrine and paracrine actions

Negative correlation with waist circumference, BMI and insulin resistance

ELISA, Immunoassay

Not easy in the House lab

van Rooij E, Levin AA et al. Circ Res. 2012;110:496-507.

Omentin-1: carotid atherosclerosis in MS

Table 1 – The comparison of clinical materials between MetS and controls.

Variable	MetS		Controls
	MetS+AS (30)	MetS−AS (30)	(30)
Age	59.93 ± 9.44	54.73 ± 11.91	54.03 ± 9.43
Gender (male/female)	16/14	17/13	13/17
Waist circumference (cm)	97.32 ± 7.26	96.57 ± 5.80	82.35 ± 4.38*
BMI (kg/m^2)	28.26 ± 3.41	26.99 ± 2.90	24.03 ± 2.56*
SBP (mm Hg)	153.67 ± 13.83	144.23 ± 14.91▲	126.00 ± 6.82*
DBP (mm Hg)	89.03 ± 11.02	89.27 ± 12.53	79.33 ± 5.15*
TC (mmol/L)	5.29 ± 0.90	4.90 ± 1.23	4.42 ± 0.62△
HDL (mmol/L)	1.38 ± 0.44	1.44 ± 0.37	1.53 ± 0.37
LDL (mmol/L)	2.72 ± 0.67	2.65 ± 1.27	2.24 ± 0.49△
TG (mmol/L)	1.95 ± 1.00	1.94 ± 1.25	1.33 ± 0.77*
FBG (mmol/L)	6.30 ± 0.87	5.85 ± 0.67▲	5.11 ± 0.52*
HOMA-IR	4.22 ± 1.25	3.41 ± 1.35▲	1.73 ± 1.09△
Omentin-1 (ng/mL)	10.66 ± 3.41	23.48 ± 5.87□	34.58 ± 4.23*

Data were showed as means ± SE. Controls versus MetS group △p <0.05; controls versus MetS group *p < 0.01; MetS−AS versus MetS+AS group ▲p < 0.05; MetS−AS versus MetS+AS group □p < 0.01. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride; FBG, fast blood glucose; HOMA-IR, insulin resistance index.

Liu R, Bu P et al. Diabetes Res Clin Pract. 2011;93:21-5.

Omentin-1: severity of CAD

CAD vs control, and CAD severity measured with SYNRAX score

Table 2. Predictors of Angiographic Coronary Artery Disease (CAD) in Univariate and Multivariate Logistic Regression Analysis.

	OR	95% CI	P
Univariate analysis (variables)			
Family history	1.05	1.03-1.16	<.005
Diabetes mellitus	2.32	1.44-3.21	<.005
Hypertension	1.63	1.23-2.34	.008
Hyperlipidemia	1.78	1.34-2.88	.023
Smoking	1.88	1.43-2.67	<.005
Omentin 1 level	1.56	1.19-2.06	<.005
Multivariate logistic regression analysis (variables)			
Family history	1.50	0.9-2.48	.12
Diabetes mellitus	1.84	1.78-2.89	<.005
Hypertension	1.15	0.85-1.85	.503
Hyperlipidemia	1.47	0.91-2.25	.089
Smoking	1.76	1.34-2.57	.009
Omentin 1 levels	1.01	1.0-1.03	.01

Table 3. Correlation Between SYNTAX Score, Omentin 1, and Clinical Parameters.

Variables	Correlation Coefficient (r Values)	P
Age	.197	.008
Diabetes mellitus	.398	<.001
Smoking	.164	.01
Hypertension	.231	.005
Hyperlipidemia	.056	.34
BMI	.01	.83
Omentin-1 levels	−.42	<.001

van Rooij E, Levin AA et al. Circ Res. 2012;110:496-507.

Omentin-1: risk of AMI and stroke

From EPIC-Potsdam cohort study: 2084 sub-cohort for 8.2 years follow-up

Table 1
Characteristics of the subcohort according to omentin-1 quartiles.

Characteristics	Quartiles of omentin-1 in the subcohort[a]				p linear trend[c]	p linear trend[d]
	Q1	Q2	Q3	Q4		
n	519	525	519	521		
Omentin-1 [ng/ml][b]	286.5 (250.6–308.6)	363.1 (343.4–380.3)	439.6 (420.0–462.8)	569.6 (517.4–642.6)		
Men [%]	41.2	36.6	37.7	33.5	0.02	0.1
Age [years]	47.4 (46.6–48.1)	48.8 (48.1–49.5)	51.9 (51.1–52.6)	53.9 (53.2–54.6)	<0.0001	<0.0001
Waist circumference [cm]	89.8 (88.8–90.7)	87.4 (86.5–88.3)	86.6 (85.7–87.5)	85.1 (84.2–86.0)	<0.0001	<0.0001
Physical activity, [h/week]	0.88 (0.73–1.03)	0.91 (0.76–1.05)	0.98 (0.83–1.13)	1.26 (1.11–1.41)	0.0005	0.01
Smoking [%]					0.3	0.5
Non-smoker	43.1	43.3	40.7	46.9		
Ex-smoker < 5 years	26.1	27.3	28.4	24.8		
Ex-smoker ≥ 5 years	7.4	6.4	8.7	8.9		
Smoker < 20 cigarette/day	16.0	14.9	17.2	12.6		
Smoker ≥ 20 cigarettes/day	7.3	8.1	4.9	6.8		
Education [%]					0.7	0.4
Unskilled or skilled	35.4	35.0	35.2	35.4		
Technical College	22.4	23.5	23.5	21.3		
University degree	42.2	41.5	41.2	43.3		
Prevalent diabetes [%]	3.7	3.8	4.6	5.9	0.07	0.0004
Antidiabetic medication [%]	1.6	1.6	3.1	3.2	0.03	0.0004
Prevalent hypertension [%]	50.7	48.7	47.4	49.6	0.6	0.06
Antihypertensive medication [%]	19.4	16.0	16.6	19.0	0.9	0.07
Lipid-lowering medication [%]	4.7	4.4	3.6	4.0	0.5	0.5
Total cholesterol [mmol/l]	5.24 (5.15–5.33)	5.26 (5.17–5.36)	5.26 (5.17–5.35)	5.37 (5.27–5.46)	0.08	0.4
HDL-cholesterol [mmol/l]	1.36 (1.32–1.39)	1.39 (1.36–1.42)	1.41 (1.38–1.44)	1.53 (1.50–1.56)	<0.0001	0.03
Triglyceride [mmol/l]	1.64 (1.55–1.73)	1.53 (1.44–1.62)	1.66 (1.57–1.75)	1.47 (1.37–1.56)	0.0003	0.7
hsCRP [mg/l]	2.57 (2.26–2.89)	1.67 (1.37–1.97)	1.89 (1.59–2.20)	1.64 (1.33–1.95)	<0.0001	0.06
Adiponectin [µg/ml]	6.99 (6.67–7.32)	7.78 (7.46–8.10)	8.23 (7.90–8.55)	9.30 (8.97–9.63)	<0.0001	<0.0001
Alcohol [g/d]	14.6 (12.9–16.3)	16.5 (14.8–18.2)	16.6 (14.9–18.2)	19.4 (17.7–21.1)	<0.0001	0.0004

Menzel J, di Giuseppe R et al. Atherosclerosis. 2016;251:415-21.

Omentin-1: risk of AMI and stroke

From EPIC-Potsdam cohort study

Table 2
Hazard ratios of MI and stroke according to quartiles and per doubling of omentin-1 levels.

	Quartiles of omentin-1 levels				p for trend	Per doubling of omentin-1	
	Q1	Q2	Q3	Q4			p-value
Omentin-1 [ng/ml][a]	286.5 (250.6–307.4)	364.2 (344.0–380.5)	439.6 (420.0–462.2)	571.9 (519.5–642.6)			
Subcohort participants (n)	519	525	519	521			
Follow-up time [years]	4245.8	4288.9	4304.1	4234.2			
MI (n = 2267)							
Cases (n)	43	45	54	60			
Sex and age adjusted	Reference	0.99 (0.63–1.54)	0.91 (0.60–1.39)	0.95 (0.62–1.46)	0.80	0.96 (0.68–1.35)	0.79
Model 2[b]	Reference	0.90 (0.56–1.44)	0.97 (0.62–1.51)	1.16 (0.72–1.83)	0.42	1.19 (0.81–1.75)	0.37
Model 3[c]	Reference	0.89 (0.56–1.42)	0.96 (0.61–1.50)	1.13 (0.71–1.79)	0.48	1.17 (0.79–1.72)	0.43
Stroke (n = 2251)							
Cases (n)	24	34	55	85			
Sex and age adjusted	Reference	1.29 (0.75–2.23)	1.73 (1.05–2.84)	2.39 (1.50–3.80)	<0.0001	2.12 (1.54–2.92)	<0.0001
Model 2[b]	Reference	1.26 (0.72–2.20)	1.63 (0.97–2.73)	2.42 (1.47–3.98)	0.0001	2.31 (1.59–3.35)	<0.0001
Model 3[c]	Reference	1.24 (0.71–2.16)	1.58 (0.94–2.66)	2.29 (1.38–3.79)	0.0003	2.22 (1.52–3.22)	<0.0001

Menzel J, di Giuseppe R et al. Atherosclerosis. 2016;251:415-21.

Galectin-3: overview

Galactin-3

β-galactoside binding lectin

- Released by activated macrophage, leukocyte and mast cell
- Regulate fibrogenesis, inflammation, cell proliferation, and tissue repair

Clinical implications

- Inflammation, scar formation
- High expression in acute and chronic LV overload
- Associated with LV remodeling
- Predict major event in acute and chronic HF

Immunoassay, ELISA

- Still not in the House lab

van Rooij E, Levin AA et al. Circ Res. 2012;110:496-507.

Galectin-3 in moderate to severe symptomatic HF

Deventer-Alkamaar Heart Failure study

NYHA Fc III/IV, LV-EF 30.9%, 6.5 years follow-up

Table 1 Baseline demographic and clinical characteristics of the study population by quartile of galectin-3 levels

Baseline characteristic	All subjects n = 232	Galectin-3 quartile				P value
		1 (<13.63 ng/mL) n = 58	2 (13.63–17.63 ng/mL) n = 59	3 (17.64–21.62 ng/mL) n = 57	4 (>21.62 ng/mL) n = 58	
Age, mean (SD) (years)	70.9 (10.0)	64.6 (11.7)	71.6 (8.9)	72.8 (8.9)	74.6 (7.0)	<0.001
Male (%)	72.4	72.4	76.3	68.4	72.4	NS
Ischemic etiology (%)	62.5	50.0	70.2	61.0	69.0	0.047
NYHA functional class (%)						
III	96	97	100	93	93	NS
IV	4	2	0	6	7	NS
LVEF, mean (SD)	30.9 (9.4)	31.1 (10.0)	29.7 (8.2)	31.9 (8.7)	31.0 (10.6)	NS
BMI, mean (SD) (kg/m^2)	26.3 (4.7)	27.9 (5.3)	25.9 (4.1)	25.8 (4.7)	25.9 (4.3)	0.046
Diabetes mellitus (%)	30	28	22	35	33	NS
COPD (%)	29	25	23	32	35	NS
Smoker (%)	13	17	12	14	9	NS
GFR, mean (SD) (mL/min)	55.0 (22.8)	72.7 (24.5)	56.0 (18.6)	49.2 (19.4)	42.3 (16.6)	<0.001
NT-proBNP level, mean (SD) (pmol/L)	436.0 (616.7)	291.1 (376.6)	353.8 (586.7)	526.5 (561.1)	651.2 (920.4)	0.005
Galectin-3 level, mean (SD) (ng/mL)	18.6 (7.8)	11.3 (1.6)	15.5 (1.3)	19.5 (1.2)	28.2 (9.0)	-

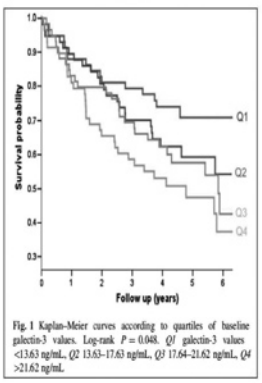
Percentages may not sum to 100 due to rounding. *P* values are from one-way ANOVA comparison of means across quartiles of galectin-3

BMI Body mass index, *COPD* chronic obstructive pulmonary disease, *LVEF* left ventricular ejection fraction, *NYHA* New York Heart Association, *SD* standard deviation, *NS* not significant

Lok DJ, van Veldhuisen DJ et al. Clin Res Cardiol. 2010;99:323–8.

Galectin-3 in moderate to severe symptomatic HF

Deventer-Alkamaar Heart Failure study



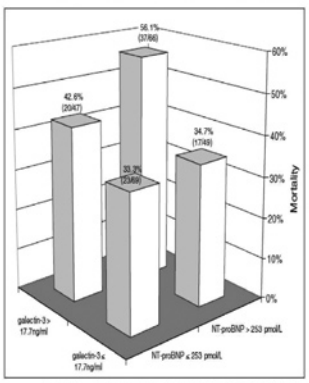


Fig. 1 Kaplan-Meier curves according to quartiles of baseline galectin-3 values. Log-rank $P = 0.048$. *Q1* galectin-3 values <13.63 ng/mL, *Q2* 13.63–17.63 ng/mL, *Q3* 17.64–21.62 ng/mL, *Q4* >21.62 ng/mL

Lok DJ, van Veldhuisen DJ et al. Clin Res Cardiol. 2010;99:323–8.

Galectin-3 in HF with preserved EF

419 admitted patients with HF and EF > 45%

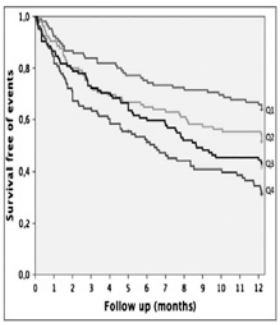


Table 3
Univariate and adjusted multivariable Hazard Ratios for galectin-3 > median (13.8 ng/ml) with all-cause mortality at 1-year follow-up.

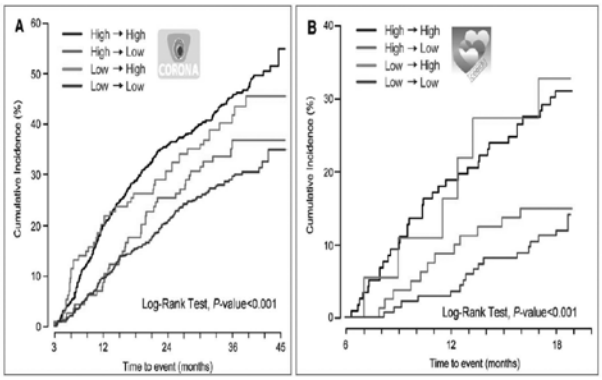
	HR (95% CI) for galectin-3	*P* value
Univariate (galectin-3 only)	1.87 (1.31 – 2.67)	<0.001
+Age	1.75 (1.23 – 2.51)	0.002
+Age + eGFR	1.63 (1.14 – 2.34)	0.007
+Age + eGFR + anemia	1.65 (1.15 – 2.36)	0.006
+Age + eGFR + anemia + Na^+	1.63 (1.14 – 2.34)	0.007
+Age + eGFR + anemia + Na^+ + NT-proBNP	1.54 (1.07 – 2.01)	0.049
+Age + eGFR + anemia + Na^+ + NT-proBNP + NYHA	1.42 (1.07 – 2.21)	0.051
+Age + eGFR + anemia + Na^+ + NT-proBNP + NYHA + Urea	1.46 (1.01 – 2.11)	0.040

The stated *P* value is associated with the regression coefficient of galectin-3 in each model. HR, Hazard Ratio; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association class; Na^+, serum sodium.

Carrasco-Sánchez FJ, Pérez-Calvo JI et al. Int J Cardiol. 2013;169:177-82.

Galectin-3 in repeated check

Cohort with CORONA and COACH studies



van der Velde AR, de Boer RA et al. Circ Heart Fail. 2013;6:219–26..

ST2: overview

ST2, as a cardiovascular risk biomarker

Member of the IL-1 receptor family

Released from cardiomyocyte under mechanical strain

ST2L: transmembrane form, sST2: soluble form

sST2

Mortality prediction in heart failure and AMI

Causal role in chronic cardiovascular disease, e.g. atherosclerosis, heart failure

IL-33/ST2 pathway in chronic heart failure

Can be performed in the House lab ALREADY!

ST2 in acutely decompensate heart Failure

sST2: high in systolic dysfunction, and high in mortality patients

Characteristics of study patients as function of left ventricular ejection fraction

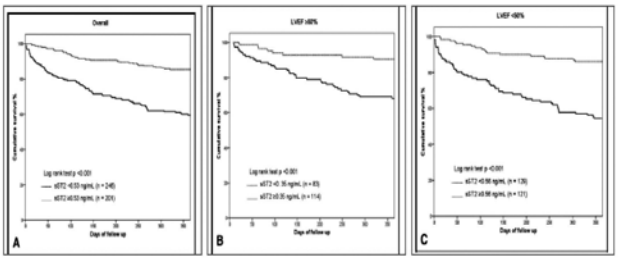
Variable	Overall (n = 447)	Left Ventricular Ejection Fraction ≥50% (n = 197)	Left Ventricular Ejection Fraction <50% (n = 250)	p Value
Left ventricular ejection fraction (%)	46 (32-60)	60 (55-65)	34 (25-42)	<0.001
Admission New York Heart Association functional class				0.46
II	102 (23%)	45 (23%)	57 (23%)	
III	156 (35%)	63 (32%)	93 (37%)	
IV	189 (42%)	89 (45%)	100 (40%)	
Estimated glomerular filtration rate (ml/min/1.73 m^2)	63 (43-86)	61 (40-83)	65 (45-90)	0.029
Blood urea nitrogen (mg/dl)	25 (18-34)	24 (18-33)	25 (18-35)	0.36
C-reactive protein (mg/dl)	3.5 (0.9-16.3)	5.2 (1-22)	2.65 (0.80-9.95)	0.013
Troponin T (ng/ml)	0.01 (0.01-0.04)	0.01 (0.01-0.037)	0.016 (0.01-0.062)	0.004
Plasma amino terminal B-type natriuretic peptide (pg/ml)	3,558 (1,646-9,250)	2,749 (1,344-6,634)	4,709 (2099-11,159)	<0.001
Soluble ST2 (ng/ml)	0.47 (0.28-0.94)	0.38 (0.26-0.79)	0.55 (0.30-1.03)	<0.001

Data are presented as mean ± SD, median (quartiles), or n (%).

Manzano-Fernandez S, Mueller T et al. Am J Cardiol.2011;107:259-67.

ST2 in acutely decompensate heart Failure

sST2: high in systolic dysfunction, and high in mortality patients



Manzano-Fernandez S, Mueller T et al. Am J Cardiol.2011;107:259-67.

ST2 in STEMI treated with primary PCI

Early risk stratification with ST2 and NT-proBNP in well-treated STEMI

CV death, non-fatal MI, non-fatal stroke, ischemia-driven revascularization

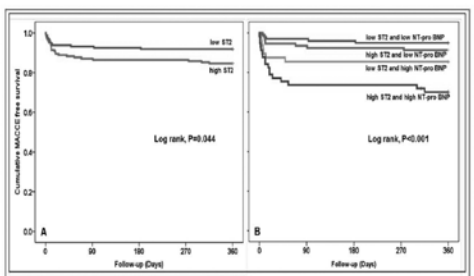
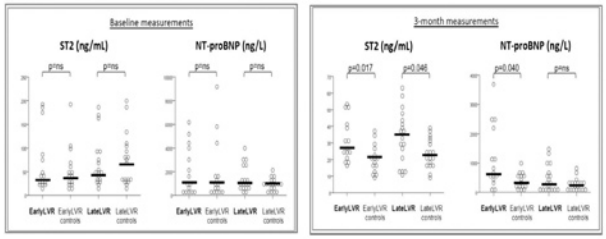


Fig 2. Kaplan-Meier survival curves for MACCE during a year following primary PCI showed high sST2 level was associated with a poorer prognosis (A) and that high sST2 and high NT-proBNP levels in combination were associated with a worst prognosis than any other levels of combination (B).

YU J, Kang WC et al. PLoS One. 2017;12:e0182829

ST2 in prediction of late LV remodeling after MI

ST2 and NT-proBNP in early, late and non-LV remodeling after ant. wall MI



Biere L, Prunier F et al. Int J Cardiol. 2018;Epub ahead of print.

ST2 in predict mortality in TAVI

401 patients treated with TAVI for symptomatic severe AS in Germany

Independent predictors for 1 year mortality

- STS score
- LV ejection fraction
- NT-proBNP
- sST2
  - but, no incremental prognostic value on STS score and NT-proBNP

Stundl A, Lunstedt NS et al. Am J Cardiol. 2017;120:986–93.

Serial ST2 in MADIT-CRT trial

Mildly symptomatic HF patients who implanted CRT

Prognostic power of sST2 and BNP at baseline

Table 2 Event rates and multivariable risk adjusted of ventricular arrhythmias, death or VA, death or HF, and death by levels of sST2 and BNP

Endpoint *n*/*N* (%) event rate	VA events 129/684 (18.9 %) 7.1 (6.0-8.4)		Death or VA 184/684 (26.9 %) 10.1 (8.8–11.7)		Death or HF 150/684 (21.9 %) 8.0 (6.8–9.3)		Death 74/684 (10.8 %) 3.6 (2.9–4.5)	
	HR (95 % CI)	*p* value	HR (95 % CI)	*p* value	HR (95 % CI)	*p* value	HR (95 % CI)	*p* value
sST2	1.18 (0.99–1.40)	0.058	1.31 (1.14–1.50)	<0.001	1.31 (1.14–1.52)	<0.001	1.45 (1.20–1.76)	<0.001
sST2[a]	1.13 (0.94–1.35)	0.212	1.23 (1.06–1.43)	0.007	1.26 (1.08–1.48)	0.004	1.41 (1.13–1.76)	0.002
sST2[b]	1.09 (0.90–1.31)	0.37	1.19 (1.02–1.39)	0.023	1.20 (1.02–1.41)	0.025	1.35 (1.08–1.69)	0.009
BNP	1.22 (1.01–1.47)	0.04	1.32 (1.12–1.56)	0.001	1.74 (1.43–2.10)	<0.001	1.78 (1.35–2.36)	<0.001
BNP[a]	1.26 (1.02–1.55)	0.03	1.29 (1.08–1.55)	0.006	1.58 (1.28–1.95)	<0.001	1.55 (1.14–2.11)	0.005
BNP[b]	1.24 (1.00–1.52)	0.046	1.25 (1.04–1.49)	0.017	1.53 (1.24–1.89)	<0.001	1.47 (1.08–1.99)	0.015

Event rate per 100 patient-years. HR (95 % CI) per one standard deviation of log-transformed biomarkers (sST2 and BNP)

[a] Model 1 adjusted for treatment arm, age, gender, ischemic etiology, diabetes, hypertension, LBBB, QRS duration, LVEF, eGFR, and NYHA class

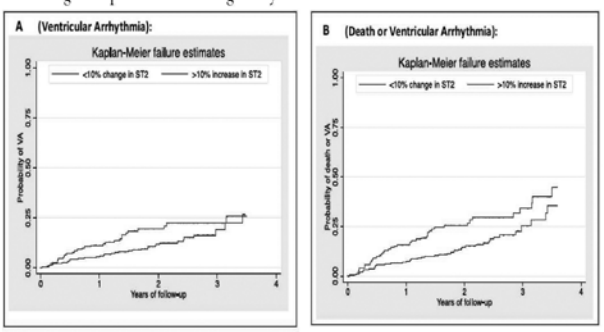
[b] Model 2, model 1 (above) and baseline sST2 or BNP

Skali H, Gerwien R et al. J CardiovascTranl Res. 2016;9:421–8.

Serial ST2 in MADIT-CRT trial

Mildly symptomatic HF patients who implanted CRT

Prognostic power of sST2 change at 1 year after CRT-D



Skali H, Gerwien R et al. J CardiovascTranl Res. 2016;9:421–8.

Conclusions

microRNA

- Cardiac specific miR: early ACS detection, therapeutic target
- House lab capability ?

Omentin-1

- Effective marker in metabolic syndrome or diabetes
- Vulnerable plaque

Galectin-3

- HF, ACS and event prediction
- ELISA, Immunoassay, but house lab (-)

sST2

- HF diagnosis, LV overload/remodeling in AMI
- Possible in house lab

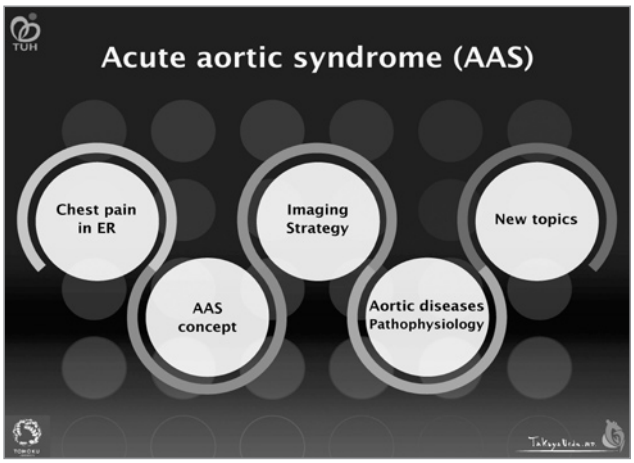
CT diagnosis of ACS and mimics - focusing the heart

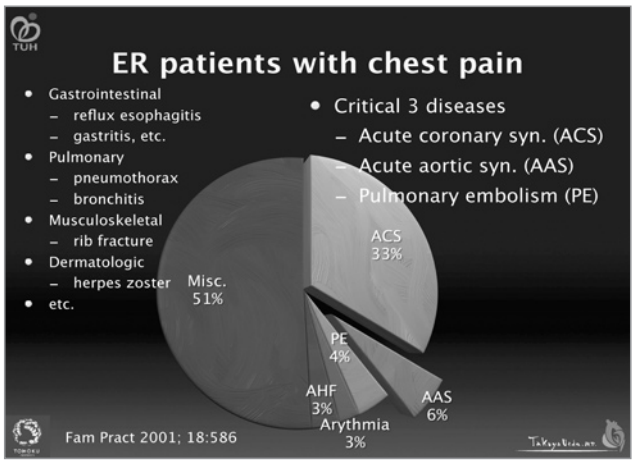
Ji Won Lee (Pusan National University Hospital, Korea)

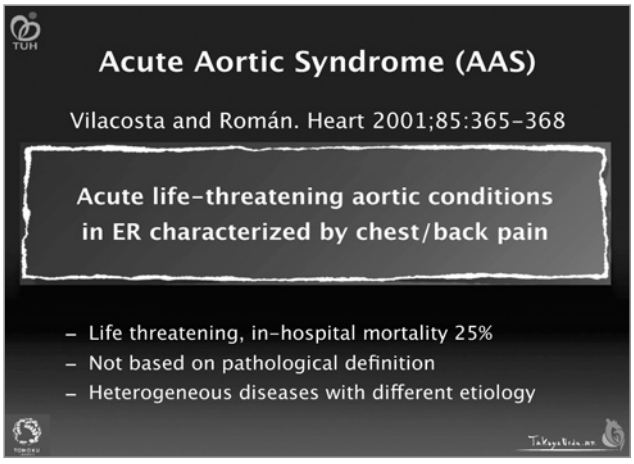
MEMO

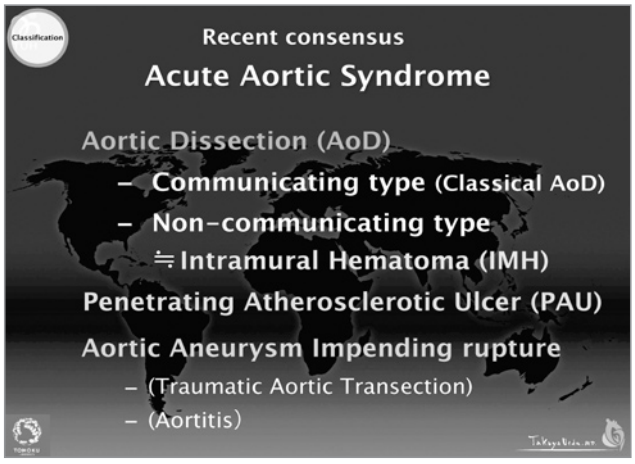
CT diagnosis of acute aortic diseases- significant mimickers of ACS

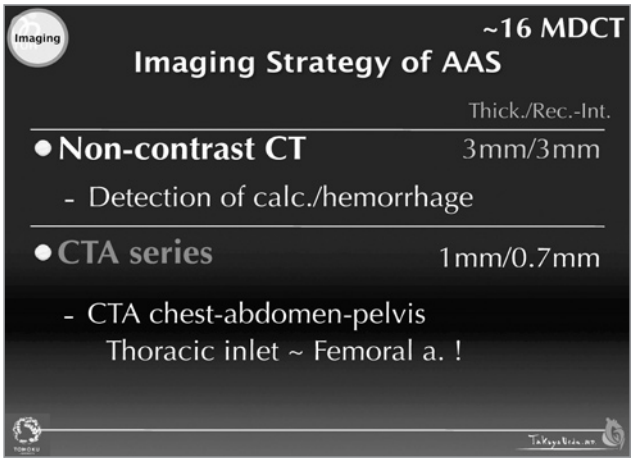
Takuya Ueda (Tohoku University Hospital, Japan)

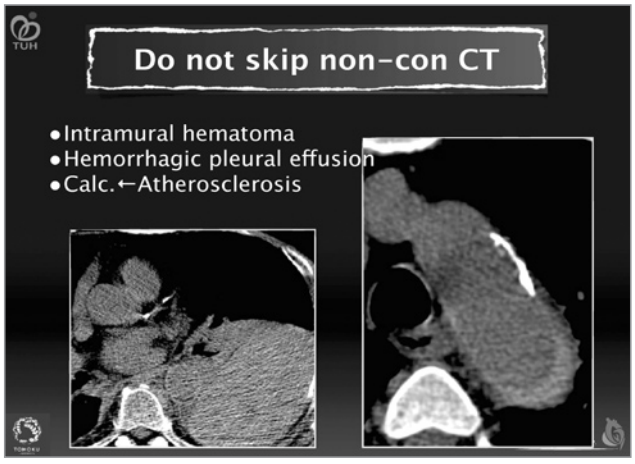


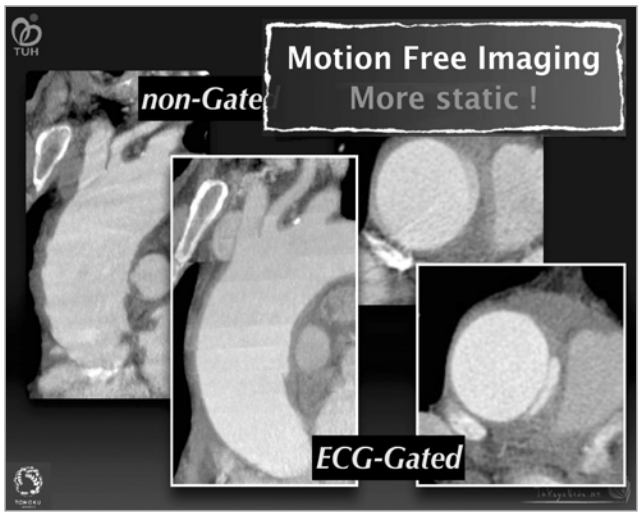








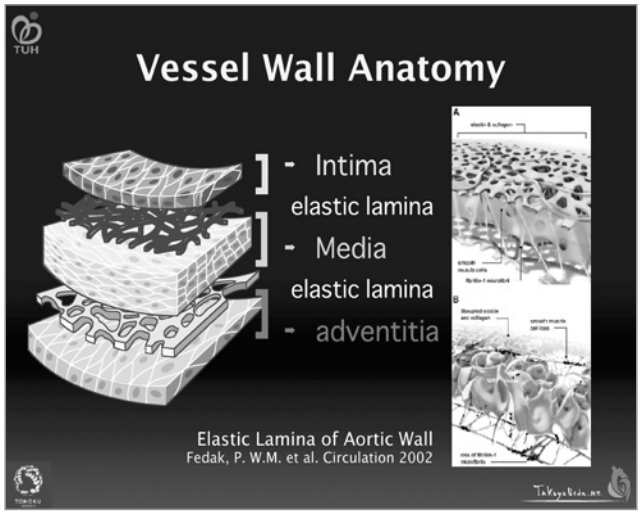


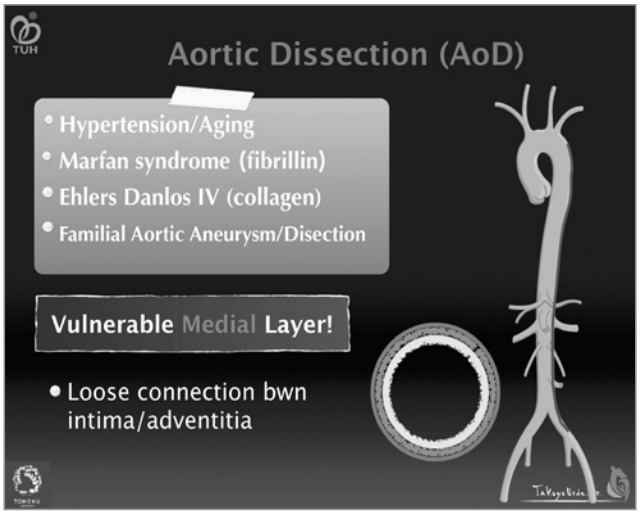


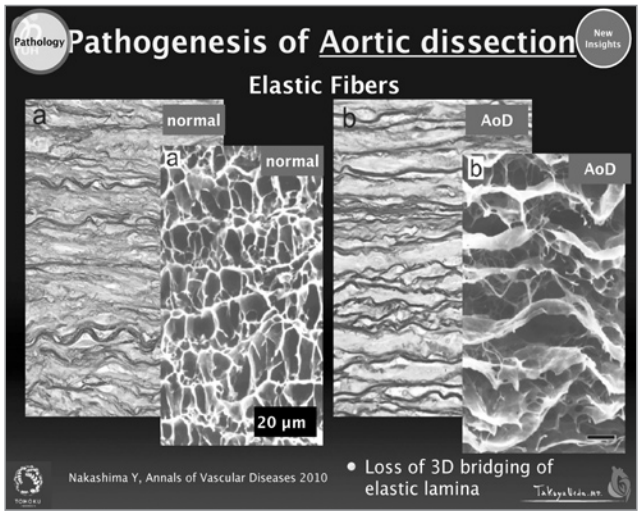
Dilemma of applying ECG-gated chest CTA in ER situation

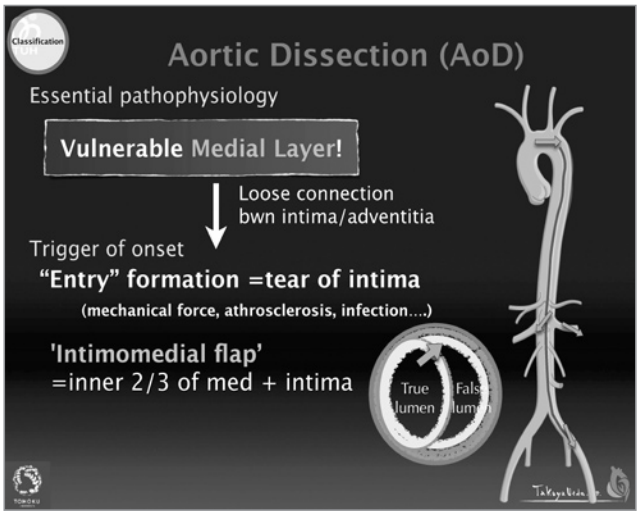
- PROS
  - High Image Quality
    entry detection, flap motion
    coronary assessment
- CONS
  - Complicated procedure
    Long scanning time in ER
    Postprocessing time

I know ECG-gated CTA is good tool,
but…. difficult to apply in ER situation….

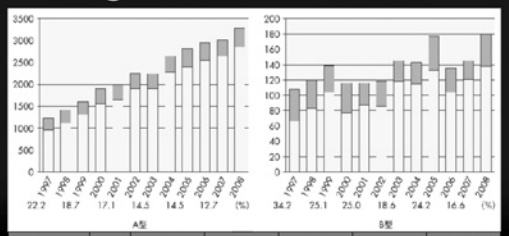








Recent result of surgical outcome of AoD



Year	Type	1997	1999	2005	2007	2014*
Perioperative mortality	A	22.2	17.1	14.5	13.0	8.5
%	B	34.2	25.1	24.2	17.6	12.2

JCS 2011 Guideline

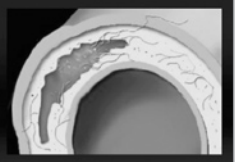
* Gen Thorac Cardiovasc Surf (2014)

	ACCF2010	Level Grade	ESC2014	Level Grade	JAMA 2016	Level Grade
Classical Aortic Dissection						
Type A	Surgery	I(B)	Surgery	I(B)	Surgery	I(B)
Type B						
non-complicated	Medical Tx	I(B)	Medical Tx (TEVAR)	I(C) IIA(B)	Medical Tx or TEVAR	I(C) IIA(B)
complicated	Surgery	I(B)	TEVAR	I(C)	TEVAR	IC
IMH						
Type A						
non-complicated	/		/		Medical Tx	IIA(C)
complicated	Surgery	IIA(C)	Surgery	I(C)	Surgery	IIA(C)
Type B						
non-complicated	Medical Tx	I(B)	Medical Tx	I(C)	Medical Tx	IIA(C)
complicated	Surgery	IIA(C)	TEVAR	IIA(C)	TEVAR	IIA(C)

Intramural Hematoma (IMH)

Traditional Concept

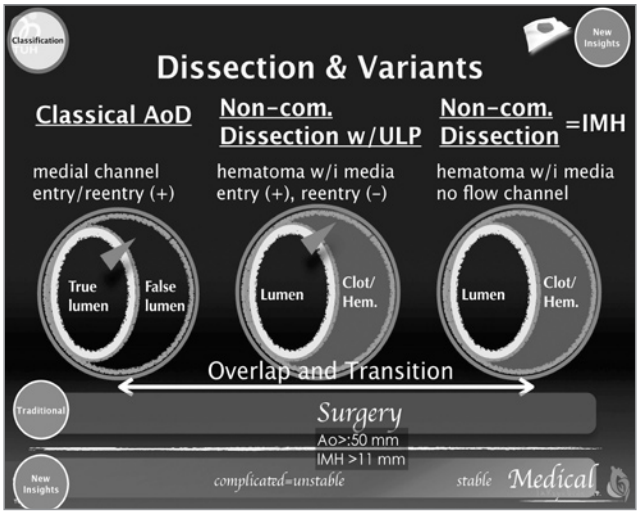
- **Definition**
  - No open flow channel
  - Hematoma within media
- **Pathology**
  - Rupture of vaso vosorum ?!



Many controversial issues!?

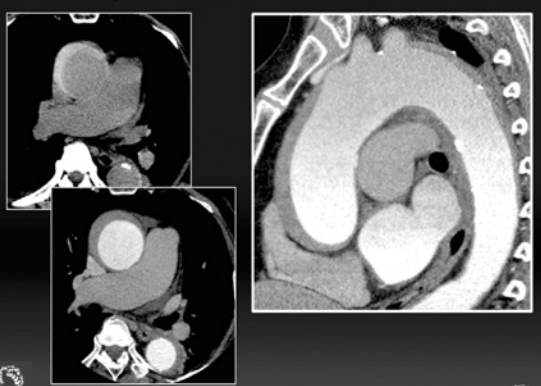
Ferco Berger et al. "Thoracic aorta - the Acute Aortic Syndrome"
Radiology Assistant: http://www.radiologyassistant.nl

Dissection & Variants

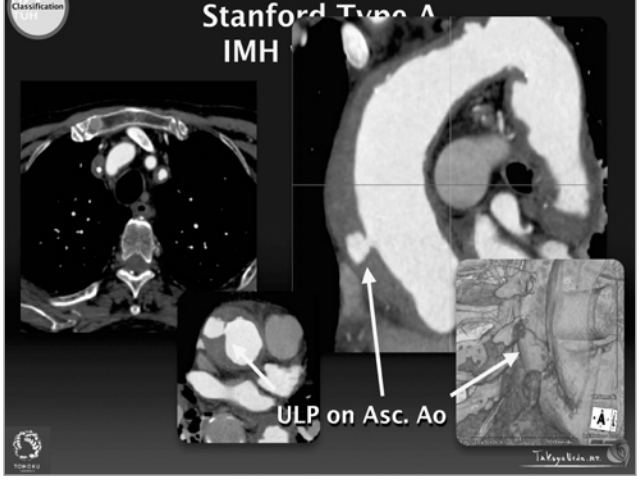


Non-com. type AoD = IMH

54 yo male w/ acute chest pain

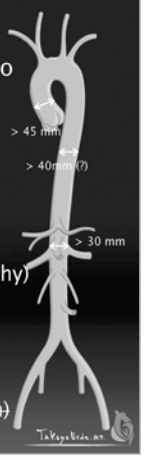


Stanford Type A IMH



Aortic aneurysm

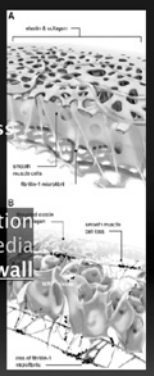
- Segmental, full thickness dilatation of Ao
- 1.5 times greater than its normal Φ
- TAA >45 mm , AAA >30 mm



- Atherosclerosis (true aneurysm)
- Infection (Mycotic An, Siphyris)
- Inflammatory AoAn (≒IgG4 related aortopathy)
- Marfan/Loies-Diez syn.
- Congenital (ex. aortopathy in TOF, BAV.)
- Trauma
- ~~Chronic Ao dissection (dissecting aneurysm)~~

(Atherosclerotic) Aneurysm

- Pathophysiology
  - mucoid degeneration
  - smooth-muscle cell loss



slow growing

Mucoid degeneration
smooth-muscle cell loss in Media
Loss of Elasticity of aortic wall
Age-related

Normal **Aneurysm**

Abdominal aortic aneurysm
at risk for rupture

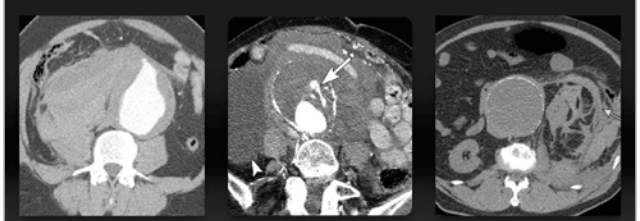
- Suspect AAA rupture in pts with
  - sudden acute abdominal or flank pain
  - shock or syncope
  - pulsatile abdominal mass
  - hematuria or GI hemorrhage
  - known-An to expand > 0.5 cm in 6M

Various condition of rupture

- Rupture
- Impending rupture
  - acute, **to rupture ? or not to rupture ? That is the question… >_<**
- Contained/concealed rupture
  - chronic, An was sealed after acute rupture
  - high ris **Do not miss an ambush, that might kill your patients !!**

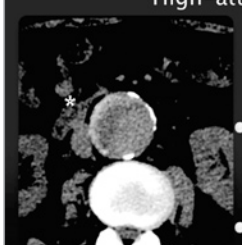
CT Signs of rupture

Retroperitoneal hematoma | Extravasation of IV contrast | Periaortic stranddling



CT Signs of impending rupture

High-attenuating crescent sign



- Famous finding !!
  - Sens. 77%, Spec. 93%
  - Mehard WB, Radiology. 1994
- But in later cohort study….
  - PPV is just 10% !!!!!
  - Boules TN, et al. Vasc Endovascular Surg. 2006

CT Signs of impending rupture

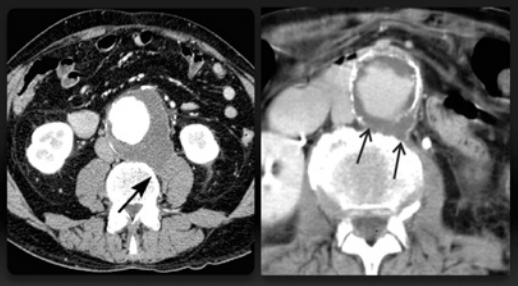
Tangential calcium sign

Focal discontinuity of intimal calcification

Rakita D. 2007 Radiographics

CT Signs of contained rupture

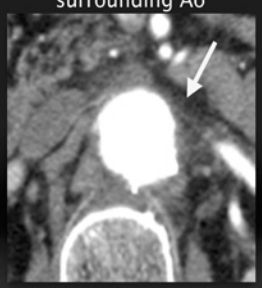
draped aorta



Schwartz SA. et al. AJR. 2007

CT Signs of contained rupture

Soft tissue density surrounding Ao



Schwartz SA. et al. AJR. 2007

Vertebral erosion

Ando M,et al. Ann Thorac Cardiovasc Surg 2003

25% in contained rupture

Penetrating Atherosclerotic Ulcer (PAU)

Clinical features

- Age: Elderly men (over 70)
- Location: Arch - Desc.
  Often multiple
- Prognosis: rupture 5-25%
- Tx: Surgery/Follow/EVAR

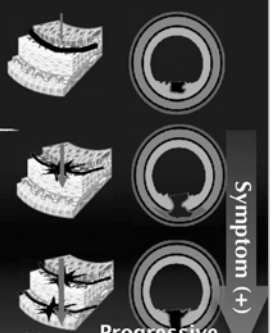
a/w Systemic atherosclerosis!!
coronary disease, aneurysm, renal diseases, ASO etc

Ulcerative lesions

Pathology

- Ulcerative plaque
  - Confined into intima
- PAU
  - Penetrates to media
- PAU impending rupture
  - Penetrates to adventitia
- Leaking PAU
  - Penetrates through adventitia

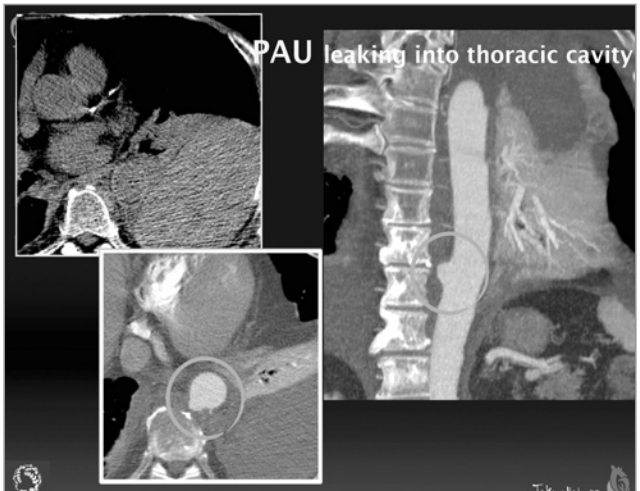
Deep

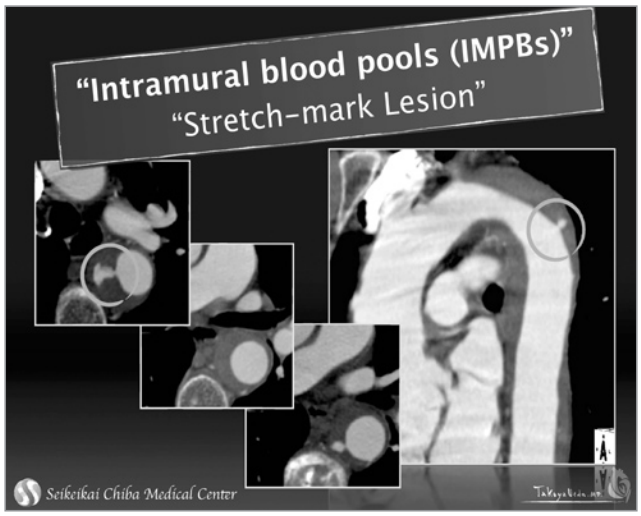


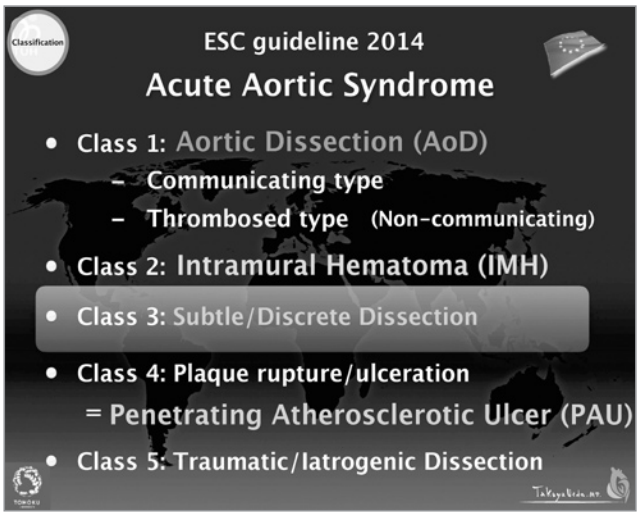
Symptom (+)

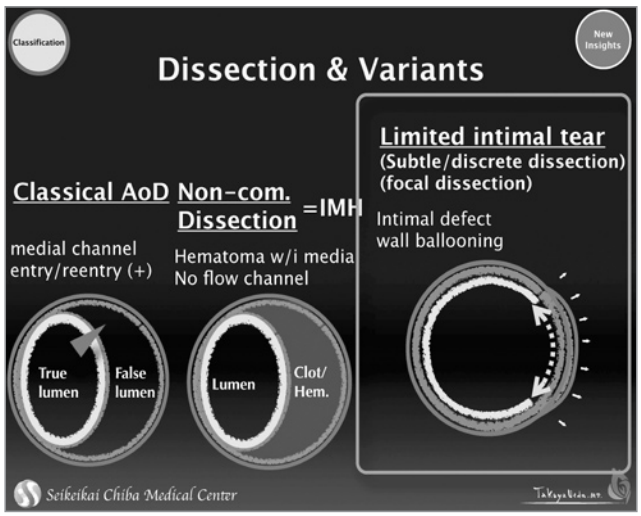
Progressive lesion

PAU leaking into thoracic cavity




"Intramural blood pools (IMPBs)"
"Stretch-mark Lesion"
Seikeikai Chiba Medical Center


Classification
ESC guideline 2014
Acute Aortic Syndrome
Class 1: Aortic Dissection (AoD)
– Communicating type
– Thrombosed type (Non-communicating)
Class 2: Intramural Hematoma (IMH)
Class 3: Subtle/Discrete Dissection
Class 4: Plaque rupture/ulceration
= Penetrating Atherosclerotic Ulcer (PAU)
Class 5: Traumatic/Iatrogenic Dissection


Classification
New Insights
Dissection & Variants
Classical AoD
medial channel
entry/reentry (+)
True lumen
False lumen
Non-com. Dissection =IMH
Hematoma w/i media
No flow channel
Lumen
Clot/ Hem.
Limited intimal tear
(Subtle/discrete dissection)
(focal dissection)
Intimal defect
wall ballooning
Seikeikai Chiba Medical Center

SESSION 6

Debate - Hypertrophic Cardiomyopathy

Chairperson **Sang-Chol Lee** (Samsung Medical Center, Korea)
Tae-Hwan Lim (University of Ulsan College of Medicine, Korea)

Presentation

How risk stratification and prevent the SCD (overall - family hx, gene, sx, ECG, echo..)
Speaker Jun-Bean Park (Seoul National University Hospital, Korea)

Surgical treatment of HCM -preop evaluation and follow-up
Speaker Joonhwa Hong (Chung-Ang University Hospital, Korea)

Role of CMR for risk stratification
Speaker Seung-Pyo Lee (Seoul National University Hospital, Korea)

Differential diagnosis of HCM mimics using CMR
Speaker Chul Hwan Park (Gangnam Severance Hospital, Korea)

Panel Discussion

Panel Dong Jin Im (Severance Hospital, Korea)
In-cheol Kim (Keimyung University Dongsan Medical Center, Korea)
Ki Seok Choo (Pusan National University Yangsan Hospital, Korea),
Wook Sung Kim (Samsung Medical Center, Korea)

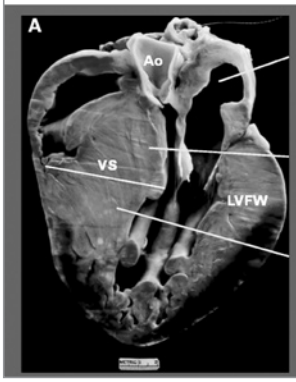
How risk stratification and prevent the SCD (overall - family hx, gene, sx, ECG, echo..)

Jun-Bean Park (Seoul National University Hospital, Korea)

Hypertrophic cardiomyopathy (HCM)

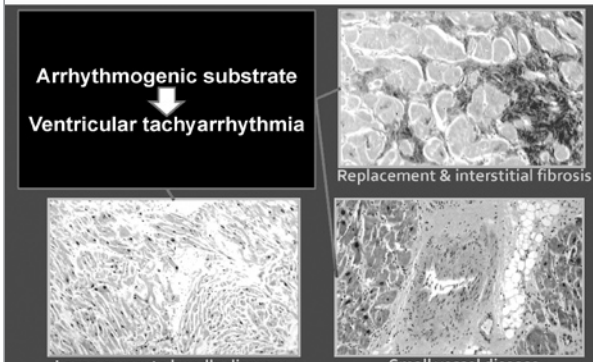
- *Morphologically*, increased LV wall thickness with/without LVOT dynamic obstruction
- *Genetically*, mutations in genes encoding components of the sarcomere

HCM pathology: gross



- LA enlargement / remodeling = atrial fibrillation ↑
- Abnormal myocardium / MV = LVOT obstruction ↑
- Supply / demand mismatch = myocardial ischemia ↑

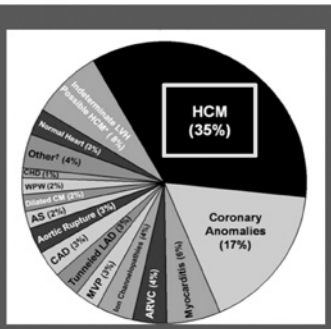
HCM pathology: microscopic



HCM-related morbidity and mortality

- Sudden cardiac death (SCD)
- Heart failure including LVOT obstrunction
- Arrhythmia, esp. Atrial fibrillation
- Embolism

HCM as single most frequent cause of sudden death in young athletes



Maron BJ et al. Circulation 2010;121:445-56

ICD indications for *secondary* prevention

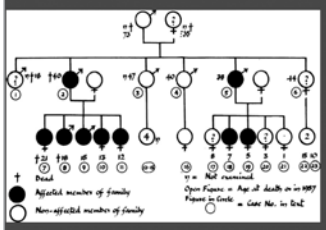
- Cardiac arrest
- Spontaneous sustained VT

Risk factors for *primary* prevention

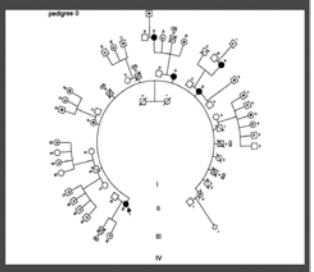
- FHx of HCM-related sudden death
- Unexplained syncope
- Abnormal exercise BP response
- Non-sustained VT
- Severe LV hypertrophy

Family history of HCM-related SCD

- History of sudden cardiac death in relatives

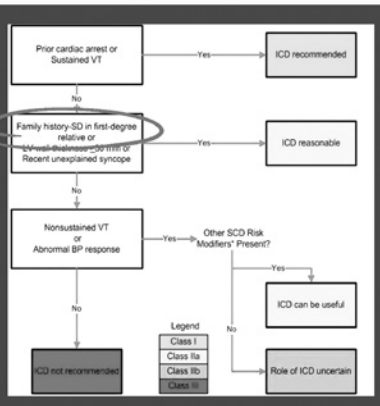


Hallman A et al. Br Heart J 1960;22:449-456



Moolman JC et al. JACC 1997;29:549-555

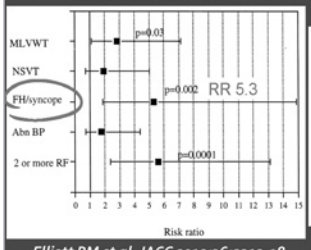
Family history of HCM-related SCD



2011 ACCF/AHA Guideline

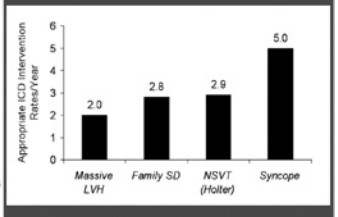
Family history of HCM-related SCD

SCD risk ratios



Elliott PM et al. JACC 2010;36:2212-18

Appropriate ICD shock rates



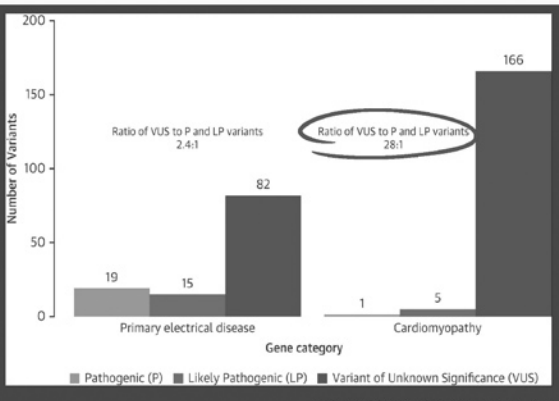
Marron BJ et al. Heart Rhythm 2016;13:1155-65

Family history of HCM-related SCD

- A family history of SCD was variously qualified to deaths in those aged >40 years or to deaths among first-degree relatives only.

Sen-Chowdhry S et al. Nat Rev Cardiol 2016;13:651-75

Gene: A long way to go……

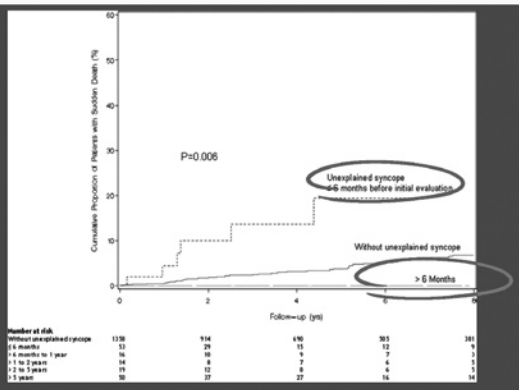


Lahrouchi N et al. JACC 2017;69:2134-2145

Unexplained syncope

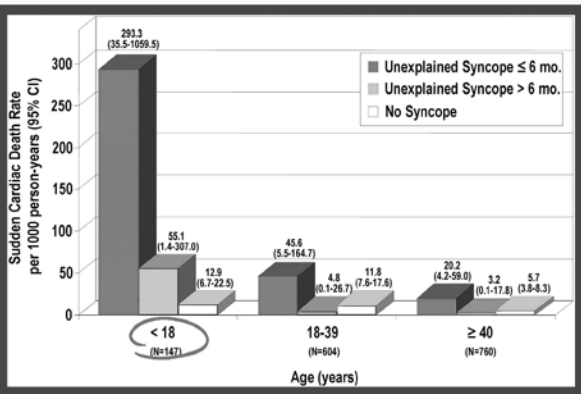
When it occurred in circumstances not clearly consistent with a neurally mediated event, i.e. without apparent explanation at rest or during ordinary daily activities, or during an intense effort

Unexplained syncope



Spirito P et al. Circulation 2009;119:1703-10

Unexplained syncope

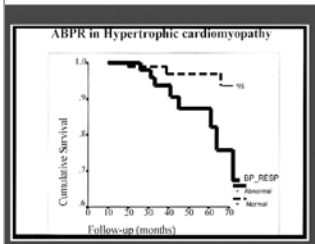


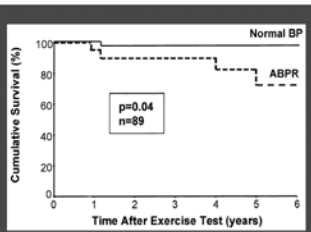
Spirito P et al. Circulation 2009;119:1703-10

Abnormal exercise BP response

A rise in SBP from baseline to peak exercise of <25 mmHg or a fall of >10 mmHg from baseline or the maximum achieved BP.

Abnormal exercise BP response





Prediction of SCD according to abnormal BP response in patients <40 YO with HCM

	Sensitivity	Specificity	PPA	NPA
Abnormal BPR	75%	66%	15%	97%

Sadoul N et al. Circulation 1997;96:2987-2991

Olivotto I et al. JACC 1999;33:2044-2051

Abnormal exercise BP response

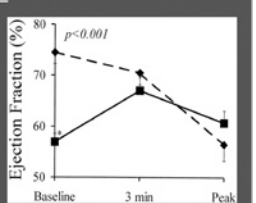
Table 2. Prevalence and Type of Perfusion Abnormalities in Patients With Normal and Abnormal BPR

	Normal BPR (n 88)	Abnormal BPR (n 17)
Abnormal perfusion imagings (%)	59 (67.1)	13 (76.5)
Fixed perfusion defects (%)	24 (27.3)	7 (41.2)
Reversible perfusion defects (%)	52 (59.1)	11 (64.7)
Left ventricular cavity dilatation (%)	9 (10.2)	8 (47.1)*
Normal perfusion imagings (%)	29 (32.9)	4 (23.5)

Abnormal exercise BP response is associated with sub-endocardial ischemia during exercise

Yoshida N et al. JACC 1998;32:1938-1042

Abnormal exercise BP response is associated with exercise-induced LV systolic dysfunction, causing hemodynamic instability associated with a high risk of SCD



Ciampi Q et al. JACC 2002;40:278-284

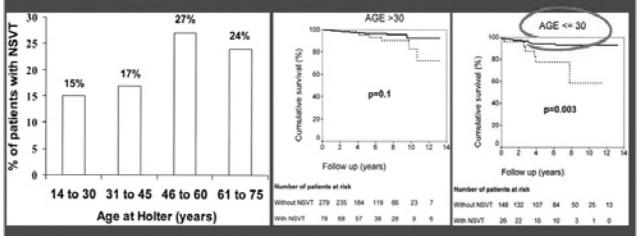
Abnormal exercise BP response

- The presence of an abnormal response was only considered as a risk factor in patients aged <40 years of age

Non-sustained VT

- Three or more consecutive ventricular extra-systoles at a rate of ≥120 bpm, lasting for <30 seconds in Holter monitoring of ECG.

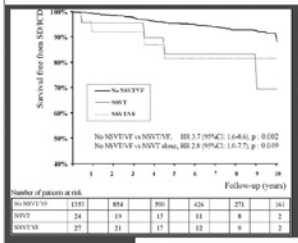
Non-sustained VT



NSVT is associated with a substantial increase in SCD risk in young patients with HCM. A relation between the frequency, duration, and rate of NSVT episodes could *not* be demonstrated.

Monserra L et al. JACC 2003;42:873-879

Non-sustained VT



NSVT during exercise is associated with an increased risk of SCD in HCM

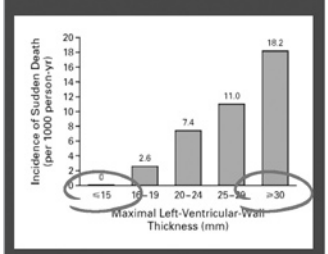
	HR	95% CI	*P*-value
Exercise NSVT/VF	3.14	1.29–7.61	0.01
Holter NSVT	2.57	1.55–4.26	0.0001
Severe LVOTO	2.41	1.08–5.53	0.03
Syncope	2.08	1.21–3.56	0.008
FHSCD	1.79	1.09–2.94	0.02
ABPR	1.43	0.86–2.36	0.2
Severe LVH	0.90	0.42–1.93	0.8

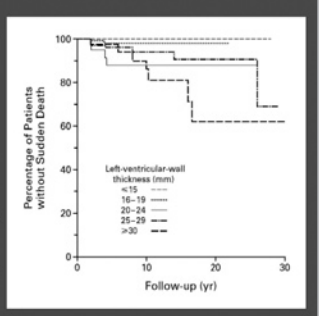
Gimeno JR et al. EHJ 2009;30:2599-2605

Severe LV hypertrophy

- The LV wall thickness in any myocardial segment of ≥30 mm in two-dimensional echocardiography

Severe LV hypertrophy





Spirito P et al. NEJM 2000;342:1778-1785

Maron BJ et al. Circulation 2010;121:445-56

Severe LV hypertrophy

TABLE 4. RESULTS OF MULTIVARIATE COX PROPORTIONAL-HAZARDS ANALYSIS OF THE RELATION BETWEEN BASE-LINE CLINICAL VARIABLES AND THE RISK OF DEATH, ADJUSTED FOR AGE.*

VARIABLE	NO. OF SUBGROUPS	SUDDEN DEATH (N=23)		DEATH DUE TO HEART FAILURE (N=15)		DEATH FROM ANY CAUSE (N=65)	
		RELATIVE RISK (95% CI)†	P VALUE	RELATIVE RISK (95% CI)	P VALUE	RELATIVE RISK (95% CI)	P VALUE
Left-ventricular-wall thickness	5	1.76 (1.19–2.60)	0.003	1.92 (1.04–3.55)	0.04	1.41 (1.09–1.81)	0.008
NYHA functional class	2	—	0.07	9.48 (2.61–34.42)	0.001	2.55 (1.26–5.18)	0.02
Left ventricular outflow obstruction	2	—	0.76	5.52 (1.55–19.65)	0.005	1.85 (1.08–3.19)	0.03
Left atrial cavity dimension	3	—	0.21	—	0.10	—	0.61
Left ventricular end-diastolic cavity dimension	3	0.48 (0.23–0.98)	0.04	—	0.22	0.70 (0.47–1.04)	0.07

*All models included age (<20, 20–39, 40–59, and ≥60 years) as a stratification factor. The subgroups for each variable are provided in Tables 2 and 3. For variables with more than two subgroups, subgroup-specific estimates of the coefficients could not be calculated, because of the small number of events, which precluded convergence of the coefficients. Relative risks were calculated from the Cox model. For variables with more than two subgroups, P values were calculated with the likelihood-ratio test, which must be interpreted as a test for linear trend of increasing (or decreasing) hazard across subgroups of the variable in question. Dashes denote variables that were removed from the final model. CI denotes confidence interval, and NYHA New York Heart Association.

Spirito P et al. NEJM 2000;342:1778-1785

Severe LV hypertrophy

	Survival estimate (95% CI)				
	No risk factors	One risk factor	Two risk factors	Three risk factors	All patients*
Wall thickness					
<15 mm	098 (096–099)	096 (093–098)	092 (087–097)	085 (073–097)	096 (093–098)
15–19 mm	097 (096–099)	095 (093–097)	090 (085–095)	081 (069–093)	094 (092–097)
20–24 mm	097 (095–099)	094 (091–096)	088 (083–092)	077 (064–090)	093 (090–095)
25–29 mm	096 (093–098)	092 (089–095)	085 (079–091)	072 (057–087)	091 (087–094)
≥30mm	095 (091–099)	090 (085–096)	081 (071–091)	066 (046–086)	088 (082–094)
All patients †	097 (095–099)	093 (091–096)	087 (082–092)	075 (062–090)	..

*For patients with different wall thicknesses modelled without risk factors.
†For patients with zero to three risk factors modelled without wall thickness.
Table 2: **5-year survival estimates in relation to wall thickness and number of risk factors**

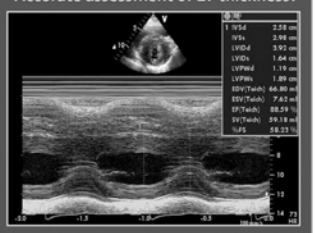
The risk of SCD associated with a wall thickness of ≥30 mm in patients without other risk factors is insufficient to justify aggressive prophylactic therapy. Most SCD occurred in patients with wall thickness <30 mm, so the presence of mild hypertrophy cannot be used to reassure patients that they are at low risk.

Elliot PM et al. Lancet 2001;357:420-424

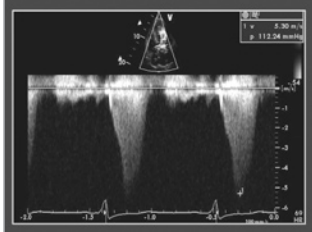
Severe LV hypertrophy

The LV wall thickness in any myocardial segment of ≥30 mm in two-dimensional echocardiography

Accurate assessment of LV thickness?



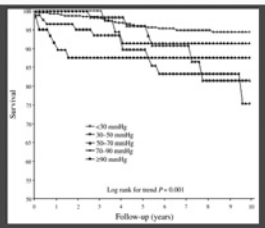
LVOT obstruction (LVOTO)

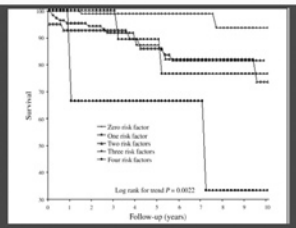


Abnormal exercise BP response

Unexplained syncope

LVOT obstruction (LVOTO)

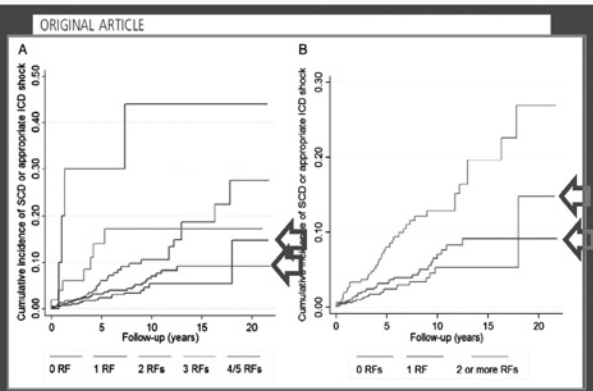




LVOTO is associated with an increased risk of SCD/ICD that is related to the severity of obstruction and the presence of other recognized risk factors for SCD. The low SCD in asymptomatic patients with LVOTO and no other SD risk markers suggests that aggressive interventions to reduce LVOTO are unwarranted in this group.

Elliot PM et al. EHJ 2006;27:1933-1941

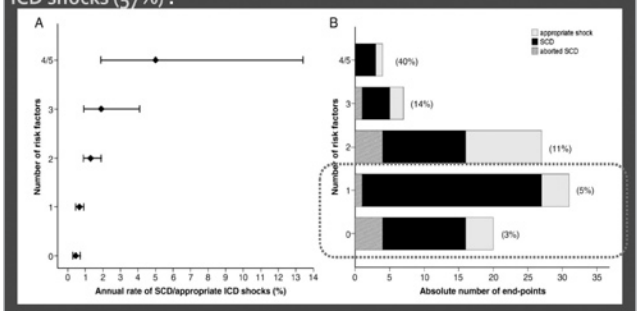
SCD prediction with risk factors... It's good?



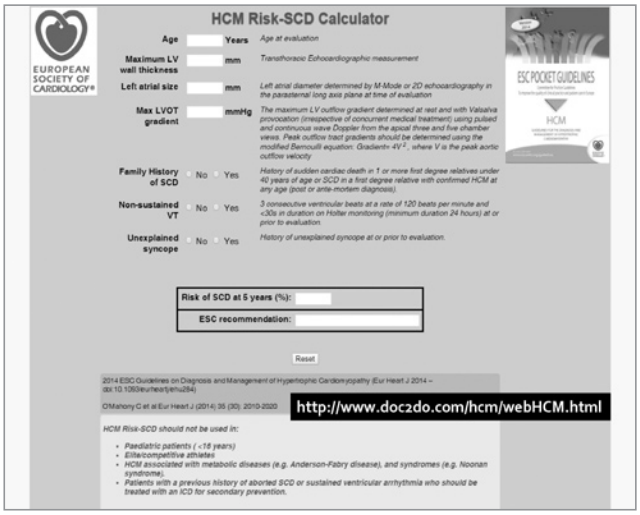
O'Mahony C et al. Heart 2013;99:534-541

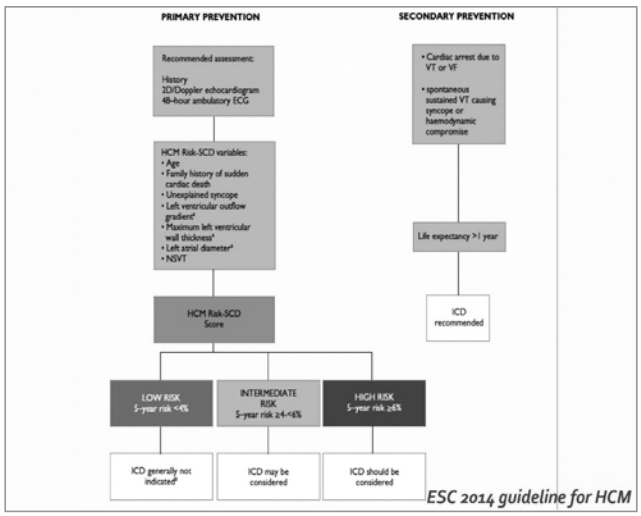
The rate vs. absolute number problem

Despite low incidence of SCD in patients with 0 or 1 risk factors, these two subgroups contributed the majority of SCD/appropriate ICD shocks (57%) !



O'Mahony C et al. Heart 2013;99:534-541



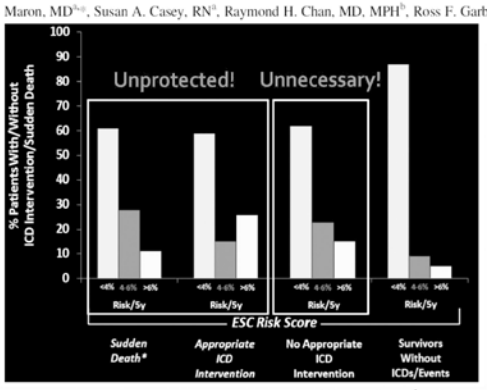


ESC 2014 guideline for HCM

Independent Assessment of the European Society of Cardiology Sudden Death Risk Model for Hypertrophic Cardiomyopathy

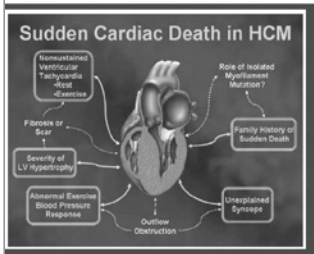
1629 HCM patients

Barry J. Maron, MD[b,*], Susan A. Casey, RN[a], Raymond H. Chan, MD, MPH[b], Ross F. Garberich, MS[a],



Maron BJ et al. AJC 2015;116:757-764

Risk stratification of SCD in HCM



Family history (+ gene)

Symptom: unexplained syncope

TMT: Abnormal BP response

Holter: Non-sustained VT

Echo: severe LV hypertrophy, LVOT obstruction

Surgical treatment of HCM - preop evaluation and follow - up

Joonhwa Hong (Chung-Ang University Hospital, Korea)

- Nothing to disclose

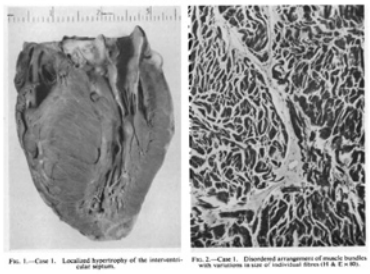
ASYMMETRICAL HYPERTROPHY OF THE HEART IN YOUNG ADULTS

BY

DONALD TEARE

From the Department of Pathology, St. George's Hospital

Received January 7, 1957

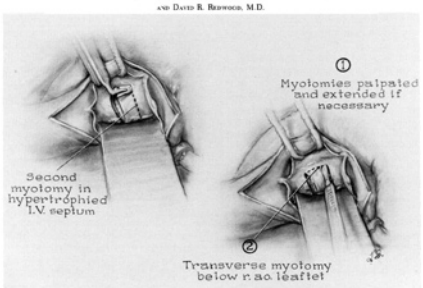


1958, British Heart Journal

Operative Treatment in Hypertrophic Subaortic Stenosis

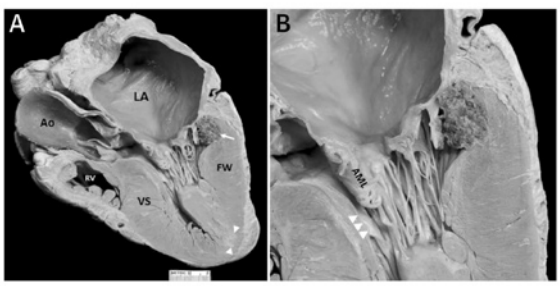
Techniques, and the Results of Pre and Postoperative Assessments in 83 Patients

By Andrew G. Morrow, M.D., Bruce A. Reitz, M.D., Stephen E. Epstein, M.D., Walter L. Henry, M.D., David M. Gunnar, M.D., Samuel B. Ironitz, M.D., and David B. Redwood, M.D.



Circulation, Volume 52, July 1975

The Heart of Dr. Morrow



JACC VOL. 67, NO. 24, 2016
JUNE 21, 2016:2900–3

Preoperative Image Studies

- Echocardiogram
- MRI
- CT

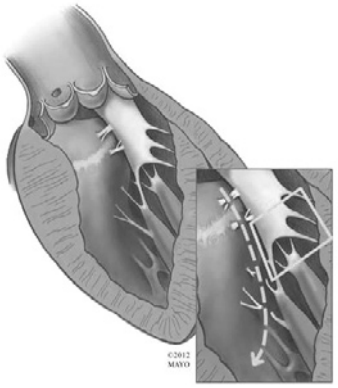
- And others

As a HCMP surgeon, what I want to know about the heart before surgery

- Is the patient indicated for myectomy?
  - Symptom
  - LVOT pressure gradient
  - Setal thickness and location
  - SAM and MR
- Does the patient have combined cardiac disease?
  - Coronary disease
  - Valvular disease
- Does the patient need ICD?
  - Family Hx of SCD
  - Septal thickness
  - Delayed enhancement or scar
  - Hx of syncope

As a HCMP surgeon, what I want to know about the heart before surgery

- Is the patient indicated for myectomy?
  - Symptom
  - LVOT pressure gradient - E
  - Setal thickness and location – C, E, M
  - SAM and MR – E, M
- Does the patient have combined cardiac disease?
  - Coronary disease - C
  - Valvular disease – E, C, M
- Does the patient need ICD?
  - Family Hx of SCD
  - Septal thickness – C, E, M
  - Delayed enhancement or scar - M
  - Hx of syncope



Most patients are referred after

- Echo
- CT
- MRI

- Holter
- Treadmil

- Coronary angio

cMR (AHA 2011)

5.3.3. Cardiac Magnetic Resonance—Recommendations

CLASS I

1. CMR imaging is indicated in patients with suspected HCM when echocardiography is inconclusive for diagnosis (180,181). *(Level of Evidence: B)*
2. CMR imaging is indicated in patients with known HCM when additional information that may have an impact on management or decision making regarding invasive management, such as magnitude and distribution of hypertrophy or anatomy of the mitral valve apparatus or papillary muscles, is not adequately defined with echocardiography (15,180–183). *(Level of Evidence: B)*

cMR (ESC 2014)

Recommendations for cardiovascular magnetic resonance evaluation in hypertrophic cardiomyopathy

Recommendations	Class[a]	Level[b]	Ref.[c]
It is recommended that CMR studies be performed and interpreted by teams experienced in cardiac imaging and in the evaluation of heart muscle disease.	I	C	148,149
In the absence of contraindications, CMR with LGE is recommended in patients with suspected HCM who have inadequate echocardiographic windows, in order to confirm the diagnosis.	I	B	126,127

cMR for Risk Stratification

On balance, the extent of LGE on CMR has some utility in predicting cardiovascular mortality, but current data do not support the use of LGE in prediction of SCD risk.

ESC 2014

CLASS IIb

1. In selected patients with known HCM, when SCD risk stratification is inconclusive after documentation of the conventional risk factors (Section 6.3.1), CMR imaging with assessment of late gadolinium enhancement (LGE) may be considered in resolving clinical decision making (184–188). *(Level of Evidence: C)*

AHA 2011

CT (ESC 2014)

- The high contrast resolution of CT provides clear delineation of the myocardium and accurate measurement of wall thickness, ventricular volumes, ejection fraction and LV mass
- Cardiovascular CT permits the simultaneous imaging of the coronary arteries and valves

Cardiac CT should be considered in patients who have inadequate echocardiographic imaging and contraindications for CMR.	IIa	C

CT (AHA 2011)

- For patients with HCM with chest discomfort, CTA would be a reasonable strategy to assess for possible concomitant CAD

Class IIa

1. **Assessment of coronary anatomy with computed tomographic angiography (CTA) is reasonable for patients with HCM with chest discomfort and a low likelihood of CAD to assess for possible concomitant CAD.** ***(Level of Evidence: C)***

Myocardial Bridge in HCMP

- Systolic compression of the muscular investment of a portion of an epicardial coronary artery
- Little information exists about its clinical significance
- Most often over the left anterior descending artery
- No symptoms to angina to myocardial infarction to sudden death
- As many as 15% of HCMP patients
- There are no recommendations or guidelines in patients with HCMP

Summary – Surgeons view

- Echocardiogram is the most important initial image study tool, and enough most of the time.
- cMR and CT can be used as supplementary image study when echocardiogram is not adequate.
- Personally, CT is preferred over MRI.

MEMO

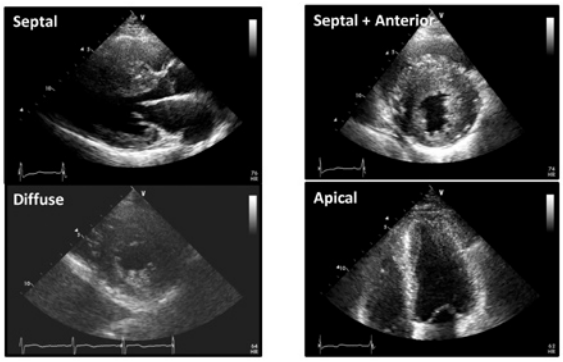
Role of CMR for risk stratification

Seung-Pyo Lee (Seoul National University Hospital, Korea)

Key Features of Hypertrophic Cardiomyopathy

- LV hypertrophy
- In the absence of 2˚ cause of hypertrophy
- Generally a genetic defect in the sarcomeric proteins
- In any segment of the LV or even the RV

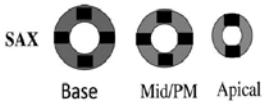
Diagnosis of HCM with 2D-echoCG



Contents of the Talk Relevant to CMR

- Cine-CMR, why they are the 'bread-and-butter' of CMR in HCM
- LGE-CMR, the part of CMR that has gained evidence in HCM
- New techniques of CMR for HCM
  - T1 mapping, extracellular volume (ECV)
  - Diffusion tensor imaging

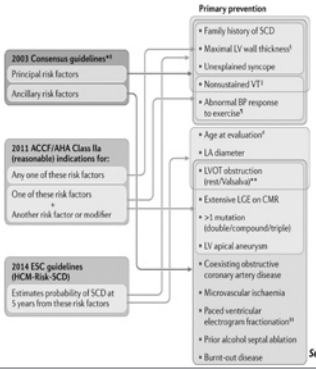
Measurement of LV Thickness in HCM



- Localization of hypertrophy
- Severity of hypertrophy

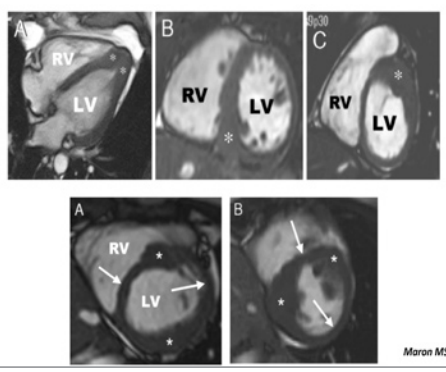
- Must include the measurement of maximal wall thickness
- In multiple segments
- At multiple levels

Degree of Hypertrophy, Essential for Predicting SCD



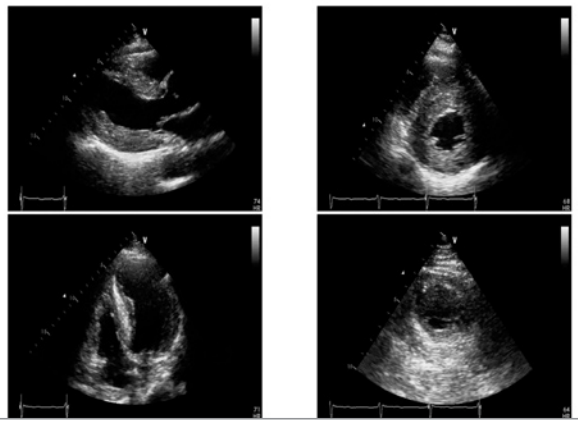
Sen-Chowdhry S et al., Nat Rev Cardiol 2016

CMR Enables Fine Phenotyping of Morphology

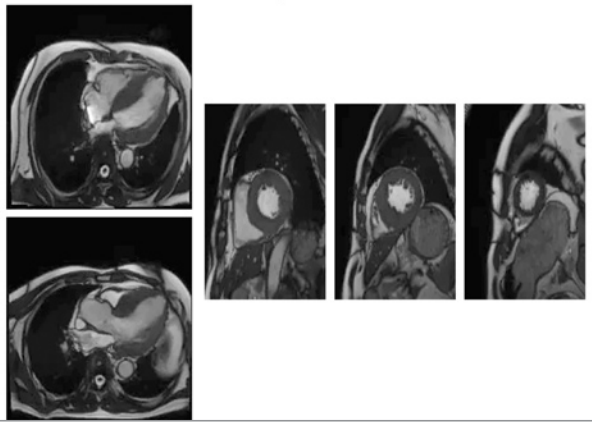


Maron MS et al., J Am Coll Cardiol 2009

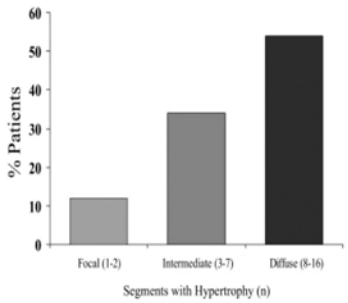
Accurate Assessment of LV Thickness?



Accurate Assessment of LV Thickness!

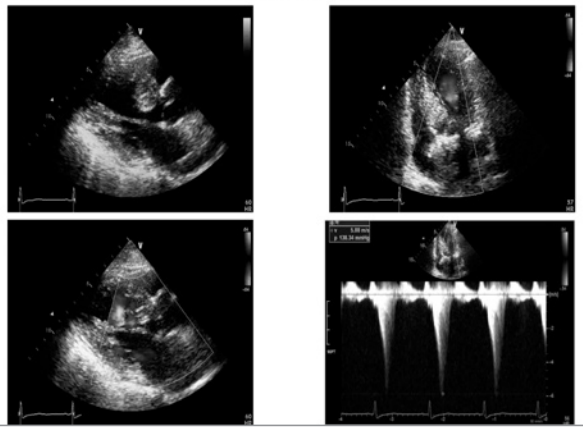


Hypertrophy can Sometimes be Very Focal!

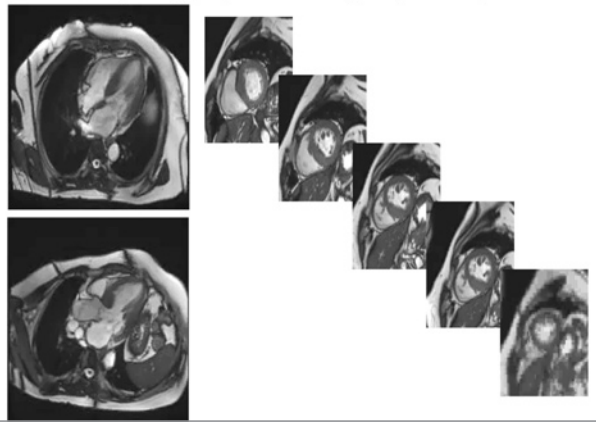


Maron MS et al., J Am Coll Cardiol 2009

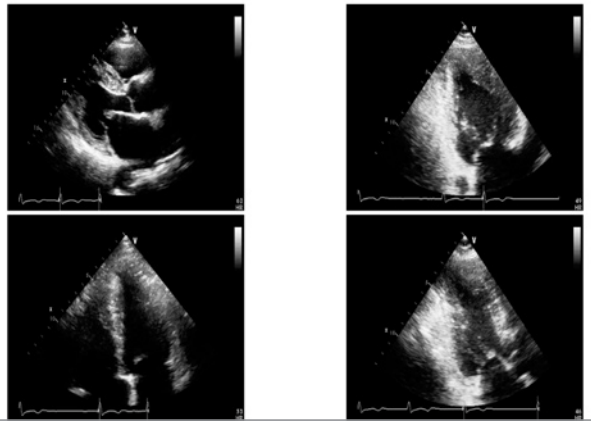
Basal Septal Hypertrophy only on EchoCG?



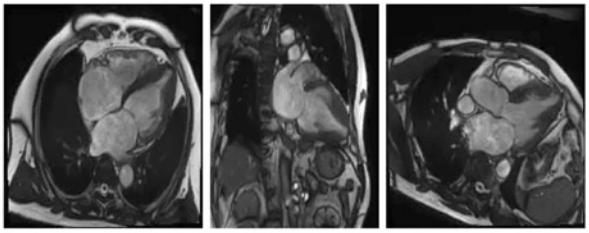
Cine-CMR, Helpful for Planning Myectomy



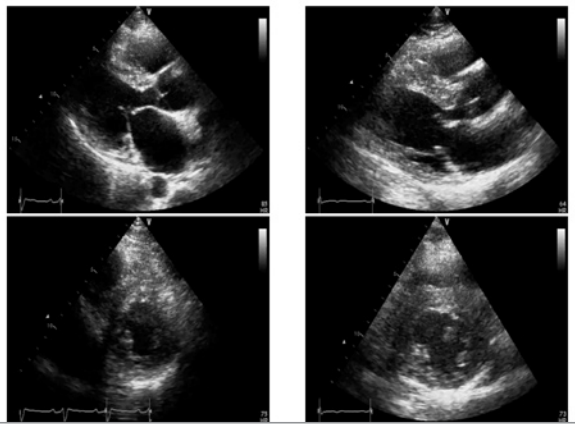
Apical Segments not Reliably Seen on EchoCG



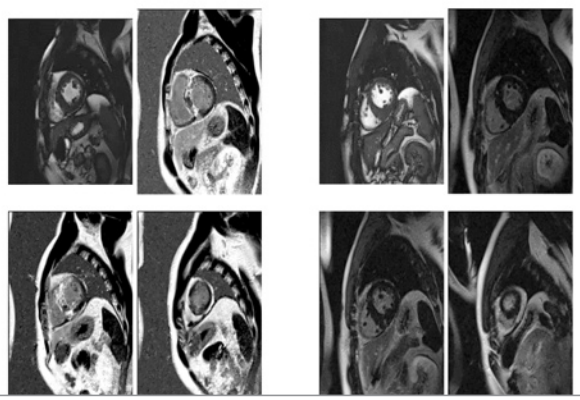
Credible Visualization of Apex with CMR



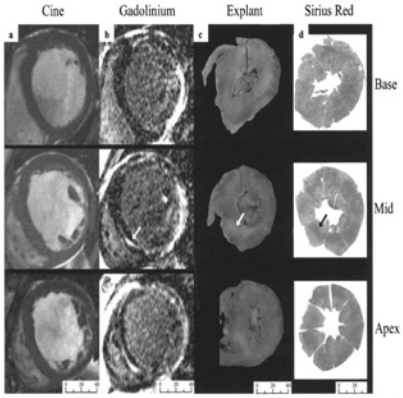
Similar EchoCG features, similar HCM?



No Way! It's Totally Different in Terms of Scar!

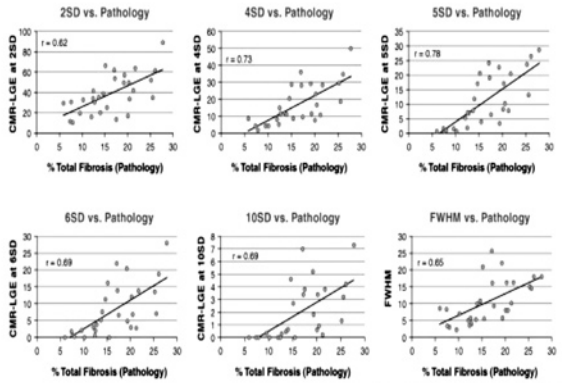


LGE, Regions of Increased Myocardial Collagen



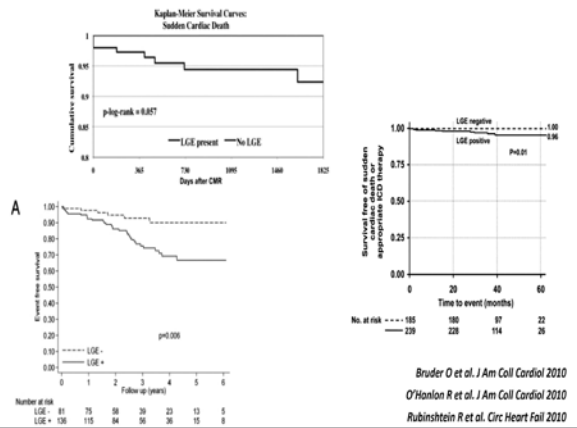
Moon JC et al. J Am Coll Cardiol 2004

LGE Reflects the Degree of Myocardial Fibrosis



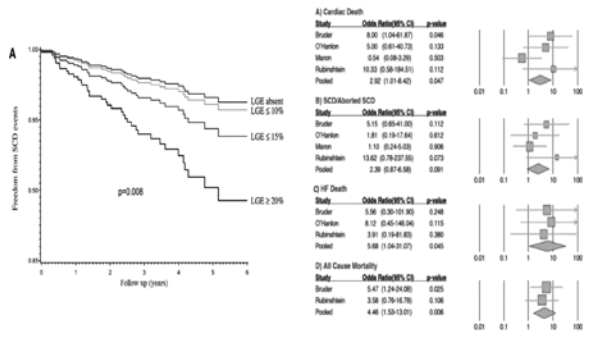
Moravsky G et al. JACC Cardiovasc Imaging 2013

LGE, a New Prognosticator in HCM?



Bruder O et al. J Am Coll Cardiol 2010
O'Hanlon R et al. J Am Coll Cardiol 2010
Rubinshtein R et al. Circ Heart Fail 2010

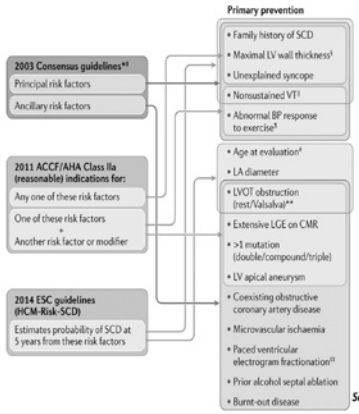
LGE, a New Prognosticator in HCM!



Chan RH & Maron MS et al. Circulation 2014

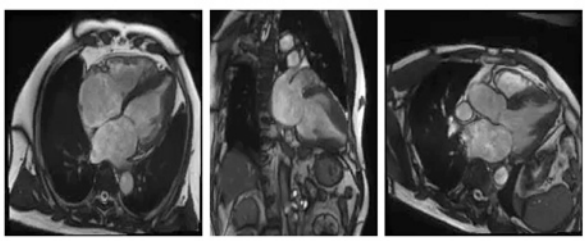
Green JJ & Salerno M et al. JACC Cardiovasc Imaging 2012

LGE, Gathering Evidence for Prediction of SCD

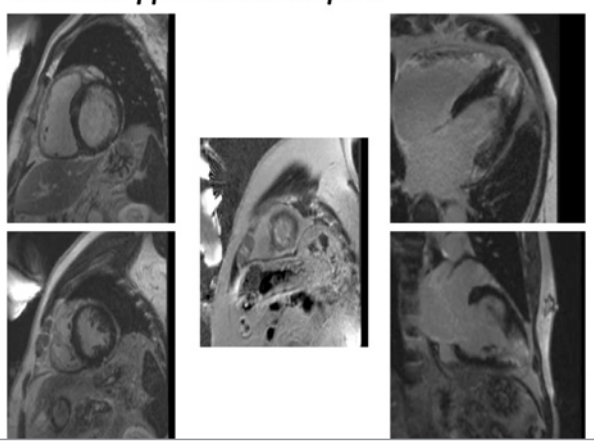


Sen-Chowdhry S et al., Nat Rev Cardiol 2016

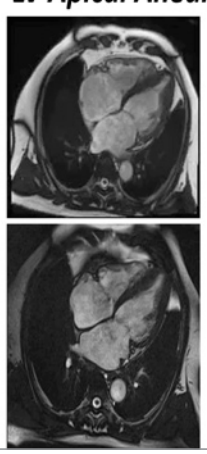
Apical HCM with Apical Aneurysm on Cine-CMR

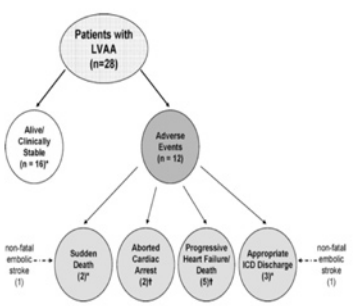


What's Happened to the Apex?



LV Apical Aneurysm, it's not Benign!



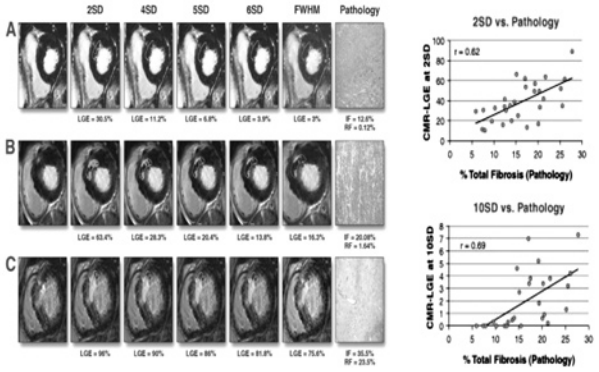


Maron MS et al., Circulation 2008

Challenges Remaining for LGE

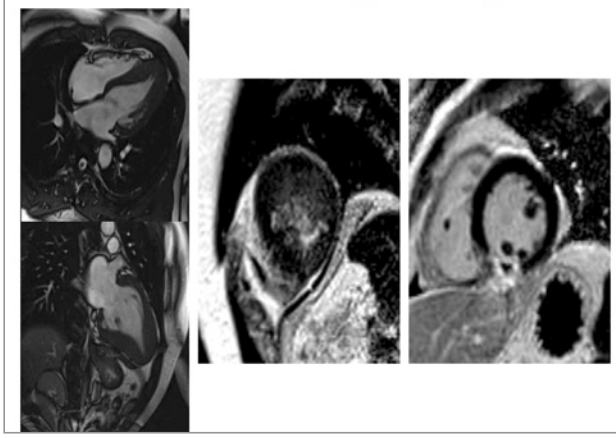
- Dichotomizes the myocardium into normal vs. abnormal
  - Less cohesive fibrosis in HCM
- Method of quantification not established
  - 2SD ~ 6SD or even full-width half-maximum method
  - Reproducibility issues
- Black, 'normal' myocardium really 'normal'?

LGE Quantification, what's the Gold Standard?

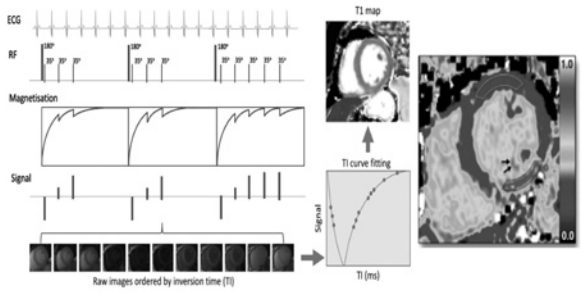


Moravsky G et al. JACC Cardiovasc Imaging 2013

How are we going to Quantify the 'Fuzzy' LGE?



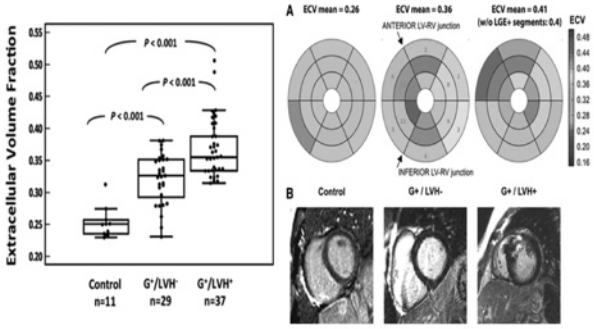
ECV Calculation using T1 Mapping



White SK et al. JACC Cardiovasc Imaging 2013

Everett RJ et al. Clin Radiol 2016

ECV Expansion in HCM-Variation Carriers

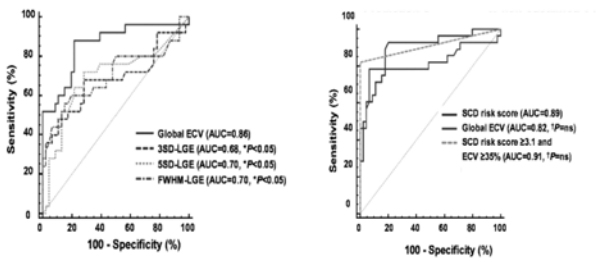


Ho CY et al. Circ Cardiovasc Imaging 2013

ECV, Superior to Conventional Parameters?

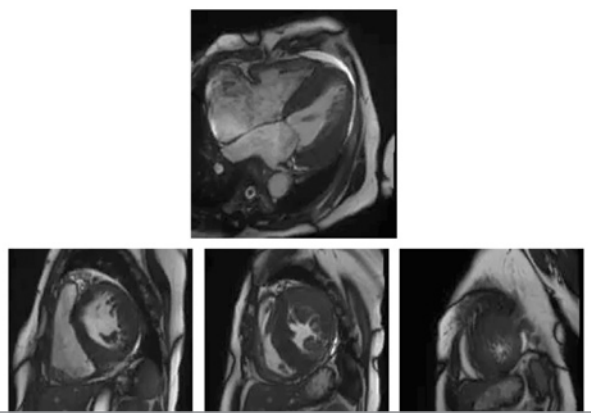
Sudden Cardiac Death

Syncope or Nonsustained VT

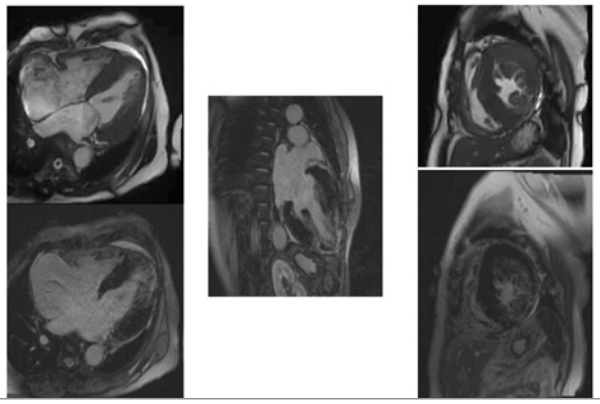


Avanesov M et al. Eur Radiol 2017

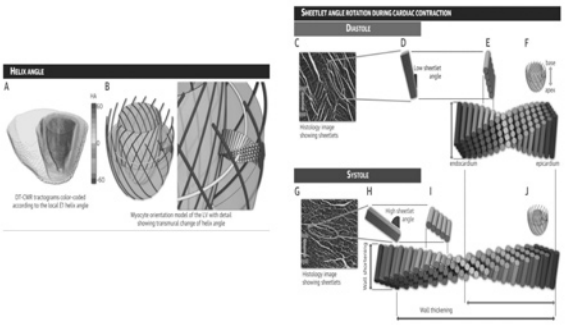
No Doubt of the HCM Dx. on cine-CMR?



No Doubt of the HCM Dx. on LGE-CMR?

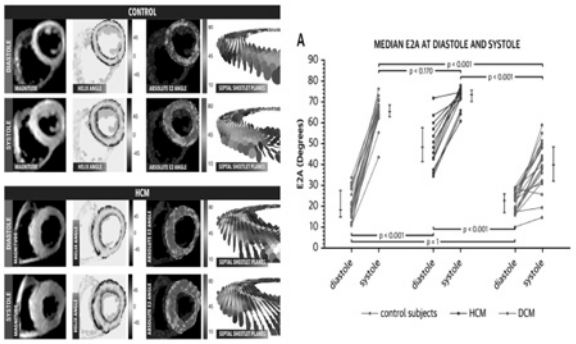


Cardiomyocyte Fiber & Sarcomere Orientation



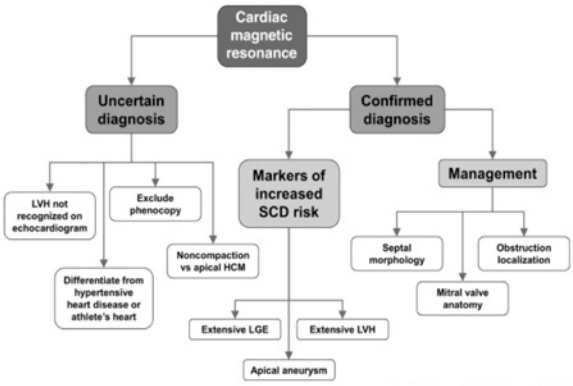
Nielles-Vallespin S et al. J Am Coll Cardiol 2017

Fiber Disorientation & Decreased Rotation in HCM



Nielles-Vallespin S et al. J Am Coll Cardiol 2017

Clinical Utility of CMR in HCM



Geske JB et al. JACC Heart Fail 2018

Clinical Utility of Various CMR Techniques in HCM

Cine imaging

Late gadolinium enhancement

ECV & Native T1

Diffusion tensor imaging

Differential diagnosis of HCM mimics using CMR

Chul Hwan Park (Gangnam Severance Hospital, Korea)

Hypertrophic cardiomyopathy (HCM), the most common genetic cardiomyopathy, is characterized by left ventricular hypertrophy (LVH) in the absence of an obvious cause.

However, various conditions including athlete's heart, hypertensive heart disease, glycogen and lysosomal storage disorders, cardiac amyloidosis, and mitochondrial cardiomyopathy mimic HCM. These HCM mimics present with LVH, which is a characteristic they share with HCM, and therefore, these conditions should be excluded before diagnosing HCM.

The differential diagnosis of HCM mimics is occasionally difficult to establish in daily routine practice. Cardiac magnetic resonance (CMR) imaging, which provides significant information about the myocardial condition, could serve as a useful tool to determine the differential diagnosis. However, conventional CMR uses a signal intensity-based qualitative technique including T1- and T2-weighted magnetic resonance images, as well as late gadolinium enhancement. The primary drawback of these techniques is a lack of quantitative assessment in that these methods only allow a comparison between the signal intensity of the remote myocardium and normal-appearing tissue or skeletal muscle. However, rapid technical innovations have offered newer cardiac MR techniques such as T1 and T2 mapping. These mapping sequences could provide quantitative values of the myocardium including the native T1 value, post T1 value, T2 value, and the extracellular volume fraction, which allows multiparametric myocardial analysis.

In this session, I will briefly review the usefulness and limitations of CMR for the differential diagnosis of HCM mimics, focusing on quantitative analysis of the myocardium.

MEMO

Day 2
May 13 (Sun.)

Luncheon Symposium II

Central Medical Service

CT motion - Introduction

GE Healthcare

GECT information introduction
- focus on the development and features of CCTA -

CT motion - Introduction

Contents

- about "ulrich medical"
- Sales and Issues
- Hardware
- Disposables
- Software & Functions
- Strong benefits

CT motion™

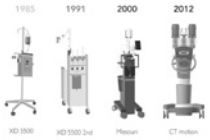
ulrich medical

100 Years ulrich medical

3대째 가업을 승계해온 회사

- 1912년 수술용 도구 제조를 시작으로 창업
- 1978년 임플란트 제품 출시
- 1985년 CT 인젝터 출시
- 1991년 전 세계 첫 MRI 인젝터 출시
- 2006년 ulrich medical USA 설립
- 2012년 창립 100주년
- 2014년 한국시장 진출 (센트럴메디컬서비스 독점 계약)

The world's first MRI injector



CT motion™

Sales and Issues

제4조(의료인과 의료기관의 장의 의무) - ⑧항

- 의료인은 일회용 주사 의료용품(**한 번 사용할 목적으로 제작되**거나 **한 번의 의료행위에서 한 환자에게 사용**하여야 하는 의료용품으로서 사람의 신체에 의약품, 혈액, 지혈 등을 투여·채취하기 위하여 사용하는 주사침, 주사기, 수액용기와 연결줄 등을 포함하는 수액세트 및 그 밖에 이에 준하는 의료용품을 말한다. 이하 같다)을 한 번 사용한 후 다시 사용하여서는 아니 된다. <신설 2016.5.29.>

개정사유 및 처벌

- 의료기관 개설자의 준수사항에 1회용 주사기 등의 사용에 관한 사항 등을 신설하여 이를 위반하여 사람의 중대한 위해를 미친 경우에는 해당 의료기관에 대하여 업인정지, 개설허가 취소, 또는 의료기관 폐쇄명령을 할 수 있도록 하여 제재의 실효성을 강화하고자 함.

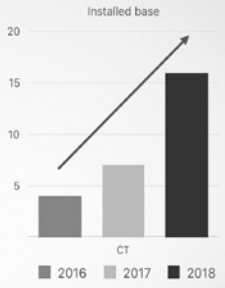
사용 현황

(2018년 4월 기준)

판매 현황

(년도별)

	4th 2016	2017	1st 2018
판매 대수	4	8	16
		합계 :	28



CT motion™

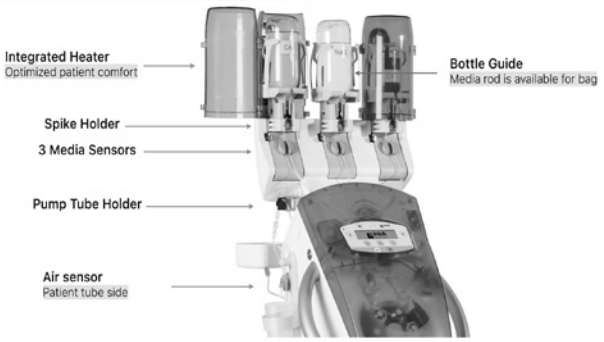
Hardware

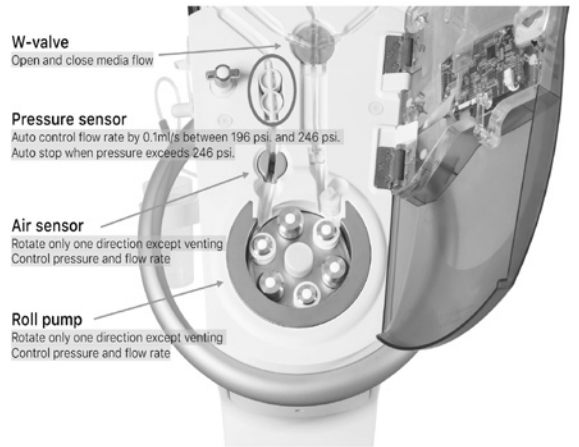
CT motion™

Ceiling version

Pedestal version

INJECTOR COMPONENTS

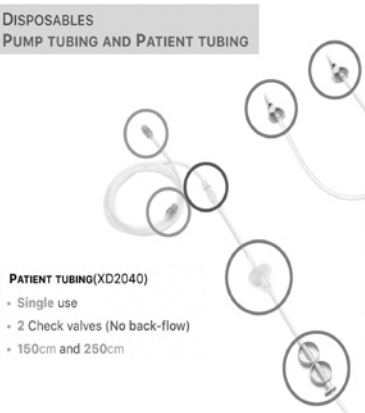




CT motion™

Disposables

Disposables
Pump tubing and Patient tubing



Pump tubing(XD8003)
- 24 Hour use for multiple patients
- 3 Spikes with bacteria filters
- 1 Particle filter
- 1 Check valve (No back-flow)

수인 제15-4125호(사용방법)
24 시간동안 사용가능하며, 다수의 환자에게 사용할 수 있습니다.

Patient tubing(XD2040)
- Single use
- 2 Check valves (No back-flow)
- 150cm and 250cm

CT motion™ Software

Manual Venting
Manual Switch
Pressure Sensor
Air Detector
Automatic Switch
Vein Check
Temporary Pressure Limit
Pause
Elapsed Time
Manual Injection
Stop Watch
SYNCOpen
CA Substitution
Tandem
Bluetooth
CT motion
Drain Down
Sleep Mode
Same Patient
KVO(Keep the Vain Open)
Start Delay
Media Detector
Remaining
Pre-filling
Auto Pressure Control
Mixing
Charging Battery
Auto Air Venting
100 Saved Programs

Features - Tandem

Tandem ON

CA1 | NaCl | CA2

Independent Injection

up to 1,000ml each

Tandem OFF

CA1 | NaCl | CA2

Auto Switching

up to 2,000ml total

Approved combinations of contrast medias

	Omnipaque 70/140/180/ 240/300/350	Visipaque 150/270/320	Isovue 150/250/300/ 350/400	Solutrast 200/250/300/ 370	Ultravist 150/240/300/ 370	Xenetix 250/300/350	Optiray 240/300/320/ 350
Omnipaque 70/140/180/ 240/300/350	■	■	■	■	■	■	■
Visipaque 150/270/320	■	■	■	■	■	■	■
Isovue 150/250/300/ 350/400	■	■	■	■	■	■	■
Solutrast 200/250/300/ 370	■	■	■	■	■	■	■
Ultravist 150/240/300/ 370	■	■	■	■	■	■	■
Xenetix 250/300/350	■	■	■	■	■	■	■
Optiray 240/300/320/ 350	■	■	■	■	■	■	■

■ Combination is approved

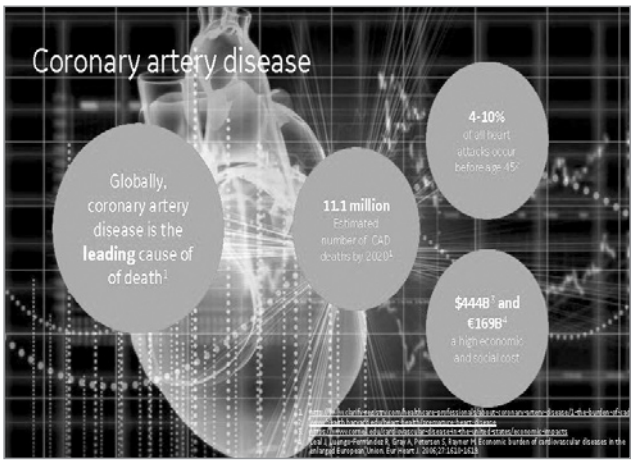
Certification
Safety with Rinsing program

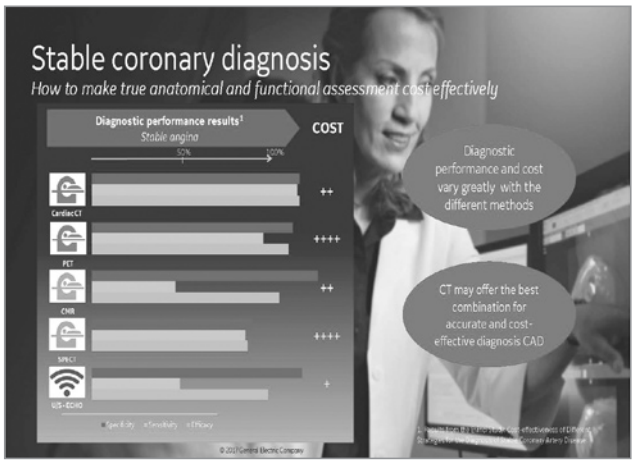
Hereby we confirm that the CT contrast agent injector XD 8000 CT motion™ is save to be used on multiple patient using several distinct contrast agents sequentially, without changing the XD 8003 pump tubing.

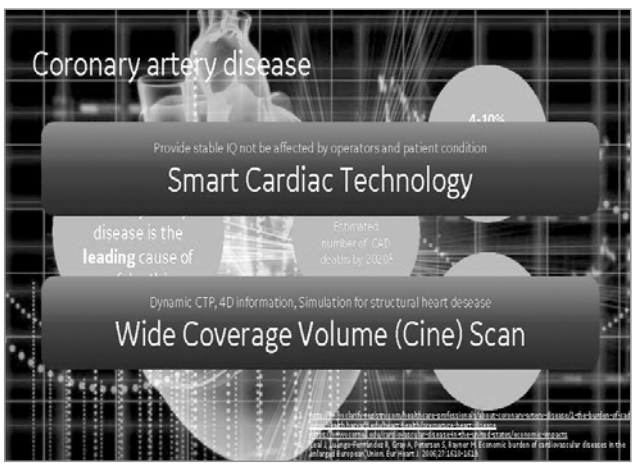
To approach this question ulrich medical authorized the GLP laboratory UL MDT GmbH to make an investigation of seven iodinated contrast media commonly used in clinical practice.

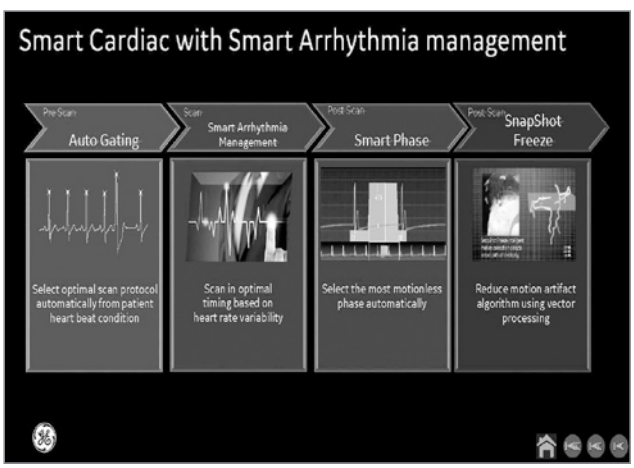
This pharmacological investigation leads to the conclusion that, when using the special rinsing program as described in the user manual to wash the pump tube system, the ulrich INJECT CT motion contrast injector is save to be used on multiple patients when using several contrast agents sequentially. There is in this case no need to place a new XD 8003 Pump Tubing. This is valid for the seven investigated contrast agents as well as for the use of local available generic contrast agents.

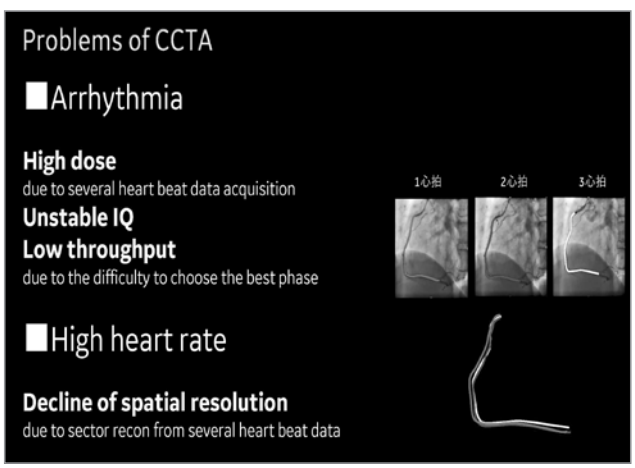
GECT information introduction
- focus on the development and features of CCTA -

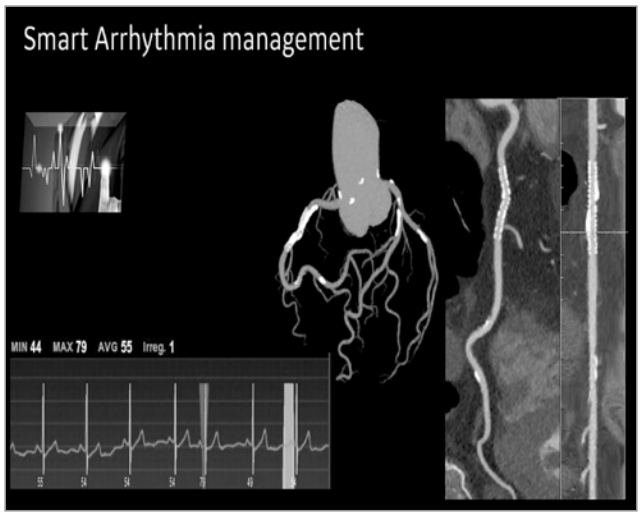


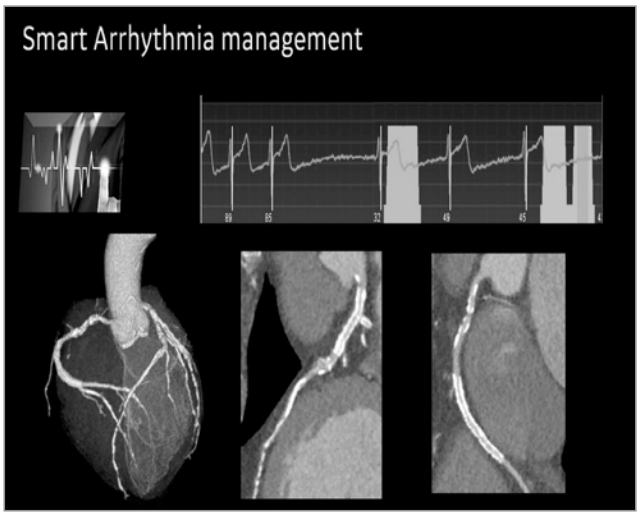


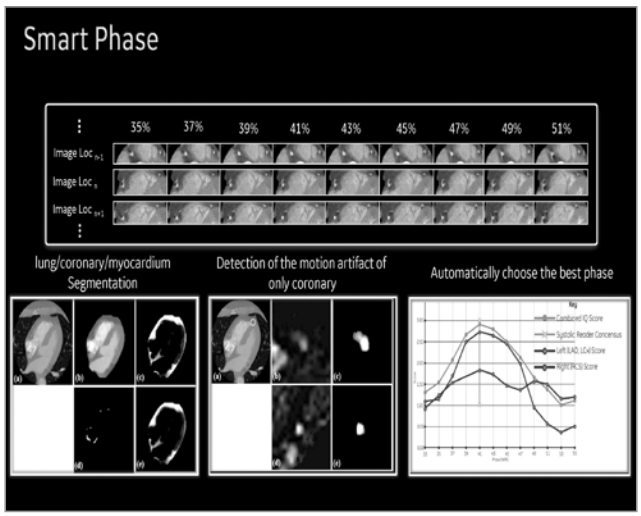


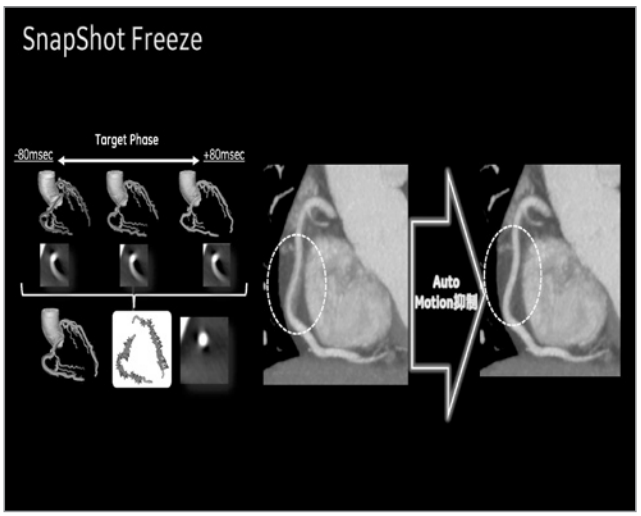


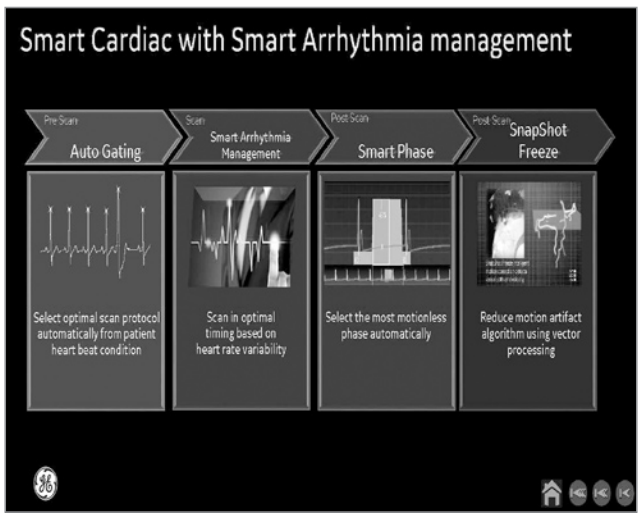


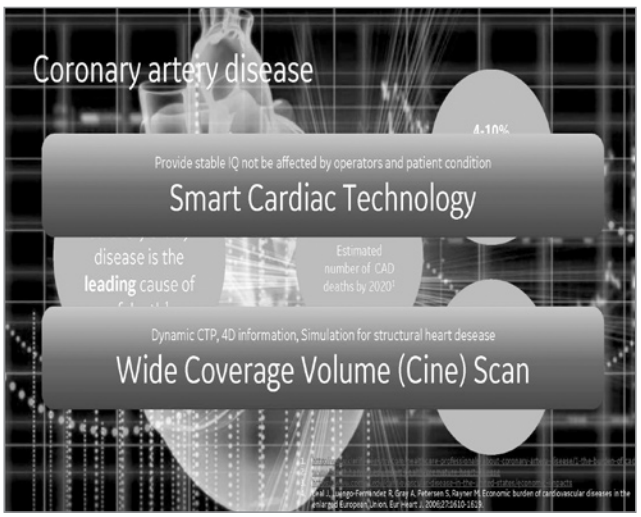

Smart Arrhythmia management
MIN 44 MAX 79 AVG 55 Irreg. 1

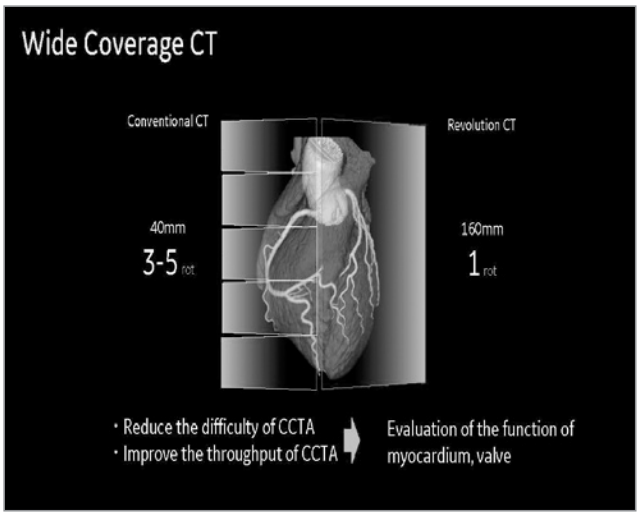

Smart Arrhythmia management

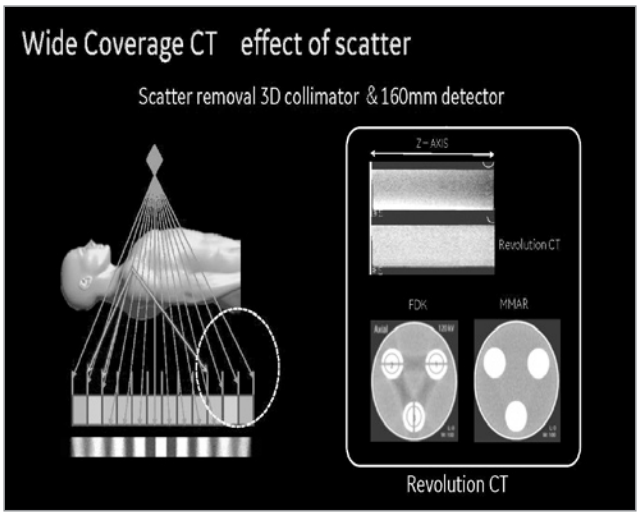

Smart Phase
35% 37% 39% 41% 43% 45% 47% 49% 51%
Image Loc n-1
Image Loc n
Image Loc n+1
lung/coronary/myocardium Segmentation
Detection of the motion artifact of only coronary
Automatically choose the best phase

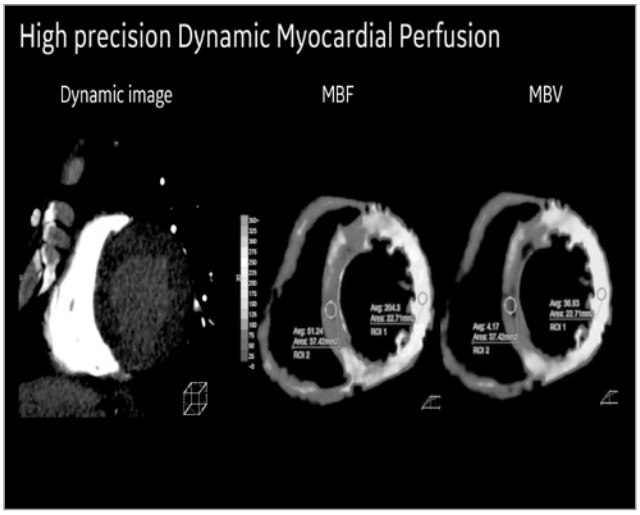

SnapShot Freeze
Target Phase
-80msec
+80msec
Auto MotionBlur

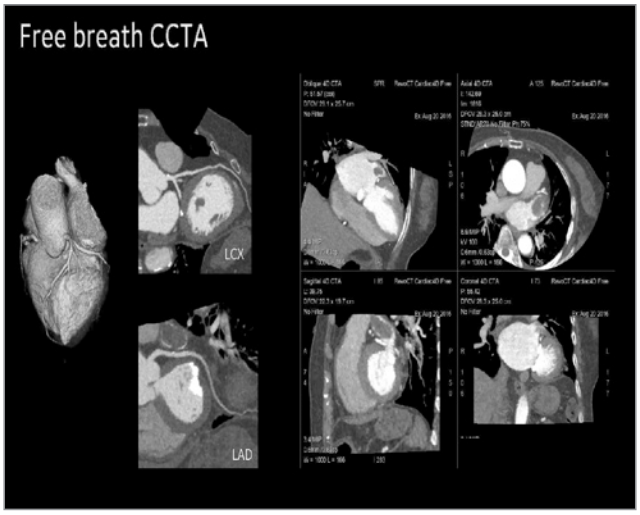

Smart Cardiac with Smart Arrhythmia management
Pre Scan
Auto Gating
Scan
Smart Arrhythmia Management
Post Scan
Smart Phase
Post Scan
SnapShot Freeze
Select optimal scan protocol automatically from patient heart beat condition
Scan in optimal timing based on heart rate variability
Select the most motionless phase automatically
Reduce motion artifact algorithm using vector processing

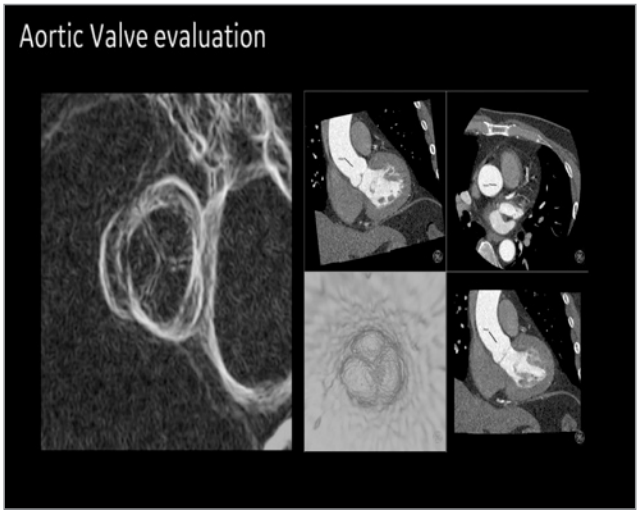

Coronary artery disease
Provide stable IQ not be affected by operators and patient condition
Smart Cardiac Technology
disease is the leading cause of
Estimated number of CAD deaths by 2020
Dynamic CTP, 4D information, Simulation for structural heart desease
Wide Coverage Volume (Cine) Scan

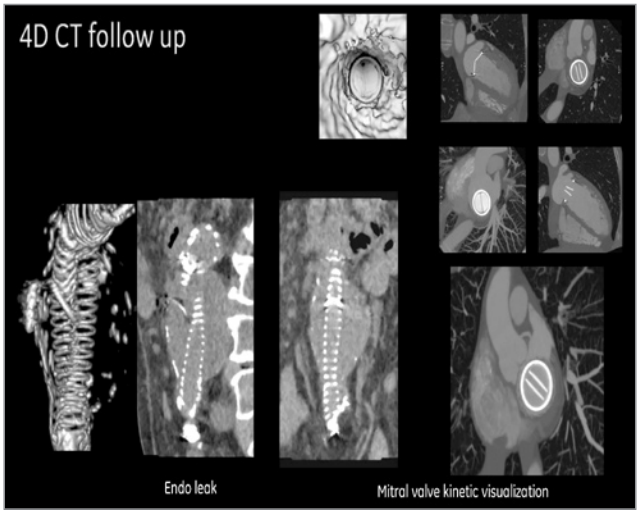

Wide Coverage CT
Conventional CT
Revolution CT
40mm
3-5 rot
160mm
1 rot
• Reduce the difficulty of CCTA
• Improve the throughput of CCTA
Evaluation of the function of myocardium, valve


Wide Coverage CT effect of scatter
Scatter removal 3D collimator &160mm detector
Z-AXIS
Revolution CT
FDK
MMAR
Revolution CT


High precision Dynamic Myocardial Perfusion
Dynamic image
MBF
MBV


Free breath CCTA
LCX
LAD


Aortic Valve evaluation


4D CT follow up
Endo leak
Mitral valve kinetic visualization


TOKYO 2020
WORLDWIDE PARTNER

SESSION 7

Cutting Edge Techniques in Cardiovascular Imaging

Chairperson **Jung Im Jung** (The Catholic University of Korea, Seoul St. Mary's Hospital, Korea)
Soon Jun Hong (Korea University Anam Hospital, Korea)

Presentation

Dual and multi-energy CT
Speaker U. Joseph Schoepf (Medical University of South Carolina, USA)

T1 mapping beyond delayed MR
Speaker Xiaohai Ma (Beijing Anzhen Hospital, China)

Viability assessment with minimal or non-contrast Imaging
Speaker Hyuk Jae Chang (Severance Hospital, Korea)

Myocardial functional assessment by CMR and echocardiography
Speaker Eui-Young Choi (Gangnam Severance Hospital, Korea)

Panel Discussion

Panel Gong Yong Jin (Chonbuk National Universtiy Hospital, Korea)
Hongseok Ko (National Medical Center, Korea)
Heesun Lee (Seoul National University Hospital Healthcare System Gangnam Center, Korea)
Hyemoon Chung (Kyung Hee University Medical Center, Korea)

Dual and multi-energy CT

U. Joseph Schoepf (Medical University of South Carolina, USA)

Disclosures

Consultant for / research support from

- Astellas
- Bayer
- GE Healthcare
- Guerbet
- HeartFlow
- Medrad
- Siemens Healthcare

Dual-Energy CT (DECT) Techniques for Cardiac Imaging

1. *Dose and Image Reconstruction*
2. *Major Applications*
   - **Perfusion Maps**
   - **Virtual Monoenergetic Images (VMI)**
3. *Minor Applications*
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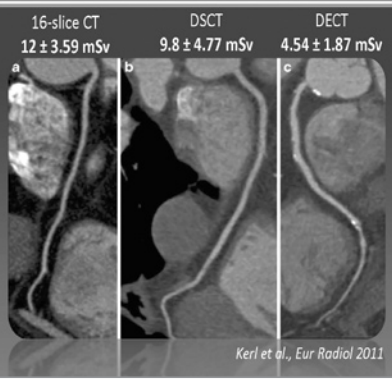
   - **Plaque Analysis**

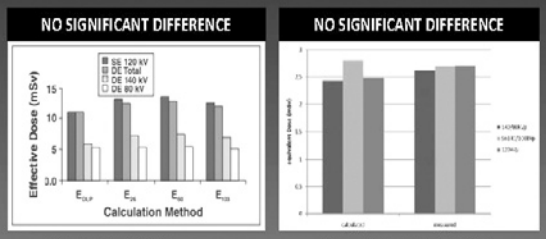
Radiation Dose



Kerl et al., Eur Radiol 2011

Radiation Dose

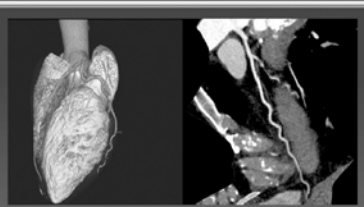
- DECT radiation doses **similar to** conventional single-energy CT



Christner JA AJR 2010

Schenzle C Invest Radiol 2010

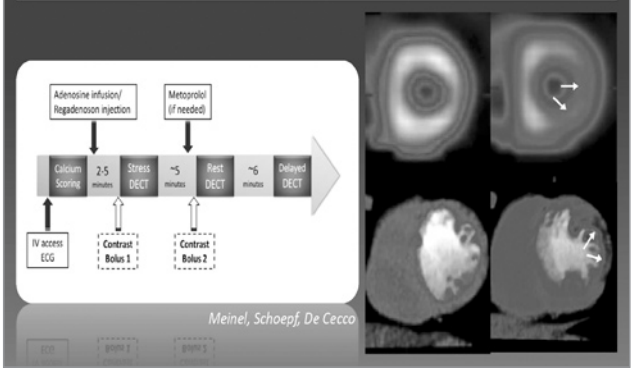
3rd dual-source DECT Generation



	Scan	kV	mAs / ref.	CTDIvol* mGy	DLP mGycm	TI s	cSL mm
FI_CaSc	4D	120	72 / 80	1.22 L	22.9	0.25	0.6
PreMonitoring	5	100	23	0.65 L	0.6	0.25	10.0
Contrast Monitoring	6	100	23	4.52 L	4.5	0.25	10.0
DE_CorAdSeq	13A	90	82 / 165				
	13B	Sn150	71 / 127	10.53 L	145.3	0.62	0.6

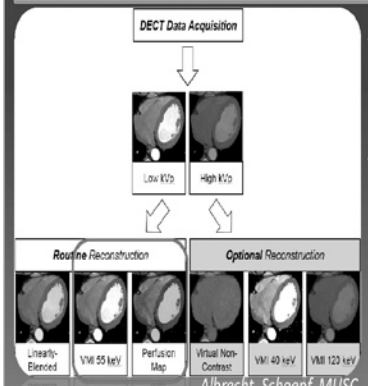
Schoepf, MUSC

Stress DECT Acquisition Protocol



Meinel, Schoepf, De Cecco

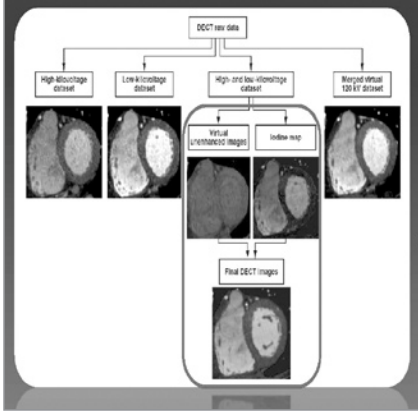
How we do it: DECT data reconstruction



- Linearly-blended images are the "standard" CCTA and are used to reconstruct curved MPRs
- In addition, we recommend routine reconstruction of
  - **VMI+ 55 keV** (*improved contrast*)
  - **Perfusion maps** (*perfusion visualization and quantification*)

Albrecht, Schoepf, MUSC

Post-Processing of Perfusion Maps



- Color-coded DECT perfusion images allow for enhanced evaluation of myocardial iodine uptake
- Iodine uptake can be quantitatively measured in mg/ml

Vliegenthart et al., AJR 2012

Dual-Energy CT (DECT) Techniques for Cardiac Imaging

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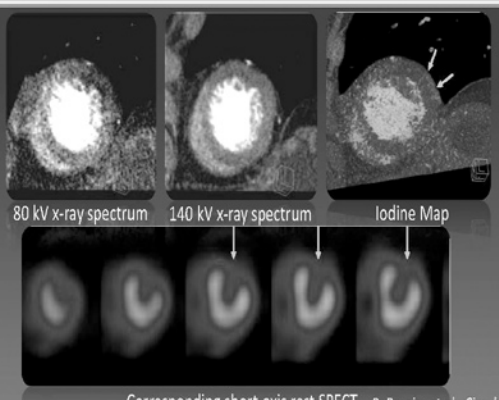
Myocardial Perfusion

- **74 yo woman**
  - Chest pain
  - Abnormal SPECT
- **DECT**
  - 2x64x0.6mm
  - 80kV/140kV
  - 0.33 s rotation time

Anatomical and Functional Assessment

B. Ruzsics et al., Circulation 2008

Anatomical and Functional Assessment



B. Ruzsics et al., Circulation 2008

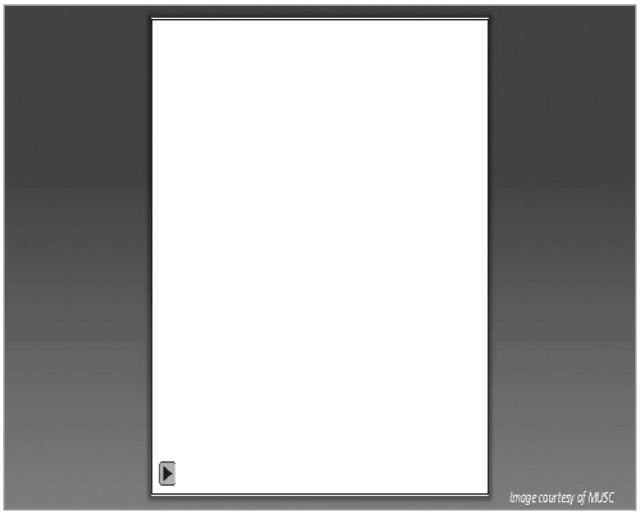
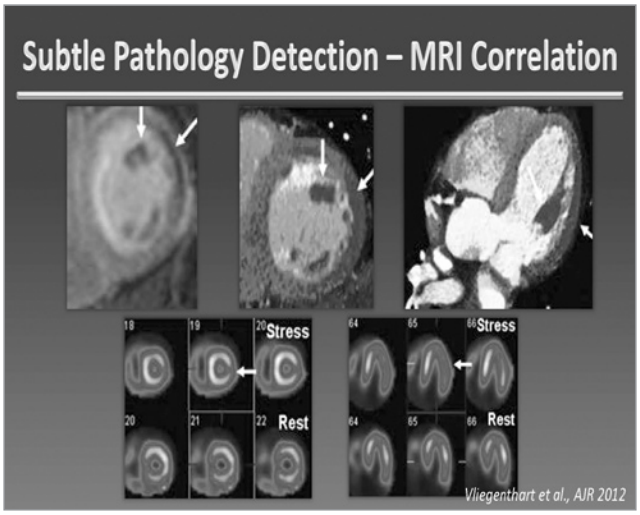
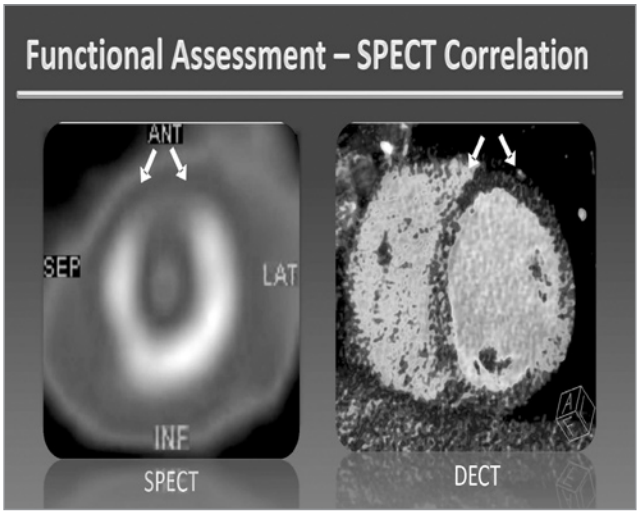
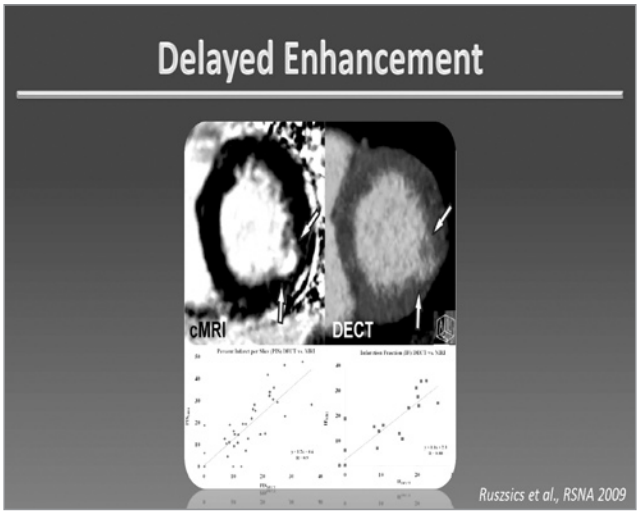
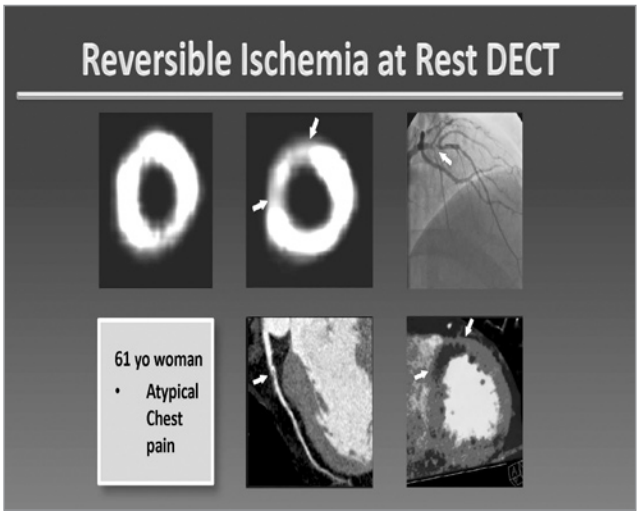


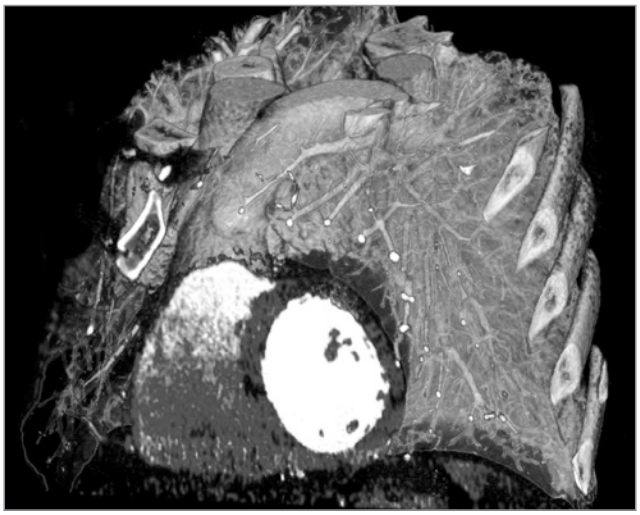
Image courtesy of MUSC


Subtle Pathology Detection – MRI Correlation
Stress
Rest
Vliegenthart et al., AJR 2012

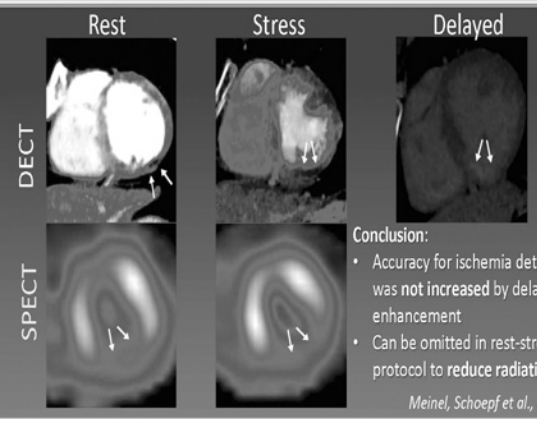

Functional Assessment – SPECT Correlation
ANT
SEP
LAT
INF
SPECT
DECT


Delayed Enhancement
cMRI
DECT
Ruszsics et al., RSNA 2009


Reversible Ischemia at Rest DECT
61 yo woman
• Atypical Chest pain



Reversible Ischemia

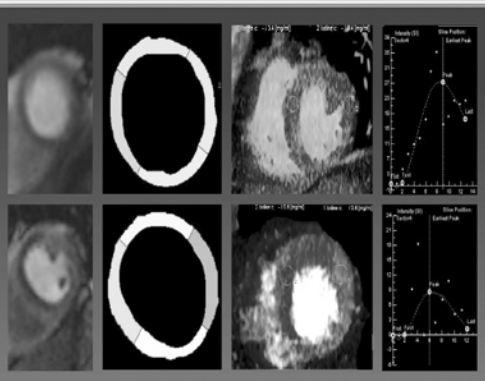


Conclusion:

- Accuracy for ischemia detection was **not increased** by delayed enhancement
- Can be omitted in rest-stress protocol to **reduce radiation**

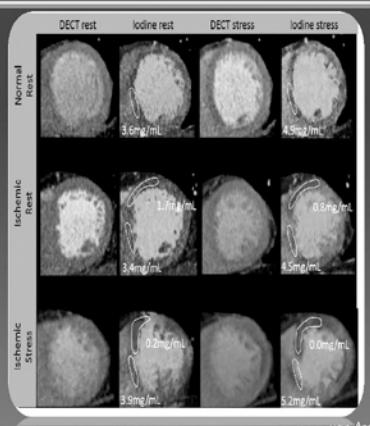
Meinel, Schoepf et al., Radiology

Quantitative DECT Perfusion



Koonce J et al., Eur Radiol 2014

Myocardial Iodine Quantification



Von Assen et al., MUSC 2017

Solving Clinical Dilemmas

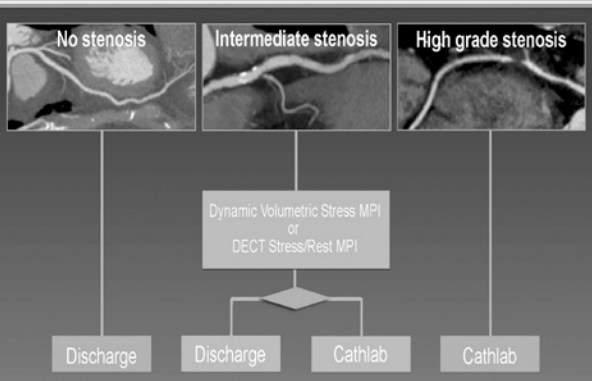


Image courtesy of MUSC

DECT Improves Accuracy

Evaluation protocol	Sensitivity (%)	Specificity (%)	AUC	p-value
cCTA positive (at least one stenosis >50%)	95%	50%	0.72	0.11
Perfusion defect on DECT myocardial iodine maps	95%	50%	0.72	0.11
Either positive	100%	33%	0.67	0.23
Both positive	90%	67%	0.78	0.04

Increased area under the curve (AUC) for significant stenosis detection

De Cecco, CN et al., AJR 2014

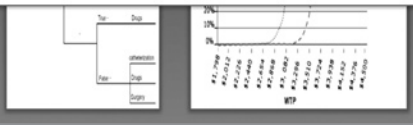
DECT vs SPECT: Cost Effectiveness

Cost-effectiveness of substituting dual-energy CT for SPECT in the assessment of myocardial perfusion for the workup of coronary artery disease

Mathias Meyer[a,c], John W. Nance Jr.[a], U. Joseph Schoepf[a,b,*], Antonio Moscariello[a,d], Markus Weininger[a], Garrett W. Rowe[a], Balazs Ruzsics[a], Doo Kyoung Kang[a,e],

Table 4
Mean costs, health outcomes, and cost-effectiveness for patients with CAD at different pre-test likelihoods.

Pre-test likelihood	Cost (US$) per patient	QALY 80%	ICER per QALY	ICER/correct diagnose 80%	ICER/QALYs 40%	ICER/QALYs 60%
SPECT	$2938	13.49	$3557	$3625	$5022	$5183
DECT	$2631	14.13	$3191	$2938	$3248	$2988
p-Value	0.0002		0.0004	0.0001	0.0001	0.0001



Dual-Energy CT (DECT) Techniques for Cardiac Imaging

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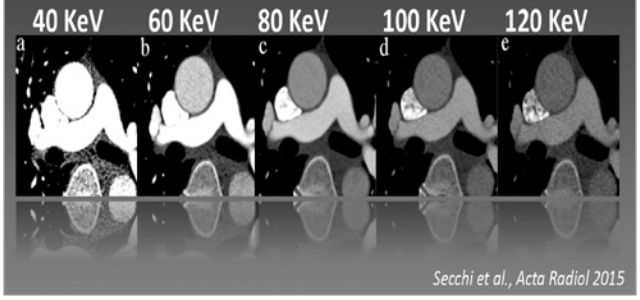
Post-processing – VMI

The benefits of the two DECT kV datasets (low kV – high contrast, high kV – low noise) are combined to a "virtual monoenergetic" image series

- **Regular image:** X-ray with spectrum of different energies
- **Monoenergetic:** virtual image (with one discrete energy)



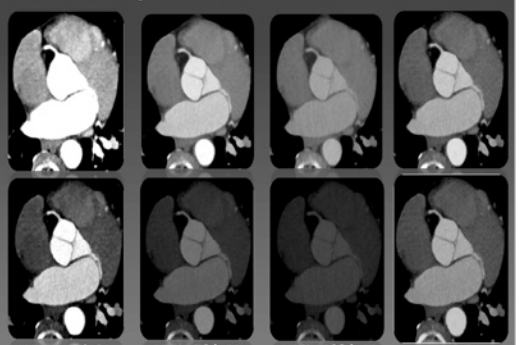
Secchi et al., Acta Radiol 2015

VMI+ for Cardiac CT

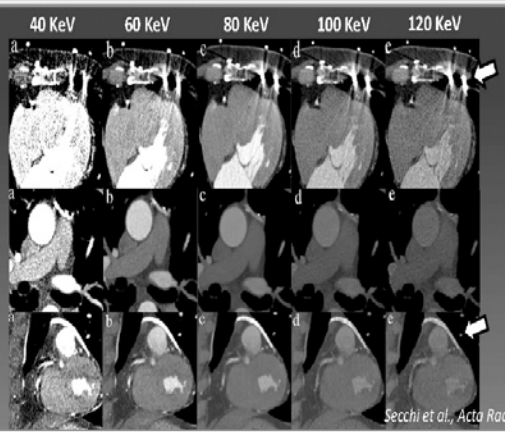
Manual adjustment of window settings is crucial – increase both width and center for low-keV

Width 600 HU
Center 150 HU

Width 1100 HU
Center 500 HU

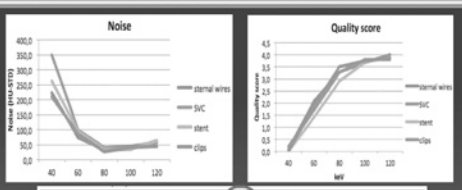


VMI - Artifact Reduction



Secchi et al., Acta Radiol 2015

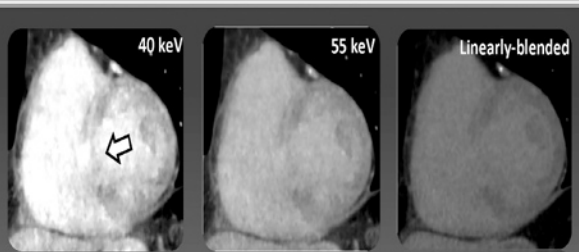
VMI - Artifact Reduction



	keV 40	keV 60	keV 80	keV 100	keV 120	P
Artifact size (mm)						
Sternal wires	8.4 ± 1.8	5.6 ± 1.8	4.0 ± 0.9	3.1 ± 0.9	2.6 ± 0.8	<0.001
SVC	21.3 ± 2.6	19 ± 2.0	17.7 ± 2.3	17.4 ± 1.9	17.4 ± 1.9	<0.001
Stents	5.9 ± 1.1	4.6 ± 0.8	3.6 ± 1.0	2.7 ± 1.1	2.7 ± 1.1	<0.001
Clips	6.4 ± 2.2	3.6 ± 1.3	2.8 ± 1.2	2.6 ± 1.1	2.2 ± 1.1	<0.001
Quality score						
Sternal wires	0.1 ± 0.3	2.1 ± 0.8	3.3 ± 0.6	3.7 ± 0.5	4 ± 0	<0.001
SVC	0.2 ± 0.5	1.7 ± 0.7	3.3 ± 0.7	3.8 ± 0.4	3.8 ± 0.4	<0.001
Stents	0 ± 0	1.4 ± 0.5	2.9 ± 0.7	3.7 ± 0.5	3.9 ± 0.4	<0.001
Clips	0 ± 0	1.9 ± 0.8	3.5 ± 0.8	3.8 ± 0.5	3.9 ± 0.4	<0.001
Noise (HU-SD)						
Sternal wires	223.1	74.5	33.3	44.7	43.9	<0.001
SVC	349.6	99.3	39.1	44.7	57.4	<0.001
Stents	261.9	93.8	33.9	35.6	62.7	<0.001
Clips	210	85.6	26.9	42.3	44.1	<0.001

Secchi et al., Acta Radiol 2015

VMI – Greater Late Enhancement



- This 64 year-old patient had history of prior MI and underwent delayed-phase CCTA
- Low-keV VMI+ reconstructions improve the visualization of iodine late-enhancement indicative for chronic infarct

Dual-Energy Techniques in Cardiac imaging

Major Applications

I. Myocardial Perfusion

II. Reconstruction of Virtual Monoenergetic images (VMI)

Minor Applications

I. Virtual Non-Contrast (VNC) images

II. Plaque Analysis

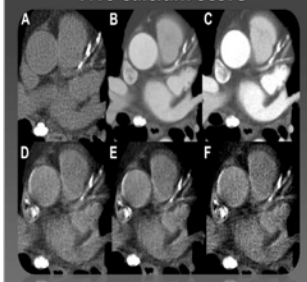
III. Calcium Subtraction

IV. Extracellular Volume Fraction (ECV)

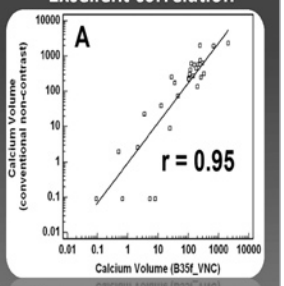
V. Myocardial Iron Quantification

DECT VNC Calcium Quantification

VNC Calcium Score



Excellent correlation



DECT may obviate the need for dedicated CT calcium scoring studies and may decrease patient radiation exposure and cost

Schwarz et al., Radiology 2012

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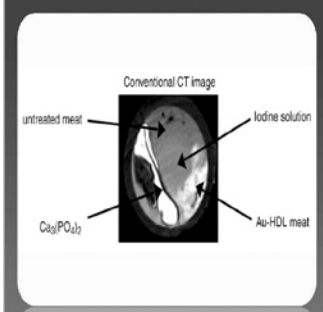
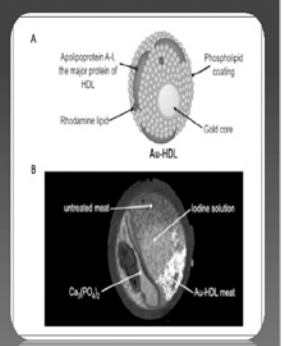
Plaque Composition





Cormode et al., Radiology 2010

Plaque Analysis

SSCT vs DSCT vs DECT: sensitivity 89.6%

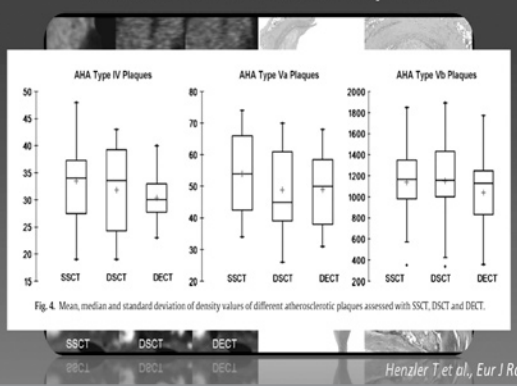


Fig. 4. Mean, median and standard deviation of density values of different atherosclerotic plaques assessed with SSCT, DSCT and DECT.

Henzler T,et al., Eur J Radiol 2011

Plaque Analysis

Plaque Composition – Dual Energy Index (DEI)

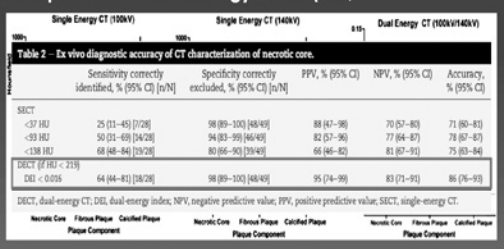


Table 2 – Ex vivo diagnostic accuracy of CT characterization of necrotic core.

	Sensitivity correctly identified, % (95% CI) [n/N]	Specificity correctly excluded, % (95% CI) [n/N]	PPV, % (95% CI)	NPV, % (95% CI)	Accuracy, % (95% CI)
SECT					
<37 HU	25 (11–45) [7/28]	98 (89–100) [48/49]	88 (47–98)	70 (57–80)	71 (60–81)
<93 HU	50 (31–69) [14/28]	94 (83–99) [46/49]	82 (57–96)	77 (64–87)	78 (67–87)
<138 HU	68 (48–84) [19/28]	80 (66–90) [39/49]	66 (46–82)	81 (67–91)	75 (63–84)
DECT (if HU < 219)					
DEI < 0.016	64 (44–81) [18/28]	98 (89–100) [48/49]	95 (74–99)	83 (71–91)	86 (76–93)

DECT, dual-energy CT; DEI, dual-energy index; NPV, negative predictive value; PPV, positive predictive value; SECT, single-energy CT.

"...With the use of the attenuation at 2 energies to create DEIs we found that the DEI of necrotic core was significantly lower than fibrous plaque and calcified plaque, and, importantly, there was no overlap in necrotic core and fibrous plaque DEIs"

Obaid DR et al., J Cardiovasc Comput Tomogr 2014

Dual-Energy Techniques in Cardiac imaging

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III. **Calcium Subtraction**

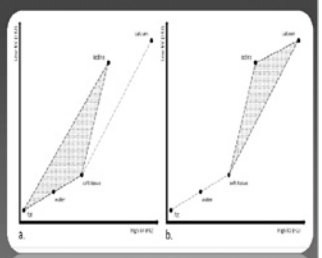
IV. Extracellular Volume Fraction (ECV)

V. Myocardial Iron Quantification

Calcium Subtraction

In the traditional three-material decomposition algorithms calcium is not represented as a reference material (a). Calcium removal may be incomplete or inaccurate.

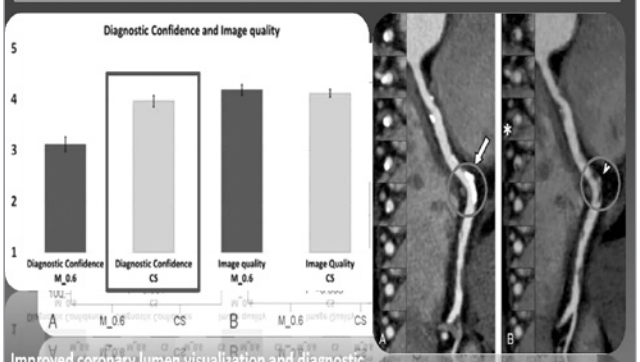
A new algorithm uses *soft tissue, iodine,* and *calcium* as the reference materials (b)



➡ **Complete subtraction of calcium and blooming from dual-energy CT image series.**

De Santis. et al., Investigative Radiology, 2017

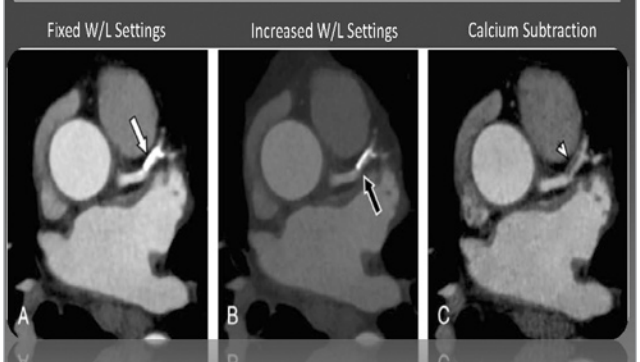
Calcium Subtraction



Improved coronary lumen visualization and diagnostic confidence in patients with heavy coronary calcifications

De Santis. et al., Investigative Radiology, 2017

Calcium Subtraction



De Santis. et al., Investigative Radiology, 2017

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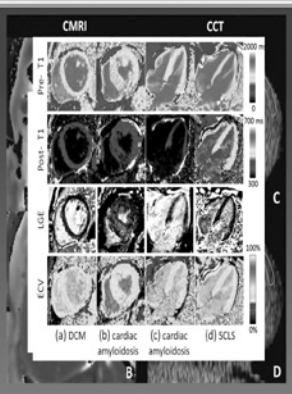
IV. **Extracellular Volume Fraction (ECV)**

V. Myocardial Iron Quantification

CT Extracellular Volume Fraction

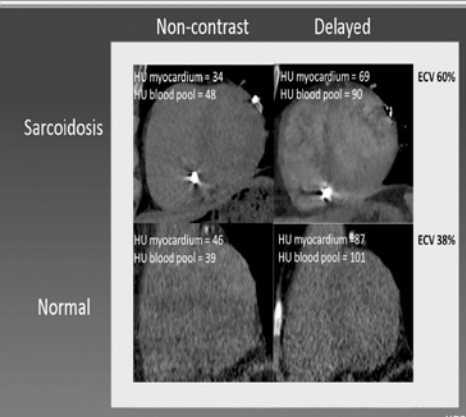
- For assessment of **diffuse** interstitial myocardial fibrosis
- Previously shown on MRI LGE and T1-mapping
- CT correlates (r=0.82) with T1-mapping cMRI
- DE-capability is currently explored



Kellman et al., JCMR, 2012

Nacif. et al., Radiology, 2012

CT Extracellular Volume Fraction



van Assen et al., MUSC 2017

Dual-Energy Techniques in Cardiac imaging

Major Applications

I. Myocardial Perfusion

II. Reconstruction of Virtual Monoenergetic images (VMI)

Minor Applications

I. Virtual Non-Contrast (VNC) images

II. Plaque Analysis

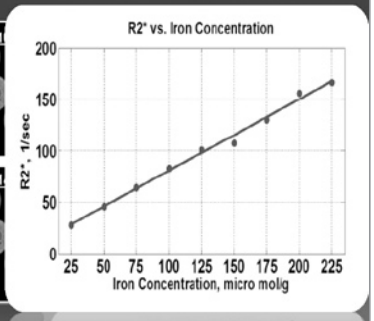
III. Calcium Subtraction

IV. Extracellular Volume Fraction (ECV)

V. **Myocardial Iron Quantification**

Myocardial Iron Quantification with DECT

DECT can be used for evaluating myocardial iron overload irrespective of the implemented imaging energy with high accuracy comparable to those from MR T2* mapping.

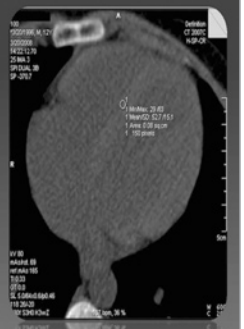


El-Sayed et al., IEEE 2014

Myocardial Iron Quantification with DECT

cDECT (septum)			
	140 kV	80 kV	Weighted average
T2* i	−0.525	−0.741	−0.597
	0.021	<0.001	0.007
	19	19	19

cDECT seems to be capable to quantify myocardial iron content in pediatric patients with thalassemia.



Hazirolan et al., EJR 2008

Conclusions and Outlook

- DECT provides morphological information + functional information
- May enhance visualization of ischemia using DECT perfusion
- Quantification of perfusion (mg/ml) beyond subjective evaluation
- Contrast optimization using VMI+
- Dose reduction using VNC
- Exciting new applications: ECV, iron

T1 mapping beyond delayed MR

Xiaohai Ma (Beijing Anzhen Hospital, China)

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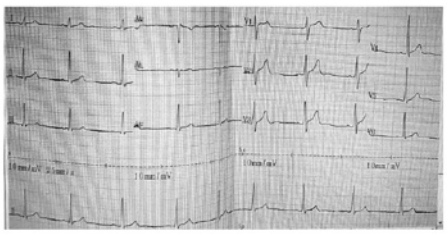
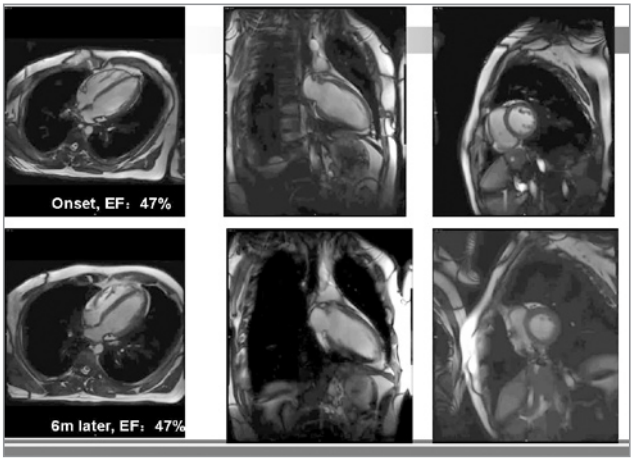
20/M，Viral Myocarditis，Heart Failure





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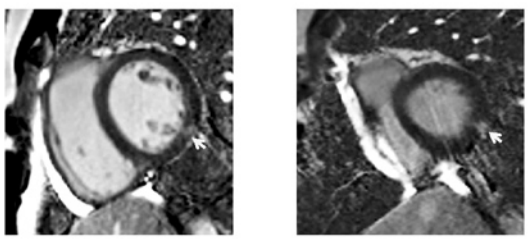

Onset　　6m later

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Beyond this, …

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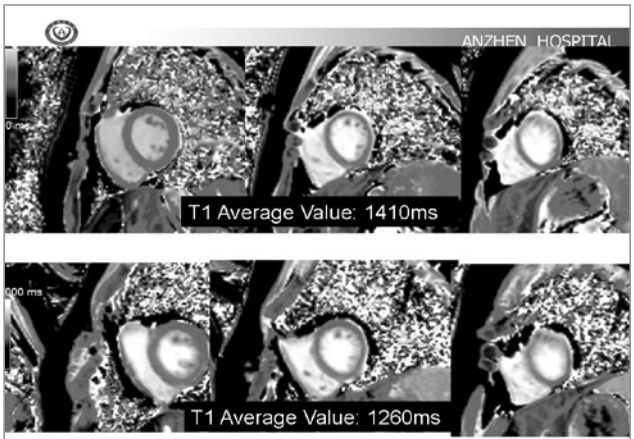

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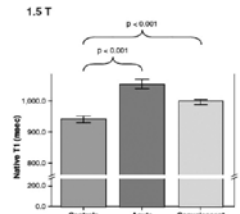
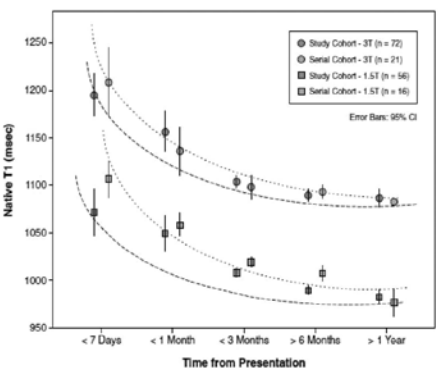


	Controls (n = 40)	Acute Myocarditis (n = 61)	Convalescent Myocarditis (n = 67)	p Value
mapping				
Native T1, ms				
1.5-T	940 ± 20	1,064 ± 37*	995 ± 19*†	<0.001
3.0-T	1,045 ± 23	1,189 ± 52*	1,099 ± 22*†	<0.001
Post-contrast T1, ms				
1.5-T	422 ± 68	373 ± 42*	383 ± 43*	0.03
3.0-T	442 ± 68	397 ± 62	426 ± 73	0.06
Lambda, %				
1.5-T	42 ± 4	50 ± 7*	46 ± 9	0.005
3.0-T	44 ± 5	53 ± 8*	45 ± 8†	0.002
Abnormal native T1, n (%)	0 (0)	60 (98)*	47 (76)*	0.001

Native T1 in Discrimination of Acute and Convalescent Stages in Patients With Clinical Diagnosis of Myocarditis

A Proposed Diagnostic Algorithm Using CMR



JACC: CARDIOVASCULAR IMAGING
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Native T1 in Convalescent Stages in Patients With Clinical Diagnosis of Myocarditis

A Proposed Diagnostic Algorithm Using CMR

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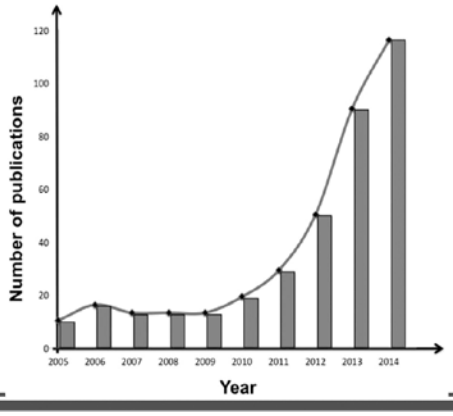
Cited publications on PubMed about T1 mapping



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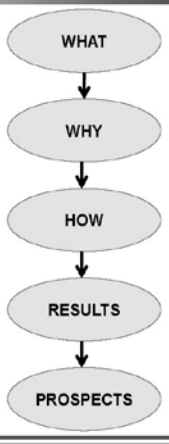
T1 Mapping

- What is T1 Mapping?
- Why do T1 Mapping?
- How to do T1 Mapping?
- How about the results?
- Knowledge gaps?
- Future directions?



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Consensus of T1 Mapping and ECV

Moon et al. Journal of Cardiovascular Magnetic Resonance 2013, 15:92
http://jcmr-online.com/content/15/1/92

Journal of Cardiovascular Magnetic Resonance

POSITION STATEMENT Open Access

Myocardial T1 mapping and extracellular volume quantification: a Society for Cardiovascular Magnetic Resonance (SCMR) and CMR Working Group of the European Society of Cardiology consensus statement

James C Moon[1,2*†], Daniel R Messroghli[3†], Peter Kellman[4], Stefan K Piechnik[5], Matthew D Robson[5], Martin Ugander[6], Peter D Gatehouse[7], Andrew E Arai[8], Matthias G Friedrich[9], Stefan Neubauer[5], Jeanette Schulz-Menger[9,10] and Erik B Schelbert[11]

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What is T1 Mapping

- **Native T1**: longitudinal relaxation time (T1) values of a given tissue when no contrast agent has been applied
- **T1 mapping**: a CMR method providing a parametric map whereby the T1 value is encoded in each pixel. T1 maps arise from a series of co-registered images acquired at different times of T1 recovery
- **ECV**: reflects the volume fraction of heart tissue that is not taken by cells

Moon JC, JCMR, 2013

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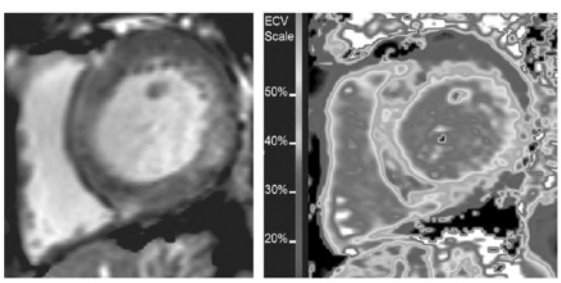
Why do T1 Mapping



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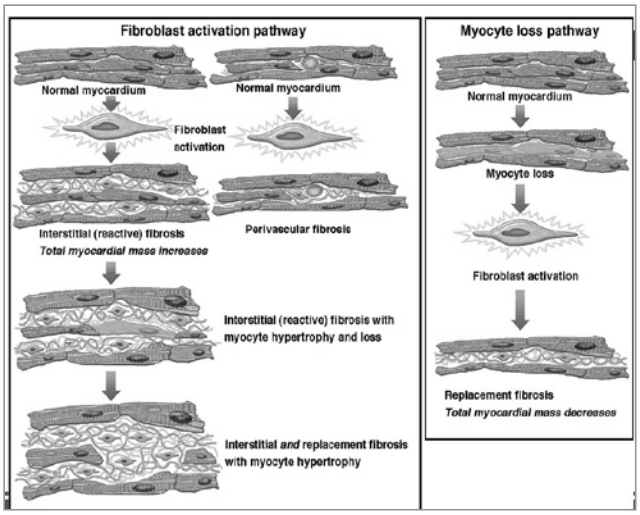
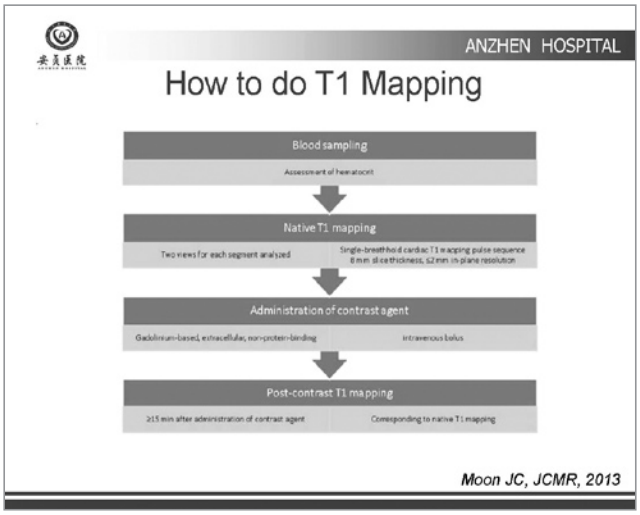

Fibroblast activation pathway
Normal myocardium
Normal myocardium
Fibroblast activation
Interstitial (reactive) fibrosis
Total myocardial mass increases
Perivascular fibrosis
Interstitial (reactive) fibrosis with myocyte hypertrophy and loss
Interstitial and replacement fibrosis with myocyte hypertrophy
Myocyte loss pathway
Normal myocardium
Myocyte loss
Fibroblast activation
Replacement fibrosis
Total myocardial mass decreases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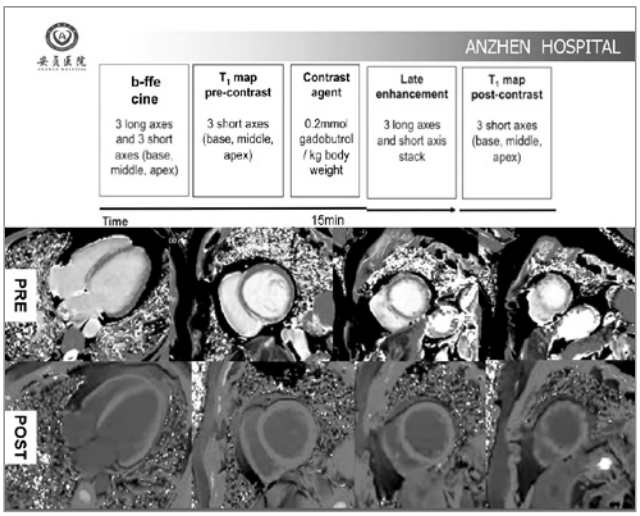
How to do T1 Mapping
Blood sampling
Assessment of hematocrit
Native T1 mapping
Two views for each segment analysed
Single-breathhold cardiac T1 mapping pulse sequence
8 mm slice thickness, ≤2 mm in-plane resolution
Administration of contrast agent
Gadolinium-based, extracellular, non-protein-binding
Intravenous bolus
Post-contrast T1 mapping
≥15 min after administration of contrast agent
Corresponding to native T1 mapping
Moon JC, JCMR, 2013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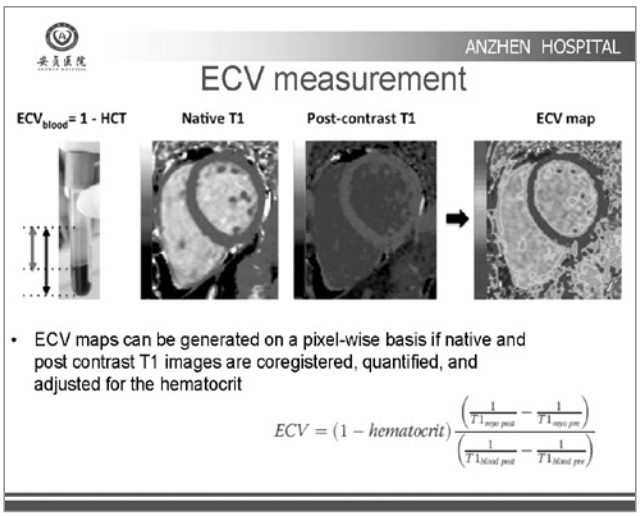
b-ffe cine
3 long axes and 3 short axes (base, middle, apex)
T1 map pre-contrast
3 short axes (base, middle, apex)
Contrast agent
0.2mmol gadobutrol / kg body weight
Late enhancement
3 long axes and short axis stack
T1 map post-contrast
3 short axes (base, middle, apex)
Time
15min
PRE
POST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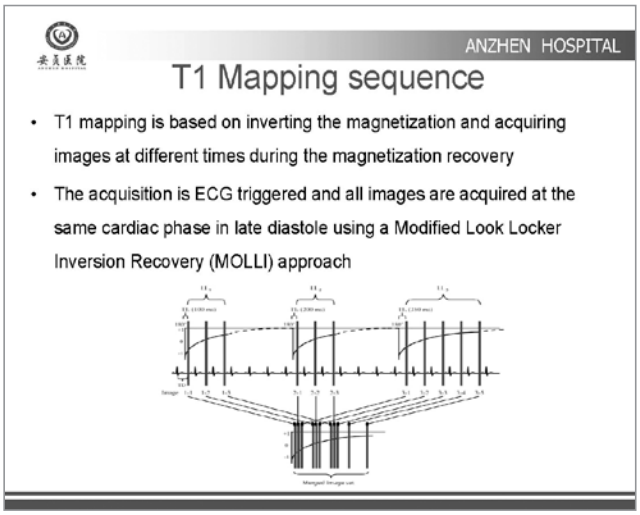
ECV measurement
ECVblood = 1 - HCT
Native T1
Post-contrast T1
ECV map
• ECV maps can be generated on a pixel-wise basis if native and post contrast T1 images are coregistered, quantified, and adjusted for the hematocrit
$ECV = (1 - hematocrit)\frac{\left(\frac{1}{T1_{myo\ post}} - \frac{1}{T1_{myo\ pre}}\right)}{\left(\frac{1}{T1_{blood\ post}} - \frac{1}{T1_{blood\ pre}}\right)}$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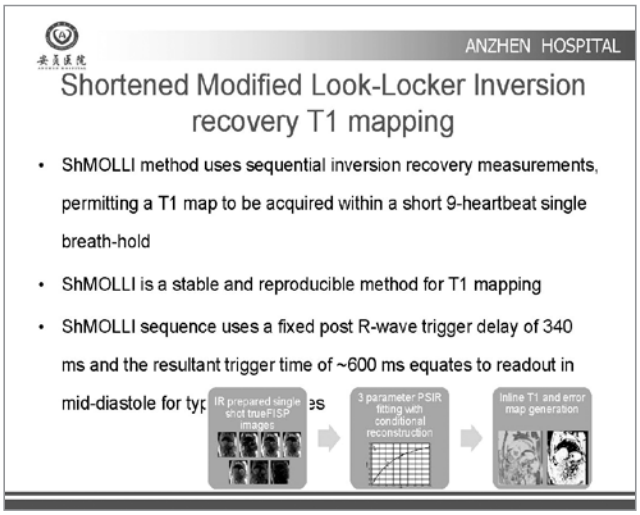
T1 Mapping sequence
• T1 mapping is based on inverting the magnetization and acquiring images at different times during the magnetization recovery
• The acquisition is ECG triggered and all images are acquired at the same cardiac phase in late diastole using a Modified Look Locker Inversion Recovery (MOLLI) approach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Shortened Modified Look-Locker Inversion recovery T1 mapping
• ShMOLLI method uses sequential inversion recovery measurements, permitting a T1 map to be acquired within a short 9-heartbeat single breath-hold
• ShMOLLI is a stable and reproducible method for T1 mapping
• ShMOLLI sequence uses a fixed post R-wave trigger delay of 340 ms and the resultant trigger time of ~600 ms equates to readout in mid-diastole for typ
IR prepared single shot trueFISP images
3 parameter PSIR fitting with conditional reconstruction
Inline T1 and error map generation

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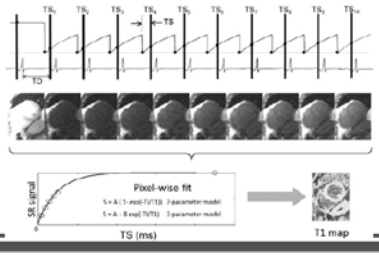
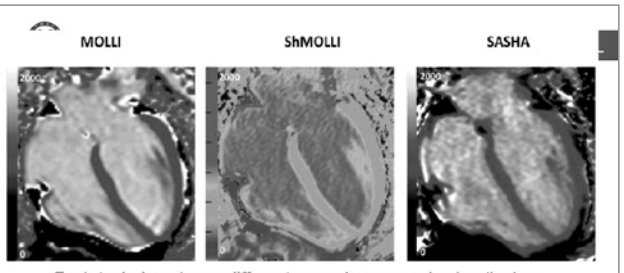
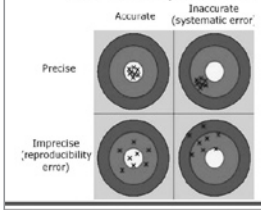
Saturation Recovery Single Shot Acquisition T1 mapping

- SASHA method using SSFP readout is very similar to the earlier Short Acquisition Period - T1 (SAP-T1) method which used a spoiled gradient recalled echo (GRE) readout





Each technique has a different normal range and color display



Kellman and Hansen JCMR 2014, 16:2

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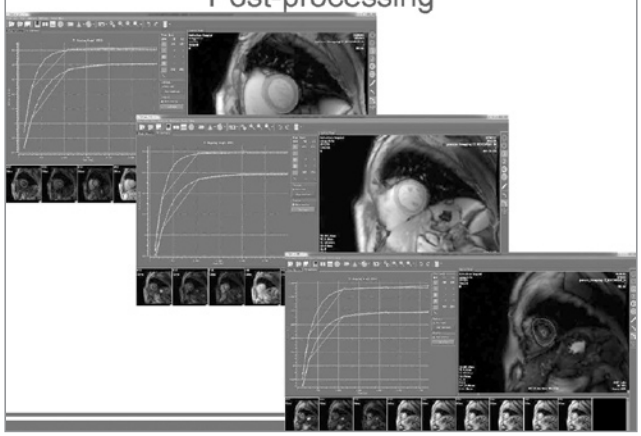
Post-processing



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How about the results

von Knobelsdorff-Brenkenhoff et al. Journal of Cardiovascular Magnetic Resonance 2013, 15:53
http://jcmr-online.com/content/15/1/53

Journal of Cardiovascular Magnetic Resonance

RESEARCH Open Access

Myocardial T_1 and T_2 mapping at 3 T: reference values, influencing factors and implications

Florian von Knobelsdorff-Brenkenhoff[1,2*], Marcel Prothmann[1,2], Matthias A Dieringer[1,2], Ralf Wassmuth[1,2], Andreas Greiser[3], Carsten Schwenke[4], Thoralf Niendorf[1,5] and Jeanette Schulz-Menger[1,2]

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T1 mapping reference values

Table 1: Select Reported Myocardial T1 Relaxation Times in Healthy Subjects

Magnet	Technique	No. of Subjects*	Age (y)	Native T1 (msec)†	Contrast-enhanced T1 (msec)	Authors	Year
1.5 T	LL	14 (8)	38 ± 10.9	1000.4 ± 126	523.3 ± 72.8	Nacif et al (27)	2011
1.5 T	MOLLI	15 (9)	33.1 ± 8.5	982 ± 46	NR	Messroghli et al (13)	2006
1.5 T	MOLLI	10 (7)	35 ± 7	976 ± 46/80	NR	Piechnik et al (19)	2010
1.5 T	MOLLI	14 (8)	38 ± 10.9	1029.4 ± 56.8	462.4 ± 62.2	Nacif et al (27)	2011
1.5 T	MOLLI	13 (7)	38.1 ± 11.1	NR	466 ± 14	Sibley et al (23)	2012
1.5 T	ShMOLLI	10 (7)	35 ± 7	966 ± 48/88	NR	Piechnik et al (19)	2010
1.5 T	ShMOLLI	21 (8)	55 ± 13	944 ± 17	NR	Ferreira et al (40)	2012
1.5 T	ShMOLLI	45 (32)	42 ± 14	941 ± 18	NR	Ferreira et al (41)	2013
1.5 T	ShMOLLI	342 (170)	38 ± 15	962 ± 25	NR	Piechnik et al (14)	2013
1.5 T	ShMOLLI	36 (22)	59 ± 4	958 ± 20	NR	Karamitsos et al (42)	2013
3 T	MOLLI	10 (7)	35 ± 7	1169 ± 45/73	NR	Piechnik et al (19)	2010
3 T	MOLLI	24 (8)	29 ± 6	1159.0 ± 39.2	NR	Liu et al (21)	2012
3 T	MOLLI	60 (30)	48 ± 17	1158.7	411.2	von Knobelsdorff-Brenkenhoff et al (43)	2013
3 T	ShMOLLI	10 (7)	35 ± 7	1166 ± 60/91	NR	Piechnik et al (19)	2010

Note.—NR = not reported.
*Number in parentheses indicates number of male subjects.

Healthy subject: T1=900~1000ms (1.5T), 1150ms (3.0T)

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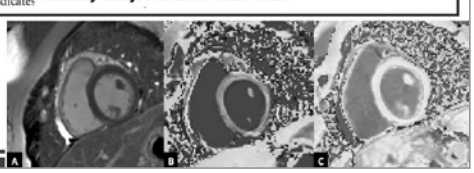
ECV reference values

Table 3: Select Reported ECVs in Healthy Subjects

Magnet	Technique	No. of Subjects*	Age (y)	ECV	Authors	Year
1.5 T	MOLLI	9 (NR)	20–50	0.217–0.262	Wong et al (24)	2012
1.5 T	MOLLI	62 (30)	43.6 ± 17.4	0.254 ± 0.025	Kellman et al (48)	2012
1.5 T	MOLLI	30 (15)	45 ± 13	0.255 ± 0.026	Miller et al (49)	2013
1.5 T	MOLLI	17 (17)	33 ± 8	0.24 ± 0.02	Florian et al (50)	2014
3.0 T	MOLLI	11 (6)	36 ± 13	0.267 ± 0.01	Lee et al (51)	2011
3.0 T	LL	9 (3)	45 ± 11	0.24	Mongeon et al (52)	2012

Note.—NR = not reported.
*Number in parentheses indicates

Healthy subjects: ECV=0.21~0.25



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Clinical Application of T1 and ECV

Messroghli et al. Journal of Cardiovascular Magnetic Resonance (2017) 19:75
DOI 10.1186/s12968-017-0389-8

Journal of Cardiovascular Magnetic Resonance

REVIEW Open Access

Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI)

Daniel R. Messroghli[1,2,3*], James C. Moon[4], Vanessa M. Ferreira[5], Lars Grosse-Wortmann[6], Taigang He[7],

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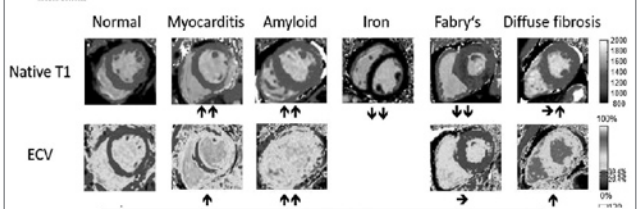

Measure	Decrease	Mild increase	Moderate or severe increase
Native T1	Anderson-Fabry, iron overload, fat, hemorrhage (athlete's heart)	diffuse fibrosis, scar, subacute inflammation	amyloid, acute inflammation, acute ischemia, necrosis
ECV	athlete's heart	diffuse fibrosis	amyloid, necrosis, scar

Messroghli et al. JCMR 2017 19:75

Ischemic cardiomyopathy

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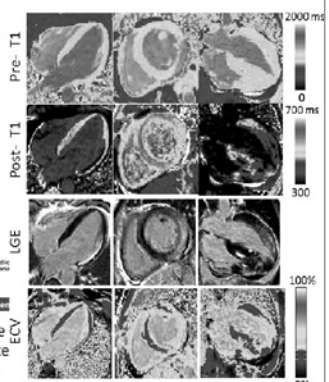
- MI: Native T1 ↑, Post T1 ↓, ECV ↑
- T1, ECV correlated with EF
- T1 Mapping is helpful for understanding post MI LV remodeling



RESEARCH Open

Extracellular volume fraction mapping in the myocardium, part 2: initial clinical experience

(a) Chronic MI (b) Acute Myocarditis (c) HCM

Nonischemic cardiomyopathy

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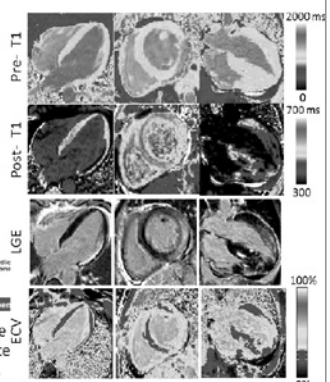
- Native T1 ↑, Post T1 ↓
- ECV ↑
- Detect early fibrosis changes
- Prognostic significance



RESEARCH Open

Extracellular volume fraction mapping in the myocardium, part 2: initial clinical experience

(a) Chronic MI (b) Acute Myocarditis (c) HCM

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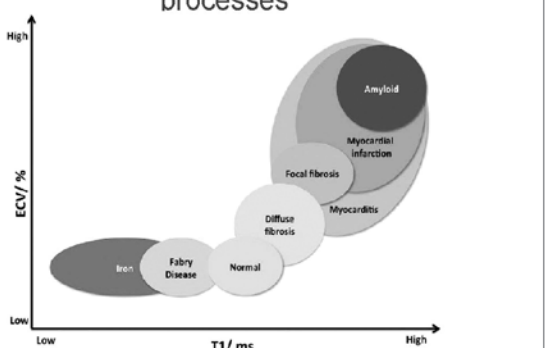
T1 mapping & ECV in various myocardial processes



Martin Ugander SCMR 2014

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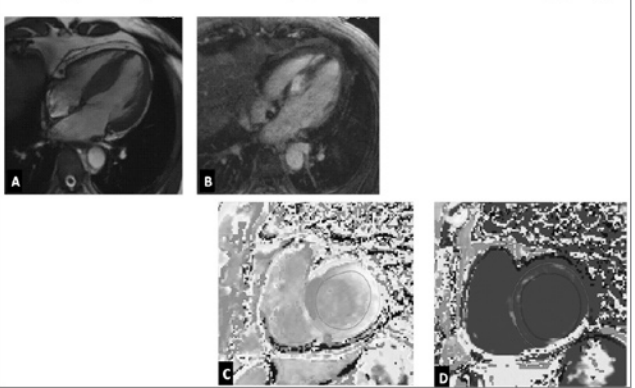
Hypertrophic Cardiomyopathy: LGE vs. T1 mapping



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RESEARCH Open Access

In-vivo T1 cardiovascular magnetic resonance study of diffuse myocardial fibrosis in hypertrophic cardiomyopathy

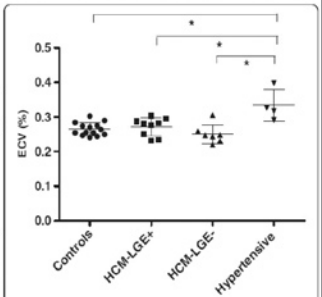

Figure 3 Extracellular volume fraction (ECV) values in non-enhanced myocardium in HCM patients and controls. The group of HCM patients is subdivided into patients with focal fibrosis on LGE (HCM-LGE+) and without focal fibrosis (HCM-LGE-). Notice that solely the group of 'hypertensive HCM' patients shows a significantly higher ECV compared to the other groups. ECV = extracellular volume fraction, HCM = hypertrophic cardiomyopathy, LGE = late gadolinium enhancement. * $p < 0.05$.

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Zhao et al. Journal of Cardiovascular Magnetic Resonance
DOI 10.1186/s12968-016-0232-7

RESEARCH

Systolic MOLLI T1 mapping with dependent pulse sequence sam scheme is feasible in patients wi fibrillation

Lei Zhao[1], Songnan Li[2], Xiaohai Ma[1], Andreas Greiser[3], Tianjing Zhang[4], Ji and Zhanming Fan[1*]

Abstract

Background: T1 mapping enables assessment of myocardial characteristics arrhythmia, atrial fibrillation (AF) is often accompanied by a variety of cardia and usually rapid ventricle rate of AF may cause inaccurate T1 estimation d magnetization recovery. We hypothesized that systolic T1 mapping with a l sequence scheme may overcome this issue.

HR	PRE	POST
50-55	5(2)3	4(1)3(1)2
56-60	5(3)3	4(1)3(1)2
61-65	5(4)3	4(1)3(1)2
66-70	5(4)3	4(2)3(2)2
71-75	5(5)3	4(2)3(2)2
76-80	5(5)3	4(2)3(2)2
81-85	5(6)3	4(3)3(3)2
86-90	5(7)3	4(3)3(3)2
91-95	5(7)3	4(4)3(4)2
96-100	5(8)3	4(4)3(4)2
101-105	5(9)3	4(5)3(5)2
106-110	5(10)3	4(5)3(5)2
111-115	5(10)3	4(6)3(6)2
115-120	5(11)3	4(6)3(6)2
121-125	5(12)3	4(6)3(6)2
126-130	5(12)3	4(7)3(7)2
131-135	5(13)3	4(7)3(7)2
136-140	5(14)3	4(8)3(8)2
141-145	5(14)3	4(8)3(8)2
146-150	5(15)3	4(9)3(9)2

a

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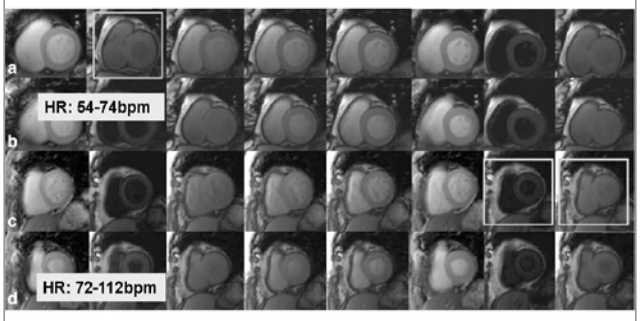

Zhao L, et al. JCMR. J Cardiovasc Magn Reson. 2016 Mar 15;18(1):13.

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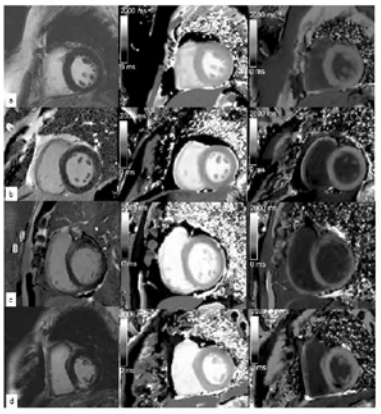

Persistent AF with HFmrEF,
EF = 49% , LGE (-),
native T1=1295 ms,
ECV=27.1%

Paroxysmal AF with HFmrEF,
EF = 48%, LGE (-),
native T1=1271 ms,
ECV=27.4%

Persistent AF with HFrEF,
EF = 39%, LGE (+) ,
native T1=1311 ms,
ECV=31.4%

Persistent AF with HFpEF,
EF = 68% , LGE (+) ,
native T1=1300 ms,
ECV=30.0%

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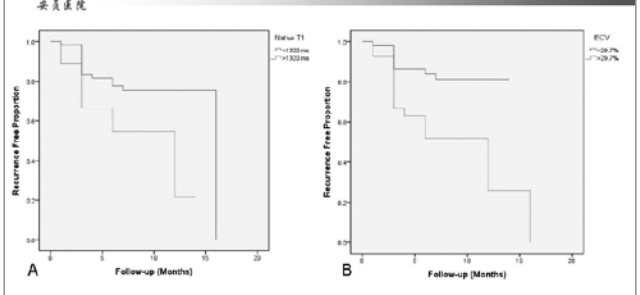

T1 mapping for predicting AF reoccurrence

Left Ventricular Myocardial Fibrosis in Patients with Atrial Fibrillation and Ventricular Dysfunction - Evaluation with Cardiovascular Magnetic Resonance T1 Mapping

Updated Insights

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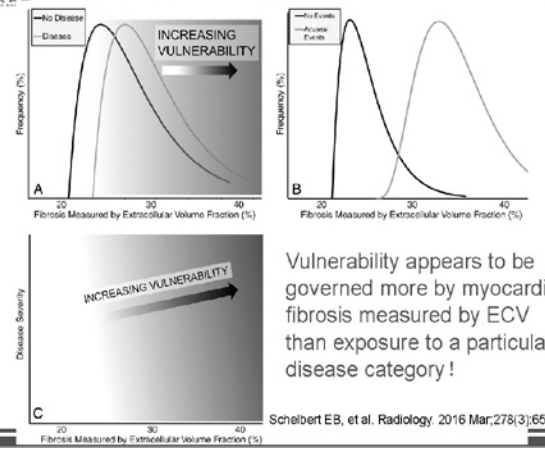

Vulnerability appears to be governed more by myocardial fibrosis measured by ECV than exposure to a particular disease category !

Schelbert EB, et al. Radiology. 2016 Mar;278(3):658-76.

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Knowledge gaps

- **Relaxometry assumptions:** the simplified model is affected by more complex molecular composition of tissue and pathology is unclear
- **Confounding factors**: measurement of a parameter of interest such as T1 may depend on other variables such as T2 or heart rate, and numerous other confounding factors
- **Partial volume effects:** depends on aspects such as wall thickness or angulation of the slice prescription
- **Post-processing**: influence the quality of parametric results, can equal or even exceed that of the acquisition strategy
- **Map analysis**: assessment of average parameter values of septal ROIs is regarded as appropriate for diffuse myocardial disease, patchy presentation require more detailed analysis of regional behavior

Messroghli *et al. Journal of Cardiovascular Magnetic Resonance* (2017) 19:75

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Future directions

- Future developments in cardiac mapping will likely focus on standardization of data acquisition and post-processing, as well as on optimizing workflows

1. Technical development and theoretical basis of test
2. Direct comparison (eg biopsy, animal models, human autopsy)
3. Detection of changes in established disease compared to normals
4. Correlation with known cardiac markers (eg echocardiography parameters)
5. Correlation with known biomarkers (eg blood biomarkers)
6. Demonstration of the test in more than one clinical scenario
7. Demonstration of test sensitivity (early disease or with age)
8. Demonstration of the ability to track change (with time, after therapy)
9. Demonstration of predictive or prognostic value of the test
10. Standardization of the test
11. Development of robust age/ethnic normal reference ranges
12. Changes in biomarker remain tied to the disease after treatment
13. Demonstration of the test as a surrogate trial endpoint
14. Clinical use and regulatory approval of the test
15. Proof that use of test improves clinical outcome

Roadmap for developing biomarkers derived from parametric mapping

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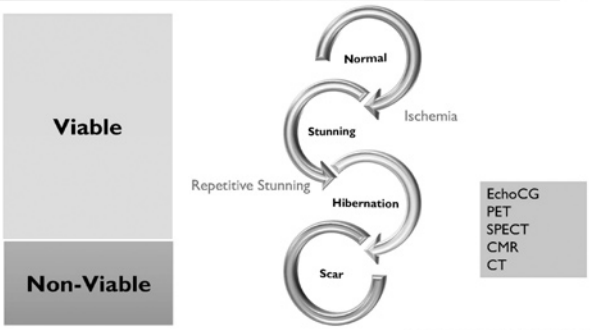
Thanks for your attention !

MEMO

Viability assessment with minimal or non-contrast Imaging

Hyuk Jae Chang (Severance Hospital, Korea)

Dysfunctional Myocardium



Chareonthaitawee et al., *JACC 2005*; **46**, 567-74

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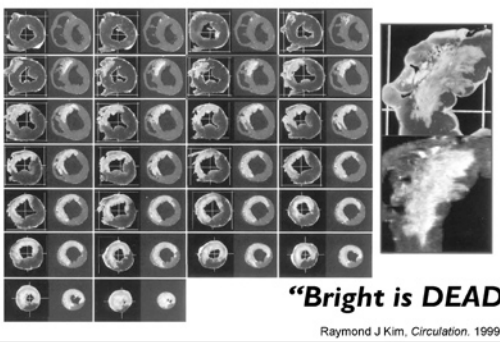
Scar Imaging using CMR



"Bright is DEAD!"

Raymond J Kim, *Circulation*. 1999;100:1992-2002

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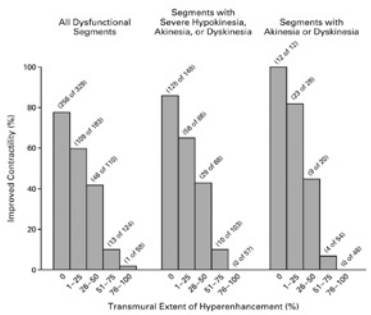
Impact of Viability Imaging using CMR on Myocardial Contractility



Kim et al. NEJM 2000;343 (20): 1445

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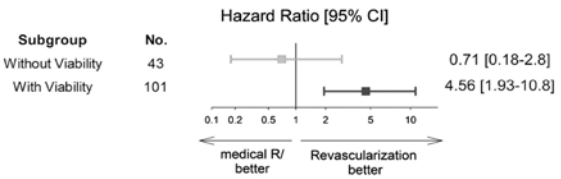
Impact of Viability Imaging using CMR on Survival

Risk of 3-Year Death According to Viability and Treatment



Gerber et al., JACC 2012; 59:825-35

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Limitations of CMR viability imaging

	PARR-2[34,35]
Patient population	Decisions about revascularization uncertain
	90% multivessel disease among patients with angiography
	34% renal disease
	19% prior CABG
Viability testing	FDG PET vs standard care
	22% viable by mismatch cutoff
Assessed ischemia or hibernation	FDG PET: Yes—hibernation

- Patients who need Viability Imaging:
  - ✓ Low EF: Hard to tolerate long scan time
  - ✓ Advanced CKD: Risk of nephrogenic systemic fibrosis/nephrogenic fibrosing dermopathy
- Expensive
- Time delay for viability imaging

Mielniczuk, Beanlands. *Circulation Cardiovascular Imaging* 2012; 5:262-70

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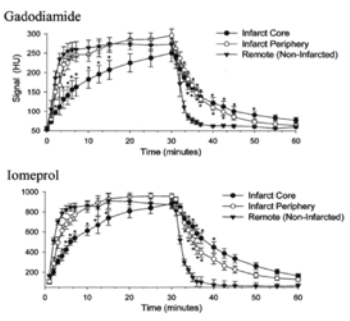
Gd and I Kinetics in Myocardial Scar



- Contrast agents for CT and MRI have similar contrast kinetics
- There have been attempts to assess myocardial viability using delayed enhancement with cardiac CT.

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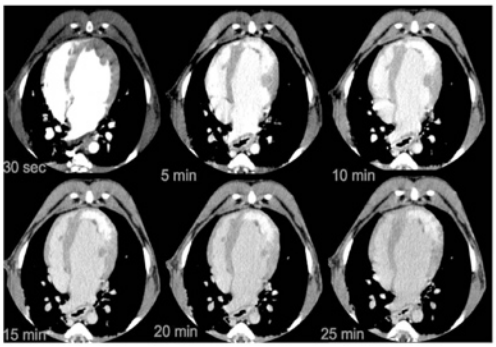
Acute Reperfused MI Animal Model using MSCT



Lardo AC et al Circulation 2006

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CT Viability Studies

Author	CT machine	Contrast amount	Voltage, tube current	Sample size	Findings
[redacted]					
Choe et al.	40-sliceMDCT (Brilliance 40, Philips)	1.5 mL/kg	120 kV, 800 effective mAs	40	- Correlation coefficient for MI size was 0.81 - Mean MI volume larger on DEMRI than DECT (26% vs 23%)
[redacted]					
Boussel et al.	Brilliance 40, Philips	No additional contrast material (after angioplasty)	80 kV and 600 mAs	19	Good agreement for number of involved segments, infarct size, and transmural extent of enhancement with both techniques (r^2 = 0.74, 0.67 and 0.76, respectively)
[redacted]					

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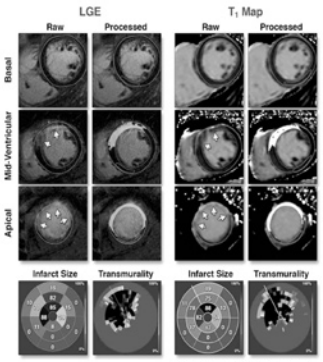
Unmet Needs with Current Viability Imaging and Possible Solutions with Cutting Edge Technologies

- **Inevitable use of contrast agent**
  - DE imaging using residual contrast agent in myocardium after conventional CAG
  - Viability MR imaging using native T1 mapping with 3T CMR imaging
- **Inefficiency of IV contrast delivery**
  - Intra-coronary contrast delivery
- **Time Delay for Viability Imaging**
  - On-Site, concurrent viability image acquisition at cath room

10

Native T1 Mapping by 3-T CMR Imaging for Characterization of Chronic Myocardial Infarctions

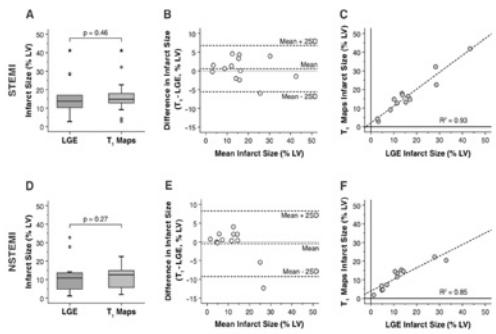


Semiautomatic Threshold Analysis to Detect and Characterize Chronic MI at 3-T in a STEMI Patient

A Kali, EY Choi, BW Choi, HJ Chang, R Dharmakumar et al, *J Am Coll Cardiol Img* 2015;8:1019–30

11

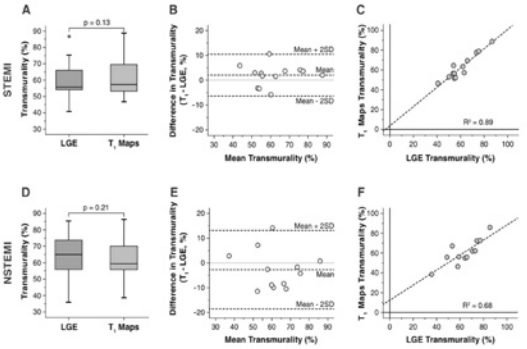
Infarct Size Comparison Between LGE Images and Native T1 Maps



A Kali, EY Choi, BW Choi, HJ Chang, R Dharmakumar et al, *J Am Coll Cardiol Img* 2015;8:1019–30

12

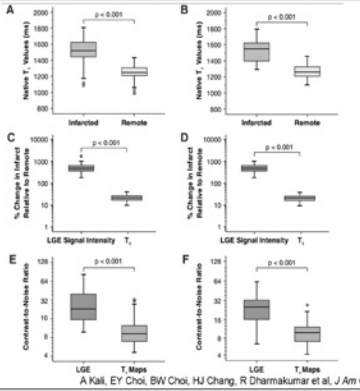
Transmurality Comparison Between LGE Images and Native T1 Maps



A Kali, EY Choi, BW Choi, HJ Chang, R Dharmakumar et al, *J Am Coll Cardiol Img* 2015;8:1019–30

13

Infarct-to-Remote Myocardium Contrast in LGE Images and Native T1 Maps

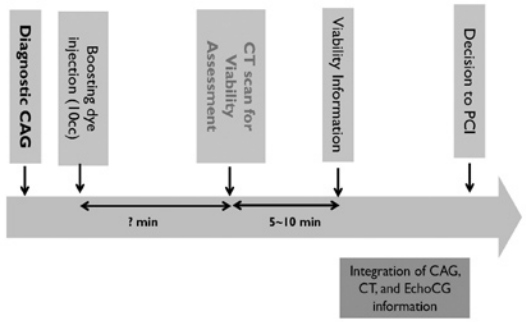


A Kali, EY Choi, BW Choi, HJ Chang, R Dharmakumar et al, *J Am Coll Cardiol Img* 2015;8:1019–30

14

Concept

Patient with Decreased LV function & Suspected CAD



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Preclinical Study with animal model Hypothesis

To evaluate a feasibility of viability assessment after conventional coronary angiography (CAG) using CardioVascular Interventional Therapeutic Computed Tomography (CVIT-CT) in swine models

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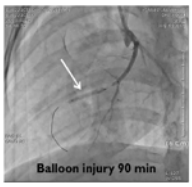
Preclinical Study with animal model Induction of MI with balloon occlusion



- 9 miniature swine models
  - Hybrid (Yukatan, Vietnam pot velly, gottigen, wild)
  - Age of 3 months
  - weights of 30kg
- Creation of MI:
  - Left anterior descending a. after 1st Dx with ballooning
  - Conventional CAG → balloon occlusion (90 min) → reperfusion

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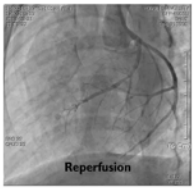
Methods Induction of MI with balloon occlusion



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I Cho, YG Jang HJ Chang et al., *JCCT* 2015;321-328

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Methods Induction of MI with balloon occlusion

- Two weeks after induction of myocardial infarction, DE images were obtained using CVIT-CT system after conventional CAG.
- Contrast Dye was injected during CAG
  - Iomeron 400, Ilsung Pharm. Korea
  - CAG 20cc, boosting shot 10cc with additional imaging
- CVIT CT system:
  - a novel combined machine of CAG system and 320-channel multi-slice CT (MSCT) scanner (Aquilion one, Toshiba) after conventional CAG.
- Voltage120kvp, Tube current 550mA
- CT imaging for Delayed enhancement performed 2, 5, 7, 10, 15, 20, 30 minutes after CAG.

I Cho, YG Jang HJ Chang et al., *JCCT* 2015;321-328

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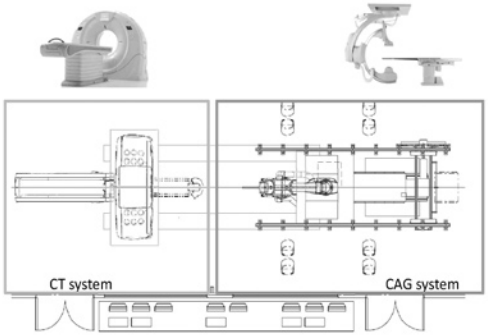
CVIT-CT System

CardioVascular Interventional Therapeutic Computed Tomography (CT) System



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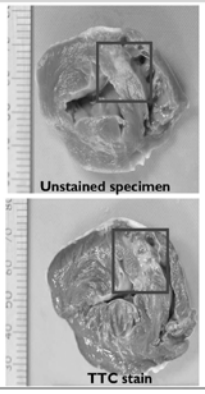
Methods
Induction of MI with balloon occlusion



- All pigs were sacrificed and heart was harvested after CAG and viability imaging.
- The heart was sliced in 10-mm consecutive sections in the short axis plane.
- All myocardial sections were embedded in a solution of 1% triphenyltetrazolium chloride (TTC).
- Infarct size was determined as TTC-negative areas as a percentage of total LV area.
- On MSCT images, infarct size per slice was calculated by dividing the DE area by the total slice area (%), and compared with histochemical analyses.
- Bland-Altman analyses /Correlation Coefficient was calculated. (Medcalc Ver.12)

I Cho,YG Jang HJ Chang et al., *JCCT* 2015;321-328

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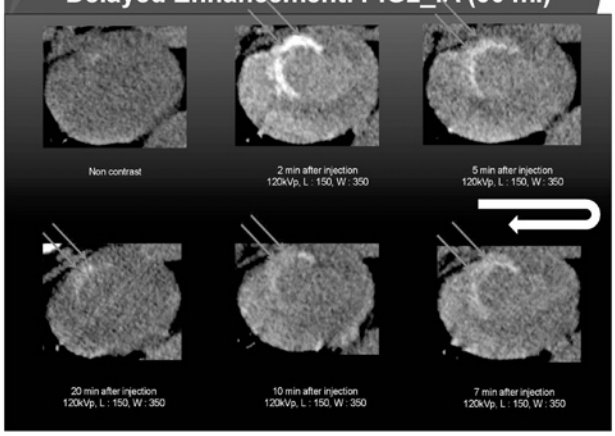
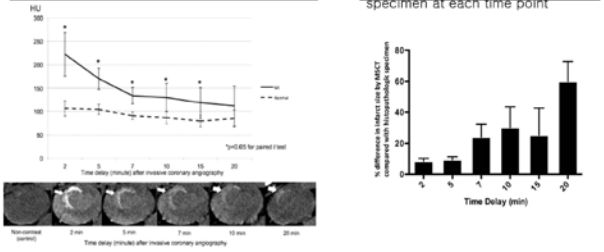
Delayed Enhancement: PIG2_IA (30 ml)



Myocardial Viability Imaging at Cath-room without Additional Contrast Injection

Time course of CT attenuation (HU) in MI tissue and remote normal myocardium

The percentage difference in infarct size by CT compared with histopathologic specimen at each time point



Best time point for viability imaging after CAG: 2-5 min

I Cho,YG Jang HJ Chang et al., *JCCT* 2015;321-328

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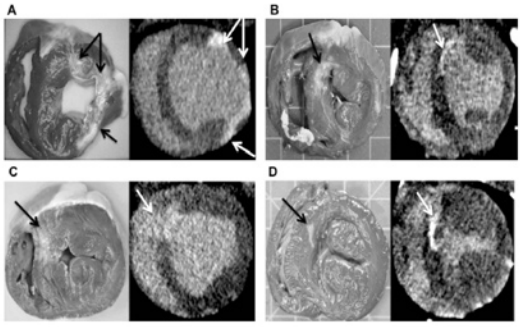
Myocardial Viability Imaging at Cath-room



I Cho,YG Jang HJ Chang et al., *JCCT* 2015;321-328

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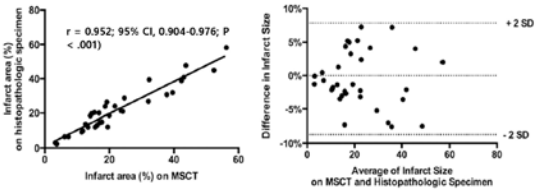
Correlation & Agreement of Infarct Size

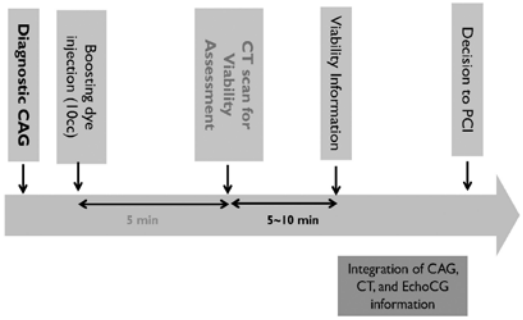


I Cho,YG Jang HJ Chang et al., *JCCT* 2015;321-328

INTEGRATIVE CARDIOVASCULAR IMAGING RESEARCH CENTER 25

Concept

Patient with Decreased LV function & Suspected CAD



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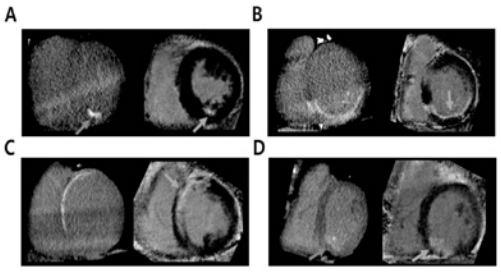
Ongoing Prospective Clinical Trial: Preliminary Analysis



Examples of visual comparisons of CT and CMR images on 4 patients (A-D).

(Red and green arrows indicate the infarcted myocardium on MSCT and CMR)

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Summary

- The limitations of current viability imaging modalities [e.g. inevitable use of contrast agent (Gd, I), time delay for viability imaging] could be overcomed by cutting edge CMR [e.g., Native T1 Mapping by 3-T CMR or CT (DE imaging with residual contrast in myocardium after conventional CAG using Hybrid CT-angio machine)].
- Additional studies, preferably in a larger patient cohort, should be needed.

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MEMO

Myocardial functional assessment by CMR and echocardiography

Eui-Young Choi (Gangnam Severance Hospital, Korea)

Assessment of accurate left ventricular systolic and diastolic function is an essential step for the diagnosis and monitoring of treatment effects of various cardiovascular diseases. Before development of current echo-Doppler technique, invasive assessment of pressure-volume relationship with load manipulation was gold standard to measure systolic and diastolic function of ventricular chambers.

However, this invasive pressure-volume relationship assessment has many problems, especially inconvenient in daily clinical practice due to invasive nature, not excellent reproducibility and need special analysis program. Improved piezoelectric crystal techniques in echo-probe, development of processing hardware and various development of analyzing software make it possible to assess ventricular function reproducibly.

By incorporating conventional two-dimensional echocardiography, (tissue) Doppler technique and speckle-tracking echocardiography, we can measure myocardial deformational function which provides myofiber functional indices in addition to traditional chamber ejection fraction and diastolic function.

Currently, echo-Doppler technique provides the best temporal resolution compared to other imaging modalities and is accepted as the best non-invasive modality for the measurement of diastolic function. Recent marked improvement in three dimensional probe technique and development of dedicated software provides new insight for three dimensional functional assessments of ventricular chamber as well as detailed information about fiber function such as area strain and shear strain.

However, echocardiography has inborn limitations in terms of acoustic window, lateral spatial resolution and observer dependency. CMR provides an ideal solution to overcome these limitations, as it can escape poor acoustic window and has excellent epicardial border delineation by current SSFP sequence and no angle dependency.

Therefore, CMR can make it possible for accurate measurement of LV mass and three dimensional cardiac chamber volumes especially in end-systolic phase. Using phase contrast image, various flows including mitral inflow can be measured three dimensionally, which can overcome limitation of some limitations of Doppler techniques such as pulmonary flow assessment and angle dependency. Tagged MRI technique also provides myocardial deformational information of principal strain and torsional value.

Especially, accurate assessment of torsion is better than current speckle tracking echocardiography technique as DICOM header has accurate information about distance between apical slice and basal slice in addition to their rotational values.

Current 4D strain can possibly provide torsional value not just twist value, but has still limitations in obtaining accurate apical rotational value due to narrow sector on 4D echo imaging. However, conventional SPAMM sequence based tagged MRI has many problems in measuring radial strain, longitudinal strain, and strain rate assessment due to limited temporal resolution and lack of reliable analyzing software.

In addition, due to problem of tag decay in end-diastolic phase and lower temporal resolution, diastolic functional assessment is not been currently accepted.

Complementary SPAMM, new sequence such as SENC, DENSE provides better myocardial deformational value including longitudinal strain and diastolic functional index than conventional SPAMM based images, although still some problems to be overcome.

Recently, feature tracking algorithm has been widely applied to cine CMR images like speckle tracking echo, this method is very convenient and easy to use, so CMR can be now used for “all in one” modality.

SESSION 8

SCCT - Beyond the Horizon

Chairperson **Byoung Wook Choi** (Severance Hospital, Korea)
Takuya Ueda (Tohoku University Hospital, Japan)

Presentation

New contrast agents for spectral CT
Speaker U. Joseph Schoepf (Medical University of South Carolina, USA)

Myocardial microcirculation
Speaker Akira Kurata (Ehime University, Japan)

Cardiovascular molecular imaging
Speaker Xiaohai Ma (Beijing Anzhen Hospital, China)

Onco-cardiology imaging
Speaker Yoojin Hong (Severance Hospital, Korea)

Research progress of cardiac CT on RSNA 2017
Speaker Jian Cao (Peking Union Medical College Hospital, China)

Panel Discussion

Panel Hwanseok Yong (Korea University Guro Hospital, Korea)
Hyun Jung Koo (Asan Medical Center, Korea)
Eun-Ju Kang (Dong-A University Hospital, Korea)
Jin Young Yoo (Chungbuk National University Hospital, Korea)

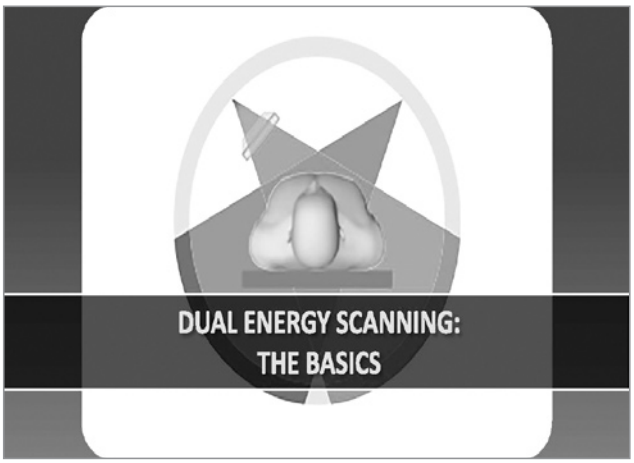
New contrast agents for spectral CT

U. Joseph Schoepf (Medical University of South Carolina, USA)

Disclosures

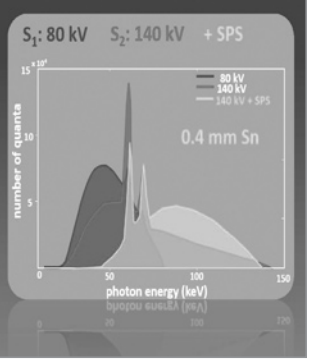
Consultant for / research support from

- Astellas
- Bayer
- GE Healthcare
- Guerbet
- HeartFlow
- Medrad
- Siemens Healthcare

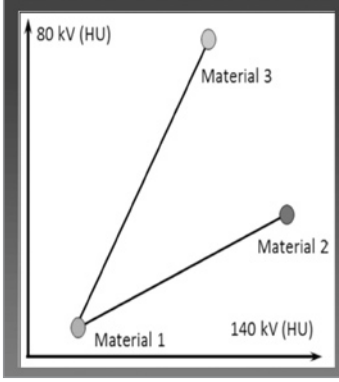


Dual Energy CT – Technical Improvements

- Dual Energy with selective photon shield
- Up to 80% improved seperation of low and high energies
- Minimized spectral overlay
- Noise reduction
- Greater dose reserve
- Complete radiation dose neutrality compared with single energy CT
- Material differentiation based on their relative absorption of X-rays at different energy levels



Dual Energy CT – Technical Improvements



The CT numbers of three known materials in the low- and high-energy images can be plotted on the y- and x-axis, respectively.

Unknown materials are then mapped onto this plot to determine the percent composition of each of the three basis materials.

Example of Dual Source DECT

1. Fat
2. Soft Tissue
3. Iodine

McCollough et al., Radiology 2015

Dual Energy CT – Techniques

Prospective DECT

Rotate-rotate: different kV at each gantry rotation	Dual Source Dual Energy	Rapid kVp Switching	Single Source Twin Beam Dual Energy
Toshiba	Siemens	GE	Siemens

Yeh et al., UCSF

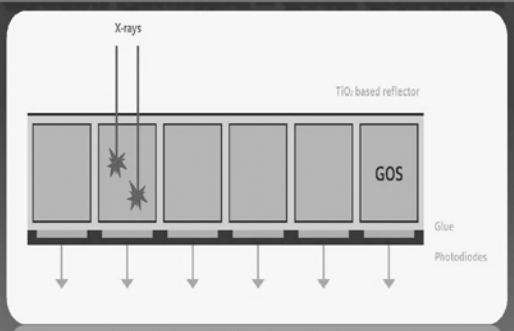
Dual Energy CT – Techniques

Retrospective DECT

Dual Layer Detector	Photon Counting
Philips	

Yeh et al., UCSF

Photon Counting – Basic Principles

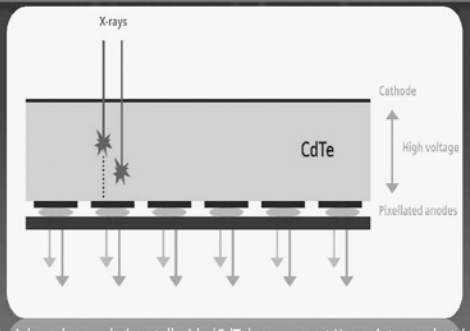


Current detectors convert X-Rays into an electrical signal in a 2-step process:

1-A scintillator layer (GOS) usually made of ceramic, converts X-rays into visible light

2-Photodiodes then convert light into an electrical current

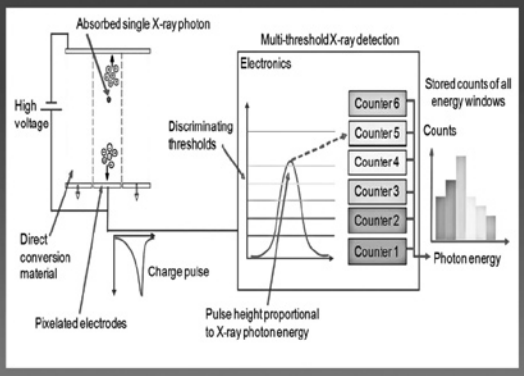
Photon Counting – Basic Principles



Certain materials such as cadmium telluride (CdTe) can convert X-rays into an electric current directly

Each X-ray generates clouds of free charged carriers -> possibility to **register each individual photon** and **measure the energy of each individual photon**

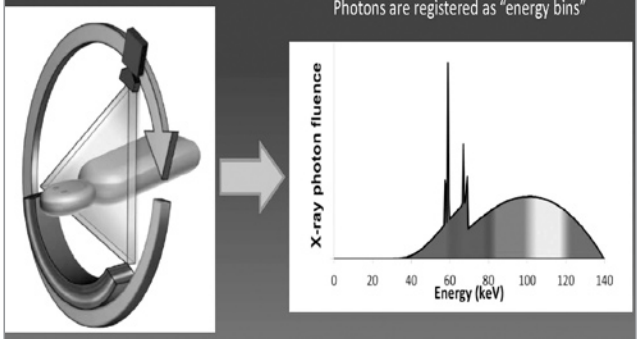
Photon Counting – Basic Principles



Boussel et al., *BJR* 2013

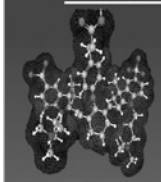
Photon Counting – Basic Principles

Photons are registered as "energy bins"



Yeh et al., *Advanced Drug Delivery Reviews* 2016

DECT and photon counting, are two major types of "spectral" CT, in which the unique, energy dependent attenuating characteristics of materials can provide new diagnostic information



A key to unlocking the capabilities of clinical spectral CT lies in the introduction of new contrast agents designed specifically for these emerging diagnostic imaging technologies

New Contrast Agents – Considerations

From a patient safety perspective, an ideal contrast agent must:

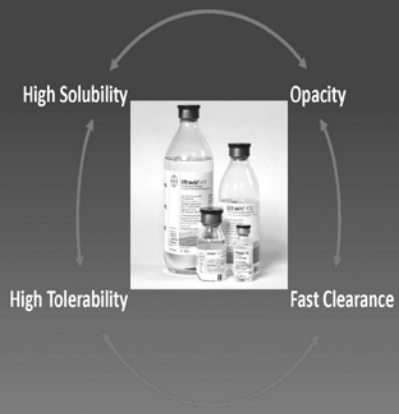
1. Contain elements that are non-toxic
2. That are formulated with physicochemical properties (viscosity and osmolality) that are compatible with high concentration delivery into the body
3. That are cleared from the body in a short time.
4. For targeted agents, off-target binding must be very low

From a practical perspective, the elements used in general-purpose CT contrast agents must be available in large quantities and at low cost.

From an imaging efficacy perspective, an ideal element for use as a conventional CT contrast agent would be one that provides high image contrast; should have dramatically different attenuation properties than current agents or structures to be differentiated from

Yeh et al., *Advanced Drug Delivery Reviews* 2016

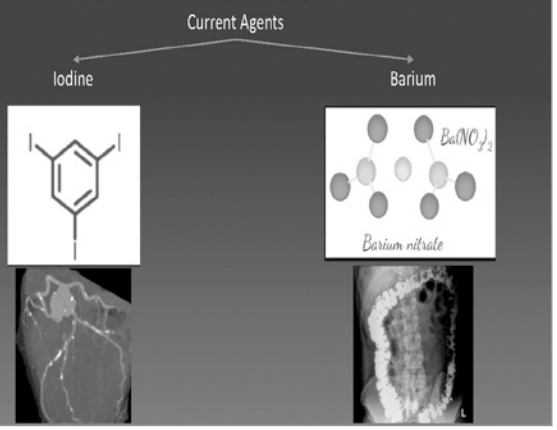
The Challenge for a New Contrast Media



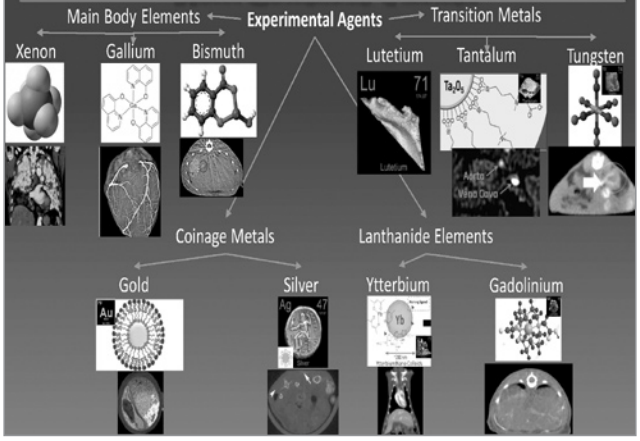
New Contrast Agents – Why?

1. Increased population of renally impaired patients
2. Need for better contrast in overweight patients (i.e. an element with a high k-edge that shows high attenuation at higher kV levels
3. Improved material differentiation with spectral CT = simultaneous use of different agents obviating the need for multiphasic imaging
4. Cell tracking and targeted imaging with nanoparticles

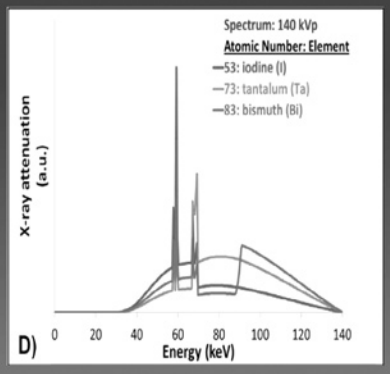
New Contrast Agents



New Contrast Agents



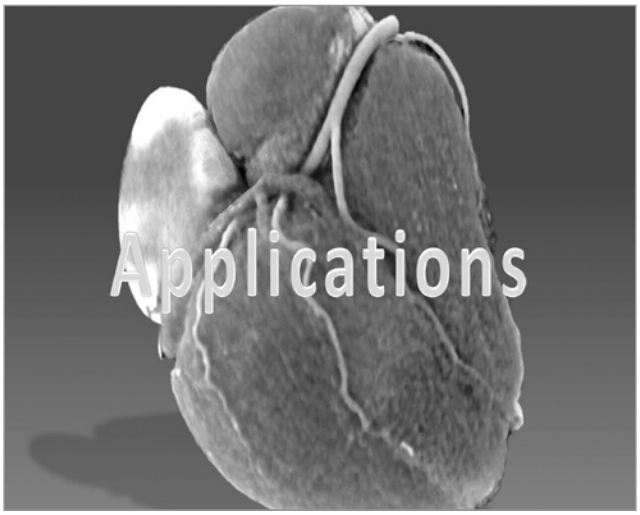
New Contrast Agents



Iodine = 33 keV

Tantalum = 67 keV

Bismuth = 91 keV



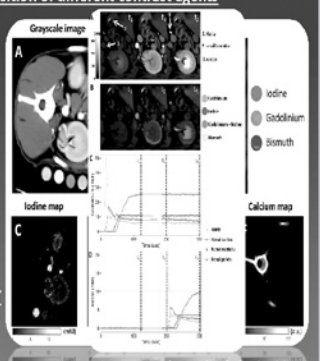
Photon Counting – Clinical Applications

Multi-energy information: Dual-Energy CT becomes **Multi-Energy CT**
Simultaneous material decomposition of different contrast agents

Multimaterial color coded can differentiate the 3 contrast agents

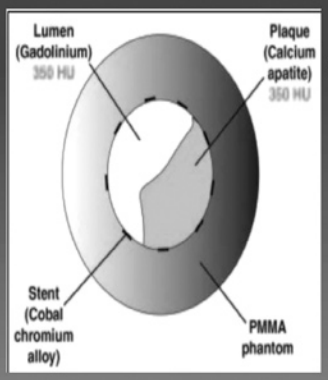
Multimaterial maps at 3 different time points show clear differentiation between the 3 contrast agents

Besides defining contrast agent concentrations, tissue enhancement at multiple phases was observed in a single CT acquisition, **potentially obviating the need for multi-phase CT scans and thus reducing radiation dose.**



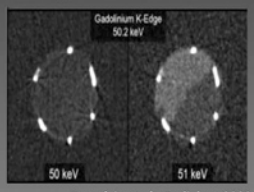
Symons et al., *Medical Physics* 2017

Gadolinium – Lumen Visualization



Stent isoattenuated to Gadolinium

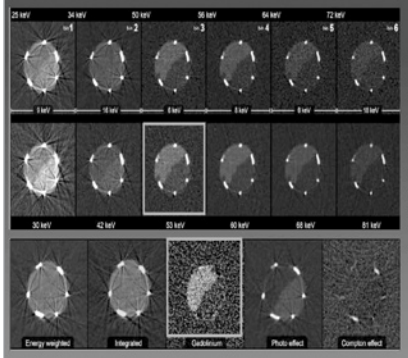
K edge Gadolinium = 50.2



Feuerlein et al., *Radiology* 2008

Gadolinium – Lumen Visualization

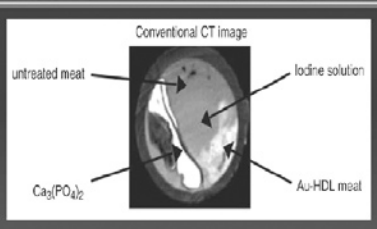
Improved Lumen Visualization



Multiple high-attenuation materials such as calcified plaque, metallic stent material, and intravascular contrast agent could be distinguished, resulting in enhanced vessel depiction and better stenosis or restenosis quantification

Feuerlein et al., *Radiology* 2008

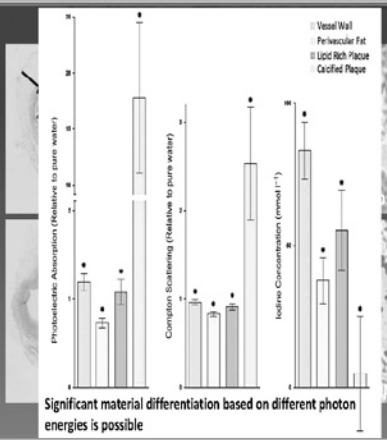
Gold Nanoparticles Targeted Imaging – Plaque Composition



Gold | Iodine | Photoelectric | Compton | **Overlay**

Cormode et al., *Radiology* 2014

Iodine – Plaque Imaging

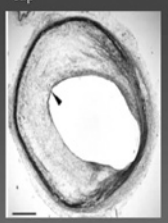


Significant material differentiation based on different photon energies is possible

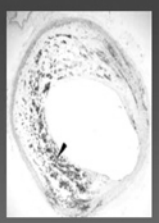
Boussel et al., *BJR* 2013

Iodine Nanoparticles Targeted Imaging – Macrophages

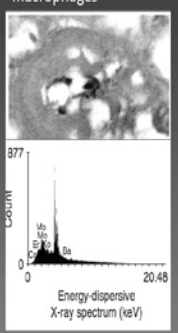
Histology of a plaque showing the fibrous cap



Fibrous cap infiltrated by macrophages



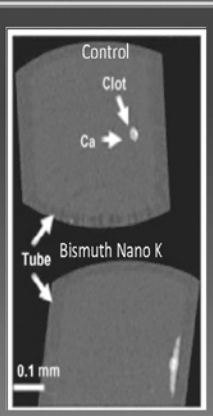
Compound N1177 accumulated in macrophages

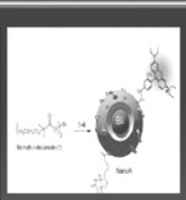


Observed correlations between the increase in the density of atherosclerotic plaques assessed by CT 2 h after the injection of N1177 and the intensity of macrophage infiltration in the lipid-rich core in the corresponding histological sections

Hyafir et al., *Nature Medicine* 2007

Bismuth Nanoparticles – Targeted Clot Imaging

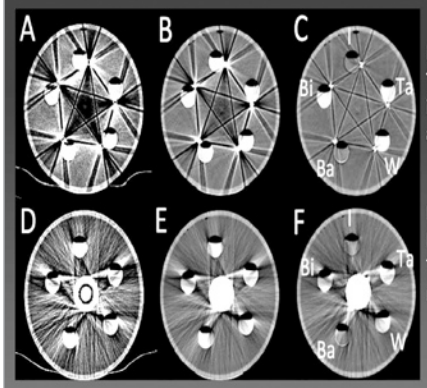




Bismuth nanoparticles bind and differentiate the fibrin surface from the calcified part of the clot

Pan et al., *Angew Chem* 2010

Metal Artifact Reduction

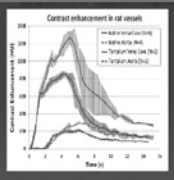


Bismuth, Tantalum and Tungsten show less decrease in enhancement and higher attenuation at high keV

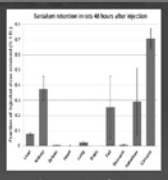
Better artifact reduction with Bismuth, Tantalum and Tungsten (C and F) while maintaining enhancement

Lambert et al., *Medical Imaging* 2015

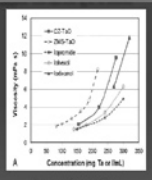
New Contrast Agents - Tantalum



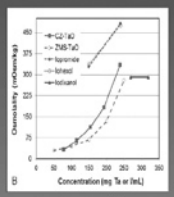
Better enhancement



Low retention



Low viscosity



Low osmolality

TABLE 3. Histopathology Analysis of Kidneys After Injection of CZ-TaO at 1500 mg Ta/kg

	Saline			CZ-TaO		
Kidney Pathology Feature	1	2	3	1	2	3
Tubular epithelium, cortex degeneration	N	N	N	N	N	1
Tubular epithelium, cortex regeneration	N	N	N	N	N	N
Tubule, cortex dilation	N	N	N	N	N	N
Cortex infiltration, mononuclear cell	N	N	>1	N	N	N
Tubular epithelium, cortex cytoplasmic droplets	N	N	N	N	N	N

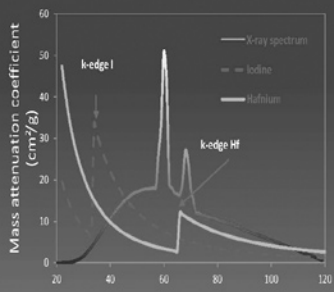
Organs harvested 48 hours after injection. Grading scale: N = normal; 1 = minimal; 2 = mild; 3 = moderate; 4 = marked; > = multifocal.
CZ indicates carboxybutane zwitterionic; TaO, tantalum oxide.

No kidney damage

Fitzgerald et al. Invest Radiol 2016

New Contrast Agents - Hafnium

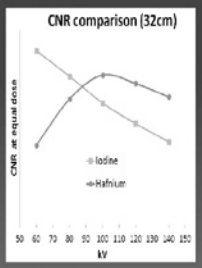
- Hafnium-(bits): Silvery metal

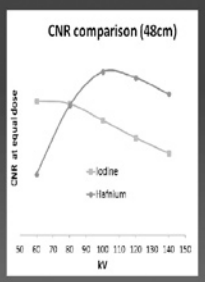


Element	k-edge keV
Iodine	33
Gadolinium	50.2
Holmium	55.6
Hafnium	**65.4**
Tantalum	67.4
Tungsten	69.5
Gold	80.7

High-Z elements (e.g. Hf) with optimum k-edge provide higher attenuation

New Contrast Agents - Hafnium

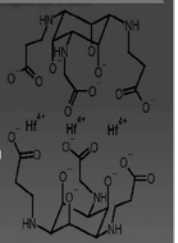




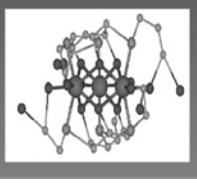
- At equal dose, Hafnium has a **higher CNR than Iodine at all tube voltages ≥ 80 kV for average sized and bigger patients**
- Iodine is better for small (pediatric patients) and at very low kV

New Contrast Agents - Hafnium

- **3 Hf^{4+} ions**
- **2 identical ligands^{5-} covering the Hf ions like a sandwich**
  - → neutral complex
- The asymmetrical ligand caries 2 propionate and one acetate chain
  - → **high water solubility**
- Molecular weight: 1282.1
  - → Hf-content: 41.8 % w/w



	Ultravist®	BAY Hafnium
Stability	stable	stable
Solubility in water	370mg I/mL	>380 mg Hf/mL
Osmolality	790 mosm/kg	860 mosm/kg
Viscosity	9.8 mPa*s	9.6 mPa*s

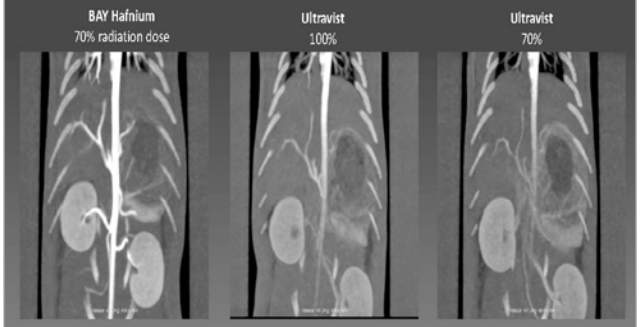


New Contrast Agents - Hafnium

- Effects of BAY Hafnium on erythrocytes were comparable to Gadovist® and less than for Ultravist®
  - → No hemolysis (free hemoglobin) was observed
  - → No histamine release
  - → No activation of the complement system was observed
- BAY Hafnium is excreted mainly through the kidneys
- Excretion was complete after 1 d. Less than 0.5% of the injected dose was present in the body after 7d (mainly in the kidney) - comparable to known extracellular contrast agents

New Contrast Agents - Hafnium

Arterial Vessels, bolus phase (same animal with 3 imaging protocols)



→ Comparable or higher CNR for BAY Hafnium with 30% radiation dose reduction compared to Ultravist® - great potential for higher dose reductions factors in CT-angiography

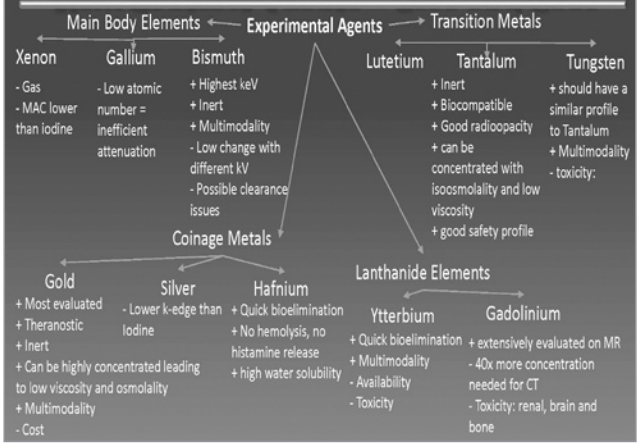
New Contrast Agents - Challenges

Atomic number (Z)	Name	Symbol	K edge (keV)	Annual production (metric tons)	Raw cost of material per 30 g dose (USD)	Concerns*
53	Iodine	I	33.2	>30,000	<1	I > 100 kVp
54	Xenon	Xe	34.6	<1		G
55	Cesium	Cs	36.0	<20	>600	T
56	Barium	Ba	37.4	6,000,000	<1	$BaSO_4$ T for IV
57	Lanthanum	La	38.9	12,000	<1	La_2O_3
58	Cerium	Ce	40.4	23,000	<1	CeO_2
59	Praseodymium	Pr	42.0	2,500	<1	Pr_6O_{11}
60	Neodymium	Nd	43.5	7000	<1	Nd_2O_3
61	Promethium	Pm	45.2			Synthetic
62	Samarium	Sm	46.8	700	<1	Sm_2O_3 A
63	Europium	Eu	48.5	100	<10	Eu_2O_3 C,A
64	Gadolinium	Gd	50.2	400	<1	Gd_2O_3 T, A
65	Terbium	Tb	52.0	10	<10	Tb_2O_3 C,A
66	Dysprosium	Dy	53.8	100	<20	Dy_2O_3 C,A
67	Holmium	Ho	55.6	10	<1	Ho_2O_3 A
68	Erbium	Er	57.5	500	<1	Er_2O_3 A
69	Thulium	Tm	59.4	50	<1	Tm_2O_3 A
70	Ytterbium	Yb	61.3	30	<1	Yb_2O_3 T, A
71	Lutetium	Lu	63.3	10	<50	Lu_2O_3 C,A
72	Hafnium	Hf	65.3	50	<20	HfO_2 C,A
73	Tantalum	Ta	67.4	<1,000	<1	Ta_2O_5 I >80 kVp
74	Tungsten	W	69.5			T
75	Rhenium	Re	71.7	45	>500	C,A
76	Osmium	Os	73.9	<1		C,A
77	Iridium	Ir	76.1	3	>500	C,A
78	Platinum	Pt	78.4	160	>1000	C,A
79	Gold	Au	80.7	2500	>1000	C,T
80	Mercury	Hg	83.1			High T
81	Thallium	Tl	85.5			High T
82	Lead	Pb	88.0			High T
83	Bismuth	Bi	90.5	8500	<1	I
84	Polonium	Po	93.1			High R

*G – gas; no stable solid compounds at room temperature.
T – toxicity.
C – cost.
A – availability.
I – imaging performance.
R – radioactivity (toxic).

Yeh et al., *Advanced Drug Delivery Reviews* 2016

New Contrast Agents – Pros and Cons



My Wish List for the Future

- **Contrast media enhanced imaging will further develop:**
  - Decrease of detection limits - potential for new, more specific compounds in MR
  - Optimized detector technology for CT - energy weighting, opportunity for new CM concepts
    - ✓ Total element decomposition for robust separation of different CM elements in CT
- **Identification of new indications for contrast media: with clear unmet medical need, real value based, patient centered & outcome orientated radiology!**

Collaboration between industry and radiologists with the aim to demonstrate the value & importance of innovation in Radiology

Conclusions and Outlook

- DECT has shown its ability for material differentiation of Iodine contrast from other structures
- Spectral CT by detecting more energy levels may allow further material differentiation through "multicolor CT"
- This could enhance plaque characterization, lumen visualization, allow the development of new contrast agents and potentially obviate the need for multiphasic scanning
- New non-iodine-based contrast materials differ in X-ray attenuation properties from current clinical contrast agents.
- May introduce profound diagnostic advantages at spectral CT and therefore may be worth long-term investment.
- Most are only investigated in vitro or on animal models as of yet
- Will need to be thoroughly vetted to minimize patient risks and ensure benefits


Thank you!
schoepf@musc.edu

MEMO

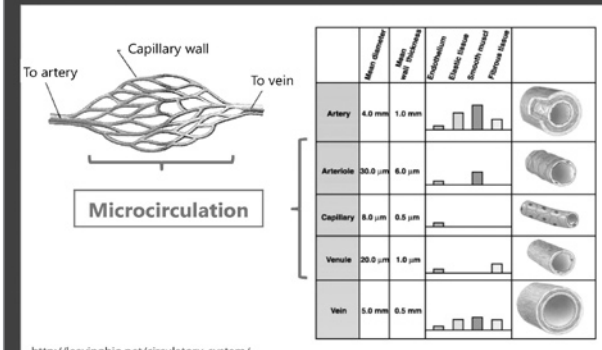
Myocardial microcirculation

Akira Kurata (Ehime University, Japan)

Contents

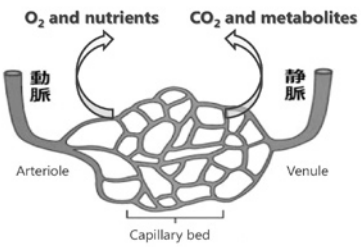
- Common knowledge
- Pharmacological aspect
- Hemodynamic aspect
- Morphological aspect
- Possible approach for microcirculation on CT

What? Where?



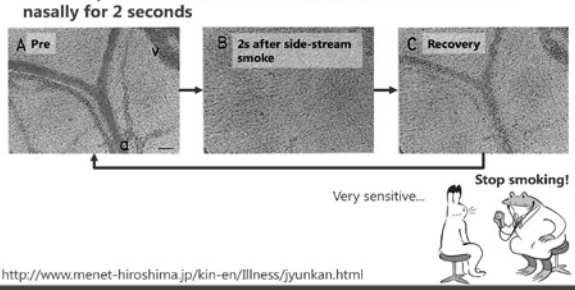
http://leavingbio.net/circulatory-system/

Function



Microcirculation (rabbit skin)

Changes in the microvessels (micro-circulation) of the rabbit skin changes in the blood vessels of the ear observed with a microscope when the rabbit was absorbed sidestream smoke nasally for 2 seconds



http://www.menet-hiroshima.jp/kin-en/Illness/jyunkan.html

Myocardial microcirculation

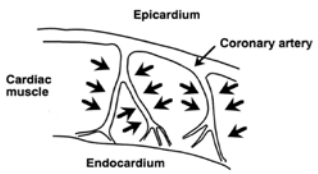


Fig. 1 Distribution of coronary arteries in the epicardium and endocardium. The coronary artery runs on the epicardial surface and turns toward the endocardium at a right angle. Arrows show the extravascular compression during systole.

(Hosokawa et al. Circ J 2011; 75: 1905-1912)

Anti-angina drug

Nitrates
- Nitroglycerin
- Isosorbide ndinitrates
- Nicorandil

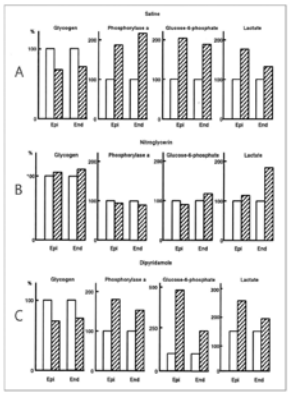
Coronary vasodilators (narrow)
- Dipyridamole
- Dilazep

Beta-Adrenergic blockers
- Propranolol
- Atenolol

Calcium antagonists
- Nifedipine
- Niludipine
- Diltiazem
- Verapamil

(Ishihara K, et al. Nihon Yakurigaku Zasshi. 1999; 113: 227-234)

Effects of the anti-angina drugs



Effects of saline, nitroglycerin and dipyridamole on changes in the endo and epicardial glycogen metabolism induced by ischemia for 3 min.

Ischemia was induced by ligation of the left anterior descending (LAD) coronary artery. Either saline (A), nitroglycerin (B), or dipyridamole (C) was intravenously injected 5 min before the coronary ligation. Ischemic myocardial samples were taken from the ischemic region of the myocardium 3 min after the coronary ligation (border bars) . The non-ischemic myocardial sample was also taken from a heart in which the coronary artery was not ligated (white bars).

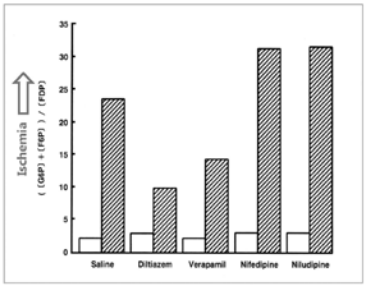
Normal myocardium

Ischemic myocardium by coronary ligation

(Ishihara K, et al. Nihon Yakurigaku Zasshi. 1999; 113: 227-234)

Kurata A, Ehime University

Effects of calcium antagonists

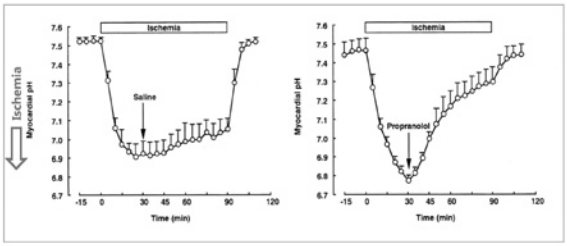


Effects of calcium antagonists on increase in the ([G6P] + [F6P]) / [FDP] of the myocardium caused by ischemia. The increase in the ratio can indicate an acceleration of anaerobic glucose metabolism. Either saline, diltiazem, verapamil, nifedipine was intravenously injected 5 min before the onset of ischemia. Calcium antagonists did not reduce myocardial ischemia.

(Ishihara K, et al. Nihon Yakurigaku Zasshi. 1999; 113: 227-234)

Kurata A, Ehime University

ATP stress static CTP (64MDCT)

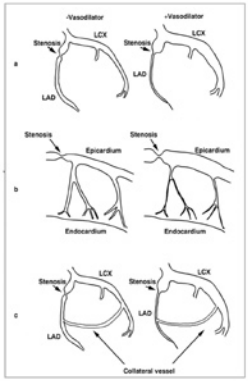


Effects of calcium antagonists on increase in the ([G6P] + [F6P]) / [FDP] of the myocardium caused by ischemia. The increase in the ratio can indicate an acceleration of anaerobic glucose metabolism. Either saline, diltiazem, verapamil, nifedipine was intravenously injected 5 min before the onset of ischemia. Calcium antagonists did not reduce myocardial ischemia.

(Ishihara K, et al. Nihon Yakurigaku Zasshi. 1999; 113: 227-234)

Kurata A, Ehime University

Coronary steal phenomenon



The coronary-steal phenomenon possibly observed when a coronary vasodilator is given.

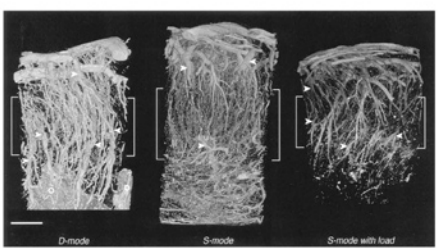
three types of coronary-steal: (a) the steal from the LAD region to the circumflex region (LCX), (b) from the endocardium to the epicardium, and (c) from the ischemic region to the normal region due to a decrease in per fusion pressure to the collateral vessel (c). The more potent the coronary vasodilator used, the more steal phenomenon could be observed.

(Ishihara K, et al. Nihon Yakurigaku Zasshi. 1999; 113: 227-234)

Kurata A, Ehime University

Hemodynamics of microcirculation

Dynamic changes in 3D architecture and vascular volume of transmural coronary microvasculature between diastolic- and systolic-arrested rat hearts



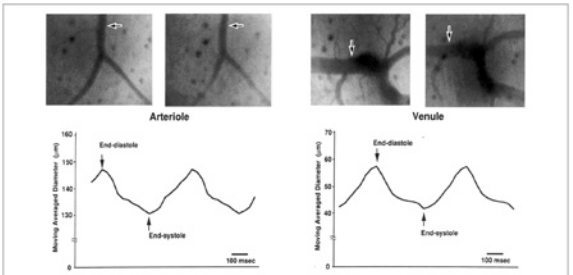
3D images of micro-vessel architecture visualized by synchrotron radiation microCT of SPring8 (left, D-mode (diastole); middle, S-mode (systole); and right, S-mode with load). Bar =1 mm.

(Toyota E, et al. Circulation. 2002; 105: 621-626)

Kurata A, Ehime University

Hemodynamics of microcirculation

In vivo observation of subendocardial microvessels of the porcine heart using a needle-probe video-microscope with a CCD Camera



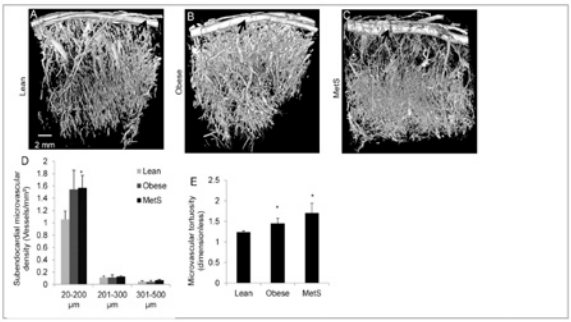
An example of the diameter change in a subendocardial arteriole (left panel) and venule (right panel) throughout a cardiac cycle

(Yada T, et al. Circ Res. 1993; 72: 939-946)

Kurata A, Ehime University

Morphological difference (pig model)

Transition from obesity to metabolic syndrome is associated with altered myocardial autophagy and apoptosis.



(Li ZL, et al. Arterioscler Thromb Vasc Biol. 2012; 32: 1132-1141)

Possible approach to microcirculation

- PET, SPECT
  - Metabolism (FDG, BMIPP)
  - Perfusion (NH_3, H_2O, Rb, Tc, Tl)
- MRI
  - Perfusion
  - Oxygen-sensitive T2 image
- CT
  - Phasic change of static CTP
  - Dynamic CTP

Phasic change of stress static CTP

Quantitative assessment of CTP in cardiac cycle

Multi-detector computed tomography detects reduced contrast enhancement during adenosine-stress in myocardial territories supplied by stenotic coronary vessels

Yasushi Koyama, Akira Kurata*, Wael A. Jaber, Neil L. Greenberg, Gardar Sigarsson, Yuichi Notomi, Hiroshi Higashino*, Shigeru Nakata*, Jitsuo Higaki*, Truhito Mochizuki*, Mario J. Garcia

	Group N (n=27)	Group S (n=19)	
Baseline			
Systolic HU	99.2 ± 21.0 †	113.7 ± 14.0 †	*p<0.0001*
Diastolic HU	109.2 ± 25.4	118.8 ± 13.3	*p<0.0001*
Adenosine stress			
Systolic HU	119.2 ± 21.7* †	102.4 ± 11.9* †	*p<0.0001*
Diastolic HU	129.3 ± 21.9*	110.9 ± 14.6*	*p<0.0001*
ΔH.U (stress- baseline)			
Systolic ΔH.U	20.0 ± 14.0	-11.3 ± 10.1	*p<0.0001*
Diastolic ΔH.U	20.1 ± 14.6	-7.8 ± 15.1	*p<0.0001*

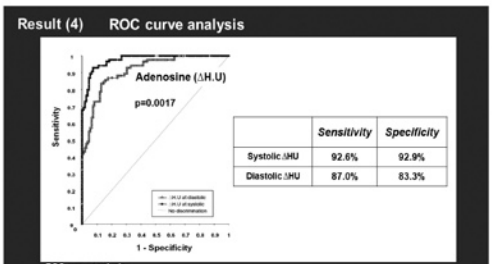
† p<0.0001 vs. diastole
** p<0.0001 vs. baseline

(Koyama Y, et al. SCCT2005)

Phasic change of stress static CTP

Quantitative assessment of CTP in cardiac cycle

Result (4) ROC curve analysis



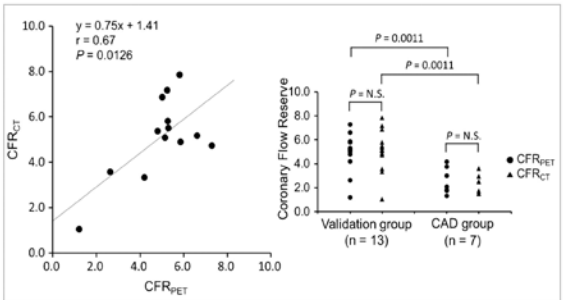
	Sensitivity	Specificity
Systolic ΔHU	92.6%	92.9%
Diastolic ΔHU	87.0%	83.3%

ROC curve analysis
- Adenosine stress MDCT was able to detect significant stenosis (≥75%), in the systolic ΔHU and the diastolic ΔHU with sensitivity 92.6% (95% confidence interval [CI] 85.9- 96.8, AUC 0.9750, ASE 0.0083, true positive (TP) 100/108, false positive (FP) 6/84, true negative (TN) 78/84, false negative (FN) 8/108) , 87.0% (95% CI 79.2- 92.7, AUC 0.9127, SE., 0.0199, TP 94/108, FP 14/84, TN 71/84, FN 14/108) and specificity 92.9% (95% CI 85.1- 97.3), 83.3% (95% CI 73.6- 90.5), cutoff ΔHU were 2.6 and 6.9 respectively by ROC curve analysis.
- In contrasting two ROC curves between the systolic ΔHU and the diastolic ΔHU using the difference of the AUC and SE, there were significant differences (Chi square 9.86, two-tailed p value 0.0017).

(Koyama Y, et al. SCCT2005)

Stress dynamic CTP

Quantification of myocardial blood flow using dynamic 320-row multi-detector CT as compared with 15O-H2O PET



(Kikuchi Y, et al. Eur Radiol 2014; 24:1547–1556)

Stress dynamic CTP

Annals of Biomedical Engineering, Vol. 42, No. 3, March 2014 (© 2013) pp. 515–525
DOI: 10.1007/s10439-013-0934-z

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Early Changes in Myocardial Microcirculation in Asymptomatic Hypercholesterolemic Subjects: As Detected by Perfusion CT

THOMAS R. BEHRENBECK,[1] CYNTHIA H. MCCOLLOUGH,[2] WAYNE L. MILLER,[1] ERIC E. WILLIAMSON,[2] SHUAI LENG,[2] TIMOTHY L. KLINE,[3] and ERIK L. RITMAN[3]

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(Received 30 May 2013; accepted 4 November 2013; published online 15 November 2013)

- dual-source CT (SOMATOM Flash, Siemens Healthcare, Germany)
  - Sequential scan mode at rest, 90 mA; 120 kV
  - ECG gated end-diastolic period with dose modulation
  - 280 ms/rotation (temporal resolution 70 ms);
  - 30 s for total scan sequence
  - Contrast, 350 mg-iodine/mL, at 5 ml/s, amount, 0.25 mL/kg
  - Dose 9.12–11.59 mSv (HR 50-60 bpm), 6.77–8.71 mSv (HR 70-90 bpm)

(Behrenbeck TR, et al. Ann Biomed Eng. 2014; 42: 515-525)

Stress dynamic CTP

Early Changes in Myocardial Microcirculation in Asymptomatic Hypercholesterolemic Subjects: As Detected by Perfusion CT

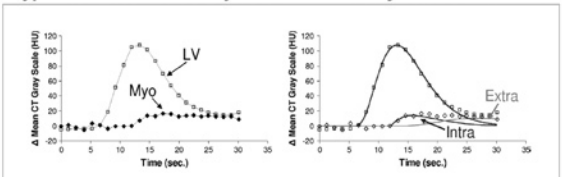


TABLE 3. CT image analysis-based parameters.

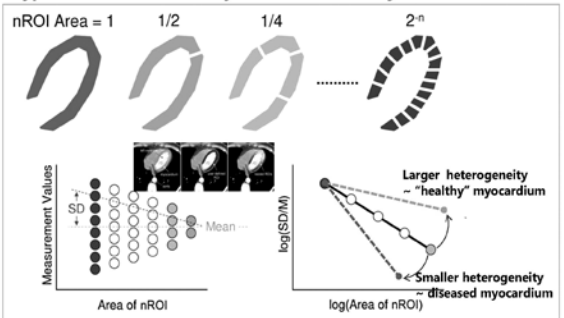
Parameter	Female control	Female at risk	Male control	Male at risk
CO/BMI (L m^2 min^{-1} kg^{-1})	0.25 ± 0.09[a]	0.20 ± 0.09[a]	0.35 ± 0.10[a]	0.33 ± 0.14[a]
Myocardial Bv (myocardium volume fraction)	0.11 ± 0.04	0.10 ± 0.03	0.10 ± 0.02	0.12 ± 0.03
Myocardial Perfusion (mL min^{-1} cm^{-3})	0.92 ± 0.54	1.07 ± 0.72	0.82 ± 0.18	1.08 ± 0.35

[a]Statistical difference across sex.

(Behrenbeck TR, et al. Ann Biomed Eng. 2014; 42: 515-525)

Stress dynamic CTP

Early Changes in Myocardial Microcirculation in Asymptomatic Hypercholesterolemic Subjects: As Detected by Perfusion CT



(Behrenbeck TR, et al. Ann Biomed Eng. 2014; 42: 515-525)

Stress dynamic CTP

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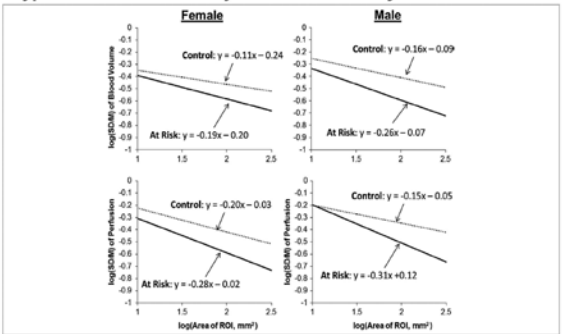
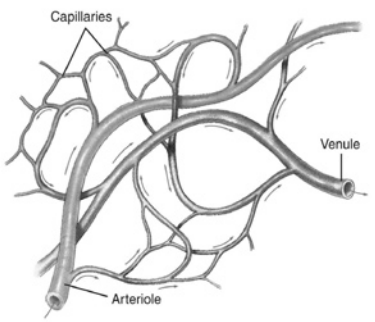


(Behrenbeck TR, et al. Ann Biomed Eng. 2014; 42: 515-525)

Take-home message

- **Myocardial microcirculation is**
  - **Complex**
  - **Sensitively affected by multiple factors (physiology, pharmacology, subclinical and disease-driven ~)**
  - **Beyond CT spatial resolution in clinical practice**
  - **(however) may be the next promising biomarker, if the methodology is established.**

Thank you very much for your attention



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Cardiovascular molecular imaging

Xiaohai Ma (Beijing Anzhen Hospital, China)

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OUTLINES

- Background
- In vivo tracing method
- Multimodal imaging of stem cells
- The commonly used stem cells
- Stem cells in the treatment of MI

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MI in CHINA

- The mortality of AMI is also increasing year by year. In 2013, the mortality rate of AMI in rural areas was much higher than that in cities

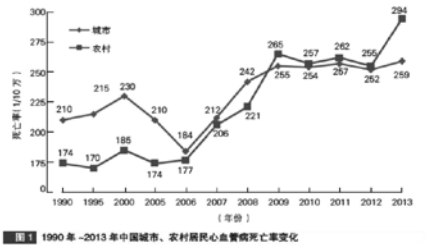

图1 1990年~2013年中国城市、农村居民心血管病死亡率变化

Chinese cardiovascular disease report 2014

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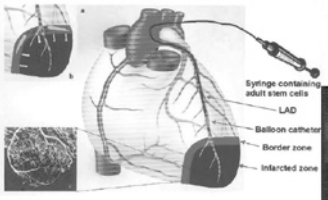
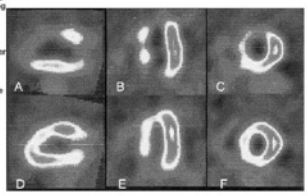
Stem cells in the treatment of AMI



SPECT: reduction of infarct size after 3 months of treatment
（30±13%→12±7%，P=0.005）



- In 2002, Strauer BE et al. confirmed the safety and effectiveness of stem cells for acute myocardial infarction for the first time in clinical practice

Circulation. 2002 Oct 8;106(15):1913-8.

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Problems to be solved by SC in the treatment of MI

- Evaluation of therapeutic effect
- Colonization and survival of stem cells after transplantation
- The mechanism of stem cells after transplantation
- Selection of stem cells

Molecular imaging is a powerful way to solve them!

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Common Molecular Imaging Probes

	PET：^{18}F-FDG
	SPECT：^{111}In-oxine, ^{111}In-tropolone, ^{99m}Tc-HMPAO
Direct labeling	MRI：SPIO, USPIO, MPIO
	US：Targeted microbubbles
	CT：Microencapsulation
	FI：Exogenous fluorescent dye
	PET：HSV1-tk
	SPECT：NIS
Reporting gene	MRI：Ferritin, transferrin receptor
	BLI：Firefly luciferase
	FI：fluorescin RFP, GFP

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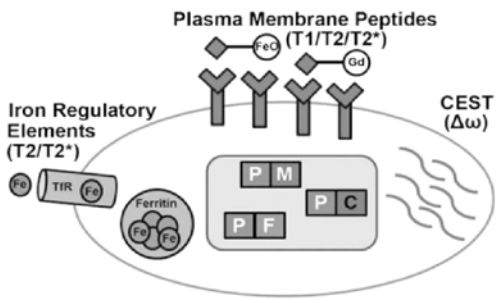
MRI value in reporting gene



Curr Cardiovasc Imaging Rep (2014) 7:9250

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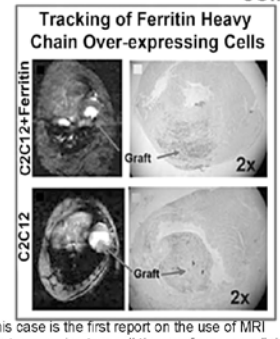
Ferritin labeling skeletal muscle myogenic cells



- Ferritin heavy chain
- Transfer into myogenic cells of skeletal muscle of mice (C2C12)
- T2 relaxation time reduced by at least 25%
- The deposition of iron particles after 4 weeks

* This case is the first report on the use of MRI reporter gene in stem cell therapy for myocardial infarction

Mol Imaging. 2010;9:201–10.

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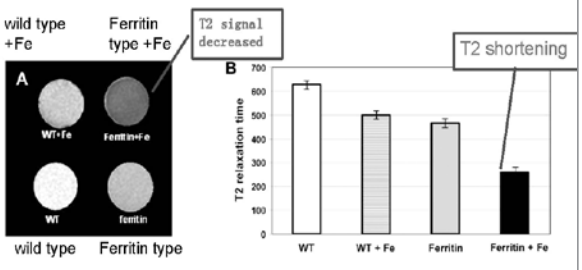
Ferritin labeling skeletal muscle myogenic cells



Mol Imaging. 2010;9:201–10.

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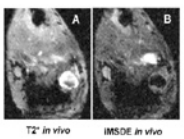
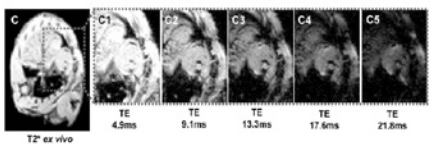
Ferritin labeling skeletal muscle myogenic cells



A in vivo T2*
B in vivo 2DIMSDE dark blood sequence



C In vitro (euthanasia 10min) T2*, T2* weighted images of different TE
The longer the TE time, the clearer the stem cells were displayed in T2*

Mol Imaging. 2010;9:201–10.

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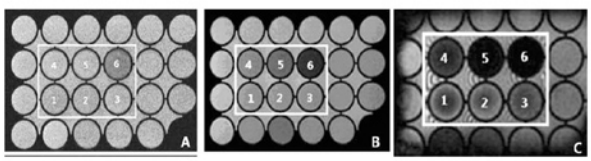
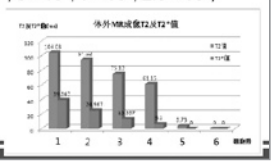
Direct labeling--USPIO Labelling mesenchymal stem cells



T1WI T2WI GRE

1→6 cells increased (ml-1) 5×10^2, 5×10^3, 5×10^4, 1×10^5, 2.5×10^5, 5×10^5



曹剑，王怡宁*，协和医学杂志，2011，2（3）：252-257.

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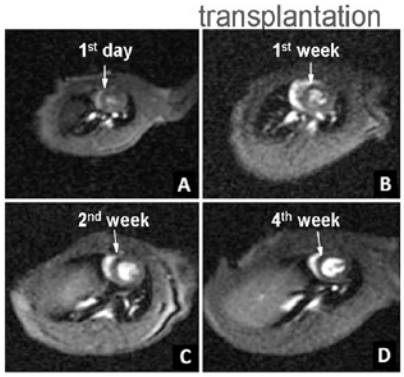
USPIO labeled MSC of rat heart MR after transplantation



A 1st day
B 1st week
C 2nd week
D 4th week

The T2 signal reduction area (arrow) was seen in the anterior wall of the left ventricle, and the size of the signal reduction area did not change significantly over time

FSPGR

曹剑，王怡宁*，中国医学科学院学报，2012，34（5），474-479.

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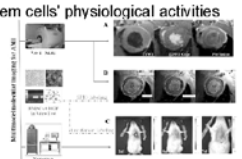
The significance of dual / multimodal tracing of SC

- No molecular imaging technology can solve all the problems of stem cell tracing
- The combination of multiple imaging modes to solve the problems in the research
  - Make up for the deficiency of single imaging mode
  - More comprehensive assessment of stem cells' physiological activities in vivo



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Issue 1: Can stem cell transplantation really survive and proliferate in vivo?

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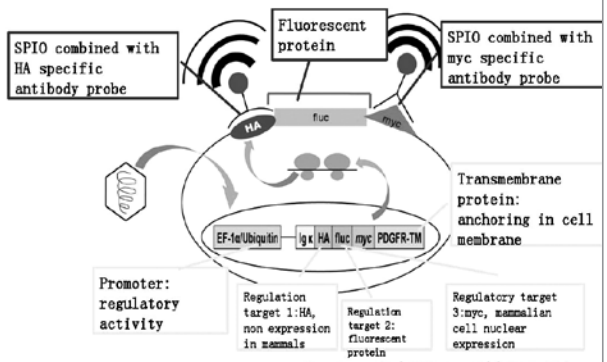
Dual modal (BLI/MRI) labeling ESC



Magn Reson Med. 2011 Nov; 66(5): 1374–1381

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Issue 2: If transplantation of SCs is effective, will the number of transplanted SCs be related to the repair of cardiac function?

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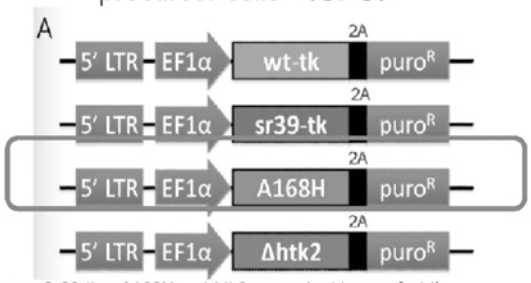
PET/BLI dual mode tracing of cardiac precursor cells （CPC）



- Sr39-tk，A168H，△htk2 are mutant types of wt-tk
- The strongest PET reporter gene was screened by previous experiments A168H

Circ Cardiovasc Imaging. 2012 Jul;5(4):481-90.

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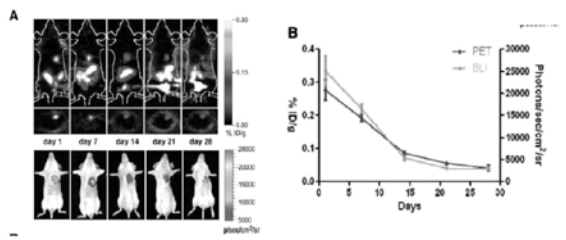
PET/BLI dual mode tracing of cardiac precursor cells （CPC）



Fluc + tk dual labeled cardiac precursor cells (CPC)
BLI+PET dual mode tracing

The simultaneous reduction of PET and BLI label at 28 days was observed

Circ Cardiovasc Imaging. 2012 Jul;5(4):481-90.

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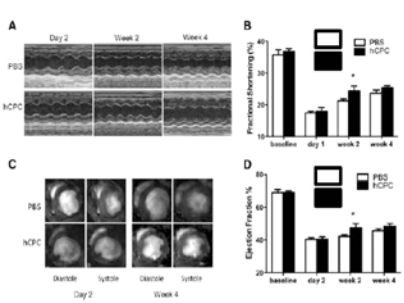
PET/BLI dual mode tracing of cardiac precursor cells （CPC）



Cardiac function was assessed by echocardiography and MRI, which was improved in the experimental group

Circ Cardiovasc Imaging. 2012 Jul;5(4):481-90.

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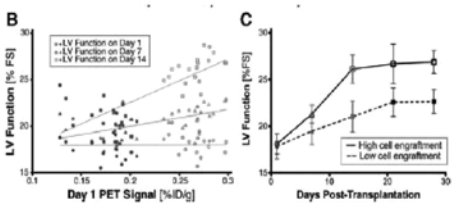
PET/BLI dual mode tracing of cardiac precursor cells （CPC）



- With increase of the number of transplanted cells, LVEF improved more
- The number of stem cell colonization is related to the improvement of cardiac function

Circ Cardiovasc Imaging. 2012 Jul;5(4):481-90.

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Issue 3: Can stem cell transplantation survive *in vivo* for a long time?

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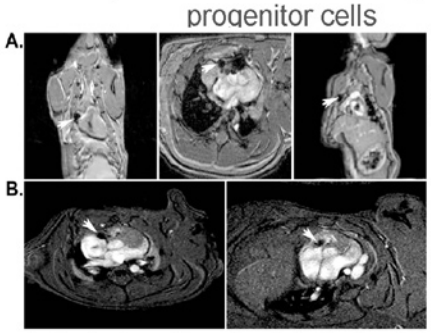
MRI/μCT dual mode tracer myogenic progenitor cells



- Implantation of myogenic progenitor cells into the atrioventricular groove of mice
- Observation of long-term tracer effect of SPIO in vivo, negative contrast agent on T2

PLoS One. 2014 Sep 24;9(9)

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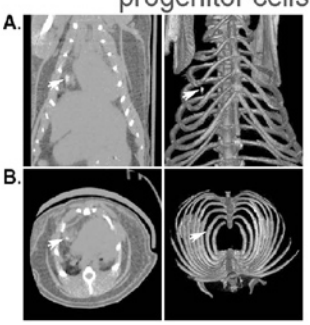
MRI/μCT dual mode tracer myogenic progenitor cells



Observation of long-term tracer effect of SPIO in vivo, negative contrast agent on μCT

PLoS One. 2014 Sep 24;9(9)

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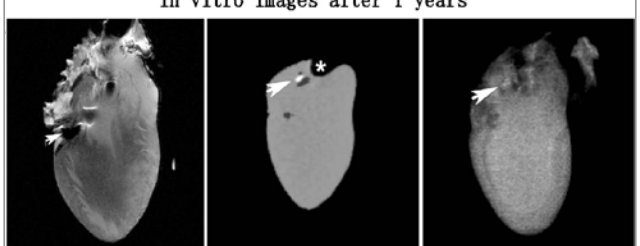
MRI/μCT dual mode tracer myogenic progenitor cells

In vitro images after 1 years



MRI　　CT (single slice)　　CT (VRT)

SPIO can serve as a long-term tracer marker, and MRI and CT can complement each other

PLoS One. 2014 Sep 24;9(9)

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Issue 4: How to assess cardiac activity in a comprehensive way?

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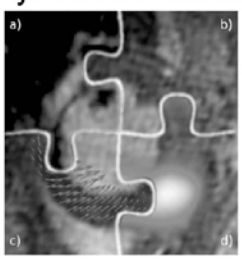
PET/MRI dual mode assessment of myocardial infarction

LGE MRI
MI area
enhanced



Cine MRI
Overall assessment
of cardiac function

DENSE MRI
assess local
myocardium movement

PET
assessment of cardiac
myocyte metabolism

Nucl Instrum Methods Phys Res A.2014 Jan 11;734B:152-155

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Issue 5: How to select suitable SC types with molecular imaging?

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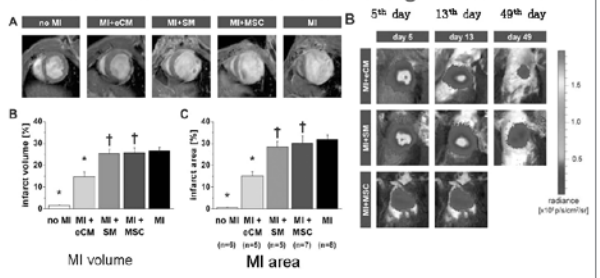
MRI/BLI dual mode screening stem cells



- Fluc label: ①eCMs ②SMs ③MSC
- Compared with the other two cells, eCMs has a longer survival time, which can significantly limit the infarct size and improve ventricular function

PLoS ONE 2013, 8(4): e61610

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embryonic stem cell (ESC)

- Advantage
  - The highest potential of division and differentiation
- Disadvantage
  - Allogeneic origin, immune incompatibility, and teratoma risk
  - Secondary ethical problems
- The results of animal experiments are good, and there is no clinical trial of ESC yet

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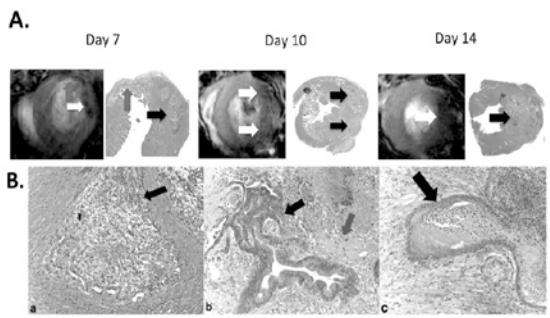
Risk of secondary teratoma secondary to embryonic stem cells



Magn Reson Med. Author manuscript; available in PMC 2012 Nov 1.

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Cardiac stem cells (CSC)

- Advantage
  - Having the ability to dividing and to differentiate myocardium
  - After MI event, the number increased rapidly and migrated
- Disadvantage
  - The number of cells is scarce
  - Short life-span of cells
  - The short life span of cells requires differentiation, and is not easy to collect and culture directly

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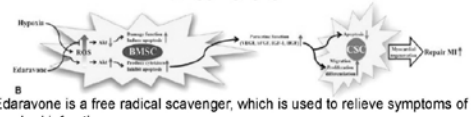
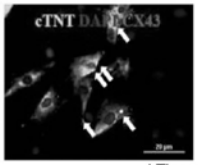
Edaravone induces BMSC to differentiate into CSC



- Edaravone is a free radical scavenger, which is used to relieve symptoms of acute cerebral infarction
- Implanting removal of serum and in vitro culture of edaravone BMSC in the MI model of mice
- BMSC activates paracrine under hypoxic and edaravone stimulation:
  - VEGF
  - bFGF
  - IGF-1
  - HGF



- cTNT and CX43 are expressed only in CSC
- BMSC apoptosis decreases, division increases, and differentiating to CSC

J Thorac Cardiovasc Surg. 2016 Mar 12.

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Induced pluripotent stem cells (iPSC)

- Regenerated and induced by embryonic cell (ESC-like cells)
- Advantage
  - Remodeling the structure and function of the myocardium in the short term
  - no ethical problem
- Disadvantage
  - Still have the possibility of inducing tumor formation

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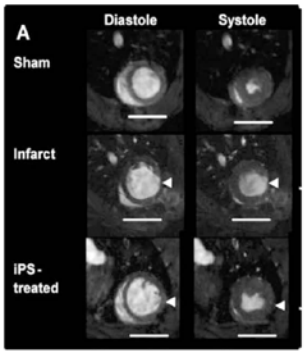
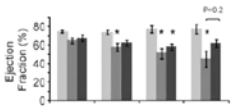
iPSCs have a trend of differentiation





- GFP labeled iPSCs was implanted in the tissue of myocardial infarction, and observed 10W
- it is not obvious in the improvement of heart function （P=0.2）
- immunohistochemistry confirmed that part of iPSCs had been differentiated into cardiomyocytes, smooth muscle cells and vascular epithelial cells in vivo

STEM CELLS AND DEVELOPMENT 2012, 21(6), 977-986

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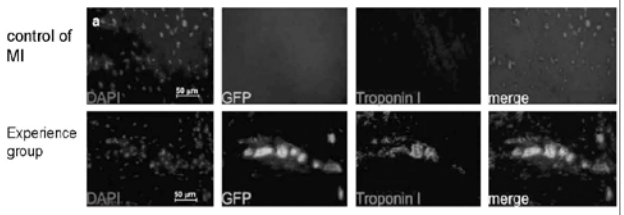
iPSCs have a trend of differentiation



Immunofluorescence results of IPSCs transplantation 10 weeks after transplantation

- Detection of apoptosis by DAPI
- GFP-labeled PSCs
- Troponin I,α-actinin labeled myocardium, SMA labeled blood vessels
- The image shows the good differentiation trend of iPSCs

STEM CELLS AND DEVELOPMENT 2012, 21(6), 977-986

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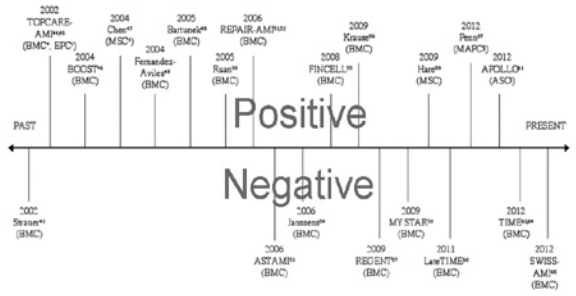
Clinical trials of SC in the treatment of AMI



J Gen Intern Med. 2013;28(10):1353–63.

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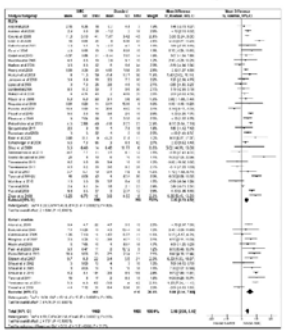
Effect of stem cells in the treatment of acute myocardial infarction



- 50 studies, 2626 patients
- BMC in treatment of MI
- LVEF improved of 3.96%
- MI area decreased of 4.03%

Circulation. 2012 Jul 31; 126(5): 551–568.

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SUMMARY

- Selecting suitable stem cells and tracing the biological behavior after stem cell transplantation by molecular imaging, revealing the therapeutic mechanism
  - ESC, CSC, iPSC have clear myocardial differentiation ability and are a hot spot for pre clinical research
  - The ability of BMC to differentiate into myocardium is controversial, but there are many clinical applications
- Dual / multimodal molecular imaging methods make up for the inadequacy of single imaging modalities
  - Selection of transplanted stem cells
  - In vivo mechanism of transplantation of stem cells
  - Dynamic monitoring of transplanted stem cells

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Thanks for your attention !

MEMO

Onco-cardiology imaging

Yoojin Hong (Severance Hospital, Korea)

Advances in cancer therapy have resulted in significant improvement in long-term survival for many types of cancer but have also resulted in untoward side effects associated with treatment.

Cancer therapies including cytotoxic chemotherapy, molecular targeted therapies, and mediastinal irradiation have been linked to myocyte damage, left ventricular dysfunction (LVD), heart failure (HF), thrombogenesis, pericardial pathology, hypertension, ischemia, conduction and rhythm disturbances, and vasospasm. HF as a result of cancer therapy has been linked to a 3.5-fold increased mortality risk compared with idiopathic cardiomyopathy

Chemotherapy induced cardiotoxicity is a well-recognized adverse effect of cancer treatment. Because it causes irreversible cardiac damage, early diagnosis, and treatment is clinically important. Especially the anthracycline class of cytotoxic agents is well known cardiotoxic agents. Although they are highly effective against a broad spectrum of malignancies including breast cancer. But they are the most notorioius agent with cumulative dose related cardiotoxicity. Considerable myocardial damage is known to occur below the known threshold level. The prevalence of chemotherapy-induced cardiotoxicity is relatively high up to nine percents. The currently used diagnostic tools include multigated acquisition (MUGA) imaging. However, these techniques require radiation exposure and lack precision, and are reported to have low sensitivity for early detection of cardiotoxicity.

Existing guidelines offer no clear consensus regarding the timing or duration of such surveillance. LVEF identification is the method most commonly used to screen for cardiotoxicity. No other imaging modalities have been specified for monitoring cardiac function during anthracycline therapy. Accordingly, a reliable, noninvasive early cardiotoxicity detection and serial monitoring method is needed. Cardiac MRI has an important role in early diagnosis and treatment of cardiotoxicity. MRI offers a much higher level of accuracy for cardiac functional analysis than echocardiography or MUGA imaging. The newly developed T1 mapping sequence is a highly accurate and attractive method for myocardial tissue characterization.

In this lecture I will discuss the role of cardiac imaging (MR or CT) in oncocardiology.

MEMO

Research progress of cardiac CT on RSNA 2017

Jian Cao (Peking Union Medical College Hospital, China)

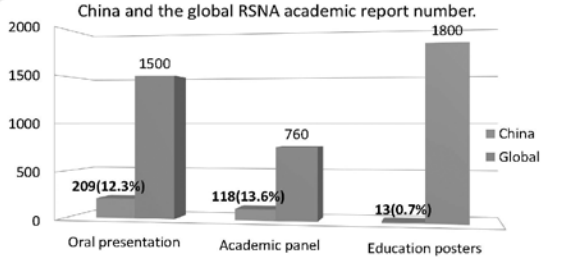
Content

1. 2017 RSNA overview
2. Research progress on Cardiac CT
3. Equipment progress on Cardiac CT

Content

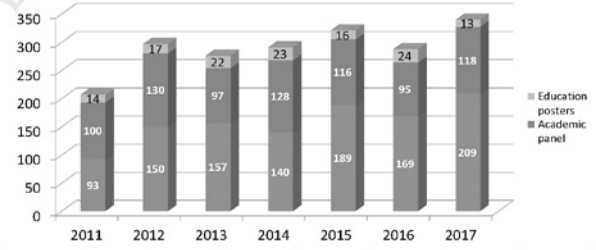
1. 2017 RSNA overview
2. Research progress on Cardiac CT
3. Equipment progress on Cardiac CT

2017 RSNA overview



- This year RSNA has about 1,500 oral presentations, 760 academic panels and 1,800 education posters.
- The number of academic reports in China accounts for 8% of the global RSNA academic report.

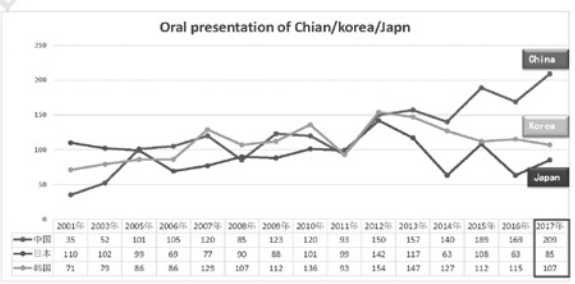
Number of academic report of Chinese scholar



Type	2011	2012	2013	2014	2015	2016	2017
academic report number	207	297	276	291	321	288	340

The total volume of academic report of Chinese scholar on RSNA is increasing.

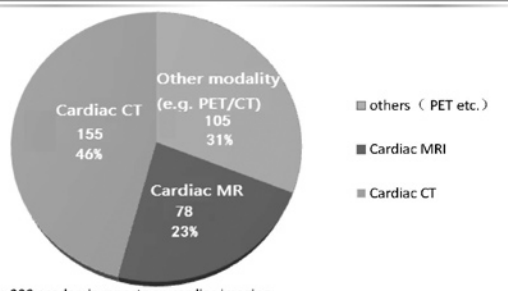
Number of oral presentations of three East Asia counties



	2001年	2003年	2005年	2006年	2007年	2008年	2009年	2010年	2011年	2012年	2013年	2014年	2015年	2016年	2017年
中国	35	52	101	105	120	85	123	120	93	150	157	140	189	169	209
日本	110	102	99	69	77	90	88	101	99	142	117	63	108	63	85
韩国	71	79	86	86	126	107	112	136	93	154	147	127	112	115	107

On 2017 RSNA Chinese scholar make far more oral presentations over Japanese and South Korean.

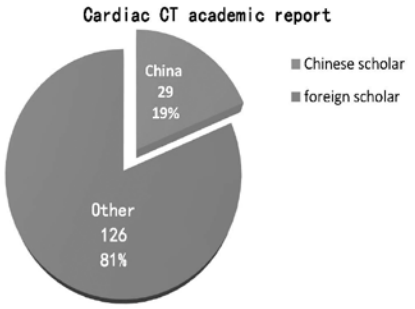
2017 RSNA cardiac imaging academic report



- There were 338 academic reports on cardiac imaging.
- There were 155 academic report about cardiac CT , accounting for 46% of all cardiac academic reports.

Retrieve "Cardiac CT" as key word,338 articles, and "Cardiac MRI" as key word, 78 articles

2017 RSNA cardiac imaging academic report

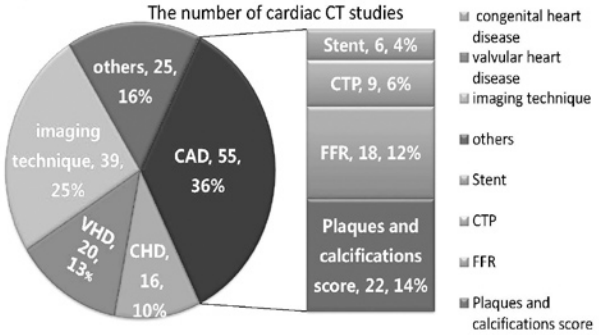


- Among all cardiac CT report, 29 were from Chinese scholars, accounting for 19% of total number.

Retrieved "China" as key word, 29 articles.

Content

2017 RSNA Cardiac CT overview



155 studies about Cardiac CT

2017 RSNA Cardiac CT overview

- Hot spot:
  - CT new technology, functional imaging (4D-CT, 3D printing, FFR, etc.) used in coronary heart disease. ;
  - Research and application of Photon counting CT;
  - Machine learning/deep learning in the application of cardiac CT
- Compare to 2016:
  - Studies on perfusion imaging decreased and FFR related studies increased;
  - Studies on new technology, machine learning increased

Photon Counting CT

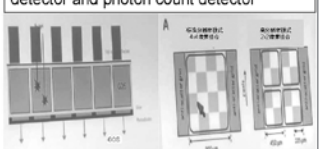
250 Micron Resolution Photon-Counting CT: Potential for Improved Imaging of Calcified Coronary Artery Stenosis Veit Sandfort et. al

Purpose: to determine the potential utility of ultra-high resolution (UHR) (250 micron PCD CT using ex-vivo hearts

Method and materials:

- N=5
- Image acquisition:
  - Hybrid energy detector (EID) :
    0.5mm resolution (D50 kernel)
  - Photon counting detector (PCD) :
    0.5mm resolution (D50 kernel)
    0.25mm resolution (S80 kernel)
- Measurements:
  - CT value of calcified plaque;
  - The volume of calcified plaque;
  - stenosis of the coronary artery.

High resolution image of hybrid energy detector and photon count detector



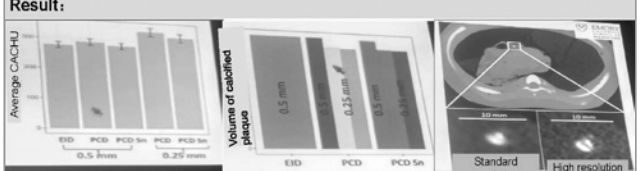
Somatom FORCE
- Hybrid energy detector.
- Comb filter.
- High resolution scanning mode.

Somatom CounT
- 2x2 sub-pixel combination.
- High resolution scanning mode (0.5 and 0.25mm)

Ulzhving, Stefan and Steffen Kappler."Photon-counting Detectors""SOMATOM Sessions.71"

Photon Counting CT

Result:



CT value of calcified plaque	Volume of calcified plaque	Stenosis of coronary artery
• There was no significant difference between EID and PCD on CT value of calcified plaque	• The volume of calcified plaques in ultrahigh resolution (0.25mm) images decreased significantly	• The ultrahigh resolution (0.25mm) image can be used to observe the degree of coronary artery stenosis more clearly.

Conclusion:

250 micron resolution photon-counting CT resulted in lower calcium volumes, reflecting less calcium blooming
250 micron resolution photon-counting CT resulted in larger lumen diameter measurements and enabled successful detection of the lumen in all calcified stenosis while standard resolution failed to depict the lumen

EID：Hybrid energy detector PCD：Photon count detector

FFR

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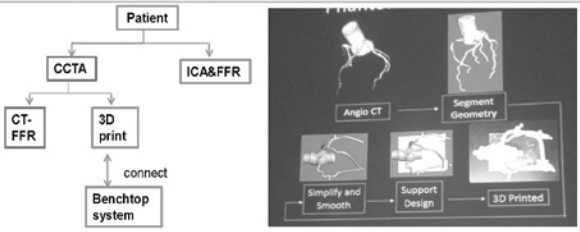
3D Printed Patient-Specific Coronary Models for Testing CT-Derived FFR

Lauren Shepard et al.

Purpose:

to develop patient-specific 3D printed coronary flow phantoms which can supplant or support expensive clinical trials for validation of CT-derived FFR technologies

METHOD AND MATERIALS:



3D printing process

FFR

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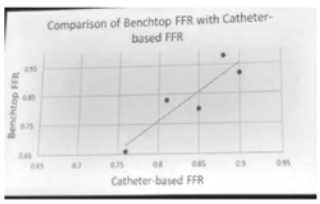
Result:



Benchtop FFR and catheter-based FFR (r=0.9)

Benchtop FFR and CT-FFR (r=0.86)

Conclusion:

This novel benchtop system can supplant the cost and risk of initial validation and optimization of CT-derived FFR technologies.

CTA enhancement protocol optimization

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Coronary Artery Enhancement for Coronary CT Angiography and Plaque Analysis: Optimization with a Test Bolus and Contrast Dilution Protocol

Veit Sandfort et. al

Purpose: three contrast injection protocols for CCTA and compared both mean levels and standard deviation of contrast enhancement

METHOD AND MATERIALS:

parameters	weight-based injection Protocol （n=60）	bolus injection Protocol 1 （n=32）	bolus injection Protocol 2 （n=59）
iodine dose	<60kg：50ml	bolus injection：20% 65ml Iopamidol	bolus injection：30% 75ml Iopamidol
	60-100kg：60ml	CCTA：X%, 65ml	CCTA：Y%, 75ml
	>100kg:70m		
injection rate	>5 ml/s	>5 ml/s	4.5 m/s
HU trigger	400HU	NA	NA

Image analysis:

- CT values of ascending aorta, descending aorta, left atrium and coronary artery;
- Changes in CT values of ascending aorta and coronary artery;

To determine the optimal time for the comparison of coronary CT angiography, and to meet the following conditions:

- HU of ascending aorta > HU of left atrium.
- HU of ascending aorta > HU of descending aorta.

X% = 20%x[(target imaging HU—aorta HU before enhancement)/(bolus injection HU—aorta HU before enhancement)]
Y% = 30%x[(target imaging HU—aorta HU before enhancement)/(bolus injection HU—aorta HU before enhancement)]

CTA enhancement protocol optimization

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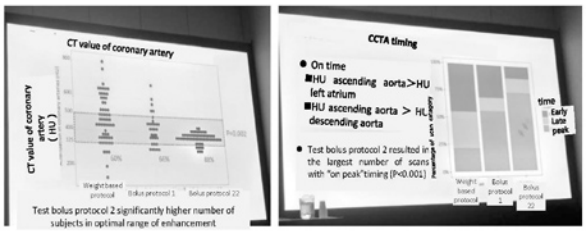
Result:



inter-study variation of the test-bolus method was significantly lower than that of the body weight injection protocol

CONCLUSION:

A test-bolus guided injection protocol with variable contrast dilution allowed greatly improved standardization of coronary and aortic attenuation levels for coronary CT angiography

Technique

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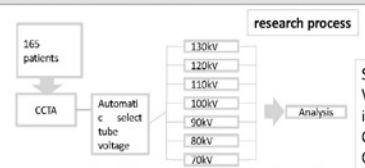
CCTA：Tube-Voltage Adapted Contrast Media Injection Protocol

Philipp L. von Knebel Doeberitz et al.

Purpose:

a simple, kVp-tailored contrast media (CM) injection protocol for coronary CT angiography (CCTA)

METHOD AND MATERIALS:



Subjective analysis:
Vascular enhancement and image noise;
Objective analysis:
CNR, SNR and CT value of coronary artery.

Tube voltage （kV）	70	80	90	100	110	120	130
Minimum iodine flow rate （gI/s）	0.7	0.8	1.0	1.1	1.3	1.4	1.7
CM （370 mgI/mL	35	39	45	40	50	60	70

Technique

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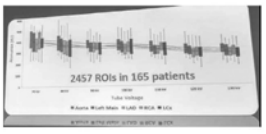
Result:

- The 70kVp protocol achieved the highest average attenuation (377 HU), significantly higher than protocols >= 110kVp (P< 0.001)
- The 80kVp protocol rendered the highest CNR (20.3), comparable to 70kVp and 90kVp (17.9 and 14.3, respectively; P> 0.05), while significant differences were found with >=100 kVp protocols (P> 0.01).
- No significant differences were found in subjective image quality (P=0.691).



The CT value of coronary artery decreased with tube voltage increase.

Conclusion:

The proposed kVp-tailored CM injection protocol allows for substantial reductions in CM administration while maintaining diagnostic vessel attenuation in CCTA.

Content

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1 2017 RSNA overview

2 Research progress on Cardiac CT

3 Equipment progress on Cardiac CT

Cardiac CT equipment progress

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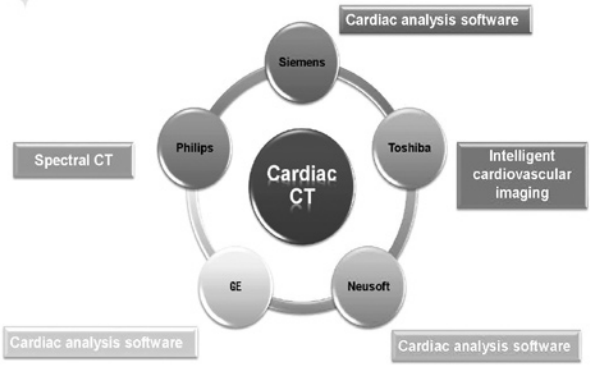
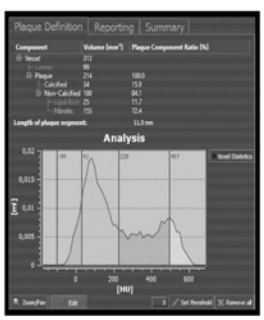


syngo.via Prototypes Coronary Plaque Analysis (Syngo Energy)

SIEMENS Healthineers



CT

- This prototype allows volumetric quantification and differentiation of lipid, fibrous, and calcified plaques.
- Advanced tools for analyzing atherosclerotic plaque morphology and characterizing different plaque composites, such as lipid and fibrous:
  - Overall Plaque Burden
  - Segment Involvement Score
  - Quantitative Remodeling Index
  - Quantitative Eccentricity Index
- Potential to assess the vulnerability of atherosclerotic lesions and evaluate strategies for stabilizing plaque

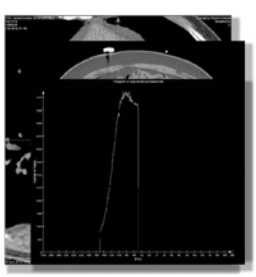
syngo.via Prototypes Coronary Plaque Analysis (SE/DE)

SIEMENS Healthineers

- Volumetric quantification and differentiation of lipid, fibrous, and calcified plaques based on both HU and Dual Energy Index

syngo.via Prototypes Cardiac Risk Assessment

SIEMENS Healthineers

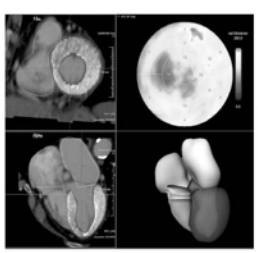


CT

- Automatic quantitative pericardial fat analysis
- Analysis of visceral fat.
- Risk assessment for cardiovascular disease and type 2 diabetes

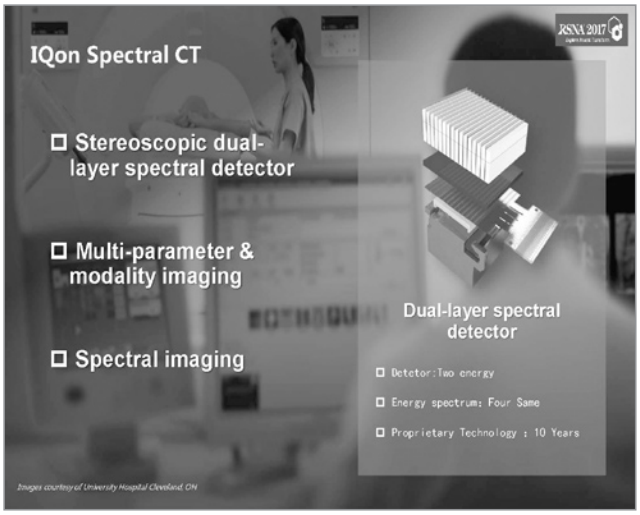
syngo.via Prototypes Cardiac Functional Analysis

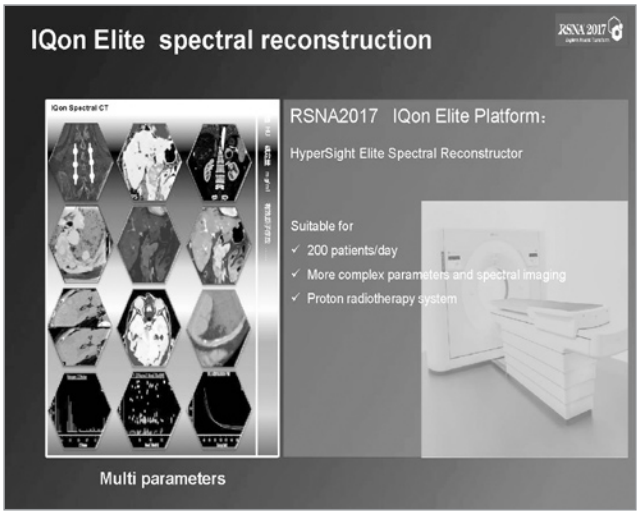
SIEMENS Healthineers

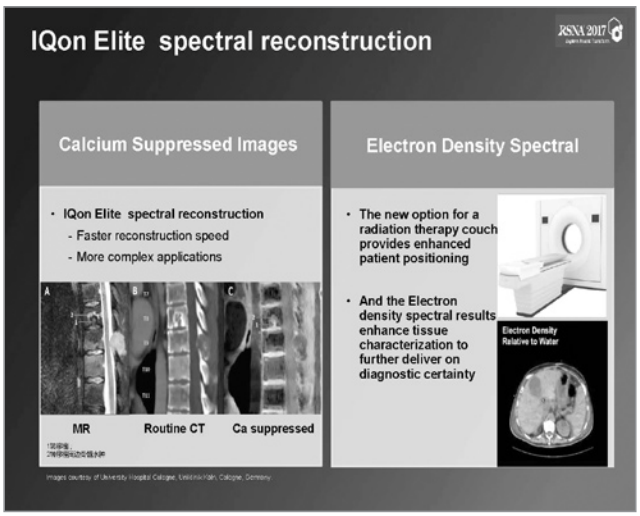


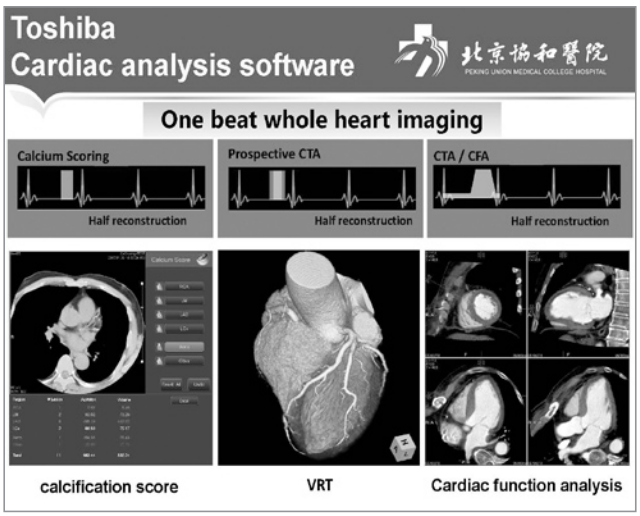
CT

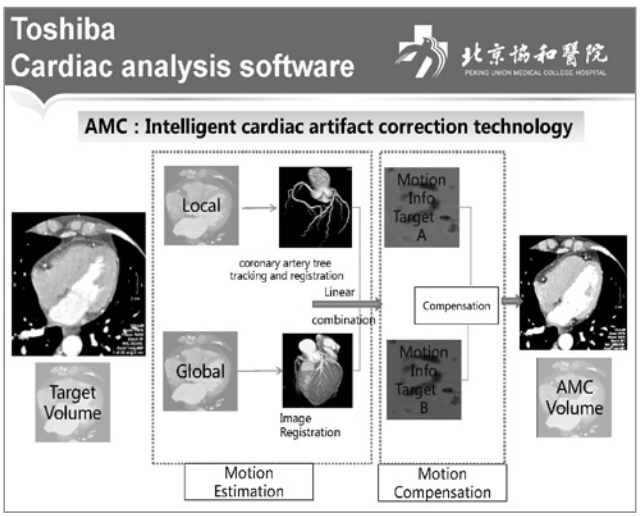
- functional analysis of the heart
- Incorporates stress and rest studies, static , dynamic myocardial perfusion, multiphase CTA, Dual Energy Perfused Blood Volume, and others
- Quantitative statistical analysis of 2D polar map-related AHA segments and user-defined ROIs in the underlying 3D data
- Automatic segmentation of left ventricle (epi- and endocardium), right ventricle, and left and right atria

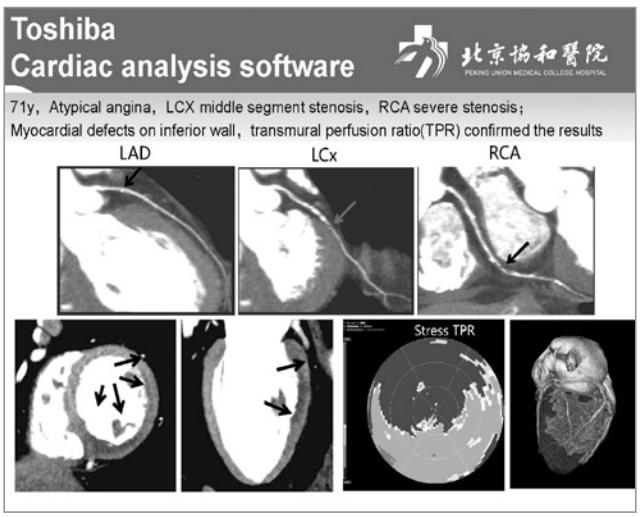

IQon Spectral CT
Stereoscopic dual-layer spectral detector
Multi-parameter & modality imaging
Spectral imaging
Dual-layer spectral detector
Detetor:Two energy
Energy spectrum: Four Same
Proprietary Technology : 10 Years
Images courtesy of University Hospital Cleveland, OH


IQon Elite spectral reconstruction
RSNA2017 IQon Elite Platform:
HyperSight Elite Spectral Reconstructor
Suitable for
200 patients/day
More complex parameters and spectral imaging
Proton radiotherapy system
Multi parameters


IQon Elite spectral reconstruction
Calcium Suppressed Images
IQon Elite spectral reconstruction
- Faster reconstruction speed
- More complex applications
MR
Routine CT
Ca suppressed
Electron Density Spectral
The new option for a radiation therapy couch provides enhanced patient positioning
And the Electron density spectral results enhance tissue characterization to further deliver on diagnostic certainty
Electron Density Relative to Water


Toshiba
Cardiac analysis software
北京協和醫院
One beat whole heart imaging
Calcium Scoring
Prospective CTA
CTA / CFA
Half reconstruction
calcification score
VRT
Cardiac function analysis


Toshiba
Cardiac analysis software
北京協和醫院
AMC : Intelligent cardiac artifact correction technology
Local
Global
coronary artery tree tracking and registration
Linear combination
Image Registration
Motion Info Target A
Motion Info Target B
Compensation
Target Volume
AMC Volume
Motion Estimation
Motion Compensation


Toshiba
Cardiac analysis software
北京協和醫院
71y, Atypical angina, LCX middle segment stenosis, RCA severe stenosis;
Myocardial defects on inferior wall, transmural perfusion ratio(TPR) confirmed the results
LAD
LCx
RCA
Stress TPR

GE Cardiac CT

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First dedicated Cardiac CT

Wide：1-beat Cardiac imaging, 14cm detector

Fast：0.24 s/r +
SSF coronary track and freeze

Accurate： "One-stop"
morphology + functional imaging

GE Cardiac CT

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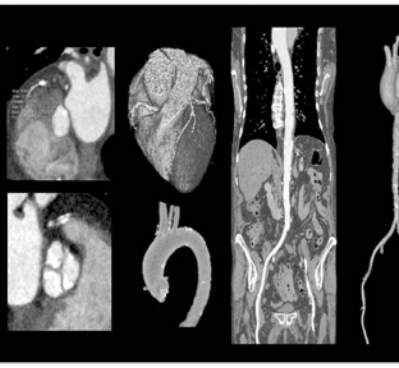
1-beat coronary artery & spectral aorta TAVR analysis with 37ml contrast

Scan type	Axial Gated Heart
Rotation time, s	0.35
Scan length, mm	160
kV	70
mA	499
ASIR-V %	50
CTDIvol, mGy	7.51
DLP, mGy·cm	120.24
Scan type	GSI Chest/abd/Pel vis
Rotation time, s	0.5
Pitch	0.992
Scan length, mm	500
mA	485
ASIR-V %	50
CTDIvol, mGy	12.25
DLP, mGy·cm	7999.0



GE Cardiac CT

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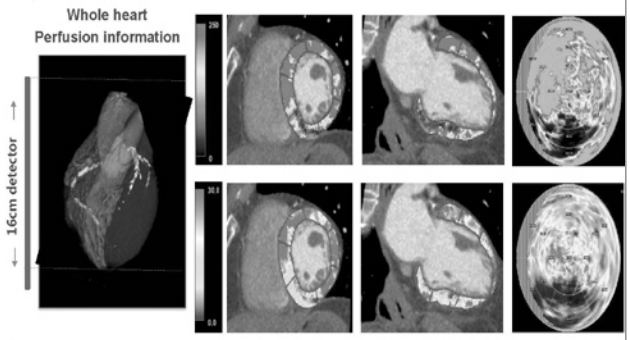
Whole heart
Perfusion information

16cm detector



GE dynamic stress myocardial perfusion 17-segment accurate analysis

GE Cardiac CT

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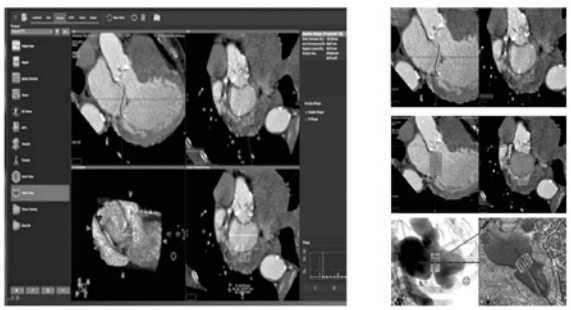
GE mitral valve analysis software



Neusoft Cardiac analysis software

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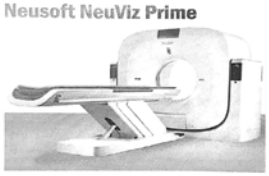
Neusoft Medical Systems Co., Ltd.
BOOTH 2538
Neusoft NeuViz Prime



"The newest NeuViz Prime express pectral CT from Neusoft Medical, Cardiac analysis software and 0.259 s/r assist in acquiring high quality medical images。"

---2017 RSNA Technology focus

Neusoft Cardiac analysis software

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Broaden Heart Rate range
- 0.259 s/r
- 25ms temporal resolution

Increase scanning success rate
- Skip premature beat
- Intelligent electrocardio-edit, auto-selection of best phase
- Motion artifacts correction

Decrease effective radiation dose
- Auto-modulation of tube current
- ClearView + iteration algorithm

Simplify workflow of scan and post-progress
- internally installed ECG monitor
- Intelligent protocol selection
- Convenient and efficient post-progress（Hidden coronary tree function）

Neusoft Cardiac analysis software

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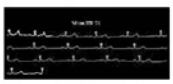
High heart rate	Low dose	"One-stop" chest pain triad syndrome
		
Retro-scan（100kVp, 750mAs, 120mm, 4s,31.2mGy, 374.6mGy.com, 5.24mSv) 350 mgI/ml contrast：60ml，5ml/s; saline：30ml，5 ml/s	Pro-scan（100kVp, 30mAs, 130mm, 4.18s,1.6mGy, 26mGy.com, 0.36mSv) 350 mgI/ml contrast：55ml，5ml/s; saline：40ml，5 ml/s	Retro-scan（100kVp, 666mAs, 377mm, 13.94s,23.5mGy, 885.95mGy.com, 15.06mSv) 370 mgI/ml contrast：65ml，3.5ml/s; saline：45ml，5 ml/s
		

Conclusion

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- With the improvement of scientific research level, the number of academic reports of Chinese scholar RSNA is increasing year by year.
- Coronary heart disease is still the most important research part in the field of cardiac CT.
- Photon counting CT,FFR, machine learning and other new technologies have become the focus of research.
- The new heart special software of each equipment manufacturer is conducive to the further analysis of cardiac structure and function, presenting a broad prospect of cardiac CT application.
- The application of new technology, new equipment and new software provides new ideas for prevention, treatment and prognosis of cardiovascular diseases.

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(최대 24시간 사용 가능)

+ Safe and reliable application

• 에어디텍터가 Pump tube 내의 기포를
즉시 감지하여 보다 안전하게 검사
- 1㎕의 기포를 감지, 누적 1ml 도달 시
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+ Economical and environmentally friendly

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• 2가지 소모품(Pump tube, Patient tube)만 사용
- Pump tube : 최대 24시간 동안 다수의 환자에게 사용 가능
- Patient tube : 환자 당 1회 사용

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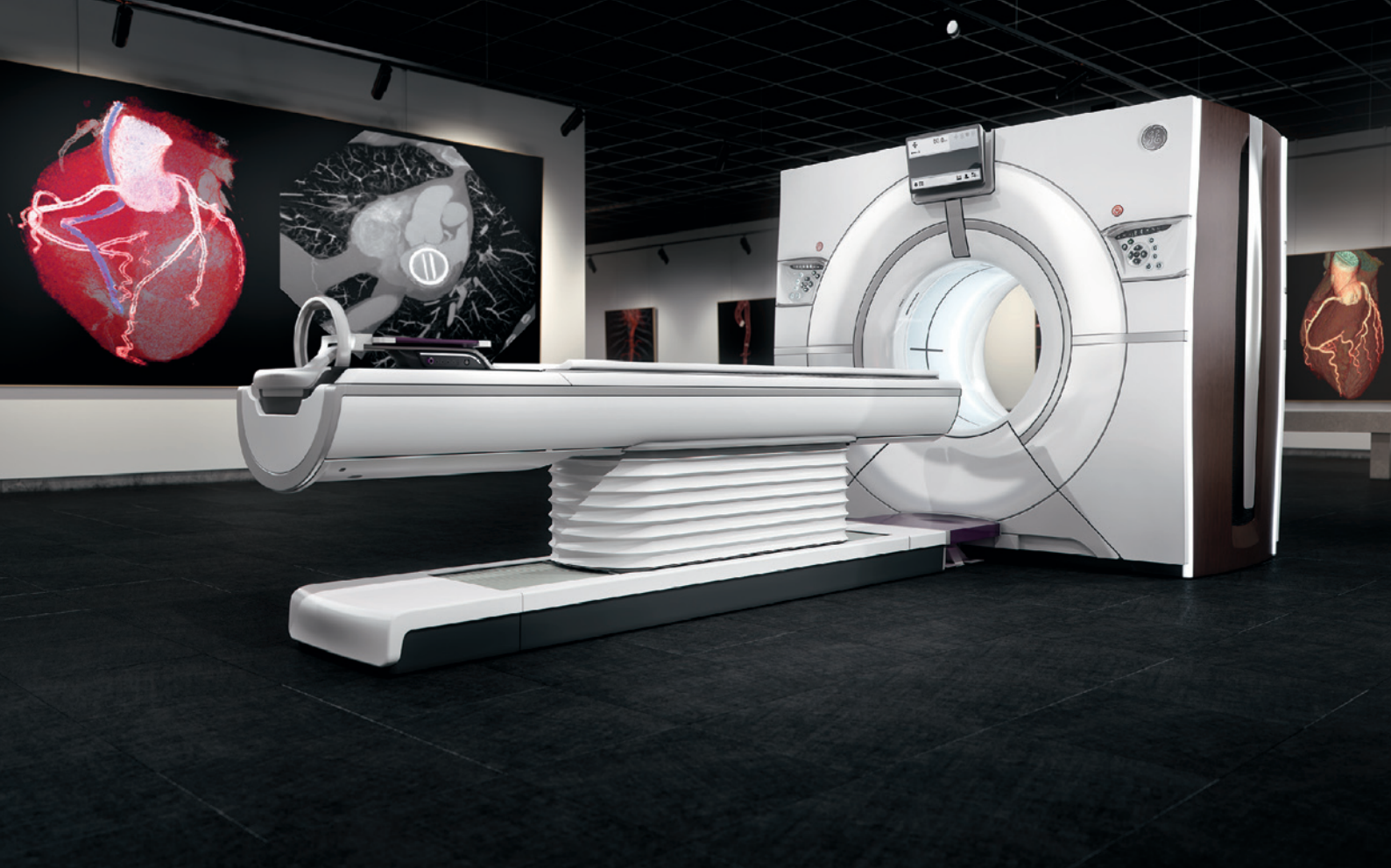

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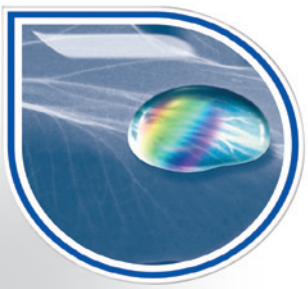

References: 1) Cademartiri F et al. High iodine concentration contrast material for noninvasive multislice computed tomography Coronary Angiography: Iopromide 370 Versus Iomeprol 400. Inv. Radiol. 2006;41(3): 349-353. 2) Schoellnast H et al. MDCT angiography of the pulmonary arteries: influence of iodine flow concentration on vessel attenuation and visualization. AJR. 2005;184:1935-1939. 3) Marchiano A et al. Does iodine concentration affect the diagnostic efficacy of biphasic spiral CT in patients with hepatocellular carcinoma? Abdom Imaging. 2005;30(3):274-80. 4) Hammerstingl et al. in "Multidetector-Row Computed Tomography". Springer 2005. Pag. 49-60. 5) Fenchel S et al. Effect of iodine concentration of contrast media on contrast enhancement in multislice CT of the pancreas. Br J Radiol. 2004;77(922):821-30. 6) Romano L et al. Enhancement and safety of iomeprol-400 and iodixanol-320 in patients undergoing abdominal multidetector CT. BJR. 2008 Dec. 8 (e-pub ahead of print).

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의료전문인용

[제품명] 울트라비스트® 300주사, 370주사 **[주성분]** 이오프로다이드 **[효능·효과]** 1. 정맥요로조영(IVP) 2. CT 조영증강: 두부, 체부 3. 혈관조영 4. 디지털감산혈관조영(DSA) **[용법·용량]** 투여 전후에 적절한 수분공급을 유지해야 한다. 조영제를 데워서 체온에 맞게 조절해서 투여하면 내약성이 훨씬 좋아진다. 투여후에는 약 30분간 환자의 상태를 관찰해야 한다. 왜냐하면 중증 이상반응의 대부분은 30분 이내에 발생하기 때문이다. 조영제로 인한 추가적인 신장해의 위험도를 줄이기 위해 가능한 최소 용량이 사용되어야 한다. 1) 정맥요로조영 (1) 성인: 울트라비스트 300주사: 체중 kg당 1 mL 투여, 울트라비스트 370 주사: 체중 kg당0.8 mL투여 (2) 소아: 울트라비스트 300주사- 신생아:1.2 gI/kg(4.0 mL/kg), 영아(1개월~2세):1.0 gI/kg(3.0 mL/kg), 유소아(2세~11세):0.5 gI/kg(1.5 mL/kg)/ 울트라비스트 370 주사- 신생아:1.2 gI/kg(3.2 mL/kg), 영아(1개월~2세):1.0 gI/kg(2.7 mL/kg), 유소아(2세~11세):0.5 gI/kg(1.4 mL/kg) 2) CT 조영증강 (1) 두부: 울트라비스트 300주사: 1~2 mL/kg/ 울트라비스트 370 주사: 1~1.5 mL/kg (2) 체부: 체부 CT 촬영시에 조영제의 양이나 주사속도는 검사하려고 하는 부위, 진단상의 문제 등에 따라 달라지며, 특히 사용하는 장비의 촬영방법의 차이, 영상재구성시간의 차이 등에 좌우된다. 3) 혈관조영- 울트라비스트 300주사 (1) 뇌혈관조영: • 대동맥궁: 50~80 mL, 경동맥: 30~40 mL, 선택적 혈관조영: 6~15 mL (2) 흉부대동맥조영 : 50~80 mL, 복부대동맥조영 : 40~60 mL (3) 사지혈관조영 • 상지동맥조영: 8~12 mL, 상지정맥조영: 15~30 mL • 하지동맥조영: 20~30 mL, 하지정맥조영: 30~60 mL/ 울트라비스트 370 주사 (1)심장 심실조영: 40~50 mL (2)관상동맥조영: 5~8 mL 4) 디지털감산혈관조영(DSA) 30~60mL 를 급속 정맥주사하면 큰 혈관, 폐동맥, 경동맥, 신동맥, 사지동맥 등이 선명하게 조영된다. **[사용상의 주의사항]** 1. 경고 1) 뇌척수강내 투여 시 중증의 이상반응이 나타날 수 있으므로 뇌수조, 척수조영에는 사용하지 않는다. 2) 숙 등 중증의 이상반응이 나타날 수 있다. 2. 다음 환자(경우)에는 투여하지 말 것. 1) 이 약 및 이 약의 구성성분, 요오드계 약물에 과민반응 및 그 병력이 있는 환자 2) 중증 갑상샘 질환 환자(요오드가 갑상샘에 축적되어 증상이 악화될 수 있다.) 3) 호모시스틴뇨증 환자에 대한 혈관조영(혈전과 색전이 증가할 수 있다.) [이상반응] 가장 빈번한(≥4%) 이상반응은 두통, 구역, 혈관확장이다. 가장 심각한 이상반응은 아나필락토이드 쇽, 호흡정지, 기관지경련, 후두부종, 인두부종, 천식, 혼수, 뇌정색, 뇌졸중, 뇌부종, 경련, 부정맥, 심정지, 심근허혈, 심근강색, 심부전, 서맥, 청색증, 저혈압, 쇽, 호흡곤란, 폐부종, 호흡부전, 흡인이다. **[전문의약품]** **[제조 및 판매자]** 바이엘코리아㈜ **[개정년월일]** 2016.08.22 **보다 자세한 사항은 제품설명서 전문 또는 바이엘 웹사이트, http://www.bayer.co.kr를 참고하시기 바랍니다.**

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제품명: 옵티레이320울트라젝트주사 주성분명: 이오버솔 [효능:효과] 옵티레이320울트라젝트주사: 〈성인〉 뇌동맥조영, 말초동맥조영, 내장/신장동맥 및 대동맥조영, 관상동맥조영 및 좌심실조영, CT 조영증강(두부, 체부), 정맥요로조영(IVP) 〈1세 이상 소아〉 심혈관조영술, CT 조영증강(두부, 체부), 정맥요로조영(IVP) [용법·용량] 가능한 최저용량을 사용한다. 조영 부위별 투여 용량은 설명서 참조 [경고] 1) 뇌척수강내 투여 시 중증의 이상반응이 나타날 수 있으므로 뇌수조, 척수조영에는 사용하지 않는다 2) 속등 중증의 이상반응이 나타날 수 있다. 제조원: Liebel-Flarsheim company, LLC 수입원: ㈜ 이미징솔루션코리아 서울특별시 강남구 테헤란로38길 10, 아이에스빌딩 6층 판매원: ㈜ 이연제약주식회사 서울특별시 강남구 영동대로 416 (대치동 코스모타워 6층) (02)793-5557 www.reyonpharm.co.kr

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아프로벨 정 전문의약품

원료약품 및 그 분량 1) 아프로벨®정 150mg, 1정 중 이르베사르탄(별규) – 150밀리그램 2) 아프로벨®정 300mg, 1정 중 이르베사르탄(별규) – 300밀리그램 **효능 · 효과** 1. 본태고혈압 2. 고혈압 치료요법으로서, 고혈압을 가진 제 2형 당뇨병 환자의 신장병 **용법 · 용량** 이 약은 식사와 관계없이 복용할 수 있다. 1. 본태고혈압 – 성인 : 이베사탄으로서 1일 1회 150mg을 경구투여하며, 효과가 충분하지 않을 경우 300mg까지 증량할 수 있다. 일반적으로 24시간 동안의 혈압조절효과는 1일 1회 75mg을 투여하는 것보다 150mg을 투여할 때 더 우수하지만, 특별한 경우(치료초기, 혈액투석 환자, 혹은 75세 이상의 고령자 등)에서는 75mg이 고려될 수 있다. 단독투여로 혈압조절이 충분치 않을 경우에 다른 혈압강하제를 병용투여할 수 있다. 특히, 낮은 용량의 이뇨제에, 히드로클로로치아짓와 병용 투여시 효과가 증가된다. 2. 고혈압을 가진 제 2형 당뇨병 환자의 신장병 – 성인 : 이 약으로서 1일 1회 150mg으로 경구 투여를 시작하여 300mg까지 증량하여 유지시키는 것이 권장된다. 이때, 필요하면 목표 혈압에 도달하기 위하여 다른 혈압강하제를 병용투여할 수 있다. · 고령자 : 일반적으로 투여량 조절이 필요치 않으나 75세 이상의 고령자의 경우에는 초회량으로서 75mg을 고려한다. · 신장애 환자 : 일반적으로 투여량 조절이 필요치 않으나 혈액투석 환자의 경우에는 초회량으로 75mg을 고려한다. · 간장애 환자 : 일반적으로 경증에서 중등도 간장애 환자에 대한 투여량을 특별히 조절할 필요는 없지만 1일 150mg을 초과하지 않을 것이 권장된다. 단, 중증의 간장애 환자에 대한 임상 경험은 없다. **경고** 임부에게 레닌-안지오텐신-알도스테론계(RAAS)에 직접 작용하는 약물들의 투여시, 태아 및 신생아에게 손상 및 사망까지도 일어날 수 있으며, 이러한 사례는 ACE억제제를 복용한 환자에서도 세계적으로 수십 례가 보고된 바 있다. 따라서 만일 임신으로 확인될 경우 즉시 이 약의 투여를 중단해야 한다. **금기** 1) 이 약 또는 이 약의 구성성분에 과민반응 환자 2) 임부 또는 임신하고 있을 가능성이 있는 여성 및 수유부 3) 중증 간장애 환자 4) 유전성 혈관부종 환자이거나, ACE억제제 혹은 안지오텐신II 수용체 길항제 치료시 혈관부종의 병력이 있는 환자 5) 갈락토오스 불내성, Lapp 유당분해효소 결핍증 또는 포도당-갈락토오스 흡수장애 등의 유전적 문제가 있는 환자(이 약은 유당을 함유하고 있음) 6) 당뇨병이나 중등도-중증의 신장애 환자사구체여과율 (60ml/min/1.73m2)에서 알리스키렌 함유제제와의 병용 7) ACE억제제를 복용중인 당뇨병성 신증 환자 **신중투여** 1) 고령자 2) 고칼륨혈증 환자 혹은 혈청 칼륨치가 높아지기 쉬운 환자 3) 경증 ~ 중등도 간장애 환자. 특히 담즙 간경변 및 담즙 정체가 있는 환자(이 약은 주로 간으로 배설되기 때문에 이러한 환자에서 혈중 농도가 상승할 수 있다.) 4) 대동맥판 및 승모판 협착증 환자 혹은 폐쇄비대심근병 환자 5) 허혈 심장병, 허혈 심장혈관 질환, 뇌혈관 장애 환자(과도한 혈압강하는 심근경색이나 뇌혈류 부전으로 인한 뇌졸중을 일으킬 수 있다.) 6) 혈류량 손실이 있는 환자(나트륨 및 혈류량이 손실된 경우 특히 초회 투여후에 저혈압 증상이 나타날 수 있다.) 7) 신장혈관고혈압 환자 8) 신기능이상 환자(과도한 혈압강하에 의해 신장 기능을 악화시킬 수 있다.) 9) 고혈압을 가진 제2형 당뇨병성 신장병 환자 10) 중증의 울혈심부전 또는 신장맥협착과 같은 신칠환 환자 11) 레닌-안지오텐신-알도스테론계(RASS)의 이중차단 : 이 약과 ACE억제제 또는 알리스키렌의 병용투여시 단독투여와 비교하여 저혈압, 고칼륨혈증 그리고 신기능 변화의 위험이 증가한다. 따라서 이 약과 ACE억제제 또는 알리스키렌의 병용은 권장되지 않는다. 병용투여의 경우, 혈압, 신기능 및 전해질을 면밀히 모니터링해야 한다. ※ 보다 자세한 내용은 홈페이지나 제품 설명서를 참고하시기 바랍니다.

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판매원 : (주)사노피-아벤티스 코리아 서울특별시 서초구 반포대로 235 (137-804), tel: 02-2136-9000, fax:02-2136-9045 제조원 : (주)한독 충청북도 음성군 대소면 대풍리 37번지 개정년월일 : 2016년 12월 23일

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