An Epidemic of Heart Disease
“The Silent Killer”

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Institute of Diabetes for Older People
Initial clinical presentation of CAD

- Angina: 35%
- MI: 10%
- Atypical CP: 20%
- Death: 30%

"If we wait for susceptible individuals to develop symptoms before deciding to treat, the earliest symptom is often sudden death. The challenge is to develop non-invasive screening methods to detect coronary arteriosclerosis in its earliest stages"

MS Brown and JL Goldstein
WOMEN & HEART DISEASE

Is your biggest worry breast cancer? Think again. ONE OUT OF THREE women will die of heart disease. What you can do to protect yourself.
Myocardial infarction is often associated with minimal coronary obstructive disease.

Percent stenosis underlying MI lesion

- <50%
- >50%

Coronary Artery Remodeling

Coronary Artery “Remodeling”

Normal vessel

No Narrowing Mild Plaque

Mild Narrowing Moderate Plaque

Severe Narrowing Extensive Plaque

Time [years]
Early detection of Coronary Artery Disease (CAD)

• **Indirect:** *Risk factors* (smoking, HTn, family h/o of CAD, diabetes, lipids, inactivity, obesity, metabolic syndrome); *blood biomarkers* (HsCRP, IL-6, BNP, etc)

• **Direct:** *Non-invasive* - ECG, Ex test, Holter, Imaging (echo, nuclear imaging, CT, MRI), *Invasive* - angiography, IVUS
Early detection of Coronary Artery Disease (CAD)

- Coronary Artery Calcium imaging using ultra-fast CT is one of the earliest non-invasive methods for detecting early CAD

CAC score: 2864 Au
JL, 31yr male
Has ED
HT, Chol 5.6,
Family H/O CAD,
Smoker
Asymptomatic
Normal ETT
CAC score 1136

Anand et al, J Nucl Cardiol 2004:11;450-57

Before angioplasty 6 months post PTCA

6 months post PTCA
Total Coronary Artery Plaque Burden and EBCT Coronary Calcium Score: defining the tip of the atherosclerotic iceberg
EBCT determines “the tip of the atherosclerotic iceberg”
Cox Proportional Hazard Survival (n=10,377)
Of EBT Coronary Calcium Screening

Women (n=4,191)

Men (n=6,186)

Source: Callister ACC 2002 abstract
Coronary Artery Calcium

- CT coronary calcium scan (CAC) is a sensitive marker of increased ‘plaque burden’, and the score is related to prognosis (patient outcome)
- Absent or minimal CAC is associated with a good outcome
- High levels of CAC may not always be associated with coronary stenosis (narrowing), thus combining with other functional imaging for detection of obstructive CAD is important for further risk stratification
Hybrid Scanner CT + SPECT

Single Photon Emission Computed Tomography (SPECT)
BJ, 67 yrs
HT, Chol 4.4
Asymptomatic
Normal ExT
CAC score 2886

Anand et al, J Nucl Cardiol 2004:11;450-57
The Epidemic of Diabetes

- **191 m** Type 2 diabetic patients worldwide\(^1\)
- **376 m** Type 2 diabetic patients by 2020 (WHO)
- **60-70%** will die from cardiovascular disease\(^2\)
- **2-4 fold increase** in development of CAD
- Identifying high-risk diabetic patients is **problematic**
  
  Often *asymptomatic*

  *Advanced disease at presentation*

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2. Gu K et al. Diabetes Care 21;1998
Coronary Artery Calcium Imaging (EBCT) Predicts All Cause Mortality: Observational Study

Shaw et al, Radiology 2003; 228: 826-33
Raggi et al, JACC 2004; 43: 1663-69
Coronary Calcium, Silent Myocardial Ischaemia and Inflammatory Biomarkers in Asymptomatic Type 2 Diabetic Subjects without Prior Cardiovascular Disease

Anand et al, Eur Heart J, 2006; 27(6): 713-21

Duration of diabetes, Glycaemic control, Conventional Risk Factors, Framingham Risk Score, CRP, IL-6, Osteoprotegrin

N=510 Diabetic patients

EBCT Coronary Calcium Imaging

CAC < 100 Agatston Units

Random Sample (n = 50)

CAC > 100 Agatston Units

All Patients

MPI

3 year follow-up (Ongoing)
Distribution of Coronary Calcium

Anand et al, Eur Heart J, 2006; 27(6): 713-21

n = 510

<table>
<thead>
<tr>
<th>Coronary Calcium Score</th>
<th>Number of Patients</th>
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<tbody>
<tr>
<td>Insignificant</td>
<td>54%</td>
</tr>
<tr>
<td>Mild</td>
<td>20%</td>
</tr>
<tr>
<td>Moderate</td>
<td>15%</td>
</tr>
<tr>
<td>Severe</td>
<td>11%</td>
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</tbody>
</table>

Insignificant: <10
Mild: 10-100
Moderate: 100-400
Severe: >400
Coronary Calcium Scores were Not Related to hs-CRP and IL-6 Levels

Anand et al, JACC, May 2006

n = 510

\[ R = 0.01 \quad p = 0.79 \]

\[ R = 0.09 \quad p = 0.33 \]
Coronary Calcification is Associated with Raised OPG Levels

Anand et al, JACC, May 2006
Asymptomatic 56 yrs old male with Type 2 diabetes and treated hyperlipidemia and hypertension.

High grade circumflex lesion confirmed angiographically and stented.
Event-Free Survival at 18 months by Cox Proportional Hazard survival Model: Death, MI, ACS, Stroke and Late Revascularisation

Coronary calcium

- 0-100 (p=0.051) RR=7.06, 0.99-50.10
- >5.0% (p<0.0001) RR=16.41, 3.59-74.92
- 1.0%-5.0% (p=0.064) RR=9.67, 0.88->100
- >1,000 (p<0.0001) RR=115.37, 14.17->900

Ischaemic Burden

- No ischaemia
- >100 (p<0.0001) RR=1.06, 0.99->100
- 101-400 (p=0.064) RR=9.67, 0.88->100
- 401-1,000 (p<0.0001) RR=69.22, 8.08->100
- >1,000 (p<0.0001) RR=115.37, 14.17->900

Anand et al, Eur Heart J 2006;27:905-912
Pre-selection of Asymptomatic Diabetics by EBCT Improves the Yield of Detection of Myocardial Perfusion Abnormalities

**DIAD study**
MPI in asymptomatic diabetics (n = 522)

**Anand et al**
MPI in asymptomatic diabetics with CAC > 100

LEFT = unselected patients, RIGHT = selected by EBCT (coronary calcium scores > 100 Agatston units)

**Graph:**
- % of All Patients
- Abnormal perfusion
- Moderate to Large reversible perfusion defects (>5%)

Wackers F et al. Diabetes Care 27;2004
Anand et al, Eur Heart J 2006;27:905-912
Progression of Coronary Artery Calcium

Anand et al, JACC 2007 (in press)

n = 398, FU 2.5 ± 0.4 yrs

- Insignificant
- Mild
- Moderate
- Severe

Baseline Coronary calcium progression categories:

- <10: Insignificant
- 10-100: Mild
- 100-400: Moderate
- >400: Severe

Percentage of patients in each category:

- <10: 15%
- 10-100: 34%
- 100-400: 65%
- >400: 55%

No Progression or Regression
Progression
Summary

• ‘Silent’ coronary atherosclerosis and ishaemia are common in diabetic patients
• Burden of CAC predicts cardiovascular outcome
• CAC and MPI imaging provide incremental diagnostic and prognostic value
• Cost of ‘initial’ functional imaging for screening would be high, thus a model with CAC imaging first may be cost effective
CT Scanners

- Electron Beam CT (EBCT)
- Multi-detector or multi-slice CT (MDCT or MSCT) - 2 to 256 slice devices: 64 slice and above for CT coronary angiography (CTA)
- Dual Source (+dual energy) 64 slice CT (Definition, Siemens)
- Hybrid and ‘micro’ scanners
Dual-Source CT SPECT: Definition

Single photon emission computed tomography (SPECT):
SPECT images are obtained following an injection of a radiopharmaceutical that is used for nuclear medicine scans. The injected medication sticks to specific areas in the body, depending on what radiopharmaceutical is used and the type of scan being performed, for example. It will show bone for a bone scan, and gall bladder and bile ducts for a hepatobiliary scan.

The radiopharmaceutical is detected by a nuclear medicine gamma camera. The camera or cameras rotate over a 360 degree arc around the patient, allowing for reconstruction of an image in three dimensions.
Computed tomography (CT): CT images are obtained while you lie on a bed that moves into a ring, or "doughnut" shaped X-ray machine. Again, the X-ray machine rotates over a 360 degree arc around the patient, allowing for image reconstruction in three dimensions. The X-ray machine from the CT scanner rotates much faster than the gamma camera, so the CT part of the study takes less time than the SPECT study.

The similarity between SPECT and CT in the method of image processing allows the images to be combined. Combining the information from a nuclear medicine SPECT study and a CT study allows the information about function from the nuclear medicine study to be easily combined with the information about how the body structure "looks" in the CT study.
Dual Source CT: Two X-ray sources and two detectors at the same time

0.33 seconds rotation speed of 1.6 tons
CT angiography
Coronary artery stents
CT angiography
Chest & abdomen
CT angiography

Heart transplant: 2 hearts
CT angiography
Aortic dissection
“Triple rule-out”
Cardiac CT Angiography

CT angiography

62 year old male with atypical chest pain

Lipid-rich stenosis, no calcium, ‘vulnerable plaque’
Direct dual energy subtraction of bone even in complicated anatomical regions

SOMATOM Definition

World’s first DSCT

Spatial Res. 0.33 mm
Rotation 0.33 sec
140/80 kV
50/210 effective mAs
Spiral Dual Energy

CM Ultravist® by Bayer Schering Pharma AG

Courtesy of University Hospital of Munich - Grosshadern / Munich, Germany
DSCT: MIP and Volume rendering

CT Coronary angiography & valve imaging
Evaluation of Aortocoronary Saphenous Vein Graft Attrition by Contrast Enhanced Electron Beam Tomography

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Anand et al; JNC 2008
61 year old man with dyspnoea on exertion & previous history of CAD (CABG: LIMA TO LAD, SVG to LCx, RCA -12 years ago; PTCA & stent to LCx SVG - 7 years ago)
CABG Graft CT angiography

Blocked bypass grafts
A High-Grade Stenosis in the RCA

Future Directions
CTA: Stent visualisation
DSCT for Detection of In-stent Re-stenosis

Pugliese et al, Heart 2007
Assessment of LV function with DSCT

Matching mitral valve and LV blood pool
Detection of Myocardial Infarction by CT and MRI

Mahnken et al: JACC 2005
Soft Plaque Visualisation
Improvements in Software

Plaque evaluation tool, assigning different colors to voxels within different ranges of CT numbers

Flohr et al: J Thorac Imaging 2007
Hybrid Scanner: CT + SPECT
Image Fusion: SPECT-CT
Future Directions: SPECT/CT
Image Fusion:
SPECT-CT
Brain Tumour
Image Fusion: Breast Cancer – Spinal metastasis
Sports injury

Image Fusion: SPECT-CT
Fate of Cardiac CT

• CT angiography is here to stay

• Low risk patients can be excluded from unnecessary invasive angiography

• DS-CT may improve diagnostic outcome

• New directions include: in-stent visualisation, soft plaque assessment, myocardial contrast enhancement and viability, valve assessment, triple rule-out, image fusion