Coronary Artery Imaging: Where we stand and where we go

Professor Lampros K. Michalis MD, MRCP, FESC
University of Ioannina
Summary

- Introduction
- Intra-coronary imaging modalities
- Hybrid coronary artery imaging modalities
- Applications
- Conclusions
Introduction

- Cardiovascular disease is the leading cause of death in the developed world
  - Population aging
  - Modern life style

- To address this problem an effort was made:
  - in developing new treatments (e.g. new wires, rotablation, DES, BVS, minimally invasive CABG)
  - in preventing events

Increased need for detailed visualization of vessel anatomy and understanding the mechanisms that are involved in the atherosclerotic process
Introduction

• Coronary artery imaging has made a considerable progress over the last 25 years
  ✓ Miniaturization of medical devices
  ✓ Advances in signal processing
  ✓ Progress in image processing
  ✓ Imaging of molecular biological phenomena

• New imaging techniques emerged for invasive and non-invasive assessment of coronary anatomy and physiology
  ➢ Already available: Coronary angiography, angioscopy, IVUS, OCT
  ➢ New intravascular modalities
  ➢ Non-invasive modalities: CT, MRI
  ➢ Hybrid modalities
Intra-coronary imaging techniques
Angioscopy

Imaging requires:

- Catheter with illumination fibres
- Proximal balloon inflation

The acquired images allow:

- Classification of the superficial plaque
- Yellow plaques → high risk plaques
- Identification of plaque disruption
- Identification of thrombus
- Assessment of stent coverage

*Uchida. J Cardiol. 2011*
New developments in angioscopy

- **Colorimetry:** quantitative color analysis
  - *Ishibashi et al. Am J Cardiol. 2007*

- **Identification of oxidised LDL:** in Evans dye oxidised LDL has a violet color
  - *Uchida. J Cardiol. 2011*

- **Identification of neo-endothelial damage after stent implantation:** Evans dye stains selectively damaged endothelial cells
  - *Uchida. J Cardiol. 2011*
New developments in angioscopy

- Near infrared fluorescence and Near Infrared Fluorescence Microscopy
- NIR has a higher penetration than the light and hence it is able to identify lipids in depth up to 700μm
- Able to identify the presence of necrotic cores and micro-calcifications in lipid rich plaques

Uchida et al. Clin Cardiol. 2011
Intravascular Ultrasound

Imaging requires:

- Insertion of a catheter with a transducer that emits and receives IVUS signal (20-70MHz)
- Pull-back of the catheter and imaging of different vascular segments

The acquired cross-sectional images allow:

- Identification of lumen, stent, vessel wall
- Quantification of their dimensions and of the plaque burden
- Classification of plaque type
- Detection the plaque rupture and the presence of thrombus

Mintz et al. J Am Coll Cardiol. 2001
<table>
<thead>
<tr>
<th>Estimate the severity of a lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Hazy” or intermediate lesions difficult to accurately assess by coronary angiography</td>
</tr>
<tr>
<td>Lesions located in diffusely diseased segments</td>
</tr>
<tr>
<td>Lesions located at the origin of side branches</td>
</tr>
<tr>
<td>Lesions located in the LMCA</td>
</tr>
<tr>
<td>Detection of restenosis or in-stent restenosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical decision making</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification of the extent, morphology and constitution of the plaque</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Guide treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Help to identify the optimal entry true lumen in CTO</td>
</tr>
<tr>
<td>POBA: Selection of balloon’s dimensions and inflation pressures</td>
</tr>
<tr>
<td>BMS, DES: Selection of optimal stent dimensions</td>
</tr>
<tr>
<td>In the treatment of complex disease e.g. small vessels, long lesions, bifurcations, LMCA</td>
</tr>
<tr>
<td>In the treatment of high risk patients e.g. renal failure, heart failure diabetes mellitus, those who cannot take long-term dual anti-platelet therapy</td>
</tr>
<tr>
<td>To identify the cause of restenosis and guide further treatment</td>
</tr>
</tbody>
</table>

| Examine final results and identify suboptimal stent expansion or dissections after percutaneous intervention |
# Intravascular Ultrasound

## Research indications

<table>
<thead>
<tr>
<th>Category</th>
<th>IVUS imaging advantages</th>
<th>IVUS imaging disadvantages</th>
<th>Preferable modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of the effect of pharmacological treatment</td>
<td>• Able to quantify changes in plaque volume&lt;br&gt;• IVUS-RF allows identification and quantification of changes in plaque's composition</td>
<td>• IVUS-RF identifies with moderate sensitivity/specificity a change from lipid to a fibrous plaque</td>
<td>IVUS</td>
</tr>
<tr>
<td>Remodelling assessment</td>
<td>• Complete arterial wall visualisation</td>
<td>• Unable to identify accurately the outer vessel wall border in segments with calcified plaques.</td>
<td>IVUS</td>
</tr>
<tr>
<td>Plaque characterisation</td>
<td>• Complete vessel wall visualisation&lt;br&gt;• IVUS-RF allows identification of the type of the plaque with good overall sensitivity and specificity</td>
<td>• IVUS-RF identifies with moderate sensitivity/specificity lipid and fibrous plaques.</td>
<td>IVUS-RF and OCT</td>
</tr>
<tr>
<td>Detection of vulnerable plaque</td>
<td>• Accurate measurement of luminal dimensions, plaque area and remodelling&lt;br&gt;• IVUS-RF allows identification of the type of the plaque with good overall sensitivity and specificity</td>
<td>• Limited axial resolution - unable to measure the fibrous cap&lt;br&gt;• Moderate sensitivity in detecting thrombus and plaque disruption/erosion&lt;br&gt;• Unable to detect macrophages or intraplaque haemorrhage</td>
<td>OCT and IVUS-RF or combination of different imaging modalities</td>
</tr>
<tr>
<td>Assessment of invasive treatments</td>
<td>• Reliable assessment of luminal, stent area and intima hyperplasia&lt;br&gt;• Precise evaluation of stent expansion&lt;br&gt;• Reliable evaluation of bioabsorbable stent recoil</td>
<td>• Limited capability in identifying vessel wall trauma (e.g. erosion, dissection) and thrombus&lt;br&gt;• Incapable of assessing stent struts coverage</td>
<td>OCT or combination of OCT and IVUS</td>
</tr>
<tr>
<td>Role of haemodynamics in atherosclerosis</td>
<td>• Complete vessel visualisation - plaque characterisation&lt;br&gt;• Multitude of automated methodologies that allows IVUS segmentation and fusion of IVUS and angiography</td>
<td>• Limited capability in detecting vulnerable plaque characteristics</td>
<td>IVUS</td>
</tr>
</tbody>
</table>
New developments in IVUS

- Advances in signal processing allowed:
  - Analysis of the radiofrequency backscatter IVUS signal and more accurate plaque characterization
    - Garcia-Garcia et al. Eur Heart J. 2011
  - Analysis of the radiofrequency backscatter IVUS signal and assessment of the vessel wall deformation (Palpography)
    - Vessel wall strain depends on the composition of the plaque (increased deformation is seen in vulnerable plaques)
      - Schaar et al. J Am Coll Cardiol. 2006
New developments in IVUS

✓ Advances in image processing permitted automated:

- Segmentation of the IVUS frames
  - Bourantas et al. Brit J Radiol. 2005

- Plaque characterization in grayscale IVUS frames
New developments in IVUS

✓ Advances in device technology

➢ Forward-looking IVUS catheter
  – Has the ability to image the vessel in an forward looking manner
  – A 45MHz transducer orientated at a 45° angle at the end of the catheter
  – Provides a forward looking cone visualization
  – Preview catheter requires a 7Fr guide catheter and provides 3-5fr/sec

Degertekin et al. IEEE Trans Ultrason Ferroelectr Freq Control. 2006
Optical coherence tomography

Imaging requires:

- Advancement of a catheter with a lens that emits lights radically to its axis
- Saline flush to clear blood
- Pull-back of the catheter and imaging of different vascular territories

The acquired cross-sectional images allow:

- Visualization of the lumen, stent, vessel
- Quantification of their dimensions, plaque volume and stent endothelialization
- Classification of the plaque type and detection of high risk plaques
- Identification of high risk plaques

Tearney et al. J Am Coll Cardiol J. 2012
Optical coherence tomography

- Accurate identification of the culprit lesion
  
  *Kubo et al. J Am Coll Cardiol. 2007*

- More accurate evaluation of stent dimensions and detection of malaposition

- Detection of stent coverage

- Assessment of ISR and plaque type
  
  *Takano et al. J Am Coll Cardiol. 2011*

- Unable to assess the pathology of the total vessel wall

- Problems with the characterization of the plaque


New developments in OCT

✓ Optical Frequency Domain Imaging (OFDI)
  - Rapidly tuned wavelength swept source
  - Produce images with a higher frame rate (160 frames/sec)
  - Permits pull-back with faster speed and thus allows the study of longer arterial segments

*Suter et al. JACC Cardiovasc Imaging 2011*

✓ Automated segmentation of OCT frames

*Sihan et al. Catheter Cardiovasc Interv. 2009*
New developments in OCT

- Assessment of macrophages accumulation
  - By measuring the normalized SD of the OCT signal in the fibrous cap
    
    Tearney et al. Circulation. 2002

- Estimation of the fibrotic composition of the plaque
  - PS-OCT: measures changes in the polarization of the OCT signal which occurs as this passes through a birefringent material (fibrous tissue)
    
    Positive predictive value: 0.89
    Negative predictive value: 0.93

  Giattina et al. Int J Cardiol. 2006
New developments in OCT

- Automatic characterization of calcific plaques using image processing techniques

New developments in OCT

✓ Micro OCT

- Axial resolution 10μm lateral resolution 20μm
- Allows identification of endothelial cells, of smooth muscle cells phenotype, macrophages, microcalcifications

✓ Poor penetration

✓ Not available for in vivo applications yet

Liu et al. Nat Med. 2011
Newer intravascular imaging modalities
Near infrared spectroscopy

Imaging requires:

- Advancement of a catheter that contains a rotating NIR light source at its tip
- The catheter is pulled-back and measurements of plaque heat are obtained at different arterial sites

Processing of the reflected signal provides:

- The chemogram
- The block chemogram
- The lipid core burden index

*Bourantas et al. Cardiovasc Ultrasound. 2011*
New developments in NIRS

- **Near infrared fluorescence molecular imaging**
  - They mark catepsin B using an activatable NIRF marker
  - NIRF was then performed which permitted identification and visualization of vessel wall inflammation
  - Response of vessel wall after stent implantation

*Jaffer et al. J Am Coll Cardiol. 2011*
Intravascular MRI

- Still under-development
- Has not implemented in humans yet
- Recently was implemented in vivo in a rabbits’ aorto-iliac arteries
  - Performed with a 3Ts scanner
  - Image resolution 300μm
  - Image acquisition 2fr/sec
- Results are promising for the future
  - Lumen
  - Vessel wall
  - Plaque characterization

Sathyanarayana et al. JACC Cardiovasc Imaging. 2010
New invasive imaging techniques

Intravascular MR spectroscopy
- Is feasible but the catheter has diameter 5.2F
- Time consuming process (51 sec for 1 frame)
- Allows only detection of the lipid rich plaques

*Regar et al. EuroIntervention. 2006*

Raman Spectroscopy
- Irradiation of the tissues with laser – analysis of the spectrum of the emitted light
- Capable to identify plaques’ composition
- Not available in clinical practice

New invasive imaging techniques

**Photoacoustic imaging**
- Based on the detection of the sound emitted by the irradiated by a laser tissue
- Can detect the type of the plaque
- Can detect inflammation
- Visualize the stent morphology
- Not available for in-vivo application

*Wang et al. IEEE Quantum Electron. 2010*

**Intravascular fluorescence spectroscopy**
- Allows detection of the superficial plaque characteristics and macrophages
- Low penetration
- Method in its infancy

*Wang et al. IEEE Quantum Electron. 2010*
Hybrid imaging techniques

Fusion methodologies that allow off-line integration of data acquired from different imaging techniques

Catheters that include two probes and allow simultaneous visualization
Hybrid imaging – IVUS

✓ IVUS and coronary angiography

- The 1st hybrid imaging technique
  - Requires identification of the regions of interest in IVUS borders
  - Extraction of the catheter path from two angiographic images
  - Placement of the IVUS images perpendicular onto the catheter path
  - Estimation of their absolute orientation

Complete visualization of vessel morphology
Accurate evaluation of the plaque volume
Accurate orientation of the plaque

These models allowed blood flow simulation and study of the association between the SS and plaque evolution.

- Plaque progresses in areas with low SS
  
  *Stone et al. Eur Heart J 2007*

- Low SS appears to promote ISR in bare metal stents and in paclitaxel eluting stents but not in sirolimus eluting stents
  
  *Papafaklis et al. J Am Coll Cardiol Intv. 2011*

- Low SS and disturbed flow can be seen in coronary bifurcations and are associated with plaque development
  
  *Papafaklis et al. Int J Cardiol. 2007*
Hybrid imaging – IVUS

Prediction

- 502 patients SS was an independent predictor of future revascularizations

Stone et al. Circulation 2012
New development for cors and IVUS fusion

Michalis L et al. submitted
Hybrid imaging – IVUS

✓ Fusion of IVUS and CT

- Requires extraction of the luminal centerline from the CT data
- Identification of correspondence (using anatomical landmarks) between the IVUS images and cross sections in the CT data
- Placement of the IVUS images onto the luminal centerline
  - Allows reconstruction of the coronary bifurcations
  - Evaluation of the capabilities of CT in assessing the extent and the morphology of the plaque
  - Unable to perform coronary reconstruction without the presence of anatomical landmarks

Hybrid imaging – IVUS

✓ Fusion of IVUS-VH and CT

- Allows detection of the distribution of the plaque in the 3D coronary geometry and comparison of the estimations
- Lumen area was overestimated by 22% by CT
- Vessel wall area was overestimated in CT by 19%
- Non calcified plaque area was overestimated in CT by 44% while the calcified plaque by 88%

Voros et al. JACC cardiolvasc interv. 2011

✓ Fusion of IVUS, NIRS and CT

Wentzell et al. Circ Cardiovasc Imaging. 2010
Hybrid imaging – IVUS

✓ Fusion of IVUS and NIRS

- Imaging is performed with the use of the TVC catheter that combines a NIRS light source and an IVUS probe.

- The catheter allows overlay of the NIRS measurements onto the IVUS images.

Garg et al. Eurointervention. 2010
Garcia-Garcia et al. Eur Heart J. 2010
Hybrid imaging – IVUS

- Fusion of IVUS and OCT
  - The ideal coronary visualization
    - Structures near the lumen (plaque rupture, erosion, thrombus etc)
    - Vessel wall

Raber et al. Eurointervention. 2011
Hybrid imaging – IVUS

✓ Fusion of IVUS and OCT

➢ Recently developed catheters that include an OCT and an IVUS probe

– Not clinically applicable yet

– The size of the probe is too big

– Electromagnetic shielding is necessary to eliminate the noise created by the motor used for rotational scanning

Li et al. Circulation. 2009
Hybrid imaging – OCT

✓ Fusion of angiography and OCT

- Available system for the co-registration of 3D QCA and OCT

- Integration of X-ray angiography and OCT using a methodology implemented to fuse IVUS/X-ray data

Tu et al. Int J Cardiovasc Imaging. 2011

Bourantas et al. Int J Cardiol. 2011
Hybrid imaging – others

✓ Fusion of IVUS and IVPA

➢ There is a catheter but it hasn’t been used in clinical practice (its safety needs to be assessed – requires time for image acquisition)

➢ Identification of plaque morphology and volume by IVUS and inflammation by IVPA

➢ Detection of stent morphology

➢ Plaque characterization

Wang et al. IEEE J Quantum Electron. 2010
Su et al. Expert Opin Med Diagn. 2010
Hybrid imaging – others

✓ Fusion of IVUS and TRFS

➢ There is a catheter but it hasn’t been used in clinical practice (TRFS signal has poor penetration, concern about vessel wall trauma)

➢ Identification of plaque morphology by IVUS and vessel inflammation by TRFS

➢ Assessment of the superficial plaque characteristics

Sun et al. Biomed Optic Express 2011
Hybrid imaging – others

✓ Fusion of OCT and NIRF

- Intravascular catheter with a 2.7mm diameter
- Able to visualize lumen morphology and inflammation
- Can detect the presence of fibrin in stented segments
- Has not been implemented in humans yet as there are concerns about the safety of the markers used for fluorescence imaging

Yoo at al. Nat Med. 2011
Applications – Comparison with non-invasive hybrid imaging techniques

- The reduced clinical applications of the hybrid invasive imaging is due to the fact:
  - Does not affect the final decision about treatment
  - It is invasive
  - There is only one hybrid catheter that can be used in clinical setting as the rest are under development while most of the fusion algorithms difficult to be used and are in the hands of specific research teams

- However the fusion of IVUS with OCT will allow:
  - Better evaluation of the composition of the plaque
  - Reliable detection of the vulnerable plaques
  - Better PCI planning and assessment of the final outcome
Applications – Comparison with non-invasive hybrid imaging techniques

- On the other hand hybrid imaging techniques have already been applied in clinical practice. The fusion of SPECT and CT allows:

  - Better assessment of the severity of a stenosis

  - Detection of the lesion in patients with multiple vessel disease that it is responsible for their symptoms

*Gaemperli et al. J Nucl Med. 2007*
Applications – Comparison with non invasive hybrid imaging techniques

- Fusion of FDG-PET and CT allow detection of the segments that there is vessel wall inflammation

- However the obtained images have a low resolution that doesn’t permit assessment of vulnerable plaque characteristics

✓ Non-Invasive imaging modalities will overcome these drawback allowing thus for detailed evaluation of plaque characteristics

✓ Fusion of invasive imaging techniques will permit us to learn more regarding mechanisms and further development of non-invasive techniques

Rogers et al. JACC Cardiovasc Imaging. 2010
Jaffer et al. J Am Coll Cardiol. 2011
Conclusions

✓ It will be a gospel for mankind if we manage to predict which plaque and when it will rupture or evolve

✓ However, to accomplish great things we must first dream, then visualize, then plan... believe... act!

A. Montapert

✓ Intravascular imaging has allowed us to see unique details and plaque characteristics and provided us an insight in the mechanisms involved in plaque development and destabilization

✓ In this challenging quest, intravascular imaging and its future developments is expected to be a valuable and indispensable ally
Thermography

Imaging requires:

- Insertion of a catheter/wire with a micro-sensor on its tip that is able to measure plaque heat
- The catheter/wire is pulled-back and measurements of plaque heat are obtained at different arterial sites

The acquired measurements allow:

- Identification of plaque inflammation that is association with increased vulnerability

_Majid et al. J Am Coll Cardiol. 2005_
_Takumi et al. J Am Coll Cardiol. 2006_