Uncertainties and modelling in the management of coronary artery disease

Professor Julian Gunn
Professor of Interventional Cardiology
Mathematical Modelling in Medicine (MMM) Group
Dept Infection, Immunity and Cardiovascular Disease
University of Sheffield
Modelling in coronary artery disease in current clinical use
Coronary artery disease

Mismatch of oxygen demand and supply: all about FLOW
The diagnostic pathway
Percutaneous coronary intervention (PCI, ‘stenting’)

Intervention guided by the angiogram
Key point: interpretation of the angiogram

Physiological assessment (Fractional Flow Reserve, FFR)
- reduces deaths/heart attacks
- reduces stent implantation
- saves money

FFR = Pd/Pa at maximum hyperemia
The vision

VIRTU
Virtual coronary physiology
VIRTUheart workflow

Angiogram

Segmentation

3D virtual mesh

Pressure and boundary Conditions selected

Flow Velocity

Pressure/ vFFR
VIRTUheart (virtual FFR): advantages

* applicable to all (not 5%)
* no invasive wire
* no drugs
* no additional time
* cheap
* anywhere in the world
* virtual stenting
* benefits of FFR
* without disadvantages
The tricky bit: the distal boundary

\[ \text{FFR} = \frac{P_d}{P_a} \]

Tuning with patient factors
Modelled vs ‘measured’ distal resistance

NARMAX:
A novel approach to boundary condition
Tuning
(S Billings)

Modelled R

‘Measured’ R

N=53 patients, 114 arteries
Accuracy of vFFR vs mFFR

N=53 patients, 114 arteries

Accuracy 92% ±0.02
Quality Assurance
NIHR i4i
A prototype tool to calculate 'virtual' myocardial fractional flow reserve (vFFR) non-invasively (VIRTU-3)

WP 1: *In silico* implementation  ['Content']
WP 2: Software development  ['Presentation']
WP 3: Clinical Revalidation ['Revalidation']
WP 4: Regulatory approval ['Application']

Apr 2017 (2y)
3D Vessel Segmentation – Old vs ...

Linear Least Squares Fit (old)
3D Segmentation: New

Fourier Representation & Optimisation (new)
Quantitative computational evaluation of response to adenosine

Methods

INPUT: Patient-specific data

G-D model of cardiovascular system (Electric/Hydraulic)

OUTPUT: Patient-specific parameters

- Prediction of adenosine response
- Prediction of effect of coronary lesion

- Gender/Weight/Height
- Heart rate
- Echocardiographic data
  - Cardiac output
  - Left-ventricle volumes
  - Ejection Fraction
- $P_r$ and $P_h$ (rest/hyperaemia)
- Significant compartments
- Auto- and Neuro-regulation
- Coronary lesions

Preliminary results

Specific patient outputs to tune

- CO (Cardiac output)
- SV (Stroke volume)
- EF (Ejection Fraction)
- HR (Heart rate)
- $P_{sys}$ (systolic aortic pressure)
- $P_{dia}$ (diastolic aortic pressure)

~ 100 parameters in total

18 parameters to tune

RMSE > 0.1

Model parameters to tune

- $ELV_{min}$ (LV diastolic elastance)
- $ELV_{max}$ (LV systolic elastance)
- $C_{es}$ (Systemic arterial capacitance)
- $RSCP$ (Systemic capillaries resistance)
- $RPCP$ (Pulmonary capillaries resistance)
- $UNV$ (Unstressed venous volume)
- 12 barocontrol parameters
Algorithm to objectively identify FFR

Problem:
1) No standard; minimum or stable $P_d/P_a$ ratio as FFR
2) Clinical decision is based on subjective interpretation
3) Signal can be altered by patient movement, cough, ectopic beats, arrhythmias

- Filter high frequencies
- Smoothing
- Find minimum and stable $P_d/P_a$

Number of lesions = 163
Number of patients = 93
Impact upon treatment

- $\Delta FFR_{\text{cath}} (0.78 \pm 0.15) \text{ vs } FFR_{\text{stable}} (0.80 \pm 0.15)$

- 14 significant to non significant (17% of significant lesion)

- $y = 0.9534x + 0.0499$

- $R^2 = 0.969$
Fast and effective computation of coronary artery haemodynamics: towards a reduced order model

Aims

- Generate a machine learning process which is able to predict the FFR for every coronary geometry taken into account.
- Develop an efficient workflow

Using 2D phantom

\[ P_a \quad P_1 \quad R_{rest} \quad R_{hyper} \]
Serial lesions -1

Velocity Contour
Pressure Contour
Streamlines
Velocity Contour
Pressure Contour
Streamlines

Velocity Profile $S_1 = 50\%$ $S_2 = 50\%$
Pressure Profile $S_1 = 50\%$ $S_2 = 50\%$

Velocity Profile $S_1 = 50\%$ $S_2 = 50\%$
Pressure Profile $S_1 = 50\%$ $S_2 = 50\%$
Serial lesions - 2

Velocity Profile $S_1=70\%$ $S_2=50\%$

Pressure Profile $S_1=70\%$ $S_2=50\%$

Pressure Contour
Velocity Contour
Streamlines

Velocity Profile $S_1=70\%$ $S_2=50\%$

Pressure Profile $S_1=70\%$ $S_2=50\%$

Pressure Contour
Velocity Contour
Streamlines
Computer modelling of coronary artery stenting: ‘virtual coronary intervention’

\[ v_{FFR} = 0.65 \]

\[ v_{FFR} = 0.94 \]
Virtual stenting:

1. Tool development
2. Validation
3. Optimal strategy
4. Clinical decisions
Validation of virtual stents

A

FFR 0.77

B

virtual stenosis

vFFR 0.75

C

FFR 0.88

D

vFFR 0.88

mFFR

0.3

0.4

0.5

0.6

0.7

0.8

0.9

1.0
Impact of VCI

- Potential to improve patient management
- Enrich a clinical trial of vFFR

(VCI guided management vs traditional angiography guidance)

Diseased artery: Baseline model

Different stent techniques modelled
FFR changes management

Does Routine Pressure Wire Assessment Influence Management Strategy at Coronary Angiography for Diagnosis of Chest Pain? The RIPCORD Study

Nick Curzen, BM, PhD; Omar Rana, MD; Zoe Nicholas, BSc; Peter Golledge, MD; Azfar Zaman, MD; Keith Oldroyd, MD; Colm Hanratty, MD; Adrian Banning, MD;

FFR changed therapy in 26%

Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: the British Heart Foundation FAMOUS–NSTEMI randomized trial

Jamie Layland1,2, Keith G. Oldroyd1, Nick Curzen3, Arvind Sood4, Kanarath Balachandran5;

FFR changed therapy in 22%
Compare vFFR to mFFR ‘virtual efficacy
VITAL VALIDATION!

[FAMOUS and RIPCORD studies]

BHF?
FFR is just a number!

Activity level
Expectations
Lifestyle

Comorbidity
Frailty

Social context
Setting
Limiting factors

- I know best!
- It takes too long!
- I can’t be bothered!
- I haven’t got time!
- It’s expensive!
- I can stent that!
- I don’t trust it!
The MDT meeting
Organisational issues
Regulatory approval
The future: What comes after FFR?

FFR is valuable, but:

- is *pressure-derived* – flow is inferred, not measured
- reflects *percentage* not *absolute* changes in coronary blood flow
- cannot provide information regarding the microcirculation
- interpretation is difficult in *serial* lesions
- reflects flow limitation relative to a hypothetically normal artery

If we could measure *absolute flow rate* within the coronaries – all these problems would be resolved!
The $Q_{\text{CFD}}$ model implemented in VIRTUheart

($Q_{\text{CFD}}$ vs $Q_{\text{actual}}$ pilot validation: bias +0.31 ml/min; SD, 2.58 ml/min)
What clinicians and patients want
Thanks