Noninvasive Fractional Flow Reserve from Coronary CT Angiography

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Why the hemodynamics for coronary artery disease?
Q: Which is a significant stenosis? Please choose one.

Coronary angiogram: left anterior descending coronary artery
This one should be a significant stenosis!

Angiography: significant

CT angiography: significant

Intravascular ultrasound: significant

Simple and Straightforward.
No room for hemodynamics!

Significant stenosis → Ischemia/Chest pain → Stent or surgery → Better prognosis
Which is a significant stenosis?

: *Anatomy vs. Ischemia*

- Stenosis severity by CT, angiography, intravascular US, ...
- Extent of the perfusion territory
- Presence of myocardial infarction
- Myocardial blood flow including collaterals
- Microvascular function

→ *Physiologic or functional evaluation*
“Fractional Flow Reserve (FFR)”

- Invasive physiologic test in a cath lab with very high spatial resolution

\[
FFR = \frac{Q^S_{\text{max}}}{Q^N_{\text{max}}} = \frac{(P_d-P_v)/R}{(P_a-P_v)/R} = \frac{\text{Distal Pr (}P_d\text{)}}{\text{Proximal Pr (}P_a\text{)}}
\]

Proximal Pressure (\(P_a\)) = 100mmHg

Distal Pressure (\(P_d\)) = 70mmHg

\(\text{FFR} = \frac{70}{100} = 0.7\)

FFR 0.7 means that 30% of myocardial blood flow was reduced due to the stenosis.
Pressure Wire + Hyperemic agent = FFRmyo

FFR vs. Myocardial ischemia

Not significant

Significant stenosis

1.0 0.80 0.75 0
Q: Which is a significant stenosis? Please choose one.

Coronary angiogram: left anterior descending coronary artery

Anatomically insignificant, but hemodynamically significant!

Anatomically significant, but hemodynamically insignificant!
FAME study

Patient with ≥ 2 vessel disease (N=1005)

Angiography-guided PCI (N=496)

FFR-guided PCI (N=509)

2 Year Death/Myocardial infarction-free survival

FFR (hemodynamics)-guided vs. Anatomy-guided
- Less stent
- Less cost
- Same procedural time
- Better clinical outcomes

Tonino, et al. NEJM 2009; Pijls, et al. JACC 2010
FFR is good for the patients and (relatively) simple………

But, requires invasive procedure and expensive (>1,000 USD)……. cannot provide 3D anatomical information…..
How to assess hemodynamics from static images?

3-D Model based on CCTA
Integration of non-invasive coronary imaging and hemodynamic lesion assessment

3-D Model based on CCTA

Hybrid imaging: CCTA + SPECT/PET

Stress CT perfusion imaging

Transluminal attenuation gradient

TAG = -15.42 (HU/10mm)

Estimation from geometry of stenosis
Computational Fluid Dynamics (CFD)

- Computational fluid dynamics (CFD) quantifies fluid pressure and velocity, based on physical laws of mass conservation and momentum balance.
- CFD is widely used in the aerospace and automotive industries for design and testing.
CFD in simple and idealized coronary models

\[
\text{FFR} = \frac{Q_{\text{max}}^S}{Q_{\text{max}}^N} = \frac{P_d}{P_a}
\]


cCTA + CFD = Pt-specific non-invasive FFR

• 2009: Project started

• Feb 2010: Collaboration with CV SIM

Potential collaboration with Cardiovascular Simulation, Inc.

Dear Dr. Koo,

Gilwook Choi (my former PhD student at Stanford) provided your e-mail address to me. Gil is company Cardiovascular Simulation, Inc. I believe that you are familiar with my company and have been doing with John LaDisa. am contacting you to inquire whether you might be interested...
Patient-specific non-invasive FFR using CT & CFD

Computational Model based on CCTA
- 3-D anatomic model from CCTA
- No additional imaging
- No additional medications

Blood Flow Solution
- Blood flow equations solved on supercomputer

Physiologic models
- Myocardial demand
- Morphometry-based boundary condition
- Effect of adenosine on microcirculation

Koo BK, EBC 2011, EuroPCR 2012
Patient-specific non-invasive FFR using CT & CFD

Computational Model based on CCTA
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Koo BK, EBC 2011, EuroPCR 2012
How can this novel technology change our daily practice?

**Current pathway**

- **CCTA**
  - >50% diameter stenosis

- **Invasive angiography**
  - >50% diameter stenosis

- **FFR**
  - FFR 0.74 → PCI

- **Current pathway**
  - >50% diameter stenosis
  - FFR 0.84 → Medical treatment

_SNUH Seoul National University Hospital Cardiovascular Center_
How this novel technology can change our daily practice?

**Novel** (risk-free, non-invasive, cost-saving) pathway

CCTA → FFR$_{CT}$ 0.74 → Invasive procedures

Invasive angiography and PCI

>50% diameter stenosis → FFR 0.74 → no ischemia

PCI

>50% diameter stenosis → Medical treatment

>50% diameter stenosis → FFR 0.84 → no ischemia
First-in-Human study

- To evaluate the feasibility and diagnostic performance of $\text{FFR}_{\text{CT}}$
- Prospective, multicenter study
- 159 vessels in 103 patients
DISCOVER-FLOW study

Diagnostic performance of $\text{FFR}_{\text{CT}}$ and CCTA

Per-vessel analysis (n=159)

- Sensitivity: $\text{FFR}_{\text{CT}} \leq 0.80 = 88$, CCTA $\geq 50\% = 91$
- Specificity: $\text{FFR}_{\text{CT}} \leq 0.80 = 40$, CCTA $\geq 50\% = 47$
- PPV: $\text{FFR}_{\text{CT}} \leq 0.80 = 92$, CCTA $\geq 50\% = 89$
- NPV: $\text{FFR}_{\text{CT}} \leq 0.80 = 92$, CCTA $\geq 50\% = 89$
- Accuracy: $\text{FFR}_{\text{CT}} \leq 0.80 = 59$

PPV: positive predictive value, NPV: negative predictive value

Clinical Evidences on Diagnostic Performance

- **DISCOVER-FLOW**
  - 5 center FIH clinical trial
  - Completed 2011
  - N=103 patients
  - Published in JACC

- **DeFACTO**
  - 17 center clinical trial
  - Completed 2012
  - N=252 patients
  - Published in JAMA

- **NXT**
  - 10 center clinical trial
  - Completed August, 2013
  - N=251 patients
  - Published in JACC
## Diagnostic performance of FFR<sub>CT</sub>

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISCOVER-FLOW</td>
<td>103</td>
<td>93%</td>
<td>82%</td>
<td>85%</td>
<td>91%</td>
</tr>
<tr>
<td>DeFACTO</td>
<td>252</td>
<td>90%</td>
<td>54%</td>
<td>67%</td>
<td>84%</td>
</tr>
<tr>
<td>NXT</td>
<td>251</td>
<td>86%</td>
<td>79%</td>
<td>65%</td>
<td>92%</td>
</tr>
<tr>
<td><strong>Total: 606</strong></td>
<td></td>
<td>90%</td>
<td>72%</td>
<td>72%</td>
<td>89%</td>
</tr>
</tbody>
</table>
Non-invasive tests/\( \text{FFR}_{\text{CT}} \)/Angiography vs. FFR

- Stress Echo
- MPI
- Angiography
- CT
- FFR\(_{\text{CT}}\)-DeFACTO
- FFR\(_{\text{CT}}\)-DiscoverFLOW
- FFR\(_{\text{CT}}\)-NXT
- CCTA
- Angiography
- MPI

Specificity vs. Sensitivity

- 30% - 100%

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3. Muller et al. JACC Intervention 2011;4
4. Min et al. JAMA 2012;308:1237-1245
7. Park et al. JACC 2012
8. Norgaard et al. JACC 2014
Clinical outcomes of FFR_{CT}-guided decision

Stable CAD symptoms; Planned non-emergent NI test or catheterization
Age ≥ 18y; No prior CAD hx; Intermediate pretest probability of CAD

### Planned NI test

- Standard NI test
- Exercise ECG
  - Stress nuclear
  - Stress echo
  - Stress MRI
  - CTA
- CTA + FFR_{CT}
- CTA
- FFR_{CT}
- No FFR_{CT}

### Planned ICA

- Standard ICA
- CTA + FFR_{CT}
- CTA
- FFR_{CT}
- No FFR_{CT}

Testing/cath performed and interpreted locally; FFR_{CT} results w/in 24–48 hrs
All F/U testing and management decisions by care team following best practices

1° — Cath w/o obstructive CAD (QCA or FFR ≤ 0.80) at 90 days
2° — MACE: death, MI, UA; Radiation (Costs; QOL)
Clinical outcomes of FFR\textsubscript{CT}-guided decision
From CTA to CT-FFR and its beyond…

Planning the treatment strategy using
Virtual revascularization & CT-derived computed FFR
Planning the treatment strategy using Virtual revascularization & CT-derived computed FFR

Before Stenting

<table>
<thead>
<tr>
<th>Stent proximal lesion only</th>
<th>Stent distal lesion only</th>
<th>Stent both</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.76</td>
<td>0.74</td>
<td>0.86</td>
</tr>
</tbody>
</table>

After Stenting

CT-derived computed FFR (FFR_{CT})

Kim KH, Koo BK, et al. JACC interv 2014
Planning the treatment strategy using Virtual revascularization & CT-derived computed FFR

Before Stenting

Angiography

After Stenting

Stent

Invasive FFR

CT-derived computed FFR (FFR_{CT})

Myocardial ischemia +

No residual ischemia

Kim KH, Koo BK, et al. JACC interv 2014
Diagnostic performance of $\text{FFR}_{\text{CT}}$ after virtual stenting to predict the residual ischemia

Kim KH, Koo BK, et al. JACC interv 2014
Virtual surgery before the surgery, with your computer

\[ \text{FFR}_{CT} \text{ after one arterial graft and 2 saphenous vein grafts} \]
Non-invasive hemodynamic measurement: Can we do more?

Coronary CT angiography + Computational fluid dynamics

Pressure

Velocity

Rest

Hyperemia
Non-invasive hemodynamic force measurement: Is this feasible?

Coronary CT angiography + Computational fluid dynamics

Simulation

Velocity
Pressure

Cauchy Stress Tensor
\[ T = -pI + \mu((\nabla \nu) + (\nabla \nu)^T) \]

Traction vector
\[ t = Tn = -pn + \mu((\nabla \nu) + (\nabla \nu)^T)n \]

Wall Shear Stress (WSS)
\[ \tau_{\text{mean}} = \frac{1}{T} \int_0^T t_s \, dt \]
\[ t_s = t - (t \cdot n)n \]

Oscillatory Shear Index (OSI)
\[ OSI = \frac{1}{2} \left( t_s - \frac{1}{T} \int_0^T t_s \, dt \right) \]

Particle Residence Time, Turbulent Kinetic Energy, ...

Seoul National University Hospital Cardiovascular Center
Non-invasive WSS assessment using cCTA and CFD

Koo BK. International Symposium on Biomechanics 2014
Association with Adverse plaque characteristics
: WSS vs. % diameter stenosis

Napkin ring sign

Positive remodeling

DS: % diameter stenosis, WSSR: resting wall shear stress, WSSH: hyperemic wall shear stress

Park JB, Koo BK, Taylor C, et al. Submitted
Novel hemodynamic index: **Axial Plaque Stress**

**Axial plaque stress** uniquely characterizes the diseased segment of both upstream and downstream.

Choi GW…Koo BK. JACC imaging 2015
Distribution of Axial Plaque Stress in patients

Choi GW…Koo BK. JACC imaging 2015
Influence of “Lesion Shape” on Hemodynamic Parameters (n=114)

% Diameter Stenosis

FFR_{CT}

| Axial Plaque Stress | (dyne/cm²) |

Choi GW…Koo BK. JACC imaging 2015
Plaque rupture at segments 6 and 7

Choi GW, TPF workshop 2014, Incheon
APS and Future Event: CASE

2011-04 CT, Asymptomatic

2012-06 Acute MI
APS and Future Event: CASE

2011-04 CT, Asymptomatic

2012-06 Acute MI

<table>
<thead>
<tr>
<th>APS</th>
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<tbody>
<tr>
<td>Upstream</td>
</tr>
<tr>
<td>Downstream</td>
</tr>
</tbody>
</table>

Choi GW…Koo BK. JACC imaging 2015
Comprehensive non-invasive assessment for CAD using cCTA and CFD

- Non-invasive hemodynamic assessment
  - Wall shear stress
  - Axial plaque stress

Mauroich_Horvat P, ..., Hoffman U. Nat Rev Cardiol 2014
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