Limits of anatomy to predict physiology

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Disclosure Statement of Financial Interest

Within the past 12 months, Nils Johnson has had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

- Grant/Research Support
  \((pending\) to institution)\n
- Non-disclosure agreements
  \((non-financial)\)

Company

- St Jude Medical
- Volcano Corporation

However, Nils Johnson has \textit{never} personally received \textit{any} money from \textit{any} commercial company.
“If you want new ideas, read old books”

- attributed to Ivan P. Pavlov

(Russian physiologist, 1849-1936, Nobel prize 1904, “Pavlov’s dog”)
Coronary Pressure
From a Physiological Index to a Clinical Tool

Thesis by
Bernard de Bruyne, MD
From the Cardiovascular Center, Aalst, Belgium

To be submitted in partial fulfillment of the requirements for the degree of
"Agrégé de l'Enseignement Supérieur"

Co-Promoters:
Jacques A. Melin, MD
William Wijns, MD

1995
“cardiologists continue to base major clinical decisions about coronary artery disease on inferences … based largely on … morphological data, such as provided by the coronary arteriogram”
CT angiogram

angiogram

infer

significance

\downarrow

decision

Invasive angiogram

Koo BK, JACC 58(19):1989, 2011, Figure 1, panel A
CT angiogram

anatomy

infer (predict)

physiology

Invasive angiogram

Koo BK, JACC 58(19):1989, 2011, Figure 1, panel A
**Anatomy** to predict physiology

%DS linked to CFR – 1974

Stenosis flow reserve (SFR) – 1986

CT-modeled FFR \((\text{FFR}_{\text{CT}})\) – 2010
Anatomic predictions

- **accurate**
  (work well on average)

- **imprecise**
  (uncertain for an individual)
Anatomy variable (here %DS)

Physiology variable (here FFR)
Measurement of uncertainty

- CT angiography resolution $\approx 0.6 \text{ mm}$
- Invasive angiography $\approx 0.2 \text{ mm}$
- IVUS $\approx 0.1 \text{ mm}$
- OCT $\approx 0.02 \text{ mm}$
- Pressure wire $\approx 1 \text{ mmHg}$
“Left main” stenosis

4.4mm  50%DS  2.2mm

ΔP

Poiseuille law: $\Delta P \propto \frac{1}{\text{radius}^4}$
Relative error $\Delta P/P = 4 \times \Delta \text{radius} / \text{radius}$

- **CTA** = $4 \times 0.6/1.1 = 218\%$ error in $\Delta P$
- **Invasive** = $4 \times 0.2/1.1 = 73\%$
- **IVUS** = $4 \times 0.1/1.1 = 36\%$
- **OCT** = $4 \times 0.02/1.1 = 7\%$
Test/retest repeatability

- FFR ±0.02
- %DS ±5-8% by QCA
- MLA ±0.3-0.6 mm²
- MLD ±0.1-0.3 mm

Johnson NP, Circ Cardiovasc Imaging 6(5):817, 2013, summary of Table 1
**Biologic variability**

Average CFR for entire LV

- Mode: 2.72 (most common)
- Mean: 3.04 ± 0.97
- Median: 2.95 (IQR 2.32-3.68)
- Range: from 0.58 to 7.13

N = 1,500 consecutive PET scans

*group vs individual*

Johnson NP, *Circ Cardiovasc Imaging* 6(5):817, 2013, Figure 1A

Unpublished, multicenter data

\[ n=4,442 \]
2013 ESC guidelines on the management of stable coronary artery disease

The traditional understanding of SCAD is that of a disease causing exercise- and stress-related chest symptoms due to narrowings of \( \geq 50\% \) in the left main coronary artery and \( \geq 70\% \) in one or several of the major coronary arteries.
Stenosis flow reserve (SFR)
• Introduced in 1986
• Gould and Kirkeeide
• Anatomy from QCA
• Modeled CFR
• Commercially available from Philips

CT-modeled FFR (FFR\textsubscript{CT})
• Introduced in 2010
• Taylor and colleagues
• Anatomy from CT angiogram
• Modeled FFR
• Commercial distribution by HeartFlow (not yet in USA)
QCA-modeled CFR

A

±0.4mm imaging resolution

reference vessel 3.5mm diameter

Fractional flow reserve (FFR)

Stenosis Flow Reserve (SFR)

0 1 2 3 4 5

B

FFRrmyo

Stenosis Flow Reserve (Angio)

0 1 2 3 4 5

0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1

Johnson NP, Circ Cardiovasc Imaging 6(5):817, 2013, Figure 3A

Bartůnek J, JACC 26(2):328, 1995, Figure 3 (bottom)
CT-modeled FFR

**A**

\[
\text{FFR by CT angiography (FFR}_{\text{CT}}) \quad \pm 0.6\text{mm imaging resolution} \\
\text{reference vessel 3.5mm diameter}
\]

**B**

\[
R = 0.72 \\
p < 0.001
\]

Fractional flow reserve (FFR)

Johnson NP, *Circ Cardiovasc Imaging* 6(5):817, 2013, Figure 4A

Koo BK, *JACC* 58(19):1989, 2011, Figure 4
CT-modeled FFR

Johnson NP, Circ Cardiovasc Imaging 6(5):817, 2013, Figure 5A
CT-modeled FFR

**DISCOVER-FLOW** (2011)
**DeFACTO** (2012)
**NXT** (2013)

DISCOVER FLOW = Koo BK, *JACC* 58(19):1989, 2011, Figure 4
DeFACTO = Nakazato R, *Circ Cardiovasc Imaging* 6(6):881, 2013, Figure 1A
NXT = Nørgaard BL, *JACC* 63(12):1145, 2014, Figure 3
# Physiology models

<table>
<thead>
<tr>
<th>Model</th>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Correlation</th>
<th>AUC</th>
<th>Accuracy</th>
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<tr>
<td>SFR</td>
<td>Bartůnek</td>
<td>1995</td>
<td>110</td>
<td>0.78</td>
<td>0.89</td>
<td>84%</td>
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<tr>
<td>Di Mario</td>
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<td>1996</td>
<td>21</td>
<td>0.57</td>
<td>0.87</td>
<td>80%</td>
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<tr>
<td>FFR&lt;sub&gt;CT&lt;/sub&gt;</td>
<td>DISCOVER-FLOW</td>
<td>2011</td>
<td>159</td>
<td>0.68</td>
<td>0.90</td>
<td>84%</td>
</tr>
<tr>
<td>DeFACTO</td>
<td></td>
<td>2012</td>
<td>407</td>
<td>0.63</td>
<td>0.81</td>
<td>69%</td>
</tr>
<tr>
<td>NXT</td>
<td></td>
<td>2014</td>
<td>251</td>
<td>0.82</td>
<td>0.90</td>
<td>81%</td>
</tr>
</tbody>
</table>

little Δ in 20 yrs
“Albeit often statistically significant, the correlations between angiographic and functional indices ... are too weak to be clinically relevant”
“too weak to be clinically relevant”

Toth G, Eur Heart J. 2014 Mar 18. [Epub ahead of print], Figure 1A