Prof Ribichini is providing this presentation on behalf of Volcano Europe
Volcano & Philips Stronger Together

<table>
<thead>
<tr>
<th>Healthy Living</th>
<th>Prevention</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Recovery</th>
<th>Home Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal Care</td>
<td>Health &amp; Wellness</td>
<td>Diagnostic Imaging</td>
<td>Image Guided Therapy</td>
<td>Patient Care &amp; Monitoring Solutions</td>
<td>Customer Services</td>
</tr>
<tr>
<td>Domestic appliances</td>
<td>Ultrasound</td>
<td>Healthcare Informatics, Solutions &amp; Services</td>
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</tr>
</tbody>
</table>

23% Diagnostic Imaging
Ultrasound
Image Guided Therapy (Volcano) Solutions

Empowering physicians to choose from an array of precise diagnostic and guidance tools supported by clinical and economic evidence.

Improving efficiency in the modern interventional suite by simplifying and increasing access to intravascular imaging and functional management.

Identify opportunities to align clinical adoption with the available level of evidence.

Innovation to address clinical utility & needs.

Continuum Of Care
FFR Use Has Grown Tremendously...
...On the Back of Strong Guidelines Support...

**CLASS IIa Level of Evidence A:** FFR is reasonable to assess angiographic intermediate coronary lesions (50% to 70% diameter stenosis) and can be useful for guiding revascularization decisions in patients with SIHD. (p32)

- Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS); European Association for Percutaneous Cardiovascular Interventions (EAPCI), Wijns W et al. Guidelines on myocardial revascularization. Eur Heart J. 2010 Oct;31(20):2501-55.
Physiology Use is Still Globally Limited* (%FFR of Diagnostic Catheterization)

*Data on file at Volcano
Physiology Use in Western Europe* (%FFR Penetration vs PCI: 11%)

* Data on file at Volcano
Innovation to Address Clinical Needs

Diagnostic Angio with Obstructive Disease
- Treatment decisions are often determined by angiography alone, with or without non-invasive tests.

Diagnostic Angio without Obstructive Disease
- Patients are sometimes told the angina-like symptoms they experience are “definitely” not their heart.

PCI Guidance for Stable Angina
- Justification to treat may be subjected to FFR, but which lesions get treated are still often driven by angiography.

PCI Guidance for Acute Coronary Syndrome (ACS)
- Non-culprit disease is sometimes submitted to non-invasive testing or staged to determine significance.

Advancing the Tools (Wires, Software, Systems)

Advancing the Science (Targeted Clinical Programs)
IVUS / VH in the assessment of coronary lesion

ESC/EACTS Guidelines on myocardial revascularization

**Recommendations**

<table>
<thead>
<tr>
<th>Class</th>
<th>Level</th>
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<tbody>
<tr>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>IIA</td>
<td>C</td>
</tr>
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</table>

**Prospect Study Published in The New England Journal of Medicine Demonstrates that IVUS and VH® IVUS Technologies Can Assess Risk of a Future Clinical Event Better Than Using Angiography Alone**

*N Engl J Med 2011;364:226-35*
Innovation to Address Clinical Needs

**Pressure/ Flow Guide Wires:**
- Verrata™
- ComboWire™
- continuous development

**Software:**
- iFR®, Pullback,
- Co-Registration, CABG Mapping. “Virtual PCI”

**System:**
- CORE FM™
- CORE™ Mobile,
- CORE™ Integrated

**Design Objectives:**
- Choice of modalities
- Simplified workflows
- Co-registered with the angiogram

- Frontline wire experience
- Durable for longer, multi-vessel procedures

**Design Objectives:**
- Choice of system options to meet individual lab needs

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Verrata™, Combowire®, Core™ Mobile, Omni™ and iFR® are registered trademarks of Volcano Corporation. Technology under development at Volcano Corporation. Verrata™, iFR® Pullback is CE Marked and FDA Cleared. iFR® is CE marked. iFR Co-Registration, CABG Mapping, “Virtual PCI,” NG Combowire™, NG Frontline are development project, Not yet CE-marked and will not be marketed or put into service until it is CE-marked.
Volcano Physiology Product Portfolio

Coronary and Peripheral Guide Wires, Hardware and Modalities

Modalities
- FFR
- CFR
- pFFR peripheral
- iFR

Hardware
- CORE™ Mobile & Integrated System
- CORE FM
- ComboMap® Console
- SmartMap® Console
- Verrata™ Pressure Wire
- PrimeWire® Prestige PLUS w/ AcuSense™
- PrimeWire® Prestige
- FloWire®
- ComboWire® XT (Combined Pressure / Flow)

CORE FM and pFFR are development programs at Volcano. Not yet CE-marked and will not be marketed or put into service until it is CE-marked.
Clinical Investment Enabling Functional Guidance

- Over 4000 patients have been studied with iFR
- Numerous prospective iFR studies have been published in peer-reviewed journals
- More than 1500 equipped with iFR worldwide

Major Enrolling Randomized Controlled Trials

Syntax II N=450

iFR in all 3 major epicardial vessels*

- \( iFR < 0.86 \)
- \( 0.86 \leq iFR < 0.93 \)
- \( iFR > 0.93 \)

**DEFINE FLAIR**

- Intermediate lesion requiring physiological assessment
- In ACS: intermediate non-culprit lesion
- \( N=2500, 1:1 \) randomisation

- **FFR**
  - **Guided PCI**
    - **FFR > 0.8**
      - Defer PCI
    - **FFR < 0.8**
      - Perform PCI
  - **IFR**
    - **Guided PCI**
      - **IFR > 0.9**
        - Defer PCI
      - **IFR < 0.9**
        - Perform PCI

**30 day, 1, 2 and 5yr follow-up**

*FFR with adenosine, IFR/FFR in side branches, all at discretion of the operator
### Clinical Investment Enabling Functional Guidance

**Total N= 10350**

<table>
<thead>
<tr>
<th>Study</th>
<th>Geographies</th>
<th>Patients</th>
<th>Endpoint Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVISE II† (2013)</td>
<td>US, EU, ME</td>
<td>800</td>
<td>• Diagnostic accuracy of iFR®/ FFR ‘hybrid approach’</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Hyperemia savings of ‘hybrid approach’</td>
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<tr>
<td>MITNEC* (2013)</td>
<td>Canada</td>
<td>500</td>
<td>• Diagnostic yield of non-invasive tests vs. FFR</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Performance of iFR® vs. FFR vs. non-invasive tests</td>
</tr>
<tr>
<td>ORBITA* (2013)</td>
<td>UK</td>
<td>300</td>
<td>• Impact of PCI on QOL metrics vs. OMT alone</td>
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<td></td>
<td></td>
<td></td>
<td>• Ability of ‘Functional Gain’ to predict QOL gains</td>
</tr>
<tr>
<td>J-DEFINE* (2013)</td>
<td>Japan</td>
<td>500</td>
<td>• Practical use and events using ‘hybrid’ iFR® / FFR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Mismatch of non-invasive and angio w/ FFR &amp; iFR®</td>
</tr>
<tr>
<td>SYNTAX II (2013)</td>
<td>EU</td>
<td>450</td>
<td>• State of the art PCI (Hybrid iFR/FFR Guided treatment and IVUS Guided implantation) vs. CABG (historical control) in moderate and high SYNTAX score patients.</td>
</tr>
<tr>
<td>DEFINE FLOW* (2014)</td>
<td>US, EU, JP, KO, ME, AF</td>
<td>500</td>
<td>• Natural history of physiology (pressure and flow)</td>
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<td></td>
<td></td>
<td></td>
<td>• Outcomes of CFR &amp; FFR quadrants (MACE)</td>
</tr>
<tr>
<td>DEFINE FLAIR* (2014)</td>
<td>US, EU, JP, KO, ME, AF</td>
<td>2,500</td>
<td>• Non-inferiority of iFR® vs. FFR (Stable, UA, ACS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Safety of deferral of non-culprit during primary PCI</td>
</tr>
<tr>
<td>iFR SWEDEHEART* (2014)</td>
<td>Sweden</td>
<td>2,500</td>
<td>• Non-inferiority of iFR® vs. FFR (Stable, UA, ACS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Predictive value of post-PCI iFR on outcomes</td>
</tr>
<tr>
<td>DEFINE Dx† (2016)</td>
<td>US, EU</td>
<td>2,000</td>
<td>• Appropriateness of patients with high risk factors to bypass nuclear and proceed to cath w/FFR</td>
</tr>
<tr>
<td>DEFINE PAD† (2017)</td>
<td>US</td>
<td>300</td>
<td>• Ability of pFFR to predict event rates following PAD stenting and atherectomy</td>
</tr>
</tbody>
</table>
Innovation to Enable Functional Guidance
Providing Choice between FFR and

iFR® Co-Reg
2017-2020

iFR Scout™
2015-2016

iFR®
2013-2014

VOLCANO
PRECISION GUIDED THERAPY

PHILIPS
A Vision for More Physiologic Guidance: iFR SCOUT

Functionally **Justified** PCI

- Is the vessel significant?
  - FFR < 0.80
  - Yes, a stent is needed.

Functionally **Guided** PCI

- Is the Vessel Significant?
  - FFR < 0.80

- Which lesion(s) are significant?
  - Physiologic pullback to identify largest increases?

- How many stents are needed?

- Have the gradients been resolved?
  - Post-PCI iFR measurements.
iFR SCOUT total vessel assessment
Male 80 Y

New Angina symptoms

PCI LAD / RCA in 2003

Culprit lesion in LCX treated with PCI

Suspicious RCA disease

iFR Pullback

IFR®
Distaal
0.91

FFR Pullback

FFR 0.83
A (Sync)Vision for Functional Guidance*

*Product under development, Not yet CE-marked, will not be marketed or put into service until it is CE-marked
Conclusions

1. Any physiologic assessment (CFR, HSR, BSR, IMR, FFR, iFR or Pd/Pa) is better than angiography alone.
2. Improving ‘angiography alone’ will be driven by
   – the right clinical investments, the right technical advancements (simpler, easier, faster)
   – robust clinical research based on outcomes
   – and educational initiatives (Courses like ETP)
3. Functionally-guided myocardial revascularization