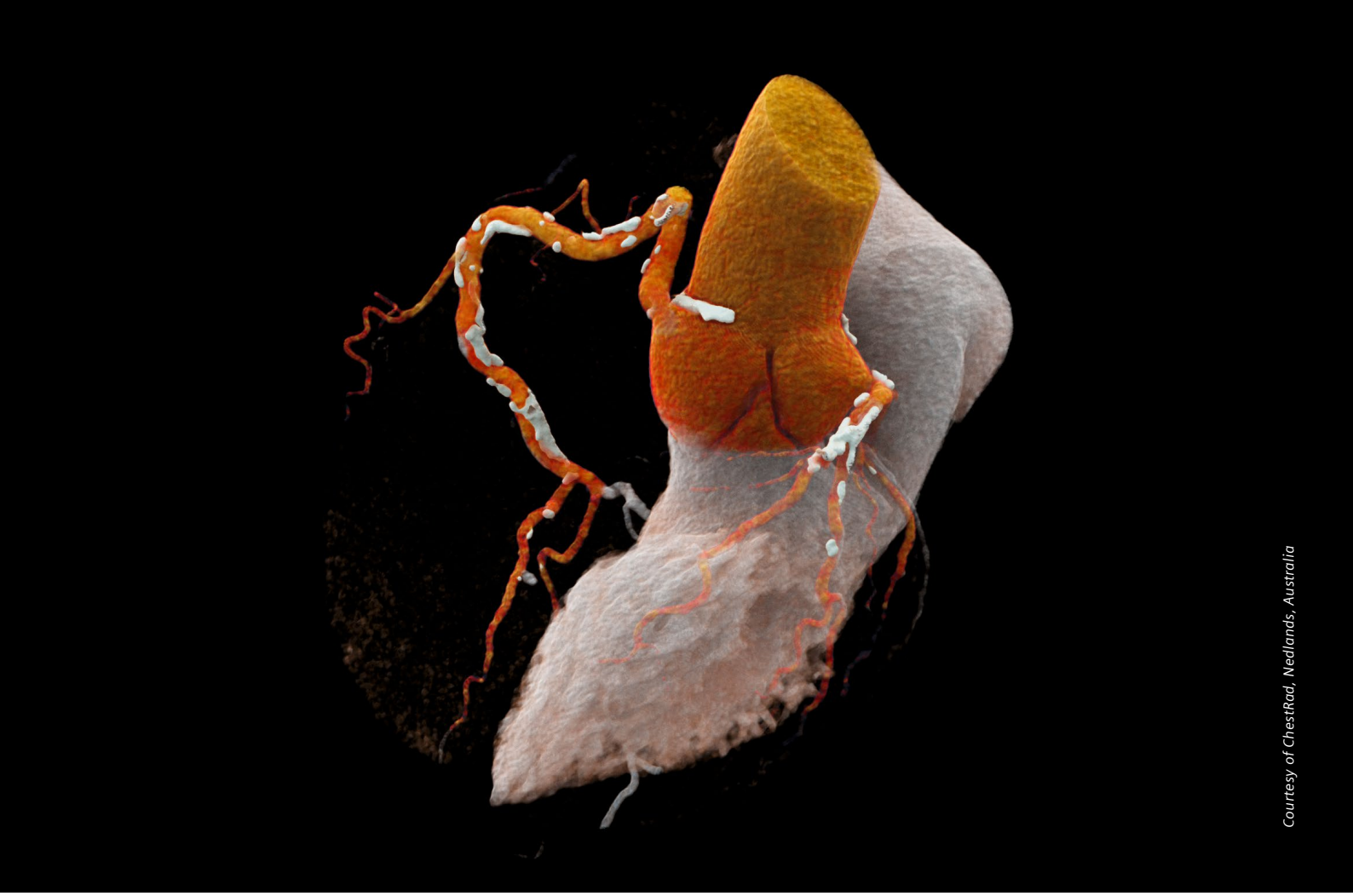


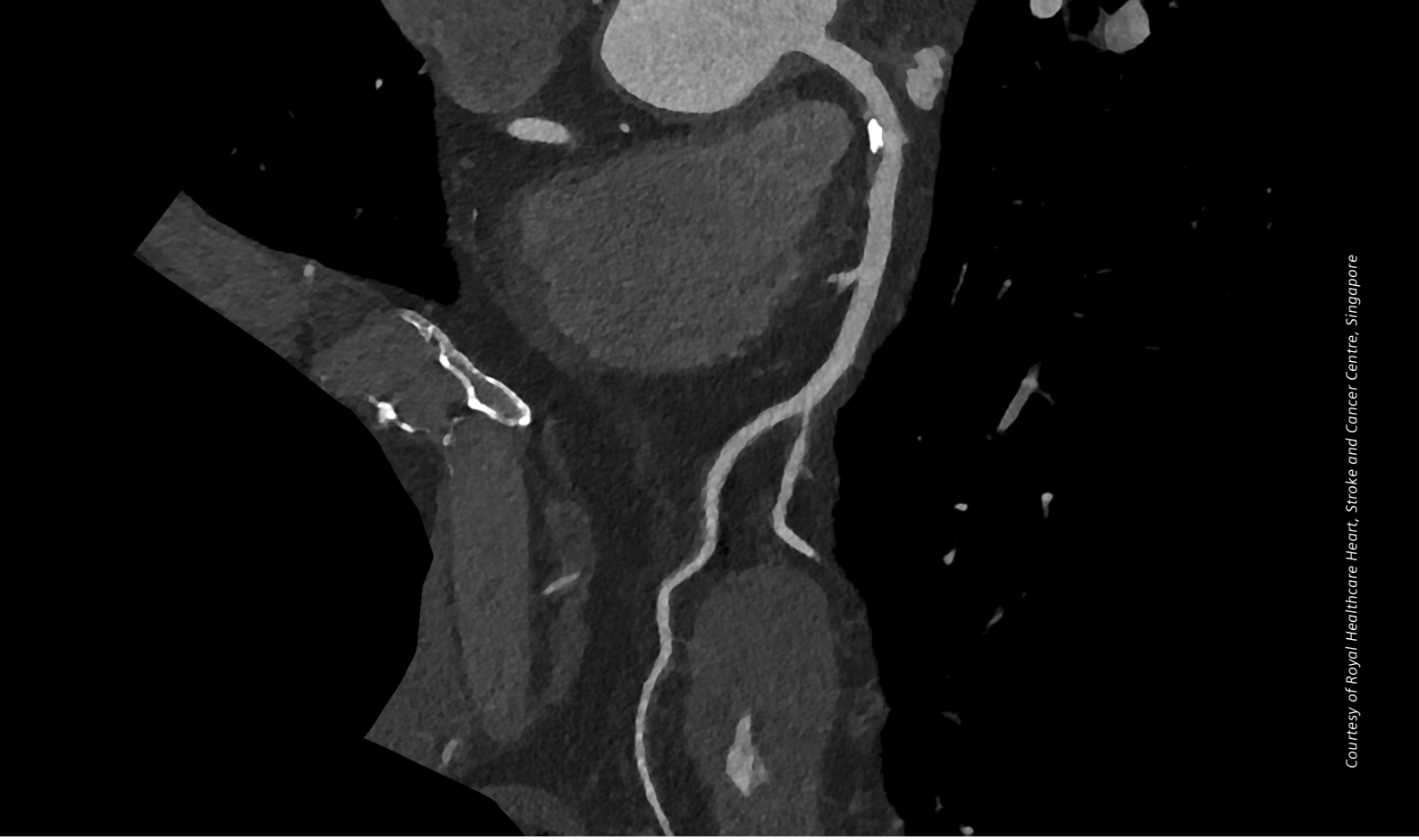
Courtesy of ChestRad, Nedlands, Australia

Whitepaper

Beyond stenosis: Sex-specific plaque morphology and management of coronary artery disease

Author: Claudia Frank

SIEMENS Healthineers



Courtesy of Royal Healthcare Heart, Stroke and Cancer Centre, Singapore

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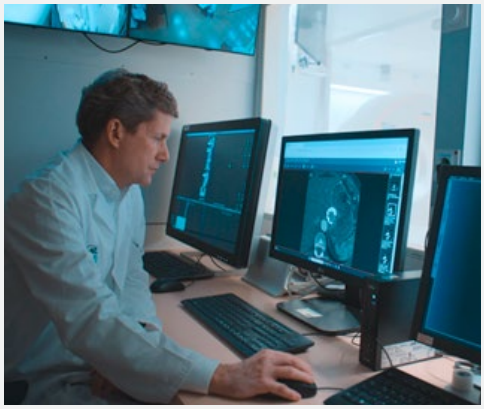

"The classical risk assessment does not work as accurately in women. And here, additional information, such as plaque morphology, becomes a decisive additional criterion: Is the patient at risk of a heart attack or not?"

Prof. Christian Loewe, MD
Radiologist
Head of the Division of Cardiovascular and Interventional Radiology
AKH Vienna and MedUni Vienna, Austria

From stenosis-based assessment to the contemporary concept of high-risk plaque

Coronary diagnostics have traditionally been based on luminal stenosis. This approach is, however, increasingly being questioned as many acute coronary syndromes are caused by lesions that are not hemodynamically significant. This is particularly relevant in women in whom non-calcified or erosion-prone plaques are more prevalent and may not be identified by conventional angiography. In younger women especially, the sensitivity of the coronary calcium score is limited, because early biologically active plaques are frequently non-calcified [1, 7].

Contemporary diagnosis has shifted to a plaque-based focus. Here, high-risk plaque is defined according to the interplay of plaque burden, composition, inflammation, remodeling, and individual thrombogenic state rather than a single morphological feature. Features include lipid-rich plaques, thin fibrous caps, positive remodeling, spotty calcifications, and the napkin-ring sign [1]. This shift affects risk stratification as well as interventional planning and decision-making [8].

Sex-specific differences in plaque biology, morphology, and progression

Serial coronary CT studies show consistent sex-related differences in plaque burden and composition. In stable coronary artery disease cohorts, women exhibit fewer lesions and lower fibrotic-lipid plaque components, with greater regression of fibrous and non-calcified plaque before age 55. In postmenopausal women, long-term data show lower baseline plaque burden and attenuated progression of non-calcified and total plaque volume compared with men. Although derived from distinct populations, these findings suggest that sex-related differences in coronary atherosclerosis are driven more by plaque composition and biological activity than by total plaque volume alone [11, 12].

Beyond morphology, inflammation also modulates plaque instability and progression. CT-based assessment of perivascular adipose tissue provides an indirect marker of vascular inflammation, and sex-specific immune and adipose responses may contribute to divergent outcomes despite similar plaque burdens [5, 7].

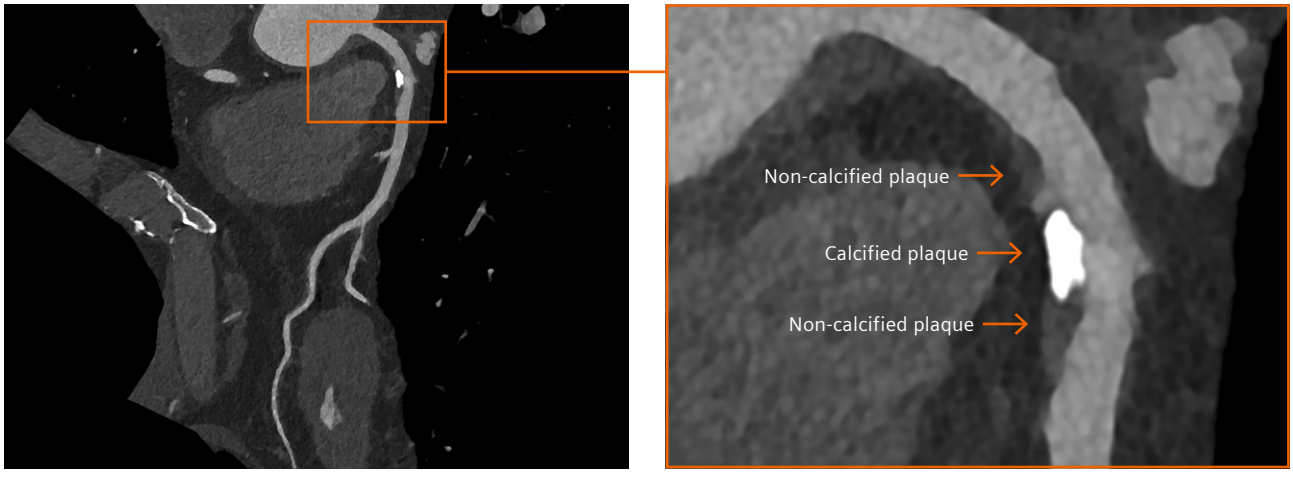

Figure 1: Non-calcified vs. calcified plaque on a photon counting CT

Courtesy of Royal Healthcare Heart Stroke & Cancer Center, Singapore

Plaque rupture versus plaque erosion: Distinct mechanisms

Plaque rupture typically arises when a lipid-rich plaque with a thin fibrous cap tears, exposing the necrotic core to the bloodstream and triggering immediate thrombus formation, that can result in partial or complete coronary artery occlusion. This mechanism is more frequently observed in men. By contrast, plaque erosion is characterized by endothelial dysfunction or denudation with an intact fibrous cap and relatively less lipid-rich and less inflamed plaque. This accounts for a substantial proportion of acute coronary syndromes and is more commonly observed in women and younger patients. Erosive lesions often show less severe stenosis and minimal calcification yet can still cause significant thrombosis. These differences help explain sex-specific variations in acute coronary syndrome presentation [1, 4].

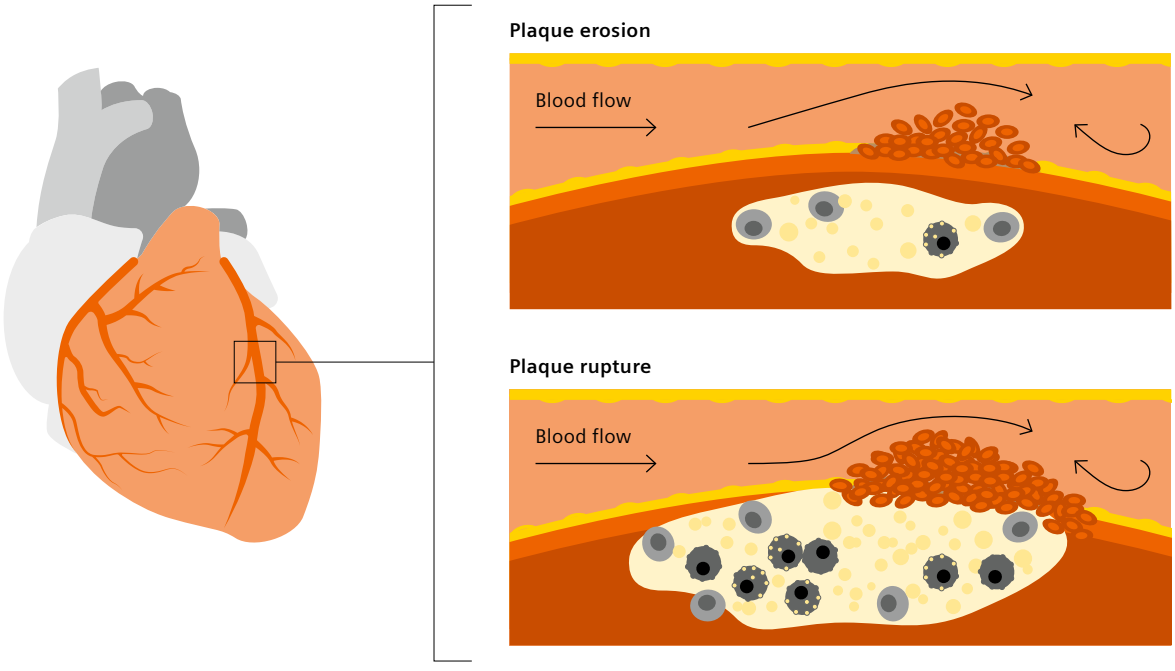

Figure 2: Plaque erosion versus plaque rupture

Imaging of high-risk plaque: Coronary CT and intravascular imaging

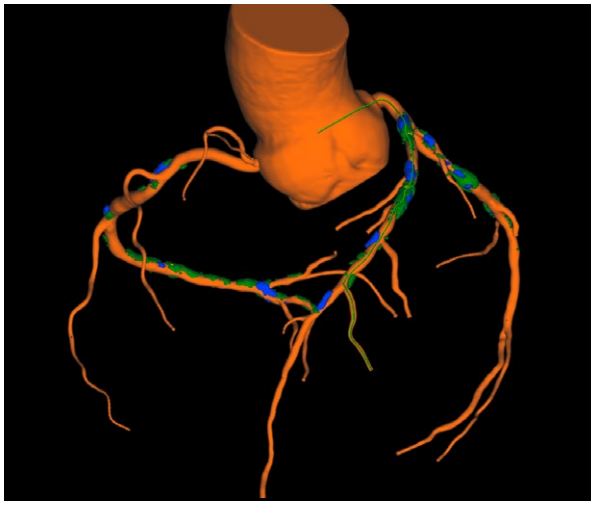

Figure 3A: Anatomical overview of the coronary tree showing plaque information based on CT data on the angiography system for CT-guided PCI

Courtesy of the Cardinal Stefan Wyszynski National Institute of Cardiology

Coronary CT allows noninvasive, reproducible quantification of plaque burden and identification of high-risk features. Modern photon-counting CT technology combined with dual source improves spatial and temporal resolution for reduced calcium blooming. This enables, in particular, a more precise assessment of mixed and non-calcified plaques. Intravascular imaging modalities, such as intravascular ultrasound and optical coherence tomography, complement CT with real-time intraprocedural plaque information that can be used during complex coronary interventions to support guidance and assessment [3, 6].

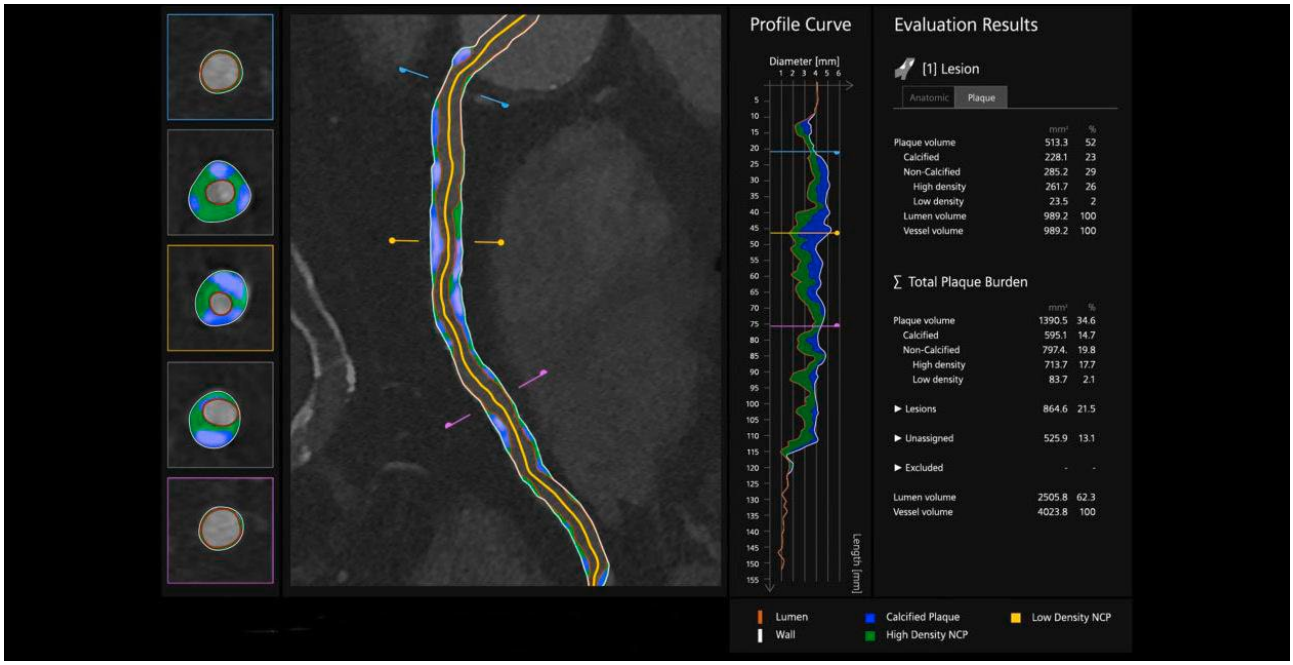

Figure 3B: AI segmented plaque characterizing both the amount and the morphology of coronary plaque

Courtesy of Semmelweis University, Budapest, Hungary

Plaque morphology and inflammation: Clinical implications for treatment strategy

Sex-specific differences in plaque morphology have therapeutic implications. Diagnostic strategies based on stenosis severity or calcium scoring may underestimate the risk, especially in women. An approach based on plaque biology enables earlier, individualized risk assessment, even in the absence of traditional risk factors [8].

Atherosclerotic plaque should be viewed as a modifiable substrate rather than merely a mechanical narrowing. Intensive reduction of low-density lipoprotein (LDL) promotes plaque stabilization and regression, which supports the early use of high-intensity statins and, when appropriate, PCSK9 inhibitors [10]. Beyond lipid burden, inflammation is another modifiable driver of risk, and anti-inflammatory therapy reduces cardiovascular events independent of LDL lowering [13]. These findings support an integrated and early lipid- and inflammation-targeted prevention strategy, complemented by comprehensive risk factor management and lifestyle intervention.

This conceptual shift extends to the interventional setting. A plaque-based perspective helps explain recurrent angina despite technically successful percutaneous coronary intervention (PCI). This is often due to diffuse plaque burden, incomplete revascularization, or non-obstructive mechanisms such as microvascular dysfunction [8]. Incorporating coronary CT imaging into preprocedural planning and intervention – potentially through CT-guided PCI – together with physiology-guided assessment and targeted intravascular imaging may improve lesion selection and reduce residual ischemia [1, 8, 9].

Conclusions

High-risk plaque is not a uniform concept. Women and men exhibit distinct patterns of plaque morphology, progression, and pathophysiological mechanisms that precipitate acute coronary events. A sex-sensitive, imaging-based, and plaque-focused strategy is therefore a key component of modern, individualized concepts for prevention, early detection, and management of coronary artery disease.

Disclaimer

The statements by customers of Siemens Healthineers described herein are based on results that were achieved in the customer's unique setting. Because there is no "typical" hospital or laboratory and many variables exist (e.g., hospital size, samples mix, case mix, level of IT and/or automation adoption) there can be no guarantee that other customers will achieve the same results.

The products/features mentioned herein are not commercially available in all countries. Their future availability cannot be guaranteed.

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