Near-Infrared Spectroscopy Enhances Intravascular Ultrasound Assessment of Vulnerable Coronary Plaque
A Combined Pathological and In Vivo Study


Objectives—Pathological studies demonstrate the dual significance of plaque burden (PB) and lipid composition for mediating coronary plaque vulnerability. We evaluated relationships between intravascular ultrasound (IVUS)–derived PB and arterial remodeling with near-infrared spectroscopy (NIRS)–derived lipid content in ex vivo and in vivo human coronary arteries.

Approach and Results—Ex vivo coronary NIRS and IVUS imaging was performed through blood in 116 coronary arteries of 51 autopsied hearts, followed by 2-mm block sectioning (n=2070) and histological grading according to modified American Heart Association criteria. Lesions were defined as the most heavily diseased 2-mm block per imaged artery on IVUS. IVUS-derived PB and NIRS-derived lipid core burden index (LCBI) of each block and lesion were analyzed. Block-level analysis demonstrated significant trends of increasing PB and LCBI across more complex atheroma ($P_{\text{trend}}<0.001$ for both LCBI and PB). Lesion-based analyses demonstrated the highest LCBI and remodeling index within coronary fibroatheroma ($P_{\text{trend}}<0.001$ and 0.02 versus all plaque groups, respectively). Prediction models demonstrated similar abilities of PB, LCBI, and remodeling index for discriminating fibroatheroma (c indices: 0.675, 0.712, and 0.672, respectively). A combined PB+LCBI analysis significantly improved fibroatheroma detection accuracy (c index 0.77, $P=0.028$ versus PB; net-reclassification index 43%, $P=0.003$), whereas further adding remodeling index did not (c index 0.80, $P=0.27$ versus PB+LCBI). In vivo comparisons of 43 age- and sex-matched patients (to the autopsy cohort) undergoing combined NIRS-IVUS coronary imaging yielded similar associations to those demonstrated ex vivo.

Conclusions—Adding NIRS to conventional IVUS-derived PB imaging significantly improves the ability to detect more active, potentially vulnerable coronary atheroma. (Arterioscler Thromb Vasc Biol. 2015;35:2423-2431. DOI: 10.1161/ATVBAHA.115.306118.)

Key Words: atherosclerotic plaque • coronary artery disease • intravascular imaging • remodeling • vulnerable plaque

 Necropsy specimens from individuals following acute myocardial infarction typically show occulsive intracoronary thrombosis overlaying a region of plaque rupture or erosion. Plaque rupture strongly associates with coronary segments abundant in lipid and inflammatory infiltrates, often encompassed by a thin fibrous cap within expansively remodeled regions. Greater plaque burden (PB) is increasingly being recognized as a common substrate wherein plaque ruptures have either already occurred or are suspected to more likely occur in the future. Accordingly, greater PB measured either invasively or noninvasively associates with incident cardiovascular events, even among individuals treated with long-term high-intensity statins. However, such quantitative plaque imaging has limited specificity for identifying plaque segments responsible for causing future myocardial infarction. Given that plaque composition is considered an important measure of plaque stability, simultaneous measurement of both coronary PB and the accompanying lipid content could potentially improve coronary risk stratification.

Combined imaging with near-infrared spectroscopy (NIRS) and intravascular ultrasound (IVUS) enables the identification and morphometric assessment of lipid-rich plaques...
Materials and Methods
Materials and Methods are available in the online-only Data Supplement (Figures 1 and 2).

Results
Clinical and Demographic Details of Heart Donors and Live Patients Undergoing NIRS-IVUS
Table 1 describes patient and vessel characteristics of the patients whose donor hearts were analyzed, as well as the clinical/demographic details of age- and sex-matched patients who underwent combined in vivo NIRS-IVUS imaging during PCI. Compared with the autopsy cohort, patients who underwent PCI were of similar age (65.9±15 versus 64.1±13 years, \( P = 0.54 \)), sex (71% versus 72% male sex, \( P = 0.99 \)), and body mass index (28.7±8.4 versus 28.6±5.8 kg/m\(^2\), \( P = 0.95 \)) and had a similar incidence of hypertension (61% versus 58%, \( P = 0.79 \)) and diabetes mellitus (33% versus 19%, \( P = 0.11 \)). Within the autopsied cohort, 45% of donors died from either a myocardial infarction or cardiopulmonary arrest, whereas 86% of the in vivo cohort underwent NIRS-IVUS during PCI after an acute coronary syndrome.

Ex Vivo Relationships Between Plaque Burden, Lipid-Core Burden, and Remodeling Indices According to Histological Group
Table 2 describes relationships between IVUS-derived PB and NIRS-derived lipid core burden index (LCBI) stratified according to plaque histological group at a 2-mm block level (n=2070 blocks). Table 2 also describes a lesion-based analysis (n=102 lesions) of autopsied vessels assessing the added relationship between coronary remodeling index (RI) to IVUS-derived PB and NIRS-derived LCBI, stratified according to lesion histological group. At a block level, increasing histological complexity was significantly associated with corresponding increments of both IVUS-derived PB and NIRS-derived LCBI (\( P_{\text{trend}} < 0.001 \) for both). Although PB did not discriminate fibrotic/fibrocalcific (group 2) from pathological intimal thickening (PIT/intimal xanthomatous plaques (group 3), there was a clear difference in block LCBI between these plaque groups.

At a lesion level, increasing histological complexity was also generally associated with corresponding increments of both IVUS-derived PB and NIRS-derived LCBI (\( P_{\text{trend}} < 0.001 \) for both). Although PIT/intimal xanthomatous (group 3) lesions contained higher PB than fibroatheromas (group 4) lesions, LCBI increased steadily across all plaque groups, reflecting the lipid-rich nature of PIT/intimal xanthoma and fibroatheromas lesions. Lesion RI were similar across plaque group 1 (0.99 [0.90, 1.1]), plaque group 2 (1.0 [0.90, 1.1]), and plaque group 3 (0.97 [0.80, 1.1]) lesions. However plaque

### Table 1. Demographic and Clinical Characteristics of Heart Donors and Age/Sex-Matched Live Cohort

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ex Vivo (Autopsy Cohort), N=51</th>
<th>In Vivo (PCI Cohort), N=43</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65.9±15</td>
<td>64.1±13</td>
<td>0.54</td>
</tr>
<tr>
<td>Male</td>
<td>36 (70.6)</td>
<td>31 (72.1)</td>
<td>0.99</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>28.7±8.4</td>
<td>28.6±5.8</td>
<td>0.95</td>
</tr>
<tr>
<td>Hypertension</td>
<td>31 (60.8)</td>
<td>25 (58.1)</td>
<td>0.79</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>17 (33.3)</td>
<td>8 (18.6)</td>
<td>0.11</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>7 (13.7)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Cardiopulmonary arrest</td>
<td>16 (31.4)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Stroke</td>
<td>15 (29.4)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Anoxia</td>
<td>6 (11.8)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Aortic aneurysm</td>
<td>2 (3.9)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Other</td>
<td>5 (9.8)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>N/A</td>
<td>37 (86)</td>
<td>N/A</td>
</tr>
<tr>
<td>Stable symptoms</td>
<td>N/A</td>
<td>6 (14)</td>
<td>N/A</td>
</tr>
<tr>
<td>Concomitant medications</td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Statins</td>
<td>N/A</td>
<td>15 (34.9)</td>
<td>N/A</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>N/A</td>
<td>12 (27.9)</td>
<td>N/A</td>
</tr>
<tr>
<td>Aspirin</td>
<td>N/A</td>
<td>20 (46.5)</td>
<td>N/A</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>N/A</td>
<td>12 (27.9)</td>
<td>N/A</td>
</tr>
<tr>
<td>Lipoprotein levels (mg/dL)</td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>LDL-C</td>
<td>N/A</td>
<td>96.3±33</td>
<td>N/A</td>
</tr>
<tr>
<td>HDL-C</td>
<td>N/A</td>
<td>39.4±13</td>
<td>N/A</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>N/A</td>
<td>112 (78, 247)</td>
<td>N/A</td>
</tr>
<tr>
<td>Coronary artery</td>
<td>N=116 arteries</td>
<td>N=43 arteries</td>
<td>0.05</td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>40 (34.5)</td>
<td>24 (55.8)</td>
<td>N/A</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>25 (21.6)</td>
<td>6 (14.0)</td>
<td>N/A</td>
</tr>
<tr>
<td>Right coronary artery</td>
<td>51 (44.0)</td>
<td>13 (30.2)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; N/A, not available; and PCI, percutaneous coronary intervention.
group 4 lesions had the highest overall RI (1.1 [1.0, 1.2], \( P_{\text{trend}} = 0.02 \) across all plaque groups), consistent with expansive arterial remodeling.

**Ex Vivo and In Vivo Relationships Between IVUS-Derived Plaque Burden and NIRS-Derived Lipid Burden**

Table 3 describes both ex vivo and in vivo relationships between PB and LCBI at a block level stratified according to tertiles of IVUS-derived PB. Across 2070 blocks of coronary segments examined ex vivo, LCBI increased significantly across each PB tertile (\( P_{\text{trend}} < 0.001 \)). Histologically, significant trends were seen across the spectrum of plaque groups and their association with tertiles of PB. The greatest proportion (91.5%) of group 1 plaques (normal/adaptive intimal thickening) was associated with the lowest (1st) tertile of PB (\( P_{\text{trend}} < 0.001 \)). By comparison, the greatest proportion (31.3%) of group 4 plaques (fibroatheromas) was associated with the highest (3rd) tertile of PB (\( P_{\text{trend}} < 0.001 \)).

Of the 43 matched patients undergoing combined NIRS-IVUS imaging in vivo during PCI, 1044 blocks were analyzed and stratified to match the tertiles of PB yielded from the autopsy analysis. In similar fashion to what was observed in the ex vivo block analysis described earlier, block LCBI increased significantly across the tertiles of PB (\( P_{\text{trend}} < 0.001 \)).

Overall, IVUS-derived PB correlated weakly, but significantly with NIRS-derived LCBI ex vivo (\( r=0.23, P<0.001 \)). Correlations according to individual AHA plaque grouping for PB and LCBI are shown in Figure 3. In vivo analyses also revealed a modest correlation between PB and LCBI (\( r=0.17, P<0.001 \)). Histological plaque grouping also correlated modestly with NIRS-derived LCBI (\( r=0.48, P<0.001 \)), but had a stronger correlation with IVUS-derived PB (\( r=0.48, P<0.001 \)).

**Intravascular Imaging Predictors of Histologically Proven Coronary Fibroatheromas**

Table 4 describes a multivariable model of IVUS and NIRS predictors for identifying histologically proven coronary fibroatheromas. In a combined model describing continuous forms of IVUS-derived PB, NIRS-derived LCBI, and RI, each of these variables were found to be relatively equivalent in identifying a fibroatheromas (PB per standard deviation [SD]: odds ratio [95% confidence interval] 2.26 [1.11, 4.58]; LCBI per SD: odds ratio 2.15 [1.11, 4.15]; RI per SD: odds ratio 2.71 [1.23, 6.02]).
Table 5 and Figure 4 describe comparisons of logistic models for plaque measures used in the discrimination of histologically proven fibroatheromas. By receiver–operating characteristic analysis, the individual $c$-indices for IVUS-derived PB, NIRS-derived LCBI, and RI to predict fibroatheromas were comparable (0.675, 0.712, and 0.672, respectively; Figure 1.

**Figure 1.** A, Schematic diagram of imaging and block histology. Chemogram (A), longitudinal intravascular ultrasound (IVUS; B), and cross-sectional IVUS analysis of plaque burden (PB; C, D). Each imaged conduit was divided into contiguous nonoverlapping 2-mm blocks (occupying sections of vessel between the dotted vertical green lines) with near-infrared spectroscopy (NIRS–IVUS coregistration. Each 2-mm block was represented by a histological slice wherein the contained atheroma underwent grading according to a modified American Heart Association (AHA) classification scheme and had IVUS-derived PB and NIRS-derived lipid core burden index (LCBI) measured. B, Schematic diagram of lesion remodeling analysis. Chemogram (A), longitudinal IVUS (B), and representative histology (C) of the most diseased 2-mm section of imaged coronary artery (defined as a lesion occupied by 3 consecutive IVUS frames). Each lesion had an IVUS-derived PB, NIRS-derived LCBI, and AHA plaque histology grade determined. The remodeling index (RI) was calculated according to a reference site (least diseased section of artery) on IVUS within 10 mm of the lesion.
However, the addition of LCBI to IVUS-derived PB resulted in a large, significant improvement for fibroatheromas prediction (c-index 0.77, \(P=0.028\) compared with PB alone). The addition of RI to the combined predictive capacity of PB and NIRS did not yield a significant increase in the c-index (c-index 0.80, \(P=0.27\); Figure 4B). Further analysis revealed that the addition of NIRS-derived LCBI to IVUS-derived PB caused a significant net reclassification improvement of 43% (\(P=0.003\)) for detecting histologically proven fibroatheromas.

**Discussion**

There is increasing interest in measuring PB for assessing cardiovascular risk and triaging risk-modifying therapies.\(^{18,19}\) This rationale has stemmed from a range of observations across pathological and prospective coronary imaging studies. Histopathologically, most coronary lesions displaying plaque rupture were of >75% diameter stenosis severity,\(^7\) complementing the original necropsy observations of Mann and Davies who found plaque disruption and healing to be most prevalent within high-grade coronary stenoses.\(^6\) More recently, invasive coronary imaging in patients with acute coronary syndrome demonstrated associations between greater PB (and lumen compromise) within ruptured plaques identified in vivo.\(^{20}\) Several prospective human coronary imaging studies uncovered the prognostic significance of baseline coronary PB.\(^{8,9,11-14,21-23}\) However, measuring PB alone has low specificity for identifying culprit segments responsible for myocardial infarction. The present analysis reinforces the link between greater PB and a higher grade plaque morphology defined histologically. Given the recent findings of associations between NIRS-derived lipid pools on chemography alone and clinical events,\(^{24}\) our findings underscore the synergistic value of plaque volumetric and compositional imaging with NIRS-IVUS for more specific vulnerable plaque detection. However, the prognostic capacity of atheroma phenotyping with dual NIRS-IVUS imaging still requires formal prospective evaluation. The ongoing Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPECT) II (NCT02171065) and Lipid-rich Plaque studies (NCT02033694) will help to reconcile this hypothesis.

A large body of evidence points to an important role for tissue composition and morphology in mediating plaque vulnerability, with consistent demonstrations of large lipid pools and inflammatory infiltrate within plaques responsible for acute coronary events.\(^{25}\) Autopsy studies show that >70% of the plaques causing fatal myocardial infarction contain a ruptured lipid core. Thrombosis without plaque rupture has been observed to occur in 20% to 30% of cases and is attributed to plaque erosion.\(^{26}\) These erosion sites often contain lipid pools or lipid cores with thick overlying fibrous caps.\(^3\) The histological demonstration of lipid in both scenarios (plaque rupture and erosion) indicates the potential importance for detecting lipid in vivo, in addition to measuring PB. Although longitudinal studies demonstrated significant associations between radiofrequency IVUS-derived fibroatheromas and incident cardiovascular events,\(^{9,11,27}\) the predominant features of such lesions were their greater PB and subsequent lumen compromise, with cardiovascular events largely driven by coronary revascularizations.\(^{28}\) Additionally, the strength of the pathological and quantitative validation of radiofrequency IVUS-derived fibroatheromas and tissue components has been questioned by some,\(^{29-31}\) whereby the amount of necrotic core expressed may relate to the presence and extent of calcium,\(^{32}\) and lipid (laden with collagen) could be misclassified as fibrofatty plaque.\(^{33}\)

On the contrary, the criterion of a target lipid core plaque (LCP; a fibroatheromas containing lipidic core \(\geq200\mu m\) thick of \(\geq60^\circ\) circumferential distribution) was defined a priori by pathologists at the United States Food and Drug Administration, serving as the benchmark for intracoronary NIRS to obtain regulatory approval. Accordingly, NIRS was
validated against this LCP definition, yielding an area under the receiver–operating characteristic curve of 0.80 for detecting LCP in ex vivo human coronary specimens. Importantly, the spectroscopic algorithm for NIRS-derived LCP captures both the lipid extent of plaque, seems unaffected by the presence of coronary calcium, and has recently been successfully used to investigate the association between lipid and calcification within coronary atheroma. Furthermore, a recent prospective evaluation demonstrated the prognostic value of NIRS-derived LCBI within a nonculprit vessel of patients with coronary disease. A limitation of this study, however, was the lack of a demonstration of the incremental prognostic value of NIRS-derived lipid over IVUS-derived PB.

Prior studies demonstrated significant associations between culprit lesion remodeling patterns and the acuity of clinical presentation. More recently, investigators revealed that a bidirectional (either extreme negative/constrictive or positive/expansive) pattern of arterial remodeling may better predict future cardiovascular events, adding further complexity to the issue of defining and categorizing coronary remodeling. Moreover, there are inherent limitations associated with measuring static RIs, representing an imperfect surrogate of what is truly a serial process. The RI, assessed statistically in the present multivariable analysis, independently predicted coronary fibroatheromas. Prediction analyses revealed that adding RI to PB significantly improved the c-index for fibroatheromas detection by almost as much as adding LCBI to PB (c-indices of 0.76 and 0.77, respectively). This finding that PB plus RI appeared to detect fibroatheromas, as well as PB plus NIRS, in autopsy specimens may not necessarily indicate that PB plus RI will predict coronary events, as well

![Figure 3](http://ahajournals.org)

**Figure 3.** Scatter plots of the relationship between intravascular ultrasound (IVUS)-derived plaque burden (PB) and near-infrared spectroscopy (NIRS)-derived lipid core burden index (LCBI). AIT indicates adaptive intimal thickening; FA, fibroatheroma; and PIT, pathological intimal thickening.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PB, %</td>
<td>2.26 (1.11, 4.58)</td>
<td>0.024</td>
</tr>
<tr>
<td>LCBI</td>
<td>2.15 (1.11, 4.15)</td>
<td>0.023</td>
</tr>
<tr>
<td>RI</td>
<td>2.71 (1.23, 6.02)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; LCBI, lipid core burden index; OR, odds ratio; PB, plaque burden; and RI, remodeling index. Odds ratios are reported from a generalized linear model accounting for the clustering of branches within hearts. Covariates in the model include donor age, sex, history of coronary artery disease, hypertension, and diabetes mellitus. Odds ratios are reported as per standard deviation (SD).
as PB plus NIRS. The performance of NIRS for fibroatheromas detection was impaired by the ability of NIRS to also detect PIT (as shown in Table 2). The ability of NIRS to detect both fibroatheromas and PIT, which has been implicated in erosion sites, may be a positive feature of NIRS imaging for detecting vulnerable plaques in vivo. Additionally, and for the above mentioned reasons, invasively assessing static coronary remodeling is also unlikely to evolve as a readily used clinical tool. Combining the measured LCBI to PB, easily measured in a prompt manner using a hybrid NIRS-IVUS catheter, demonstrated similar significant improvement for detecting coronary fibroatheromas. Moreover, adding the RI to a combined NIRS-IVUS assessment did not significantly improve the c-index for fibroatheromas detection.

Several caveats of the present analysis warrant further consideration. The seminal validation of NIRS to detect LCP yielded a receiver–operator curve c-index of 0.80.16 By contrast, the present analysis demonstrated that the combined index of PB and LCBI for detecting coronary fibroatheromas yielded a receiver–operator curve c-index of 0.77. There are several potential reasons for these differences. We defined lesions on the basis of the single most diseased 2-mm block of coronary artery measured with IVUS (n=102) and tested the predictive capacity of NIRS (for measuring LCBI) and IVUS (for measuring PB and RI) to associate with fibroatheromas. This approach differed markedly from that of Gardner et al who assessed in excess of 2600 contiguous coronary blocks of 2 mm length with a predefined LCP definition set by the United States Food and Drug Administration. Differences between chemogram signals and histological findings could have also affected the results. For example, NIRS detects both necrotic cores (cholesterol-rich regions with tissue necrosis) and lipid pools (areas of lipid with intact cellular structures). However, coronary fibroatheromas contain NC, whereas intimal xanthomas and pathological intimal thickening contain lipid pools. Furthermore, lesions were selected only if IVUS PB analysis was available, which may not have been present in the setting of coronary bifurcations or extensive calcium, precluding identification of the external elastic membrane boundary. However, our approach was the only valid means for simultaneously assessing inter-relationships between remodeling, PB, and LCBI against gold standard plaque histology.

In conclusion, we demonstrate that adding NIRS-derived LCBI to PB significantly improved the ability to identify coronary fibroatheromas. Therefore, an index of PB and LCBI,
obtained during hybrid NIRS-IVUS intracoronary imaging, holds promise for identifying vulnerable coronary atheroma in vivo.

Acknowledgments
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Disclosures
Dr Maddern received research support and speaker honoraria from InfraRedX. Dr Maddern is the employee of InfraRedX. Dr Sum is the employee of InfraRedX. Dr Muller is the employee of InfraRedX, with stock ownership in InfraRedX. Dr Maehara received speakers’ fees from St Jude Medical and a research grant from Boston Scientific Corporation and InfraRedX. Dr Mintz received grant support from InfraRedX and grant support from Nycomed from Volcano, Boston Scientific, and St Jude Medical. Dr Nicholls received research support from InfraRedX, AstraZeneca, Resverlogix, Eli Lilly, Novartis, Anthera, and Roche and consulting fees from Merck, AstraZeneca, Takeda, Roche, Omthera, Amgen, CSL Behring, and Boehringer Ingelheim. The other authors report no conflicts.

References


**Significance**

Pathological studies demonstrated the dual significance of plaque burden (PB) and lipid composition for mediating coronary plaque vulnerability, and there remains intense interest in developing and validating catheter-based intracoronary imaging modalities for prospectively identifying high-risk plaque segments serving as the potential substrate for future coronary events. In this analysis, we evaluated relationships between intravascular ultrasound–derived PB and arterial remodeling with near-infrared spectroscopy (NIRS) –derived lipid content (lipid core burden index) in ex vivo and in vivo human coronary arteries. Although greater coronary PB and lipid content each associated with more advanced and potentially vulnerable forms of coronary atheroma defined histologically, the high specificity of NIRS to detect lipid enabled a more accurate discrimination of active (pathological intimal thickening/intimal xanthomas and fibroatheromas) versus quiescent (adaptive intimal thickening and fibrous/fibro-calcific) plaques. Histologically proven fibroatheromas, considered the most likely substrate for provoking intracoronary thrombosis, harbored the highest PB and lipid core burden index and more commonly occurred within expansively remodeled coronary segments. The addition of NIRS to conventional gray-scale PB assessment resulted in a large and significant improvement for correctly reclassifying coronary fibroatheromas, with good accuracy. In vivo comparisons of 43 age- and sex-matched patients (to the autopsy cohort) undergoing combined NIRS–intravascular ultrasound coronary imaging yielded similar correlation between PB and lipid core burden index to those demonstrated ex vivo. Hence, the following data underscores the potential of PB and lipid core burden index, obtained during hybrid NIRS–intravascular ultrasound intracoronary imaging, for identifying vulnerable coronary atheroma in vivo. Prospective large-scale clinical studies are currently underway evaluating the prognostic utility of this hybrid imaging technology.