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Intracoronary Near-Infrared Spectroscopy (NIRS) Imaging for Detection of Lipid Content of Coronary Plaques: Current Experience and Future Perspectives

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Abstract Acute coronary syndromes are frequently caused by "vulnerable" coronary plaques with a lipid-rich core. In 1993 near-infrared spectroscopy (NIRS) was first used to detect the lipid (cholesterol) content of atherosclerotic plaques in an experimental animal study. NIRS was then carefully validated using human atherosclerotic plaques (ex vivo), and has subsequently been developed for intracoronary imaging in humans, for which now an FDA-approved catheter-based NIRS system is available. NIRS provides a "chemogram" of the coronary artery wall and is used to detect lipid-rich plaques. Using this technology, recent studies have shown that lipid-rich plaques are very frequent in the culprit lesion of patients with an acute coronary syndrome, and are also common in non-culprit coronary lesions in these patients as compared to patients with stable coronary disease. First studies are evaluating the impact of statin therapy on coronary NIRS-detected lipid cores. Intracoronary NIRS imaging represents a highly interesting method for coronary plaque characterization in humans and may become a valuable tool for the development of novel therapies aiming to impact on the biology of human coronary artery plaques, likely in combination with other intracoronary imaging techniques, such as optical coherence tomography.

Keywords Intracoronary near-infrared spectroscopy (NIRS) Imaging · Lipid content of coronary plaques · Acute coronary syndromes · Chemogram · Coronary lesions

Introduction

Atherosclerotic plaques with a large lipid core are a frequent cause of acute coronary syndromes [1]. In 1993 near-infrared spectroscopy (NIRS) was first used for atherosclerotic plaque imaging in an experimental animal model [2]. In further ex vivo validation studies, NIRS was found to accurately detect the lipid (cholesterol) content of human atherosclerotic plaques [3]. In 2001, a device prototype for intracoronary imaging was developed [4]. Recently, NIRS received US Food and Drug Administration approval [5]. NIRS provides a "chemogram" of the wall of the coronary artery and aims to detect lipid-rich plaques [6].

NIRS Catheter

A commercially available catheter-based NIRS imaging system has been developed. This NIRS imaging system consists of a 3.2 French catheter (InfraReDx, Burlington, Massachusetts, USA), a pullback, rotation device, and a dedicated console comprising a laser light source and a computer for algorithmic data processing [7]. The catheter comprises the rotating core with optical fibers that deliver and collect near-infrared light [7]. The light is emitted into a sample by the NIR spectrometer, which subsequently measures the proportion of light that is returned over the range of optical wavelength [6]. The NIRS system uses wave lengths of 800 to 2500 nm, converting a diffuse reflectance signal from an object to produce a spectrum. Subsequently, a computer analyzes the spectra and produces an algorithm to demonstrate a chemogram, that corresponds strongly to the lipid content [5] (Figs. 1 and 2).

Experience Using NIRS for Coronary Plaque Imaging in Humans in Vivo

Non-invasive imaging modalities including computed tomography or magnetic resonance have a limited resolution for precise plaque characterization [5]. Therefore, catheter-based intravascular imaging methods, such as optical coherence

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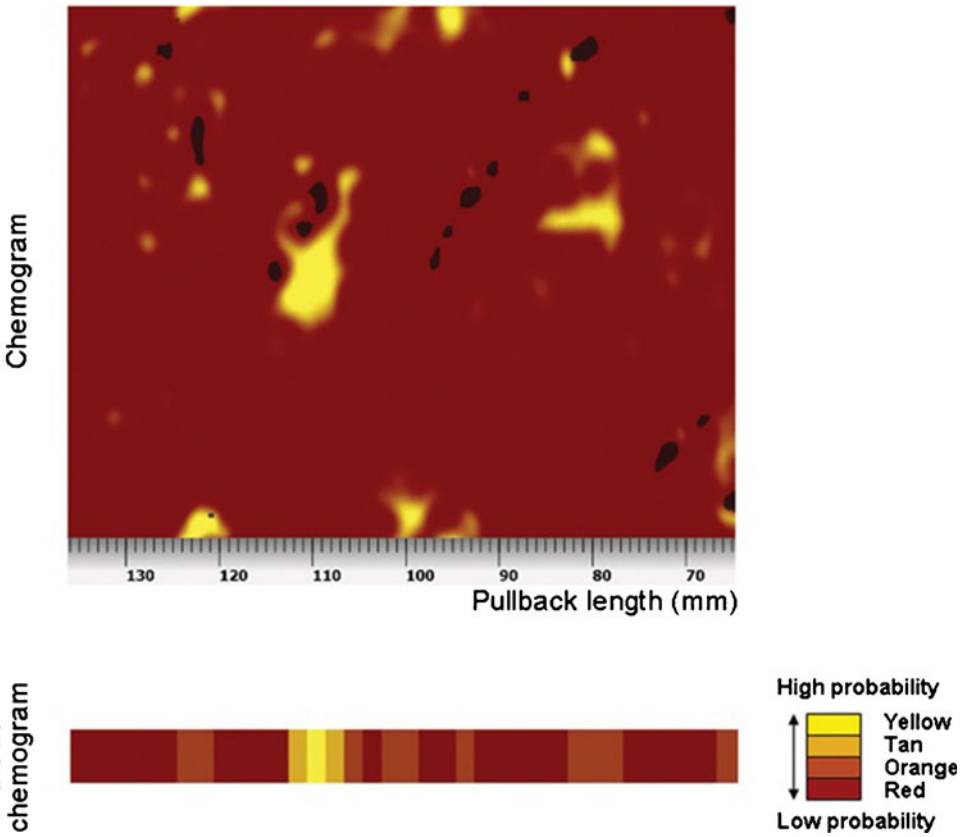

Fig. 1 An example of near-infrared spectroscopy (NIRS). A 'chemogram' is shown detecting a colour map of the artery wall and indicates the location and intensity of coronary lipid content. The horizontal-axis of the chemogram represents the pullback position and the vertical-axis represents the circumferential position in degrees (0–360°). Adapted and modified from: Choi B et al. Eur Heart J 2013;34:2047–2054

tomography (OCT) and NIRS are highly valuable for detailed characterization of coronary atherosclerotic plaques, and have become available within the last years.

As described above, the NIRS imaging system allowing for plaque assessment was carefully validated against atherosclerotic plaque autopsy specimens, and can nowadays be used in humans in vivo [7, 8]. A summary of recent clinical investigations is outlined in Table 1. NIRS provides excellent spectra through blood and despite heart movement by using short scanning acquisition cycles [7]. The PROSPECT study suggested, that a plaque burden of >70 %, thin-cap fibroatheroma, and minimal luminal area ≤4.0 mm^2 are predictors of overall long-term adverse cardiovascular events [9]. NIRS has been established as a very accurate modality to characterize plaques with different lipid content [8]. Madder et al. have shown, that target lesions responsible for acute coronary syndrome are frequently composed of lipid core plaque with a high lipid core burden index (LCBI) [10]. The presence of lipid core plaque may address the high-risk setting for subsequent coronary events, which needs to be further investigated in future studies [11, 12]. Interestingly, both culprit and non-culprit lesions contained lipid core plaque more frequently in ACS patients as compared to patients with stable angina [10].

Moreover, the study by Pu et al. have recently supported the notion, that combining NIRS with IVUS can lead to a better plaque characterization [13]. In addition, the three-dimensional reconstruction of coronary anatomy by ANGIOCARE Software permits the identification of the lipid core plaque location and therefore the association among vessel geometry, endothelial shear stress and plaque composition [14].

Implications for Guiding Therapy

The impact of short-term intensive statin treatment on a lipid plaque content has been investigated in a first study using NIRS demonstrating changes in lipid composition [15]. Several small studies have examined the potential impact of plaque evaluation by NIRS for interventional coronary therapy [16–18]. It is well known, that 3-15 % of percutaneous coronary interventions (PCIs) are complicated by periprocedural myocardial infarction (MI) due to the distal embolization by intraluminal thrombus and/or lipid-core plaque content [19–21]. First studies suggest that edge dissections or plaque disruptions may be more common when stents end within a lipid core plaque [22]. Dixon et al. have documented, that in 16 % of lesions lipid core plaque may extend

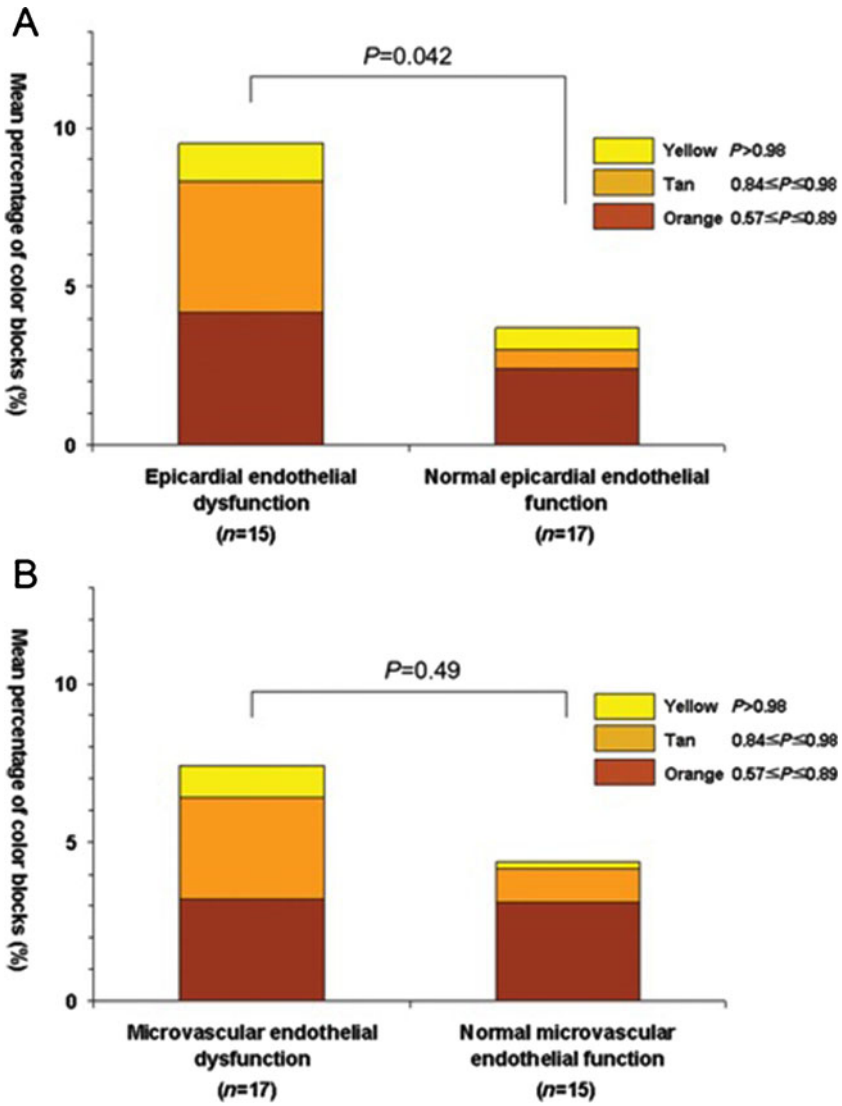

Fig. 2 Near-infrared spectroscopy (NIRS) imaging indicates the lipid-core containing plaques are substantially more frequent in human coronary arteries with endothelial dysfunction. Adapted and modified from: Choi B et al. Eur Heart J 2013;34:2047–2054

beyond the margins of the lesion as assessed by angiography [23]. This further points to limitations of QCA alone in the evaluation of lesion- and subsequently stent length [23]. Notably, the NIRS-identified lipid core plaque has been described to be strongly associated with a high risk of thrombus formation or periprocedural myocardial infarction [17, 18, 24].

Future Perspectives

NIRS is likely to become a sensitive modality for coronary plaque characterization. NIRS could be an interesting tool to investigate novel lipid-modulating and other cardiovascular therapies aiming to prevent adverse coronary events [17, 23]. However, a potential limitation of NIRS may be its inability to assess the depth of a lipid core and the measurement of lipid volume has not been validated so far [5]. NIRS may therefore be used in combination with other imaging modalities, such as IVUS or OCT. In this respect, a combined imaging catheter has recently been developed (TVC Imaging System, MC 7 system, InfraReDx, Burlington, Massachusetts, USA), combining both, an IVUS probe and NIRS light source. This catheter is being used in the IBIS-3 (Integrated Biomarker and Imaging Study 3) to investigate the effects of rosuvastatin therapy on the lipid-rich coronary atherosclerotic plaques [25].

Table 1 Intracoronary human NIRS studies

Study	Year	n* patients	Aim	Conclusion
Caplan J.D. et .al [6] *JACC*	2006	6	Initial clinical experience in stable CAD	High quality NIRS spectra can be obtained in patients in vivo
Waxman, S. et .al [7] *JACC Cardiovasc Imaging*	2009	106	To determine whether catheter-based NIRS signals from coronaries of patients are similar to those from autopsy specimens and to assess initial safety of NIRS device	Spectral data were safely obtained by NIRS similarly to those from autopsy specimens; results demonstrated the feasibility of invasive detection of coronary LCP
Raghunathan, D. et .al [17] *Am J Cardiol*	2011	30	To examine whether an association exists between the presence and extent of LCP detected by NIRS performed before PCI with postprocedural MI	PCI of LCP-positive lesions is associated with increased risk for MI after PCI
Goldstein, J.A. et .al [18] *Circ Cardiovasc Interv*	2011	62	To analyze the relationship between the presence of a large LCP detected by NIRS and periprocedural MI	NIRS provides rapid, automated detection of extensive LCPs that are associated with a high risk of periprocedural MI
Brugaletta, S. et .al [26] *JACC Cardiovasc Imaging*	2011	31	To compare the findings of NIRS, IVUS virtual histology and grayscale IVUS obtained in matched coronary vessel segments of patients undergoing coronary angiography	Larger plaque area by grayscale IVUS was more often associated with either elevated percentage VH necrotic core or LCP by NIRS
Madder, R.D. et .al [10] *Circ Cardiovasc Interv*	2012	60	To determine the frequency of LCP at target and remote sites in ACS vs. stable angina	Target lesion responsible for ACS were frequently composed of LCP; LCPs often were found in remote, non-target areas; LCPs were more common in patients with ACS vs. stable angina patients
Pu, J. et .al [13] *Eur Heart J*	2012	66	To evaluate NIRS combined with IVUS to provide novel information of human coronary plaque characterization	Combining NIRS and IVUS contributes to the plaque characterization
Dixon, S.R. et .al [23] *Am J Cardiol*	2012	69	To compare the target lesion length using NIRS combined with angiography vs. angiography alone	Patients undergoing stent implantation could have LCP extending beyond the intended treatment margins as defined using QCA alone
Brugaletta, S. et .al [27] *JACC Cardiovasc Imaging*	2012	202	To explore a relationship between lipid plaque composition by NIRS and angiographic severity of coronary artery disease	Patients with highest Syntax score have a higher LCBI
Brilakis, E.S. et .al [16] *Catheter Cardiovasc Interv*	2012	9	To investigate whether use of an embolic protection device might prevent complications of LCP interventions	Use of embolic protection devices frequently resulted in embolized material retrieval after stenting of native coronary artery lesions with large LCP
Brugaletta, S. et .al [28] *JACC Cardiovasc Imaging*	2012	68	To assess LCP distribution in nonculprit coronary arteries using NIRS	LCP were mainly located in proximal portions of the LAD and LCX, and more uniformly distributed in the RCA;
Kini, A.S. et .al [15] *JACC*	2013	87	To determine the impact of short-term intensive statine treatment on intracoronary plaque lipid content	Short-term intensive treatment with statine may reduce lipid content in obstructive coronary lesions
Papayannis, A.C. et .al [24] *Catheter Cardiovasc Interv*	2013	9	To examine the association between presenting LCP (by NIRS) and poststenting thrombus formation (by OCT)	Stenting large LCPs may be associated with intrastent thrombus formation
Townsend, J.C. et .al [29] *Am J Cardiol*	2013	100	To investigate, whether coronary bifurcations have higher levels of intracoronary LCP than non-bifurcation regions	Coronary bifurcations do not appear to have higher levels of intracoronary LCP than their comparative non-bifurcation regions
Maini, A. et .al [30] *J Inv Cardiol*	2013	77	To evaluate LCP modification with coronary revascularization and its correlation with periprocedural MI	Plaque modification may be performed successfully using interventional methods and can be evaluated with NIRS; axial plaque shifting is an acute prognostic marker for postprocedure MI
Madder, R.D. et .al [31] *JACC Cardiovasc Interv*	2013	20	To describe NIRS findings of culprit lesions in STEMI	Plaques causing STEMI have a high LCBI
Zynda, T.K. et .al [32] *Catheter Cardiovasc Interv*	2013	78	To determine if there was a relationship between angiographic lesion complexity and the extent of LCP identified by catheter-based NIRS	Angiographic SYNTAX score weakly correlated with lipid core burden index
Choi, B.J. et .al [33] *Eur Heart J*	2013	32	To investigate whether coronary endothelial dysfunction is associated with the LCP in patients with early CAD	Patients with early CAD and endothelial dysfunction had a higher lipid content in the vascular wall than patients with normal endothelial function;

ACS acute coronary syndrome; *CAD* coronary artery disease; *IVUS* intravascular ultrasound; *LAD* left artery descending; *LCBI* lipid core burden index; *LCP* lipid core-containing plaque; *LCX* left circumflex artery; *MI* myocardial infarction; *NIRS* near-infrared spectroscopy; *PCI* percutaneous coronary intervention; *QCA* Quantitative Coronary Angiography; *RCA* right coronary artery; *STEMI* ST-segment elevation myocardial infarction; *number of patients

Compliance with ethics Guidelines

Conflicts of Interest Dr. Milosz Jaguszewski and Dr. Roland Klingenberg reported no conflicts of interest relevant to this article.

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