Journal of Cardiology 65 (2015) 134–142

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Reproducibility of intravascular ultrasound radiofrequency data analysis (virtual histology) with a 45-MHz rotational imaging catheter in ex vivo human coronary arteries

Takashi Muramatsu (MD, PhD)[a,b], Hector M. García-García (MD, PhD)[a,c,*], Salvatore Brugaletta (MD, PhD)[d], Jung Ho Heo (MD)[e], Yoshinobu Onuma (MD, PhD)[a], Russell J. Fedewa (PhD)[f], Anuja Nair (PhD)[g], Yukio Ozaki (MD, PhD)[b,**], Patrick W. Serruys (MD, PhD)[a]

[a] Thoraxcenter, Erasmus Medical Center, Rotterdam, The Netherlands
[b] Department of Cardiology, Fujita Health University Hospital, Toyoake, Japan
[c] Cardialysis B.V., Rotterdam, The Netherlands
[d] Department of Cardiology, Thorax Institute, Hospital Clinic, Barcelona, Spain
[e] Division of Cardiology, Department of Internal Medicine, Kosin University Gospel Hospital, Busan, South Korea
[f] Biomedical Engineering Department, Cleveland Clinic, Cleveland, OH, USA
[g] Volcano Corporation, Rancho Cordova, CA, USA

ARTICLE INFO

Article history:
Received 24 March 2014
Received in revised form 1 May 2014
Accepted 7 May 2014
Available online 18 September 2014

Keywords:
Intravascular ultrasound
Virtual histology
Reproducibility
Ex vivo
Coronary artery disease

ABSTRACT

Background: Despite the frequent use of spectral analysis of intravascular ultrasound radiofrequency data (VH® IVUS) in clinical studies, the assessment for reproducibility using this with high frequency IVUS remains unexplored.
Purpose: The aim of this study was to examine the reproducibility of VH IVUS using 45-MHz rotational IVUS in ex vivo human coronary arteries.
Methods: Data were collected using 45-MHz VH IVUS (Revolution®, Volcano Corporation, San Diego, CA, USA) via a series of pullbacks from eight human coronary artery specimens. Imaging data were analyzed by two independent observers. Intraobserver and interobserver reproducibility were assessed using five pullbacks from five vessels. The intercatheter reproducibility was assessed using three different catheters in each of the five vessels. The intracatheter reproducibility was assessed between the two sequential pullbacks from each of the 15 catheters used in the intercatheter assessment.
Results: Geometrical measurements consistently showed low variability (relative difference <10%) and excellent intraclass correlation coefficients (ICCs), ranging from 0.88 to 1.00. With respect to the compositional measurements, the relative differences were predominantly higher than those of geometrical measurements. In particular, fibrous-fatty area showed a higher relative difference (17.5% in intercatheter assessment) compared to fibrous, necrotic core, and dense calcium areas (6.5%, 8.4%, and 6.4%, respectively). However, each compositional measurement also showed acceptable reproducibility (ICCs ranging from 0.82 to 1.00).
Conclusions: The 45-MHz rotational VH IVUS technology had acceptable reproducibility with respect to geometrical and compositional assessments in ex vivo human coronary arteries. These data are crucial when designing future longitudinal studies addressing geometrical measurements and plaque characterization by 45-MHz VH IVUS.

* Corresponding author at: Thoraxcenter, Erasmus Medical Center, z120, Dr Molerwaterplein 40, 3015 GD Rotterdam, The Netherlands. Tel.: +31 10 206 28 28; fax: +31 10 206 28 44.
** Co-corresponding author at: Department of Cardiology, Fujita Health University Hospital, 1-98, Dengaku, Kutsukake, Toyoake 470-1192, Japan. Tel.: +81 562 93 2312; fax: +81 562 93 2315.
E-mail addresses: hgarcia@cardialysis.nl (H.M. García-García), ozakiyuk@fujita-hu.ac.jp (Y. Ozaki).

http://dx.doi.org/10.1016/j.jjcc.2014.05.004
0914-5087/

Introduction

Intravascular ultrasound (IVUS) facilitates the assessment of extent, distribution, severity, and morphology in human atherosclerotic coronary arteries [1–3]. In the field of interventional cardiology, IVUS has been used not only for therapeutic decision making [4,5], but also for clinical research evaluating serial changes in atherosclerotic coronary plaque size and composition [6–10]. The spectral analysis of IVUS radiofrequency data (VH® IVUS) facilitates plaque characterization. This VH IVUS technology (Volcano Corporation, San Diego, CA, USA) classifies plaque components as fibrous, fibrous-fatty, necrotic core, or dense calcium [11,12]. The predictive accuracy of the 20-MHz VH IVUS technology was previously examined by direct comparison with pathohistology of ex vivo (97%) and in vivo (95%) human coronary arteries [12,13]. These studies illustrated the clinical significance of VH IVUS images to assess the distribution of the tissue components within the plaque [14]. Indeed, distributions of these components might reflect the clinical characteristics of patients [15] and were also associated with cardiovascular risk score [16]. A previous clinical trial demonstrated that the presence of a thin-cap fibroatheroma detected by VH IVUS was an independent predictor of future cardiac events [17]. It should also be noted that, in the IBIS-2 study, an Lp-PLA_2 inhibitor darapladib (GlaxoSmithKline, Philadelphia, PA, USA) was studied with regard to its capabilities to modify plaque components. One of the key findings was that Lp-PLA_2 inhibition with darapladib interferes with necrotic core expansion as assessed by VH IVUS [18]. This study highlighted the potential of VH IVUS to detect changes in plaque that are related to the mechanism of action of the investigational drugs. Since the fate of coronary plaques is related to their histological composition [19], valid plaque characterization could provide clinically relevant information and become a therapeutic target for future studies regarding pharmacological intervention [7–9,18] and bioresorbable scaffold implantation [20,21].

The first commercially available VH IVUS system was developed with 20-MHz solid-state array IVUS. A new-generation 45-MHz rotational VH IVUS has been developed and produces better resolution images that might improve plaque characterization. However, there have been no published data in terms of reproducibility that is crucial for longitudinal studies. Therefore, the aim of this study was to assess the reproducibility of geometrical and compositional measurements using 45-MHz rotational VH IVUS in ex vivo human coronary arteries.

Methods

Samples and imaging procedure

A total of nine harvested specimens of human coronary arteries were used for this study. The mean age of the donors was 61.3 years, and all coronary artery specimens showed severe atherosclerotic plaque. The specimens were pinned on a custom-made room-temperature-vulcanizing silicone elastomer using needles in a dissecting tray filled with saline during imaging. The elastomer has acoustic impedance comparable to water in order to minimize ultrasonic artifacts within the IVUS image. A 3.2-French, 45-MHz rotational IVUS catheter (Revolution®, Volcano Corporation) was inserted from the ostium to the distal end of the specimen. IVUS data were acquired with a pullback speed of 0.5 mm/s. An electrocardiogram simulator (430B ECG simulator, Medi Cal Instruments, Inc., Lewis Center, OH, USA) was used to trigger the VH IVUS data acquisition at a frequency of 60 beats per minute.

45-MHz VH IVUS data analysis

The IVUS data were recorded with a commercially available IVUS console that was enabled for 45-MHz ultrasound backscatter data acquisition (s5 Imaging System, Volcano Corporation). In each pullback, the region of interest (ROI) was defined using distal and proximal side branches. The same side branches were used as anatomical landmarks for each pullback data within a given vessel. Contour detection of vessel lumen and media–adventitia interface was independently performed by two experienced IVUS analysts. QIvus Version 2.1 software (Medis, Leiden, The Netherlands) was used for the off-line contour detection, and the virtual histology (VH) images were processed with the contours using the VH OEM Version 2.0.2 software (Volcano Corporation) that was modified specifically to assess tissue characterization in ex vivo data in the absence of blood attenuation.

Reproducibility assessment

In this study, we assessed the intraobserver, interobserver, intracatheter, and intercatheter reproducibility. Among the nine vessels (i.e., coronary artery specimens); one vessel was excluded from the current analysis because of poor specimen quality due to severe damage. For the assessment of intraobserver reproducibility, five pullbacks from five vessels were randomly selected and analyzed twice at an interval of 2 weeks by the same observer (i.e., agreement between 1st and 2nd analyses). For the assessment of interobserver reproducibility, the same five pullbacks as used for the intraobserver assessment were analyzed by two independent analysts (i.e., agreement between observer 1 and observer 2). In addition, five vessels were evaluated by three catheters each with two sequential pullbacks per catheter, leading to the capability of multiple assessments: intracatheter reproducibility comparing two sequential pullbacks with 15 catheters (i.e., agreement between 1st and 2nd pullbacks), and intercatheter reproducibility comparing the first pullback of catheter 1, catheter 2, and catheter 3 in each vessel (i.e., agreement among three catheters).

We applied the frame-level analysis for the assessment of intraobserver and interobserver reproducibility because all the same frames (i.e., crosssections) should be analyzed, while the segment-level analysis was applied for the assessment of intracatheter and intercatheter reproducibility because the analyzed crosssections could be different between the pullbacks even after matching the segments with the landmark side branches. Each component of geometrical and compositional measurements was compared under the aforementioned conditions.

Statistical analysis

Descriptive variables are presented as means ± standard deviations (SDs). The reproducibility with corresponding 95% confidence intervals (CIs) was determined using intraclass correlation coefficients (ICCs). Bland–Altman plots were generated to estimate the limit of agreement (LOA) defined as the mean difference of measurements between the two conditions ± 2 SD [22]. Statistical analysis was performed with PASW 18 software (SPSS Inc., Chicago, IL, USA).

Results

Intraobserver agreement

The mean length of ROI was 20.5 ± 4.1 mm for the five pullbacks. Geometrical and compositional data of the matched frames are shown in Table 1. The relative intraobserver differences in geometrical measurements were negligible. Of note, the relative