

Computer-Assisted Quantitative Analysis of New Interventional Treatment Methods

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Abstract

Recently Bioresorbable metal scaffolds have been added to the treatment choices for coronary artery disease. They can replace permanent metallic implanted stents and to assess their clinical performance several imaging methods were applied amongst which intravascular ultrasound (IVUS). However, standard quantitative analysis of IVUS data neglects both the three-dimensional nature of the coronary arteries as well as the influence of cardiac motion. In order to improve the accuracy of the IVUS analysis over the past years several new processing algorithms and semi-automated tools have been developed. This study evaluates if the application of these new methods would result in a different evaluation of a new coronary treatment method by reanalyzing a clinical study previously assessed by older analysis methods.

1. Introduction

Coronary stents, such as bare metal stents (BMS) and drug-eluting stents (DES), are normally used to treat coronary artery disease. The need for scaffolding is confined to the period, 3 to 6 months, following the intervention, after that, there are no further benefits and their presence could even cause adverse events such as late stent thrombosis and chronic inflammation [1]. Additionally, permanent metallic stents alter the vasomotion of the stented segments and they require long-term antiplatelet treatment to avoid thrombosis [2, 3]. To overcome these drawbacks the bioresorbable metal scaffold (AMS) has been introduced as an alternative therapy, and for studying these new scaffolds several imaging methods were applied [4, 5]. One of the imaging methods mostly used to evaluate new stent platforms is intravascular ultrasound (IVUS). Standard quantitative IVUS analyses are performed on a series of tomographic cross-sectional images acquired at 1s intervals of IVUS

pullback at a speed of 0.5 mm/sec.

These methods underestimate the three-dimensional (3D) nature of the coronary artery and the catheter displacement in the vascular lumen as well as the influence of the cardiac motion which induces a saw-tooth shaped appearance of the coronary segment in reconstructed longitudinal views and it may result in inaccurate analyses [6]. To overcome these limitations several post-processing and analysis methods/tools have been developed such as retrospective ECG-gating, semi-automated contour detection, correction methods if different IVUS catheters or consoles have been used within longitudinal studies and software to analyze tissue composition such as by example Echogenicity software [7-10]. The objective of this study is to reevaluate a clinical trial with the new methods, which was previously analyzed by the older methods and to evaluate if this would result in a different study outcome [5].

2. Methods

The study design and the previous applied imaging methodology have been previously published. In this study retrospective ECG-gating, correction for the use of different ultrasound consoles and catheters, semi-automated contour detection and Echogenicity analysis were applied (Fig.1).

2.1. Quantitative IVUS

Before IVUS quantitative analysis, the IVUS data were retrospectively image-based gated by the Intelligate method [8, 11]. This method is based on identification of the near end-diastolic frames from recorded non-ECG-gated IVUS data and builds a new gated study. The advantages of gating are a smooth appearance of the coronary vessel in longitudinal reconstructed views, which results in a much better performance of the applied automated contour detection algorithms, instead of the typical saw-tooth shape appearance of Non-Gated IVUS

(Fig. 2) and more importantly it results in an improved accuracy.

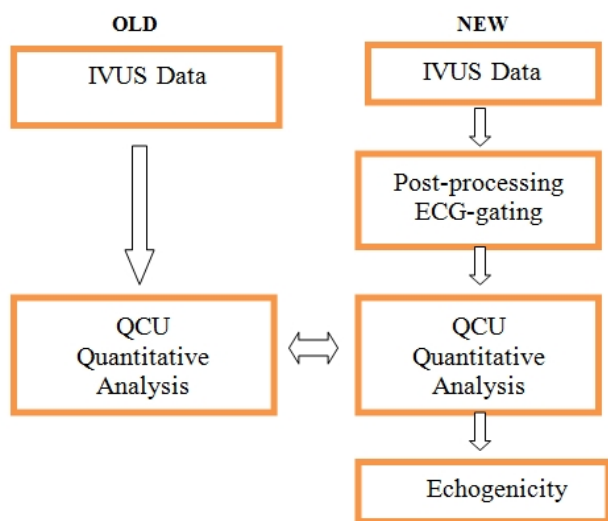


Figure 1. Flow-chart of the study measurement setup.

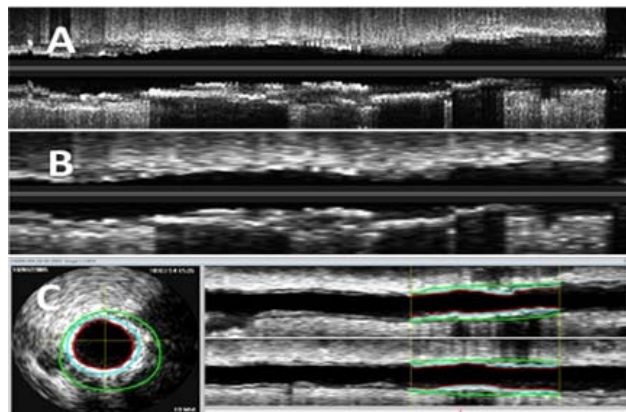


Figure 2. Panel A, shows a non-gated longitudinal IVUS reconstruction. Panel B, shows the retrospective gated equivalent IVUS dataset. Finally panel C, shows the contour detection of the scaffolded segment.

2.2. IVUS analysis

All IVUS studies were analyzed with the dedicated CURAD Vessel Analysis software (Curad, Wijk bij Duurstede, The Netherlands) QCU analysis software [9]. The Curad software focuses on the tracing of contours in reconstructed longitudinal cut-planes (L-Mode displays). This L-mode analysis improves the feasibility to

recognize relevant tissue structures and it enables semi-automatic contour tracing. Baseline and follow-up IVUS studies were analyzed simultaneously, side-by-side, onto a single screen to allow accurate matching between these studies acquired at different time points (e.g. baseline vs. follow-up). The comparison between the IVUS studies at the different time points was based on a comparison of the scaffolded segments rather than on a match between individual IVUS cross-sectional images. The scaffolded segments were determined by the first and the last cross-sectional IVUS cross-section in which scaffold struts could be identified.

To match the 4 months follow-up data, in which the stent struts were not always visible, landmarks such as calcium spots and side-branches were also used. The contours of the lumen-intima interface, the scaffold and the outer vessel border were used to determine the areas and volumes of the vessel and to assess the plaque tissue composition.

2.3. Differential echogenicity analysis

Automated echogenicity analysis software, previously published, was applied to quantify the plaque composition and to assess the absorption process of the bioresorbable metal scaffolds [12]. In brief, the mean grey-value of the adventitia, situated just outside the elastic external membrane (EEM), is used to classify tissue components as hypoechoic or hyperechoic, respectively gray-values lower and higher than the mean adventitia level. Fibrous plaque is characterized as tissue having a gray-level intensity similar or higher than that of the adventitia, while “softer” tissue has a lower grey-level intensity. Echogenicity was measured after implantation and at 4 months follow-up.

To study the absorption of the scaffold and the plaque three different regions were analyzed (Fig. 3):

- 1) The region between lumen and stent-contour to focus on the absorption of the scaffold.
- 2) The region between lumen and EEM-contour to assess the absorption of the scaffold for long-term follow-up when scaffold disappears.
- 3) The region between the scaffold and the EEM-contour to focus on possible peri-scaffold plaque changes.

2.4. Statistical analysis

Continuous variables are expressed as mean \pm SD and the comparisons between the same measurements at different time points were performed with a 2-tailed paired *t* test. Values <0.05 were considered statistically significant.

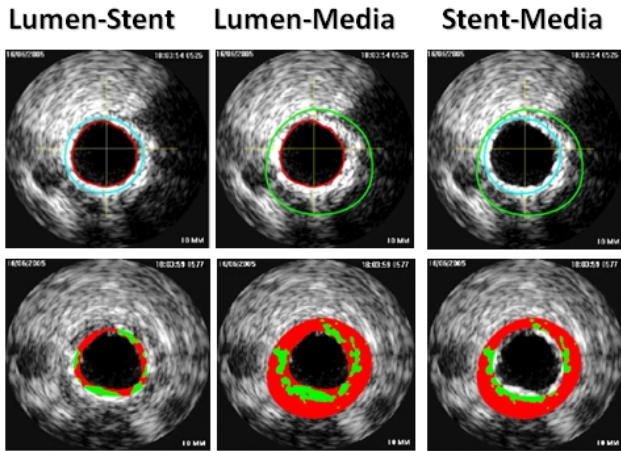


Figure 3. To study the absorption of the scaffold and the plaque three different regions within the IVUS data were analyzed.

3. Results

The overall analysis included 37 lesions that underwent an IVUS examination at both post-implantation and at 4 months follow-up (Table 1). The overall final minimum stent CSA after implantation was 6.4 ± 2.0 mm², stent volume was 118.5 ± 33.2 mm³, lumen volume was 109.3 ± 31.8 mm³ and the EEM volume index was 266.5 ± 75.0 mm³.

IVUS Characteristics: comparison between Gated and non-Gated data						
	BL Gated	BL non-Gated	4M FUP Gated	4M FUP non-Gated	Δ % Gated	Δ % non-Gated
Stent length index(mm)	15,4±2,1	15,9±4,1	15,2±2,2	16,2±4,1	-1,3	1,8
Minimum stent CSA(mm ²)	6,4±2,0	6,2±1,5	4,2±1,9	4,2±1,6	-34,3	-32,2
Minimum vessel CSA(mm ²)	14,5±4,5	14,6±4,2	12,8±5,1	12,6±4,4	-11,7	-13,7
Stent volume index(mm ³)	118,5±33,2	116,5±40,2	91,6±44,2	95,0±38,9	-22,7	-18,4
Lumen volume index(mm ³)	109,3±31,8	116,9±40,0	79,3±40,9	74,9±32,8	-27,4	-36
EEM volume index(mm ³)	266,5±75,0	254,4±84,4	250,3±96,3	242,8±87,4	-6,07	-4,5
Intimal hyperplasia follow-up(mm ³)			13,5±6,7	20,4±14,4		

Table 1. IVUS measurement results.

3.1. Four month follow-up

After 4 months follow-up the late lumen loss (LLL) was the combined effect of a decrease in EEM area (change from baseline to 4 months = -16.2 ± 67.7 mm³) and neointima formation (at 4 months follow-up = 13.5 ± 6.7 mm³).

At 4 months follow-up the average % hyperechogenicity of the plaque showed a decrease (%hyperechogenicity after stenting = 12%, after 4 months = 6.7%). In 17 patients with pre- and post-implantation IVUS and at 4 months follow-up, the lumen-media %hyperechogenicity showed at 4 months values lower than those at pre-intervention, probably due to the increase of the plaque over time (pre-implantation = 8%, after stenting = 12.2%, after 4 months = 6.3%). The plaque area mean shows, indeed, an increase of the plaque of 9.7% after 4 months (after stenting = 10.3 ± 3.3 mm², after 4 months = 11.3 ± 3.8 mm², $p=0.03$) (Table 2).

Change from baseline to 4 months follow-up: gated and non-gated				
	Gated	n	Non-gated	n
Minimum stent CSA change(mm ²)	-2,3 ± 1,8	36	-2,0 ± 1,3	43
Minimum vessel CSA change(mm ²)	-1,7 ± 3,1	37	-1,8 ± 1,9	42
Stent volume change(mm ³)	-28,0 ± 35,7	36	-23,9 ± 32,9	35
Lumen volume change(mm ³)	-30,0 ± 34,4	35	-45,2 ± 40,5	35
EEM volume change(mm ³)	-16,2 ± 67,7	35	-18,9 ± 45,4	29

Table 2. Four months follow-up results ECG- vs. non-gated analyses.

3.2. Comparison to previous analyses

Comparison of the outcomes using the newer methods compared to the outcome generated previously showed that the percentage change between BL and FUP of the parameters such as minimum stent cross-sectional area (Δ% gated: -1.3; Δ% non-gated: 1.8), the stent volume index (Δ% gated: -22.7; Δ% non-gated: -18.4) and the EEM volume index (Δ% gated: -6.07; Δ% non-gated: -4.5), resulted in higher percentages for the gated data as compared to non-gated acquired data.

Other parameters such as the minimum vessel cross-sectional area (Δ% gated: -11.7; Δ% non-gated: -13.7), the lumen volume index (Δ% gated: -27.4; Δ% non-gated: -36) showed percentages lower than those generated applying the older methods.

Finally, the volume of intimal hyperplasia at follow-up by gated data was much lower than the volume acquired by non-gated analyzed IVUS data (gated: 13.5 ± 6.7 mm³ vs. non-gated: 20.4 ± 14.4 mm³; respectively).

4. Discussion

This study shows that the developments within image processing methods can help to improve the evaluation of new therapies amongst which such as the here described

and studied bioresorbable scaffolds. Important parameters such as scaffold lengths and volumes (of lumen, stent and vessel) were all different as compared to the parameters acquired by the older methods (Table 1) [5]. Indeed, the percentage change ($\Delta\%$) between post-implantation and the 4 months follow-up data, generated by retrospective gating was much lower than the percentage change by non-gated IVUS analysis (e.g., $\Delta\%$ of lumen volume index between gated and non-gated analysis was 8.6%).

In the future, the advantages of the bioresorbable scaffolds could fully replace the drug-eluting stents and the bare metal stents to treat the coronary artery disease, for this reason we need to assess the behavior and the absorption of the new platforms with imaging methods more sophisticated than the older methods because it could have serious implications onto the interpretation of the performance of this new bioresorbable scaffold platform [1]. This study shows that by using newer quantitative tools the quantified amount of neointima hyperplasia is more than 33% less, a significant finding as in-stent restenosis is often used as an end-point in long-term follow-up studies of coronary stents. Using more accurate analysis methods also reduces the amount of measurement noises and thus increases the sensitivity of the analysis which ultimately will lead to a necessary smaller amount of patients to be included.

4.1. Limitations

This study was limited to a small cohort of patients who were enrolled ($n=37$), however, this is often the case in first-in-man studies. Other limitations were that the IVUS data was recorded on analog video-tape, which has a lower quality than the digital recordings we have today.

5. Conclusion

Improved imaging processing and computer-assisted quantitative analysis methods results in more accurate quantitative parameters allowing reducing the number of patients to be included in prospective studies and it should be considered to re-analyze previous studies analyzed by older methods.

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