Cardiovascular Revascularization Medicine 20 (2019) 775–781

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Validation of a Novel System for Co-Registration of Coronary Angiographic and Intravascular Ultrasound Imaging☆

Khalil Houissa [a], Nicola Ryan [b], Javier Escaned [b], Nick L. Cruden [c], Neal Uren [c], Tristan Slots [d], Peter Kayaert [e], Stéphane G. Carlier [a,*]

[a] UMONS, Hôpital Ambroise Paré, Mons, Belgium
[b] Hospital Clínico Universitario San Carlos, Madrid, Spain
[c] Royal Infirmary of Edinburgh, Edinburgh, UK
[d] Pie Medical Imaging, Maastricht, Netherlands
[e] Universitair Ziekenhuis Gent, Gent, Belgium

ARTICLE INFO

Article history:
Received 20 May 2018
Received in revised form 29 October 2018
Accepted 29 October 2018

ABSTRACT

Introduction: Intravascular ultrasound (IVUS) is a useful adjunct to guide percutaneous coronary intervention (PCI). Correlating IVUS images with angiographic findings can be challenging. We evaluated the utility of a novel co-registration system for IVUS and coronary angiography.
Methods and results: A 3-D virtual catheter trajectory was constructed from separate angiographic imaging runs using bespoke software. Intravascular ultrasound images were obtained using a commercially available mechanical rotational transducer with motorized pullback. Co-registration of ultrasound and angiographic images was then performed retrospectively based on the length of pullback, the 3-D trajectory and the start position of the catheter. Validation was performed in a spherical phantom model and in vivo in the coronary circulation of patients undergoing coronary angiography and intravascular imaging for clinical purposes. 111 paired angiographic and IVUS runs were performed in 3 phantom models. The differences between the reference length and the length measured on the 3D reconstructed path was -0.01 ± 0.40 mm. Intra-observer variability was 0.4%.
We enrolled 25 patients in 3 European hospitals and performed 35 co-registration attempts with an 86% success rate. 71 landmarks were selected by the first operator, 68 by the second. Differences between angiographic and IVUS landmarks were -0.22 ± 0.72 mm and 0.05 ± 1.01 mm, respectively. Inter-observer variability was 0.23 ± 0.63 mm.
Conclusion: We present a novel method for the co-registration of IVUS and coronary angiographic images. This system performed well in a phantom model and using images obtained from the human coronary circulation.
Classifications: Innovation, intravascular ultrasound, other technique

1. Introduction

Although coronary angiography remains the gold standard for the assessment of coronary artery diseases (CAD), it only shows a projected shadow of the coronary lumen unable to provide reliable information on plaque vulnerability or to address the true extent of atherosclerosis [1,2]. Intravascular ultrasound (IVUS) allows detailed visualization of the arterial wall and is useful in delineating culprit lesions, moderate plaque and stent under expansion [3]. These two imaging modalities are complementary for optimal guidance of percutaneous coronary intervention (PCI). However, difficulties correlating important IVUS findings to angiographic images limit the routine use of IVUS during PCI. Angiography/IVUS co-registration methods aim to make vessel mapping easier. Currently available co-registration methods have several disadvantages [4–9]: manual indication of common anatomical positions in both modalities and contrast filled angiographic projections are needed. For others, excessive X-ray exposure comes from real-time angiographic tracking of the imaging transducer position necessary during pullback. We present the first multicenter evaluation of a new co-registration of IVUS and angiograms using the 3D catheter path of the imaging wire [10].

Abbreviations: 2-D, Two dimensional; 3-D, Three dimensional; CAD, Coronary artery disease; ECG, Electrocardiogram; OCT, Optical Coherence Tomography; PCI, percutaneous coronary intervention; QCA, quantitative coronary analysis; SD, standard deviation; IVUS, intravascular ultrasound.

☆ Conflicts of interest: T Slots is employed by Pie Medical Imaging. All other authors report no conflicts of interest.

* Corresponding author at: UMONS, Faculté de Médecine et de Pharmacie, Service de Cardiologie, Avenue Maistriau, 25, 7000 Mons, Belgium.
E-mail address: Stephane.CARLIER@umons.ac.be (S.G. Carlier).

https://doi.org/10.1016/j.carrev.2018.10.024
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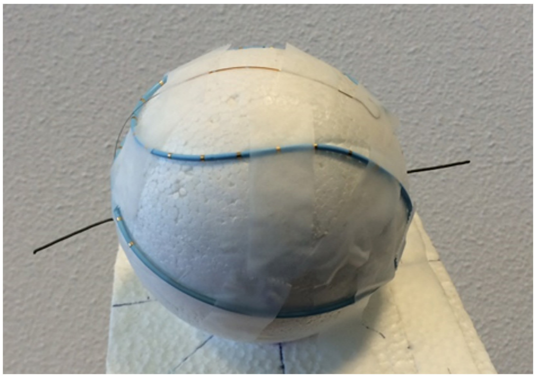

Fig. 1. The phantom sphere with three catheters of different lengths.

2. Methods

In summary, our method is based on a 3D vessel centerline generated from two separate angiogram runs obtained with the IVUS catheter in place. One run uses contrast to serve as a roadmap and the other does not require contrast. In both angiograms, the 2D path of the catheter is marked, starting at the IVUS transducer. Co-registration is then possible knowing the true length in the 3D angiogram and the position of the first IVUS frame.

We initially performed an off-line validation in a phantom to assess the accuracy of the 3D reconstruction. After obtaining feasibility data, we performed real time co-registration in patients.

2.1. Phantom validation

Our phantom consisted of a sphere with three catheters placed around it. Each catheter was marked every 10 mm and had a total length of 30, 90 and 174 mm (Fig. 1). The phantom was placed under an X-ray system (Siemens Axiom Artis®) and several angiographic projections recorded. Thereafter 3D reconstructions of each catheter were obtained using several combinations of projections (Fig. 2). A single operator, blinded to the real catheter lengths, performed measurements of the distance between landmarks. Measurements were repeated by the same operator four weeks apart. The two data sets were measured using the IV-LINQ co-registration system (Pie medical, Maastricht, NL). We compared the actual catheter length with the measured length to determine the accuracy of 3D reconstruction.

2.2. Clinical validation

- Co-registration technique [10]

Co-registration using the 3D catheter path of the imaging catheter is as simple as ABCD, as described previously by Carlier et al. [10]:

A. Advancing imaging catheter.
B. Biplane or two angiograms (preferably orthogonal, at least 30° apart) are acquired during breath holding with the vessel of interest placed in the isocenter.
C. Contrast injection in one of the angiograms used as the roadmap image. Angiograms are sent via DICOM to the co-registration workstation.
D. Digital transfer of the motorized IVUS pullback streamed real-time to the co-registration workstation.

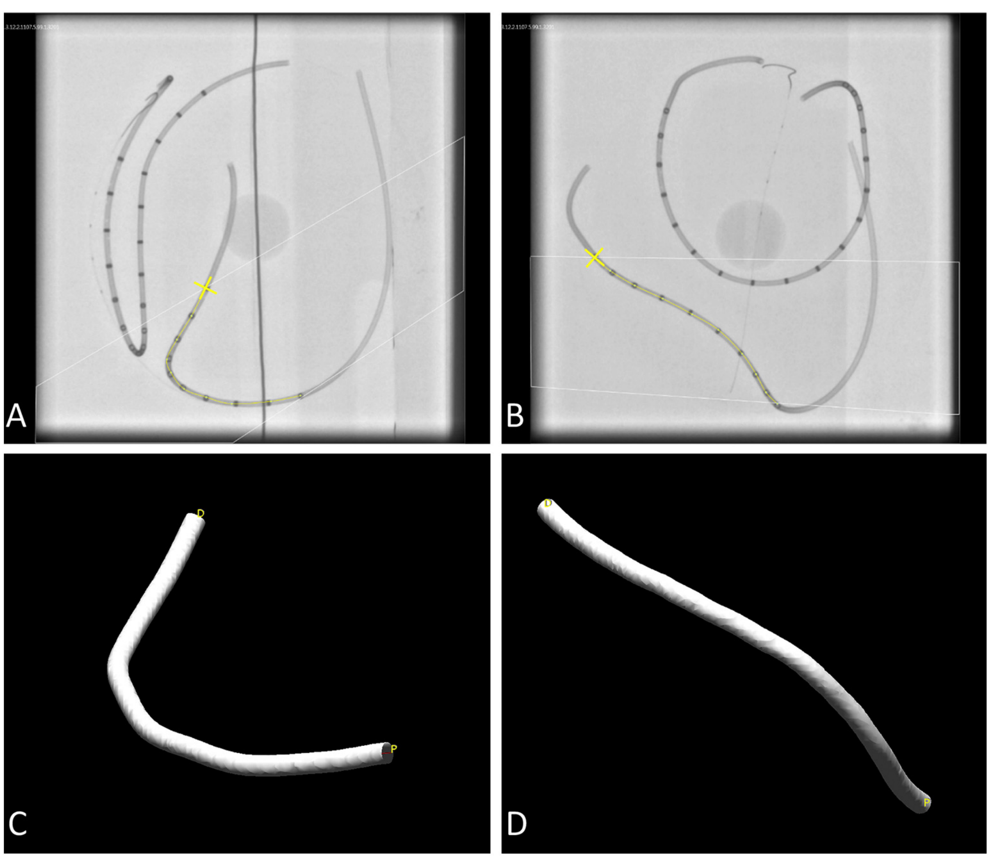

Fig. 2. Example of 3D reconstruction of phantom. Two projections at least 30° apart are selected (A and B). The catheter path is marked in the two projections beginning on a same distal reference. Panel C and D shows the 3D reconstruction of the catheter path.

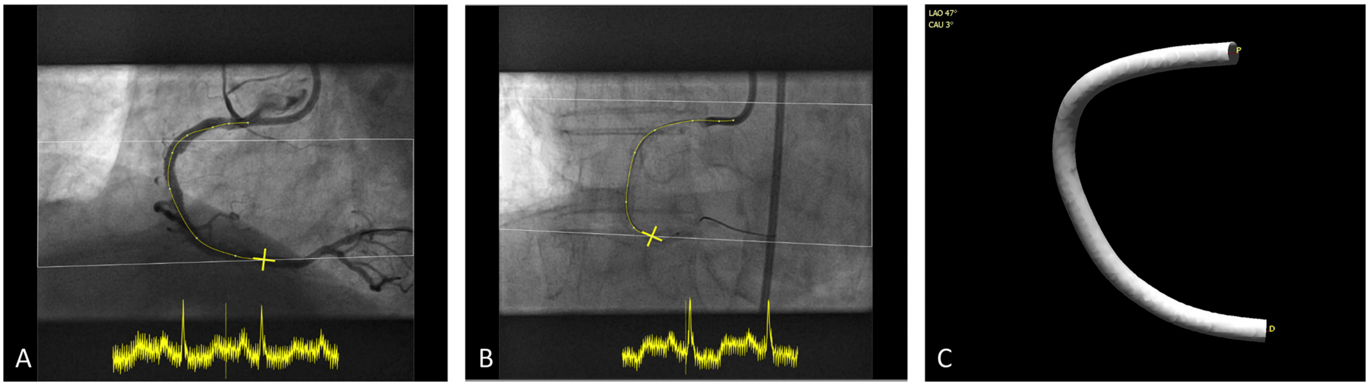

Fig. 3. Steps for 3D angiographic reconstruction of the IVUS catheter: two angiograms are acquired at least 30° apart (A and B). Only one angiogram is filled with contrast (A). The user indicates the IVUS tip and marks further the catheter path in the two projections. Panel C shows the 3D reconstructed IVUS catheter path.

In both angiograms the user indicates the 2D path of the catheter starting at the imaging tip in end-diastolic frames. Thereafter the system automatically calculates the true 3D catheter path length without foreshortening or out-of-plane magnification. IVUS co-registration is then based on the starting point of the trajectory that will be matched to the first recorded IVUS frame. From this starting point, a distance mapping algorithm co-registers each IVUS frame with the 3D catheter path (Figs. 3–4). Offline processing is also possible using an IVUS pull-back recorded in a DICOM file.

- Study population

We enrolled 25 patients in three European hospitals (*UZ Brussels-Belgium*, *Royal Infirmary of Edinburgh-UK and Hospital Clínico Universitario San Carlos*, *Madrid-Spain*). The study population included all comers, undergoing clinically indicated coronary angiography and IVUS. All patients provided written informed consent for storage and use of patient data. Systems used were *Siemens Axiom Artis®*, *Philips Allura®*, *GE Discovery®* in combination with Boston *Scientific iLAB 2.7®* or *Polaris®*. All IVUS studies were performed with a Boston Scientific Opticross™ 40 MHz coronary imaging catheter using a motorized pull-back speed of 0.5 mm/s.

- Data analysis

A central corelab evaluation in the University of Mons (UMONS), Belgium assessed the offline accuracy of the co-registration, using *CAAS Workstation 7.2.1 IV-LINQ software* (*Pie Medical Imaging*, *Maastricht*, *The Netherlands*). Side branches or visible stent edges were first located on angiograms, the exact location was then marked on the IVUS run. Thereafter we measured the mismatch length between angiographic and IVUS locations of these preselected land-marks (Fig. 5). Two operators blinded to the other's results performed the analysis. Quantitative coronary analysis (QCA) was performed with the CAAS Workstation 8.0 (Pie Medical Imaging, Maastricht, the Netherlands).

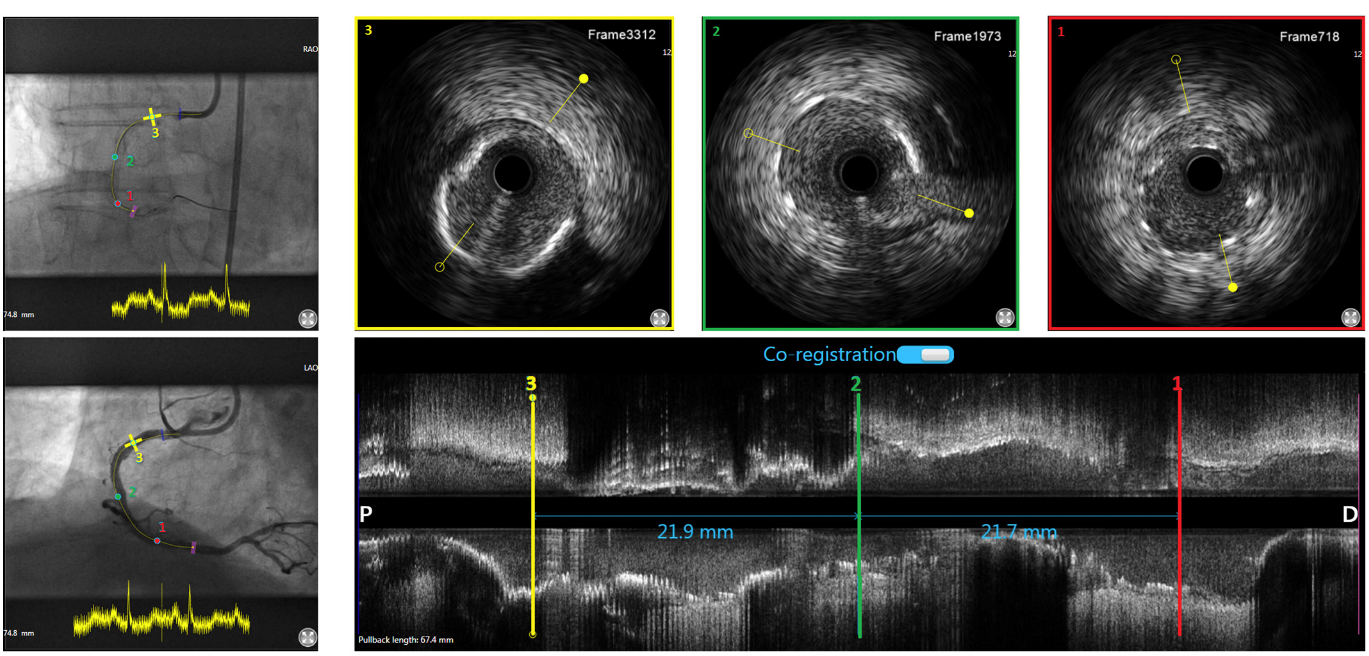

Fig. 4. Example of co-registration on the right coronary artery. Distal reference corresponding to the position of the IVUS tip before starting pullback is marked in pink, which will be matched to the first recorded IVUS frame. From this starting point, each IVUS frame is located on the angiogram in real time: (1) distal stent edge, (2) side branch, (3) heavy calcified plaque. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

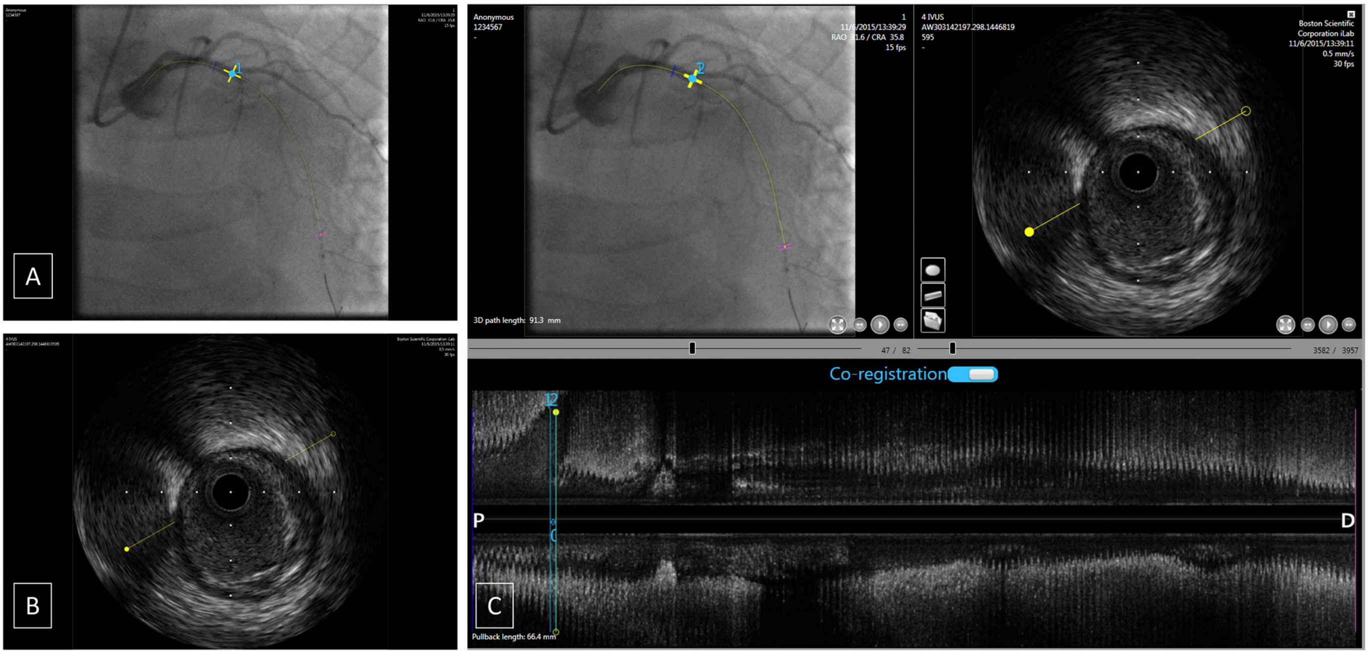

Fig. 5. Example of side branches selection. A: Diagonal is marked on angiogram (landmark 1). B: Diagonal is bookmarked on IVUS (landmark 2 on panel C). C: Mismatch between the two landmarks is then calculated.

2.3. Statistical analysis

- Phantom validation

Differences between the measured length on the 3D reconstructed phantom path and the real catheter length were expressed as mean ± standard deviation (sd). Intraobserver variability was assessed using a Bland Altman plot.

- Clinical validation

Mismatch between IVUS and angiographic landmarks was expressed as mean ± sd. The *ANOVA* test was used to look for a correlation between mismatch and the distance of the landmark from the distal reference (IVUS tip) (Statistical analysis was performed using *IBM SPSS Statistics 20*®). Interobserver variability was assessed using a Bland Altman plot.

3. Results

3.1. Phantom validation

We obtained 37 paired angiograms of the phantom and used a total of 111 3D reconstructions of the three catheters. For these recordings, no IVUS was performed nor co-registration. The mean ± sd difference between the reference length and the one measured on the 3D reconstructed path was −0.01 ± 0.4 mm. The intra-observer variability was 0.4%.

3.2. Clinical validation

Twenty-five patients were included and 35 co-registration attempts were performed without any clinical complications. Patient characteristics: average age 66-years (21 to 91), with 80% male. The majority of interrogated vessels were the LAD (52%) or RCA (32%), with less LCx (12%) and ramus (4%). Five attempts were excluded, giving an 86% success rate. In 3 cases, the two angiographic projections were inappropriate for a 3D reconstruction of the coronary segment of interest and we noticed in 2 other cases that the position of the IVUS probe was different in the two angiographic projections, compared to landmarks such as a side branch, due to inadvertent probe shifting between

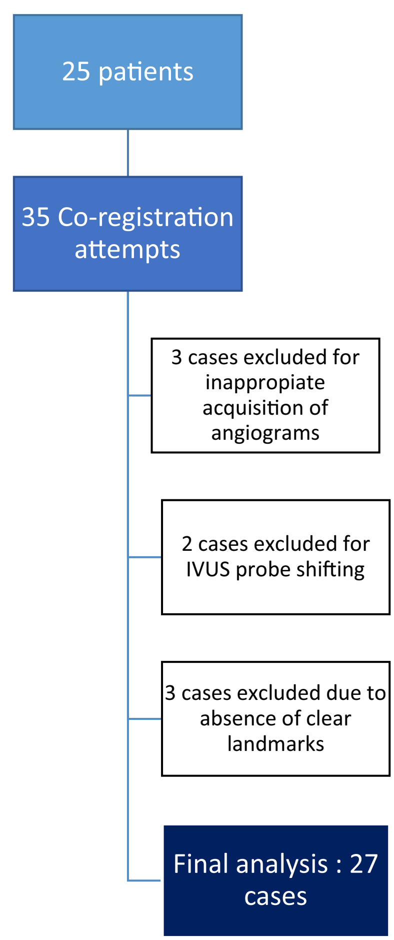

Fig. 6. Clinical validation: the study design.

the two angiograms. An additional three cases were excluded from the analysis due to the absence of clear landmarks to map (Fig. 6). Vessels of interest were the left anterior descending artery in 17 cases, the right coronary artery in seven and the left circumflex in three. All lesions were de novo lesions. Reference diameter by QCA was 2.69 ± 0.54 mm, lesion length 13.1 ± 6.7ranging from 3 to 33 mm, with an average diameter stenosis of 38 ± 25%. Average time to perform co-registration from loading the angiograms until co-registration was less than 1 min. Seventy-one landmarks were selected by the first operator, 68 by the second in IVUS pullbacks of up to 100+ mm. The position of these landmarks ranged from 2 to 98 mm from the start of the IVUS pullback (mean ± sd = 39.7 ± 21.7 mm). Fig. 7 demonstrates the mismatch between IVUS and angiographic mapping in function of the position of the landmarks from the start of the IVUS pullback. The bias on this mismatch was not correlated to the distance between the chosen landmark and the distal reference ($p = 0.99$). Differences between angiographic and IVUS landmarks were −0.22 ± 0.72 mm and 0.05 ± 1.01 mm respectively for observer 1 and 2. After pooling the common landmarks analysed by the two operators, we observed a low inter-observer variability: mean ± sd (obs 1–obs 2) = 0.23 ± 0.63 mm as demonstrated on Fig. 8.

4. Discussion

We present the results of a novel method for co-registration of coronary angiographic and IVUS images based on generation of a virtual 3D catheter path within the coronary circulation. Using this technique, we observed successful co-registration in over 85% of cases with a good accuracy.

The limitations of coronary angiography in assessing the true extend of atherosclerosis is well recognised. Several studies demonstrated that the visual interpretation of angiograms is often associated with a misjudgement of plaque severity [1,11–13]. Intravascular ultrasound offers detailed cross sectional views of the arterial wall, helping the cardiologist choose the correct stent size based on accurate assessment of luminal and vessel dimensions, lesion length and volume of plaque burden. Although not a universal finding, a number of studies have demonstrated improved outcomes with IVUS guided PCI, particularly in the era of drug eluting stents [14–17], essentially related to a lower rate of target lesion revascularisation [18,19]. Despite this, IVUS remains underused in almost all cardiovascular catheterisation laboratories worldwide because of cost constraints but also due to the difficulties locating IVUS findings in the angiogram.

The aim of co-registration methods is to combine the accurate and valuable information provided by IVUS with the usual interpretation of the coronary tree as presented by angiography. Several studies propose different concepts for co-registration of angiography and IVUS or other intravascular imaging modalities. Sonka's group [4,5] and Slager et al. [8,9] proposed accurate methods to locate IVUS images along a 3D reconstructed vessel, with an exact IVUS images orientation allowing calculation of shear stress and other hemodynamic studies. However, these methods require a long post processing analysis unsuitable for daily use during PCI procedures. An alternative approach was described by Tu & al [6] who reported a good co-registration accuracy (mean registration error 0.03 ± 0.45 mm, measured in 22 patients and a total of 56 landmarks). Nonetheless their co-registration technique requires two contrast angiograms and manual labelling of landmarks. This presumes the presence of identifiable side branches or stent edges, which is not always the case. Other proposed techniques are based on tracking the imaging tip under ECG triggered fluoroscopy [7], and even though satisfactory results have been reported (median registration error below 1.5 mm), the radiation exposure concerns are a major limiting factor for an eventual wider use. St Jude Medical offers an angiography-OCT co-registration but to date no studies regarding its accuracy have been published. A recent randomized study of 200 patients evaluating stent implantation guided by this automated coregistration of OCT and angiography did not reduce geographical miss defined as edge dissection or significant residual disease either by angiography or OCT [20].

The aforementioned methods are therefore either complex and demand heavy workflow or require excessive radiation exposure or contrast use. This paper evaluates a new co-registration method that aims

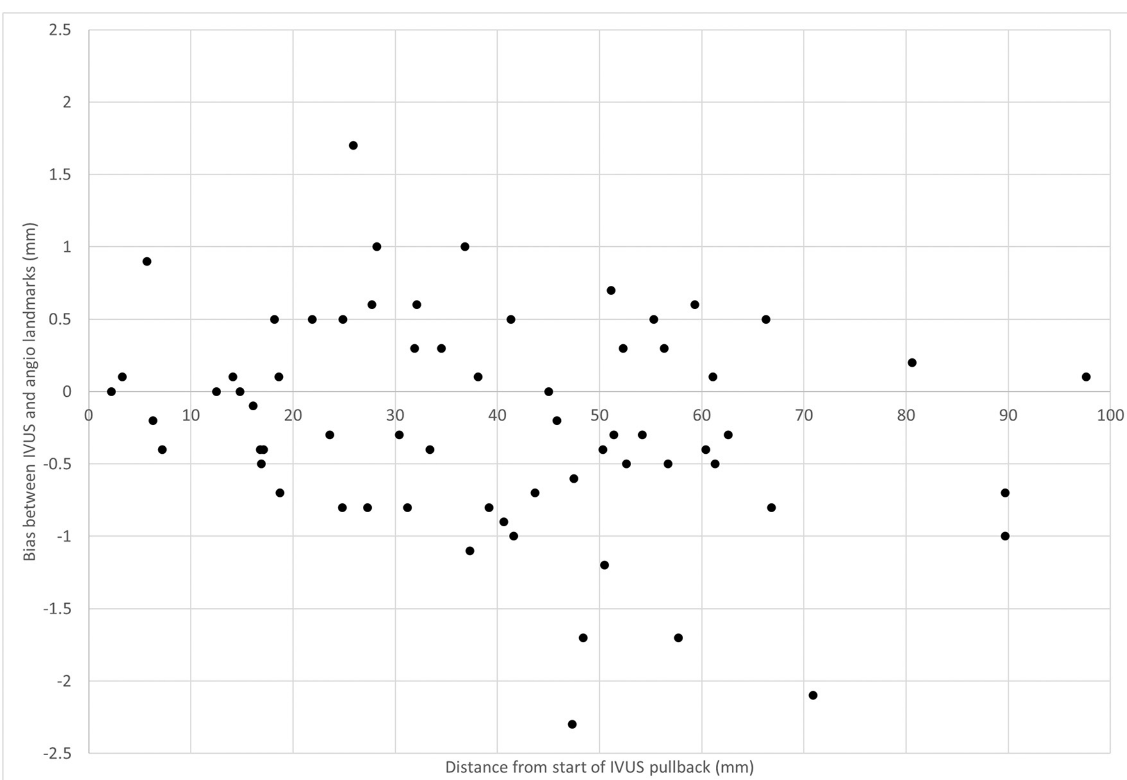

Fig. 7. Absolute angiogram/IVUS measured mismatch in function of the position of the landmark from the start of the IVUS pullback.

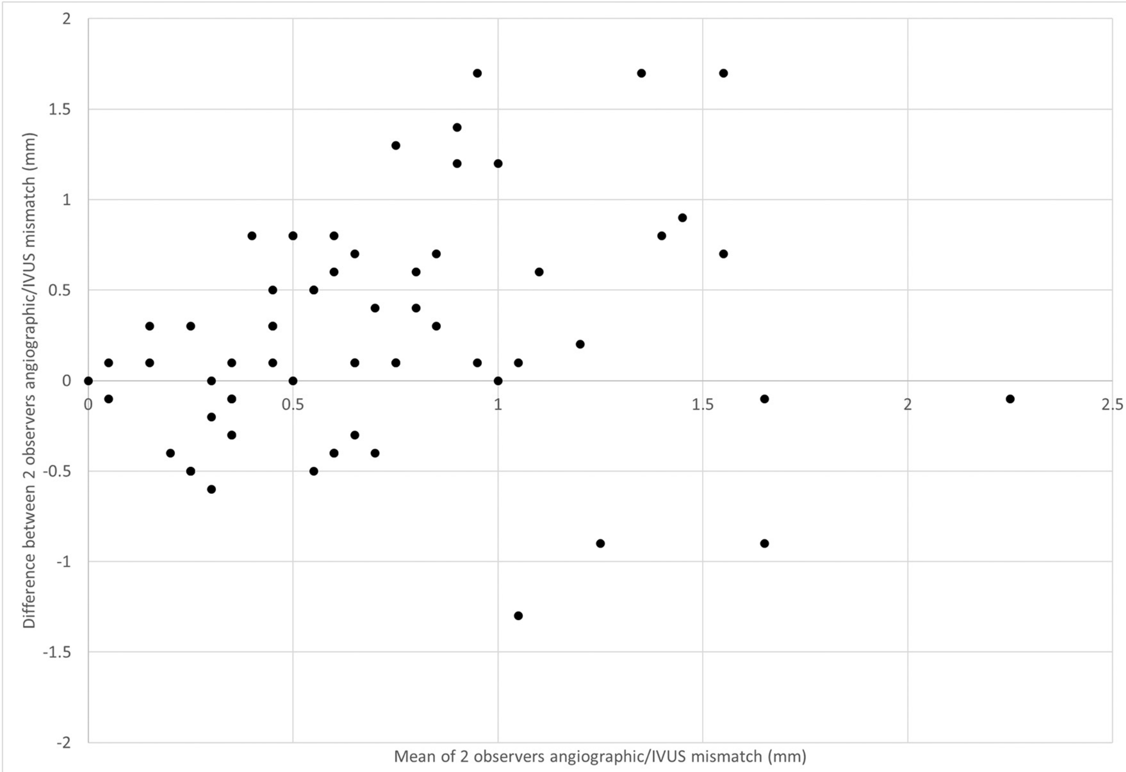

Fig. 8. Bland Altman plot of the inter-observer variability on absolute angiogram/IVUS measured mismatch.

to transcend the previously described weaknesses by proposing a simplified work flow with no need for additional X-ray exposure or contrast injection. The primary results demonstrate the feasibility of this technique. However, some limitations must be mentioned:

1. Angiogram acquisitions must be performed strictly in the isocenter otherwise 3D reconstruction and therefore co-registration will be distorted. Currently developments are ongoing to allow the use of non-isocenteric angiograms.
2. The catheter tip is used as reference, which supposes that any displacement of the catheter between angiograms acquisitions and IVUS run or any speed variations due to breathing or important cardiac motion may skew co-registration accuracy.
3. The track length is calculated according to the known automated pullback speed. This limits the usage of manual pullback.
4. This study enrolled a limited number of patients and used only one IVUS system and one IVUS probe type (Boston Scientific Opticross™) for all cases. It is plausible that this technique may be less accurate with other IVUS systems.

5. Conclusion

This first multicenter clinical evaluation of a new angiography/IVUS co-registration method demonstrates that it is accurate and robust when acquisitions guidelines are fulfilled. Upcoming studies will explore its feasibility with other IVUS system and ongoing technical developments may facilitate non-isocentric angiographic acquisitions. Further clinical studies must evaluate the real impact on improving PCI results, which remains the final aim of all co-registration methods.

Impact on daily practice

Co-registration of angiography and IVUS potentially simplifies PCI by allowing easier identification of appropriate landing zones as well aiding in the choice of more accurate stent size and lengths. This system minimises both radiation and contrast exposure reducing the risks to patients undergoing IVUS guided PCI. The impact of this system on improving PCI results still needs to be evaluated.

References

[1] Topol EJ, Nissen SE. Our preoccupation with coronary luminology the dissociation between clinical and angiographic findings in ischemic heart disease. Circulation 1995;92:2333–42.
[2] Radico F, Cicchitti V, Zimarino M, De Caterina R. Angina pectoris and myocardial ischemia in the absence of obstructive coronary artery disease: practical considerations for diagnostic tests. JACC Cardiovasc Interv 2014;7:453–63.
[3] Mintz GS. Clinical utility of intravascular imaging and physiology in coronary artery disease. J Am Coll Cardiol 2014;64:207–22.
[4] Wahle A, Prause PM, DeJong SC, Sonka M. Geometrically correct 3-D reconstruction of intravascular ultrasound images by fusion with biplane angiography—methods and validation. IEEE Trans Med Imaging 1999;18:686–99.
[5] Wahle A, Prause GPM, Birgelen CV, Erbel R, Sonka M. Fusion of angiography and intravascular ultrasound in vivo: establishing the absolute 3-D frame orientation. IEEE Trans Biomed Eng 1999;46:1176–80.
[6] Tu S, Holm NR, Koning G, Huang Z, Reiber JHC. Fusion of 3D QCA and IVUS/OCT. Int J Card Imaging 2011;27:197–207.
[7] Wang P, Ecabert O, Chen T, Wels M, Rieber J, Ostermeier M, et al. Image-based co-registration of angiography and intravascular ultrasound images. IEEE Trans Med Imaging 2013;32:2238–49.
[8] Slager CJ, Wentzel JJ, Schuurbiers JCH, Oomen JAF, Kloet J, Krams R, et al. True 3-dimensional reconstruction of coronary arteries in patients by fusion of angiography and IVUS (ANGUS) and its quantitative validation. Circulation 2000;102:511–6.
[9] Krams R, Wentzel JJ, Oomen JA, Schuurbiers JC, Andhyiswara I, Kloet J, et al. Shear stress in atherosclerosis, and vascular remodelling. Semin Interv Cardiol 1998;3:39–44.
[10] Carlier S, Didday R, Slots T, Kayaert P, Sonck J, El-Mourad M, et al. A new method for real-time co-registration of 3D coronary angiography and intravascular ultrasound or optical coherence tomography. Cardiovasc Revasc Med Med Mol Interv 2014;15:226–32.
[11] Nissen SE. Pathobiology, not angiography, should guide management in acute coronary syndrome/non-ST-segment elevation myocardial infarction: the non-interventionist's perspective. J Am Coll Cardiol 2003;41:103S–12S.
[12] Zir LM, Miller SW, Dinsmore RE, Gilbert JP, Harthorne JW. Interobserver variability in coronary angiography. Circulation 1976;53:627–32.
[13] Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS, et al. A prospective natural-history study of coronary atherosclerosis. N Engl J Med 2011;364:226–35.
[14] Zhang Y, Farooq V, Garcia-Garcia HM, Bourantas CV, Tian N, Dong S, et al. Comparison of intravascular ultrasound versus angiography-guided drug-eluting stent

implantation: a meta-analysis of one randomised trial and ten observational studies involving 19,619 patients. EuroIntervention 2012;8:855–65.

[15] Klersy C, Ferlini M, Raisaro A, Scotti V, Balduini A, Curti M, et al. Use of IVUS guided coronary stenting with drug eluting stent: a systematic review and meta-analysis of randomized controlled clinical trials and high quality observational studies. Int J Cardiol 2013;170:54–63.

[16] Jang J-S, Song Y-J, Kang W, Jin H-Y, Seo J-S, Yang T-H, et al. Intravascular ultrasound-guided implantation of drug-eluting stents to improve outcome: a meta-analysis. JACC Cardiovasc Interv 2014;7:233–43.

[17] Ahn J-M, Kang S-J, Yoon S-H, Park HW, Kang SM, Lee J-Y, et al. Meta-analysis of outcomes after intravascular ultrasound-guided versus angiography-guided drug-eluting stent implantation in 26,503 patients enrolled in three randomized trials and 14 observational studies. Am J Cardiol 2014;113:1338–47.

[18] Steinvil A, Zhang Y-J, Lee SY, Pang S, Waksman R, Chen S-L, et al. Intravascular ultrasound-guided drug-eluting stent implantation: an updated meta-analysis of randomized control trials and observational studies. Int J Cardiol 2016;216:133–9.

[19] Hong S, Kim B, Shin D, et al. Effect of intravascular ultrasound–guided vs angiography-guided everolimus-eluting stent implantation: the ivus-xpl randomized clinical trial. JAMA 2015;314(20):2155–63.

[20] Koyama K, Fujino A, Maehara A, et al. A prospective, single-center, randomized study to assess whether automated coregistration of optical coherence tomography with angiography can reduce geographic miss. Catheter Cardiovasc Interv Oct 22 2018. https://doi.org/10.1002/ccd.27854 [Epub ahead of print].