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A randomised trial of sheathless versus conventional access for transradial interventions

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Introduction

Recent studies have reported a high rate of transradial access (TRA)-induced vascular injury which leads to chronic intimal thickening and is associated with radial artery spasm (RAS) and radial artery occlusion (RAO)[1–3]. This is likely to be caused by radial artery puncture, sheath introduction and sheath friction caused by radial artery inner diameter-sheath outer diameter (RAID/SOD) mismatch. However, using optical coherence tomography (OCT), post-procedural radial artery (RA) damage was also found in the proximal part of the RA, where the vessel has a larger diameter and RAID/SOD mismatch is less likely to be the cause of vascular damage. One of the possible mechanisms is intimal damage caused by the space between the guidewire and the catheter tip which shaves the vessel wall ("razor" effect) **(Figure 1)**[4].

A sheathless catheter introduction system may reduce both RAID/SOD mismatch and the razor effect by a smooth wire-to-catheter transition. To evaluate these two potential effects, we designed a trial to measure intimal and medial radial artery injury, comparing sheathless TRA (SLTRA) with the RAILWAY™ Sheathless Access System (Cordis, Cardinal Health, Milpitas, CA, USA) to conventional TRA (CTRA).

Methods

Details regarding the procedures, data collection and definitions are available in **Supplementary Appendix 1** and **Supplementary Figure 1**-**Supplementary Figure 3**.

Results

A total of 597 patients were screened for the trial **(Supplementary Figure 1)**, of whom 51 were enrolled. Two patients did not undergo OCT; one OCT was not analysable. The main reason not to include patients was logistic, and a maximum of one patient per day was enrolled due to time constraints in the cath lab. Baseline and procedural results are presented in **Supplementary Table 1** and **Supplementary Table 2**.

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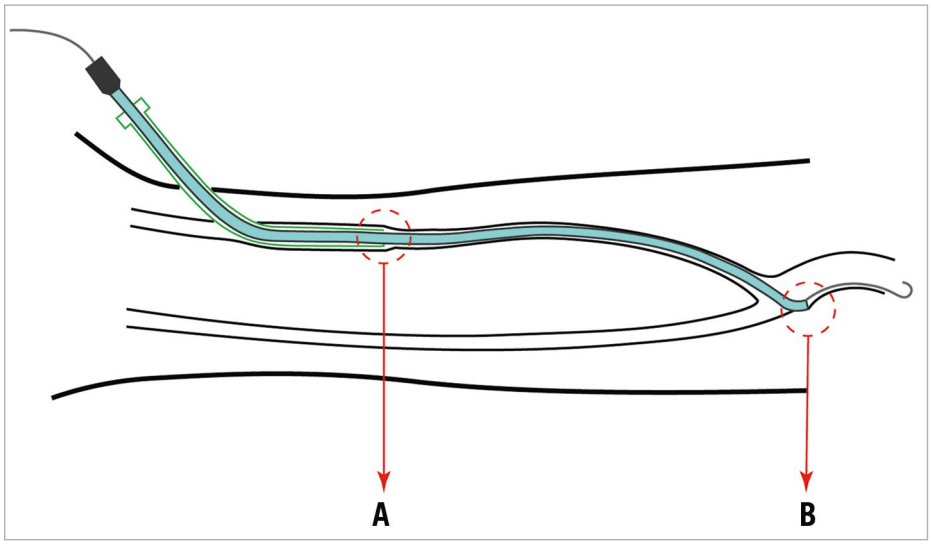

Figure 1. *Mechanisms of radial artery injury caused by the transradial access. A) Oversized sheath outer diameter (SOD) compared to the radial artery internal diameter (RAID). B) Razor effect of the catheter tip edge. Green represents the sheath outer layer, light blue the guiding catheter and the grey line the guidewire.*

ENDPOINTS

The occurrence of the predefined composite primary endpoint did not differ significantly between the CTRA and SLTRA groups (9 [35%] vs 14 [56%], respectively, p=0.27) **(Table 1)**. The interobserver agreement of the primary endpoint was low (kappa 0.45), mainly driven by the component intimal tears (kappa 0.30). The agreement of the other endpoints medial dissection and thrombus was substantial (kappa 0.73 and 0.83, respectively). Secondary endpoints are shown in **Supplementary Table 3**.

Table 1. OCT endpoints.

	CTRA (n=23)	SLTRA (n=25)	*p*-value
Primary (combined)			
Any injury proximal or distal	9 (39%)	14 (56%)	0.27
Secondary (localisation of injury)			
Proximal injury	6 (26%)	9 (36%)	0.54
Distal injury	3 (13%)	6 (24%)	0.47
Secondary (type of injury)			
Intimal tears	8 (35%)	5 (20%)	0.34
Medial dissection	0 (0%)	6 (24%)	0.02
Thrombus	2 (9%)	6 (24%)	0.25

Discussion

No reduction in vascular injury of the radial artery was shown using the RAILWAY Sheathless TRA System. Also, no reduction in other predefined endpoints was seen.

The frequency of vascular damage in the control group of our trial was in line with the results of two recent OCT studies[3,5]. In other trials, sheathless access reduced RAS[6], probably as a result of a more favourable RAID/SOD ratio[7]. Although RAID/SOD mismatch was not present in our SLTRA group, there was no protective effect on distal or proximal RA injury measured by OCT. There were more medial dissections in the SLTRA group. Forward movements of the RAILWAY dilator system may induce medial damage during introduction of the guiding catheter (GC). Another cause may be the introduction of normal instead of hydrophilic coated GCs, as used in other SLTRA systems.

Contrary to other studies[3,5], we found a low interobserver agreement when evaluating intimal tears (IT). OCT imaging of the intima is prone to false images, for example by suboptimal blood clearance. On the other hand, medial dissections and intraluminal thrombi are easily visible with OCT.

Our findings may have important consequences for the use of SLTRA in daily practice. SLTRA is feasible as an alternative access strategy and its procedural success rate is comparable to CTRA[8,9]. On the other hand, in our cohort the technique did not seem to reduce vascular damage. Therefore, SLTRA may not be appropriate as a standard access technique to prevent vascular injury, but it may be beneficial in selected patients, for example patients scheduled for procedures mandating large bore catheters or for populations with small radial arteries.

Limitations

One limitation of the trial is the lack of historical OCT data in patients undergoing SLTRA. Also, for logistic reasons, one patient a day was included, which might have introduced selection bias, although we have no data about the reasons for excluding patients. In addition, the study was not powered to detect any clinical endpoint. Moreover, the relationship between OCT-detected injury and clinical outcome is not known.

Conclusion

SLTRA is not related to reduced vascular injury when compared to CTRA, as evaluated by OCT imaging.

Impact on daily practice

No preventive effect of the RAILWAY Sheathless Access System on radial artery injury was seen in this study. Adoption of a sheathless technique as a standard procedure for 6 Fr TRA does not seem appropriate.

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Conflict of interest statement

R.J. van Geuns reports grants and personal fees from Abbott Vascular, outside the submitted work. N. van Royen reports grants from Abbott, Philips, and AstraZeneca, personal fees from Castor, Medtronic, Bayer, and Boston, and grants from Biotronik, outside the submitted work. The other authors have no conflicts of interest to declare.

References

1. Costa F, van Leeuwen MA, Daemen J, Diletti R, Kauer F, van Geuns R, Ligthart J, Witberg K, Zijlstra F, Valgimigli M, Van Mieghem NM. The Rotterdam Radial Access Research Ultrasound-Based Radial Artery Evaluation for Diagnostic and Therapeutic Coronary Procedures. *Circ Cardiovasc Interv.* 2016;9:e003129.

2. Wu SS, Galani RJ, Bahro A, Moore JA, Burket MW, Cooper CJ. 8 french transradial coronary interventions: clinical outcome and late effects on the radial artery and hand function. *J Invasive Cardiol.* 2000;12:605-9.

3. Yonetsu T, Kakuta T, Lee T, Takayama K, Kakita K, Iwamoto T, Kawaguchi N, Takahashi K, Yamamoto G, Iesaka Y, Fujiwara H, Isobe M. Assessment of acute injuries and chronic intimal thickening of the radial artery after transradial coronary intervention by optical coherence tomography. *Eur Heart J.* 2010;31:1608-15.

4. Patel T, Shah S, Pancholy S, Deora S, Prajapati K, Coppola J, Gilchrist IC. Working through challenges of subclavian, innominate, and aortic arch regions during transradial approach. *Catheter Cardiovasc Interv.* 2014;84:224-35.

5. Di Vito L, Burzotta F, Trani C, Pirozzolo G, Porto I, Niccoli G, Leone AM, Crea F. Radial artery complications occurring after transradial coronary procedures using long hydrophilic-coated introducer sheath: a frequency domain-optical coherence tomography study. *Int J Cardiovasc Imaging.* 2014;30:21-9.

6. Horie K, Tada N, Isawa T, Matsumoto T, Taguri M, Kato S, Honda T, Ootomo T, Inoue N. A randomized comparison of incidence of radial artery occlusion and symptomatic radial artery spasm associated with elective transradial coronary intervention using 6.5-Fr Sheathless Eaucath Guiding Catheter vs. 6.0 Fr Glidesheath Slender. *EuroIntervention.* 2018;13:2018-25.

7. van der Heijden D, van Leeuwen MA, Janssens GN, Hermie J, Lenzen M, Ritt MJ, van de Ven PM, Kiemeneij F, van Royen N. Endothelial dysfunction and the occurrence of radial artery spasm during transradial coronary procedures: the ACRA-Spasm study. *EuroIntervention.* 2016;12:1263-70.

8. Noble S, Tessitore E, Gencer B, Righini M, Robert-Ebadi H, Roffi M, Bonvini RF. A Randomized Study of SheathLess vs Standard Guiding Catheters for Transradial Percutaneous Coronary Interventions. *Can J Cardiol.* 2016;32:1425-32.

9. Chiam PT, Liu B, Wong AS, Wong PE, Lim ST, Koh TH, Lim VY. Comparison of novel 6.5 Fr sheathless guiding catheters versus 5 Fr guiding catheters for transradial coronary intervention. *EuroIntervention.* 2011;7:930-5.

10. Garg N, Madan B, Khanna R, Sinha A, Kapoor A, Tewari S, Kumar S, Goel PK. Incidence and predictors of radial artery occlusion after transradial coronary angioplasty: Doppler-guided follow-up study. *J Invasive Cardiol.* 2015;27:106-12.

Supplementary data

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The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-19-00380

Supplementary data

Supplementary Appendix 1. Methods

Study design and population

This proof-of-concept trial has a prospective, multicentre, randomised, open-label design. The study protocol was registered at the Netherlands National Trial Register (NTR7081) and approved by the local ethics committee and performed in accordance with the Declaration of Helsinki. Between 18 January and 9 April 2018, patients scheduled for elective coronary angiography were screened in three Dutch PCI centres. Inclusion criteria were met if patients were admitted for transradial coronary angiography with the option for an ad hoc coronary intervention, and were older than 18 years of age and able and willing to give informed consent. Excluded were patients who a) had severe renal dysfunction (eGFR <30 ml/min), b) had previous TRA through the same radial artery, c) were admitted for intervention for ST-elevation myocardial infarction, or d) were admitted for work-up for valve disease. After screening and the informed consent procedure, 51 patients were eligible to enter the trial. A brief flow chart is presented in **Supplementary Figure 1**. Patients were randomised to SLTRA or CTRA in a 1:1 fashion, using block randomisation, stratified per including centre.

Radial access

All patients received preprocedural sedative medication and local anaesthesia (lidocaine). If patients were randomised to SLTRA, a 6 Fr guiding catheter (BRITE TIP™; Cordis, Cardinal Health, Milpitas, CA, USA) was advanced directly into the radial artery using the 6 Fr RAILWAY Sheathless Access System (Cordis). After radial artery puncture with an open 21 G access needle, a 0.021" hydrophilic access wire was inserted. After removal of the needle, a small skin incision was made. Then, a 5 Fr dilator was used to predilate the radial artery and to inject the radial artery cocktail. After removal of the dilator, a 0.021" compatible RAILWAY dilator was inserted over the access wire. After this, the wire was removed and the GC was

advanced over the RAILWAY dilator. Next, the dilator was removed and the GC was reloaded with a 0.035" guidewire and the 0.035" compatible RAILWAY dilator. The GC/RAILWAY system was advanced over the wire up to the subclavian artery to ensure smooth passage. The dilator was then removed and angiography completed. GC exchange was performed using the 0.035" compatible RAILWAY dilator. The type and number of coronary catheters used were left to the discretion of the operator in both study arms. CTRA was performed according to the local protocol, using a Seldinger technique with a 21 G needle and a 0.021" hydrophilic access wire. Over this wire a 6 Fr Glidesheath Slender® (Terumo Corp., Tokyo, Japan) with an outer diameter of 2.46 mm was introduced and the same GCs were used. All patients received a radial artery cocktail containing verapamil (5 mg), nitroglycerine (0.2 mg) and heparin (5,000 IU) before the procedure. Extra heparin was given in case of PCI according to the patient's weight. After the procedure, haemostasis was achieved according to the local protocol, including two hours of compression with a compression device. Patent haemostasis was not mandated by the protocol.

Procedure

After radial access, coronary angiography and intervention were performed. The number of catheters used, the frequency of catheter passages and crossovers to another access site were registered as well as procedural length, fluorescence time and contrast use. Catheter types were predefined as Judkins left, Judkins right, EBU, Amplatz or other. Upper limb pain was noted using a visual analogue score (VAS) from 0-10. Also, radial artery spasm was scored when two out of the following were present: persistent forearm pain, pain in response to catheter manipulation, pain response to catheter withdrawal, difficult catheter manipulation after being "trapped" by the radial artery, considerable resistance on withdrawal of the sheath. Before and one month after the procedure, patients underwent hand function questionnaires.

OCT

The Ilumien™ FD-OCT system was used with the OPTIS™ Dragonfly™ catheter (St. Jude Medical, St. Paul, MN, USA). After coronary angiography with or without intervention, the GC with or without sheath was pulled back until the catheter tip reached the ostium of the radial artery. No extra radial artery cocktail was mandated by the protocol. The OCT catheter was advanced in the GC just until the tip of the OCT catheter reached the tip of the GC. Then, the GC was pulled back 72 mm to facilitate OCT scanning without the necessity of forward movements of the OCT catheter, preventing vascular damage. The first OCT pullback was performed to visualise the proximal part of the RA (proximal OCT run) and a second OCT pullback was performed distally (distal OCT run) **(Supplementary Figure 2)**. To evaluate the radial artery internal diameter/device outer diameter ratio, the intima-to-intima distance of the most distal non-spastic segment was measured. All OCT images were analysed by two experienced physicians, blinded to the clinical data and randomisation.

Questionnaires for hand function

The QuickDASH DLV and CISS questionnaires were taken before and one month after the procedure. The QuickDASH consists of 11 items to measure physical function, symptoms and their consequences on daily life, scored from 1-5. A difference of 14 points in a QuickDASH score is considered to be a minimal clinically important difference (MCID). The validated Cold Intolerance Symptom Severity (CISS) questionnaire is able to detect cold intolerance. Cold intolerance is defined as abnormal pain of the hand and fingers after exposure to cold that leads to significant functional impairment, which commonly occurs after a variety of upper extremity injuries. Pathological cold intolerance is defined as a CISS score >30.

Radial artery occlusion (RAO)

The radial artery was palpated after the procedure. If RAO was suspected, this was confirmed by ultrasound or Doppler study, defined as the absence of antegrade flow. Pulse Doppler interrogation of waveform was done to rule out collateral flow suggesting upstream occlusion. Biphasic or triphasic signals were taken as normal flow, while a monophasic signal was considered as collateral flow from an upstream block in the artery [10].

Endpoints

The primary endpoint was a composite of the following signs of acute radial injury, detected by post-procedural radial OCT: a) intimal tears (IT), defined as luminal surface discontinuity with or without an intimal flap that was restricted within the intima, b) medial dissections (MD), defined as a luminal surface disruption that extended into the media either in a radial or in a circumferential direction, and c) intraluminal thrombi (TR), defined as high-backscattering protrusions inside the lumen of the artery with signal-free shadowing in the OCT image **(Supplementary Figure 3)**.

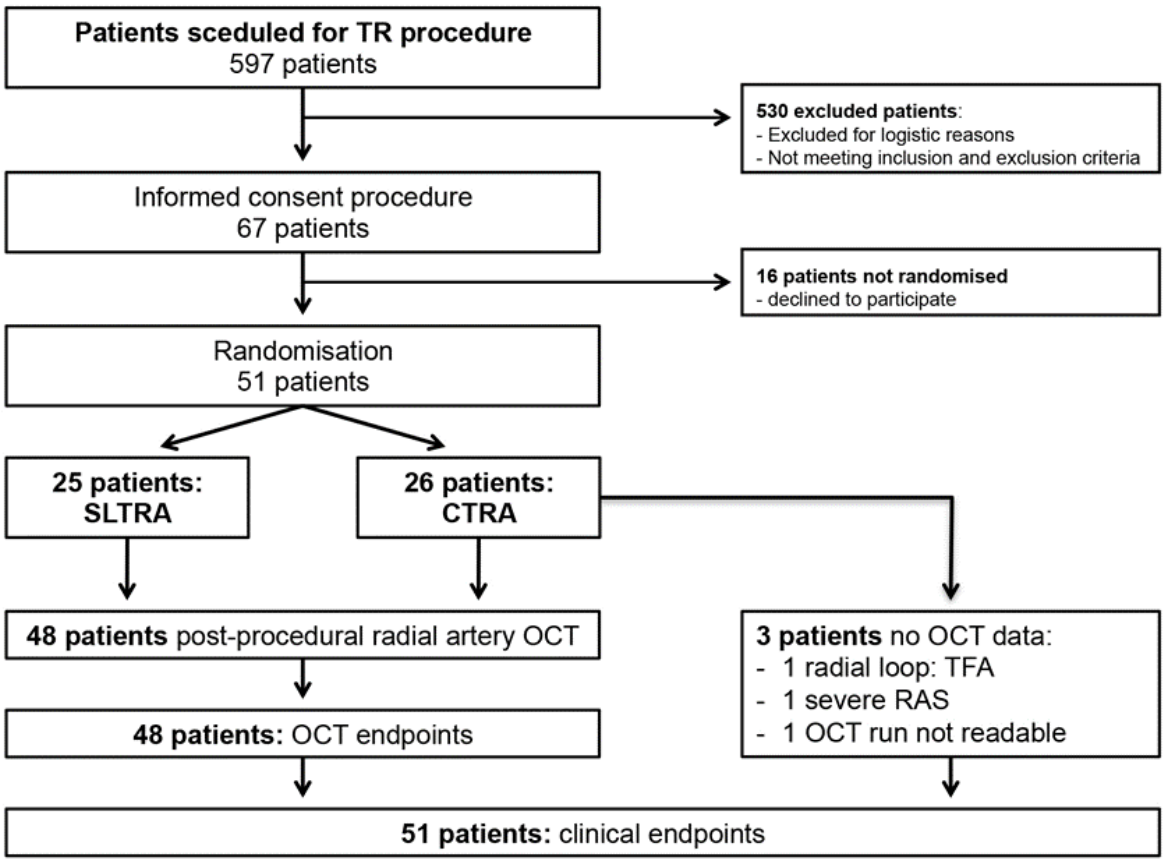
In addition to the separate parameters of vascular injury and localisation of injury (proximal or distal), several pre-defined procedural and clinical outcome parameters were evaluated as secondary outcome. First, procedural progress, consisting of procedural time until radial OCT, fluoroscopy time until radial OCT, crossover to contralateral radial artery or femoral artery and the total amount of contrast used were noted. Secondly, radial artery spasm was noted, defined as two out of five characteristics: persistent forearm pain (extending beyond the period of catheter manipulation), pain response to catheter manipulation (manoeuvres of the catheter other than withdrawal, such as rotation or small movements to obtain optimal catheter position), pain response to catheter withdrawal, difficult catheter manipulation after being "trapped" by radial artery and considerable resistance on withdrawal of the sheath. Also, difference in procedural pain score (VAS), occurrence of RAO after the procedure, hand

dysfunction (QuickDASH score) and cold intolerance (CISS score) at one month were compared between the treatment groups.

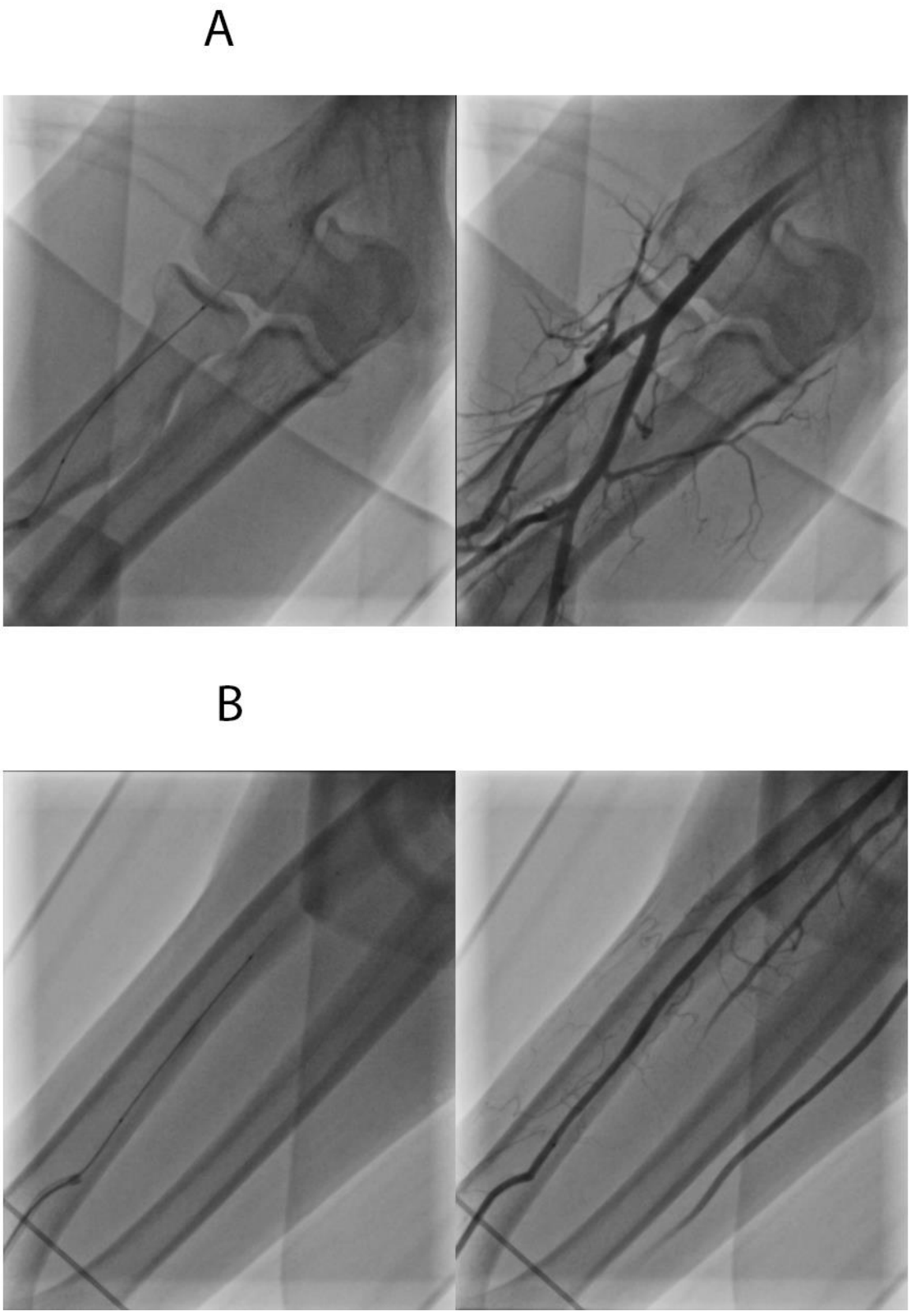
Statistical analysis

Baseline characteristics and endpoints were tabulated and compared between the two groups (SLTRA and CTRA). The Kolmogorov-Smirnov test was used to test the variables in our study population for normality. Continuous variables are presented as mean±standard deviation (SD) in case of a normal distribution and as median (interquartile range [IQR]) otherwise. Categorical variables are expressed as frequencies (percentages). Continuous baseline characteristics were compared between groups using an independent samples t-test for normally distributed variables and the Mann-Whitney test for random variables that were not normally distributed. Categorical variables were compared between groups using the chi-square test. All statistical tests were two-tailed, and a p-value of <0.05 was considered statistically significant. To test the interobserver agreement of the OCT data between the two physicians, the kappa value of these binary variables was determined.

No data about the absolute reduction of vascular damage measured by OCT were available. We expected an important reduction in vascular injury, based on the concept of less RAID/SOD mismatch and prevention of the “razor” effect measured by OCT. The only radial OCT data available show injury in 43% of the distal segments. So, to retain power in this proof-of-concept study, we hypothesised an absolute reduction of 25% in the incidence of vascular injury in patients undergoing an SLTRA procedure compared to a CTRA procedure, namely from 40% [3] to 15%. To test this hypothesis at a type 1 error probability of 5% and a type II error probability of 20%, a sample size of 50 patients would be needed. All statistical analyses were performed with SPSS for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).



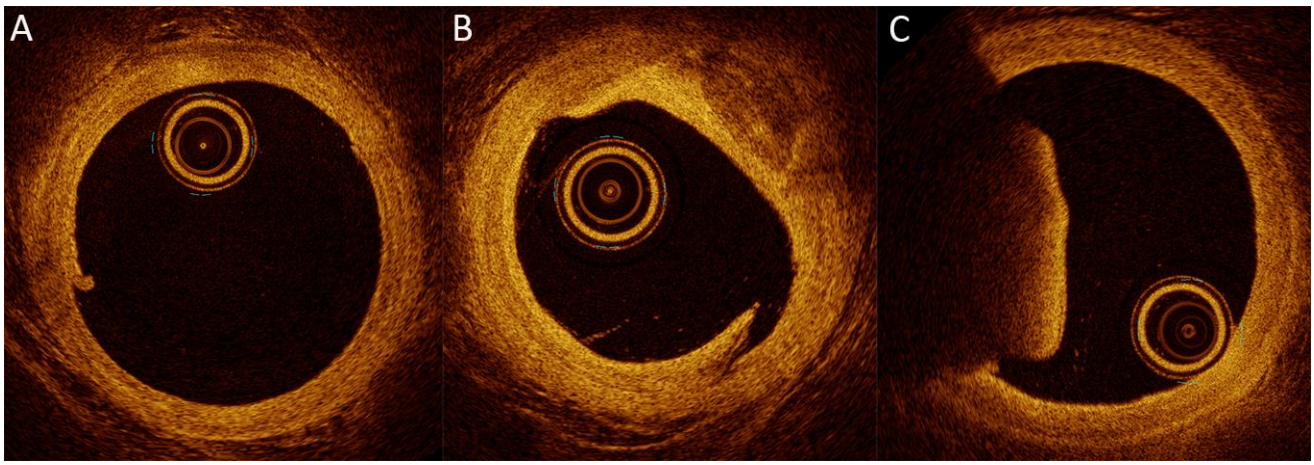
Supplementary Figure 1. Flow chart.



Supplementary Figure 2. Examples of OCT catheter positions during scanning of the radial artery.

A) Proximal run.

B) Distal run.



Supplementary Figure 3. Types of vascular injury.

A) Intimal tear (IT).

B) Medial dissection (MD).

C) Intraluminal thrombus (TR).

Supplementary Table 1. Baseline characteristics.

	CTRA (n=26)	SLTRA (n=25)	*p*-value
Age, years±SD	65±9	66±7	0.94
Gender, male	16 (62%)	12 (48%)	0.40
Diabetes	6 (23%)	4 (16%)	0.73
Hypertension	16 (62%)	12 (48%)	0.40
Hypercholesterolaemia	12 (46%)	2 (8%)	**<0.01**
Smoking	6 (23%)	5 (20%)	1.00
Family history	12 (46%)	7 (28%)	0.25
MI	2 (7.7%)	4 (16%)	0.42
CABG	0 (0%)	0 (0%)	-
PCI	3 (12%)	2 (8%)	1.00
PAD	3 (12%)	0 (0%)	0.24
Renal failure	0 (0%)	0 (0%)	-

CABG: coronary bypass grafting; MI: myocardial infarction; PAD: peripheral artery disease; PCI: percutaneous coronary intervention; SD: standard deviation

Supplementary Table 2. Procedural data.

	CTRA (n=26)	SLTRA (n=25)	*p*-value
TRA right RA	25 (96%)	23 (92%)	0.49
Type of procedure			
CAG only	18 (69%)	14 (56%)	0.39
CAG+PCI	5 (19%)	10 (40%)	0.13
CAG+FFR/imaging	3 (12%)	1 (4%)	0.61
Medication during procedure			
Radial artery cocktail	26 (100%)	25 (100%)	-
Heparin, IU (median, IQR)	5,000 (1,250)	5,000 (1,500)	0.78
GP IIb/IIIa blocker	0 (0%)	0 (0%)	-
Catheters used			
1	6 (23%)	7 (28%)	0.76
2	18 (69%)	18 (72%)	1.0
3	2 (8%)	0 (0%)	0.49
Type of catheter used			
Judkins left	24 (92%)	25 (100%)	0.49
Judkins right	19 (73%)	17 (68%)	0.76
Other	3 (12%)	1 (4%)	0.61
Number of catheter passages			
1	6 (23%)	7 (28%)	0.76
2	14 (54%)	18 (72%)	0.25
3	5 (19%)	0 (0%)	0.05
4	1 (4%)	0 (9%)	1.0
Total (median, IQR)	2 (0.5)	2 (1.0)	0.12
Arterial dimensions			
Radial artery internal diameter, mm (mean±SD)	2.57±0.43	2.70±0.43	0.30
RAID/DOD ratio <1	13 (57%)	0 (0%)	**<0.01**
Bleeding complications			
Access-site bleeding	1 (4%)	4 (16%)	0.19
Bleeding requiring longer hospitalisation	1 (4%)	1 (4%)	1.0
Bleeding requiring vascular surgery	0 (0%)	0 (0%)	-

CAG: coronary angiography; FFR: fractional flow reserve; IQR: interquartile range; IU: international units; PCI: percutaneous coronary intervention; RAID/DOD ratio: radial artery internal diameter/device outer diameter ratio

Supplementary Table 3. Other secondary endpoints.

	CTRA (n=26)	SLTRA (n=25)	*p*-value
Secondary (procedural progress)			
Procedural time, min (median, IQR)	19 (12)	23 (33)	0.15
Contrast use, ml (median, IQR)	55 (56)	70 (70)	0.41
Fluoroscopy time, min (median, IQR)	4.8 (3.9)	4.4 (11.0)	0.74
Crossover to other access site	1 (4%)	1 (4%)	1.00
Secondary (patient comfort)			
VAS procedural pain (median, IQR)	2 (5)	2 (4)	0.60
VAS pain score after procedure (median, IQR)	1 (1)	1 (1)	0.54
Pathological cold intolerance	4 (15%)	5 (20%)	0.73
QuickDASH MCID	1 (4%)	1 (4%)	1.0
Radial artery spasm	5 (19%)	1 (4%)	0.19
Radial artery occlusion	0 (0%)	1 (4%)	0.49

IQR: interquartile range; MCID: minimal clinically important difference; VAS: visual analogue scale