Conventional or Ultrasound guided puncture technique for the distal radial artery, direct comparison study
Sound Distal Trial.

Version 3.0 Oct 2025.

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Contents

Abbreviations 3
1. PROTOCOL SUMMARY 4
2. SCHEMATIC STUDY DESIGN 5
3. SYSTEMATIC PROTOCOL STUDY SYNOPSIS 6
4. BACKGROUND 7
5. STUDY OBJECTIVES 8
Primary outcome 8
Secondary outcomes 8
6. STUDY DESIGN 9
7. INFORMED CONSENT 12
8. SCREENING AND ENROLMENT 12
9. INCLUSION CRITERIA 12
10. EXCLUSION CRITERIA 12
11. RANDOMIZATION 13
12. STUDY SITE INVESTIGATORS 13
13. PROCEDURAL DETAILS 14
13.1 Pre-procedural assessments 14
13.2 Ultrasound echoardiography methodology 15
13.3 Coronary angiogram and Percutaneous coronary intervention 20
14. POST PROCEDURE FOLLOW-UP 21
15. MEDICATION RECOMMENDATION 21
16. TREATMENT FAILURES 21
17. ADVERSE EVENTS 21
Adverse events definition and classification 21
Expected adverse events 21
18. DATA COLLECTION 23
18.1 Data collection 23
18.2 Protocol deviations 23
18.3 Record retention by study site 23
18.4 Monitoring of data to source documents 23
19. STATISTICS AND ANALYSIS 23
19.1 Sample Size 23
19.2 Statistical analysis 23
20. REGULATORY REQUIREMENTS 24
20.1 Institutional Review Board and Ethics Committee: IRB/IEC 24
20.2 Insurance 24
20.3 Confidentiality 24
20.4 Publication Policy 24
20.5 Intellectual Property 24
20.6 Publication 24
21. FUNDING 24
22. SCHEDULE 25
23. REFERENCES 25

Abbreviations

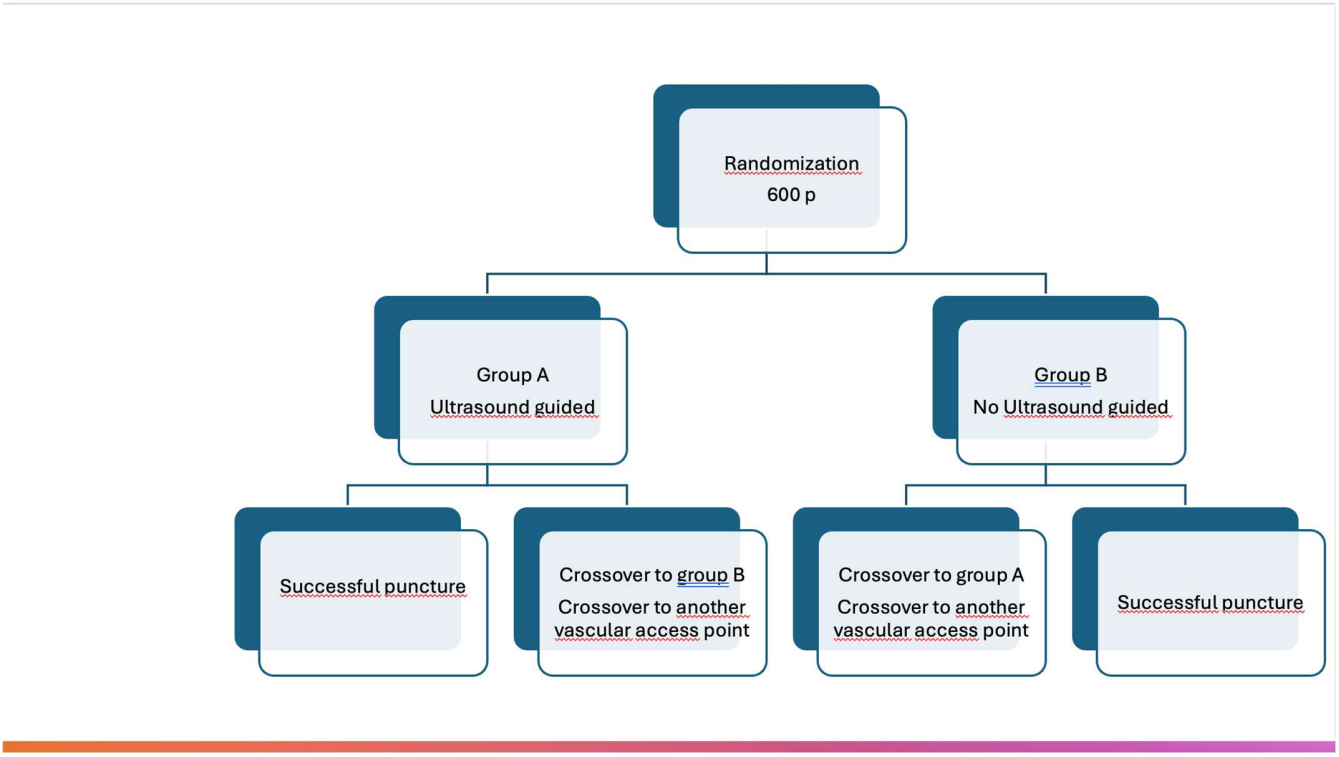
AE Adverse Event
dTRA Distal transradial Access
TRA Trans Radial Access
CAD Coronary Artery Disease
MACE Major Adverse Cardiovascular Events
US Ultrasound echography
RAO proximal radial occlusion
PCI Percutaneous coronary intervention
DRA distal radial access
AS anatomical snuffbox
CV cephalic vein
SBRN superficial branches of the radial nerve
SAX Short-axis
LAX long-axis
OOP out-of-plane
IP in-plane
DNTP Dynamic Needle Tip Positioning
MI Myocardial infarction
TVR Target Vessel Revascularisation
CABG Coronary artery bypass graft surgery

1. PROTOCOL SUMMARY

Over the last few years, a new approach using distal radial access had been employed for a various types of percutaneous interventions. The purpose was to further decrease the rate of vascular complications and proximal radial occlusion (RAO).
The feasibility of distal radial access in several specific groups of patients for conventional, complex coronary and non-coronary procedures was extensively studied and showed a variable rate of success between different operators, using different techniques.
The main limitation is the rate of failure in cannulation that is related to the smaller diameter of the distal radial artery and the anatomic variability at the level of access site puncture. One of the solutions advocated by Hadjivassiliou et al. is the use of ultrasound-guided distal transradial acces (dTR)A, which is expected to reduce failure and complication rates.
A recent monocentric, single operator pilot study indicated a lower failure rate with ultrasound than conventional dTRA, without significant differences in puncture time and complication rate between the two approaches.
A specific ultrasound algorithm for distal radial puncture was recently developed and is currently used in our clinical daily practice, showing a 100% rate of success, in a selected group of patients that had favorable anatomic features. Imaging the distal radial artery by ultrasound could potentially be safer, select the proper candidates for this technique and increase the rate of successful cannulation.
However, to date, the comparison of feasibility and safety between ultrasound-guided and conventional dTRA has not been reported.
The SOUND Distal trial is a pilot study measuring the reproducibility, rate of success, rate of complications and quality puncture measures.

The primary outcome is comparing the rate of success of dTRA cannulation between conventional and echo guided puncture. Secondary outcomes include quality puncture measures differences between the two approaches regarding patient scale pain/puncture time and number of attempts.
Other secondary end points include technic reproducibility among operators and the total rate of complications for both approaches.

2. SCHEMATIC STUDY DESIGN



3. SYSTEMATIC PROTOCOL STUDY SYNOPSIS

Title: Conventional or Ultrasound guided puncture technique for the distal radial artery: direct comparison study.

Short title **Sound Distal Trial.**

Design : A multi-center, prospective, randomized pilot study comparing the feasibility and safety between a specific ultrasound-guided and conventional dTRA puncture
Objectives Improving the vascular site access of the distal radial artery for percutaneous procedures by the use of ultrasound guided puncture

Primary endpoint: rate of success of dTRA cannulation

Secondary endpoints:
technical reproducibility, rate of complications and puncture quality measures: patient pain scale/puncture time /number of attempts
Other secondary end points include technic reproducibility among operators for both approaches and the total rate of complications.
Treatment -The rate of successful PCI/ The rate of vascular access site conversion/ The rate of non vascular complications
Follow-up -During hospitalization and Clinical follow up at 30 days and 12 months

Inclusion criteria
Patient older than 18 years requiring diagnostic angiography or PCI.
The subject has stable or acute coronary syndrome, or a positive functional study documenting ischemia.
The subject is eligible for PCI.
The subject is male, or a non-pregnant female.
The subject gives consent prior to study inclusion.

Exclusion criteria Pregnant and/or breast-feeding females.
Patients who intend to have a major surgical intervention within 6 months of enrolment in the study at the level of the vascular site access.
Patients who previously participated in this study.
The subject has suffered a stroke or transient ischemic neurological attack or cerebrovascular accident within the past six months, or has any known intracranial mass, arteriovenous malformation, aneurysm or other intracranial pathology.

Number of patients 600
Study duration 9 Months
After 6 Month - consultation check

4. BACKGROUND

Recently, distal radial access (DRA), a novel transradial access site, has gained worldwide recognition as an effective alternative route for interventional vascular procedures. DRA has shown great efficiency in various coronary procedures, leading to its increasing adoption as an alternative to the traditional trans-radial approach (TRA). This shift began in 2017 when Kiemeneij published his initial experience with anatomical snuffbox access.

Anesthesiologists were the pioneers in using DRA as an alternative site for perioperative blood pressure monitoring in cardiac pediatric and adult patients. Amato et al. (1977) and Pyles et al. (1982) reported the use of DRA when conventional vascular sites failed to provide successful puncture.

DRA offers several advantages. It protects the proximal radial artery from occlusion by preserving antegrade flow to the arm through the superficial palmar arch branch. Additionally, DRA avoids direct mechanical injury to the proximal radial artery during puncture and cannulation. Compared to the traditional radial approach at the wrist, distal radial access provides improved comfort for both patients and operators during catheterization. It also facilitates faster hemostasis, reducing nursing staff time. Moreover, DRA enables the possibility of reopening a chronic total occlusion of the proximal radial artery through a retrograde approach.

While DRA appears to be the safest vascular access for interventional procedures, it presents challenges in terms of puncturing and cannulating a smaller, more angulated, and difficult-to-palpate artery. To address this, ultrasound (US) guidance for DRA has been introduced and extensively discussed in various publications. US offers multiple advantages, such as evaluating arterial characteristics (size and tortuosity), determining the feasibility of DRA, estimating the risk of vascular injury, and assessing pain related to equipment-artery diameter mismatch.

By using US guidance, a better selection of suitable candidates for DRA can be made, while also allowing direct visualization of the target vessel. This approach reduces the rate of failures associated with blind puncture, enabling physicians to adopt DRA more widely. In our practice, we follow a specific US DRA guidance protocol, which is fully described in the methodology section of this study. The protocol includes a comprehensive evaluation of the anatomical features of the distal radial artery, selection of the optimal puncture site, and the short-axis out-of-plane technique.

These aspects not only enable a clean and less painful puncture but also prevent hematoma formation that can occur with blind puncture, particularly when the cannulation of the distal radial artery is too deep, lacking the advantages of a strong bone floor and easy and fast compression. Furthermore, the conventional palpation technique may inadvertently cause trauma to the extensor tendons of the pollicis or result in accidental puncture of the cephalic vein or superficial branches of the radial nerve.

Despite the potential advantages of US-guided DRA, they have not yet been fully incorporated into current practice. Puncture and cannulation are still primarily performed using pulse palpation. The aim of this study is to investigate the rationale for vascular ultrasound during distal radial access and compare the specific US-guided protocol with the standard palpation technique. Our hypothesis is that US-guided DRA will increase the success rate of the first attempt and result in faster procedures with fewer redirects, attempts, and bleeding complications.

5. STUDY OBJECTIVES

Since published rates of successful ultrasound guided cannulation of dTRA are limited and in absence of objective imaging measures to properly select candidates for this particular vascular access, this study is designed as a pilot study in order to assess the potential benefits of ultrasound imaging compared to conventional puncture for obtaining dTRA.
The null hypothesis is that there is no difference in the success rate of obtaining dTRA between a US or non-US guided approach.

The primary endpoints of the study will be the first-wiring pass success rate.

Secondary endpoints

1) The total number of attempts needed for the first-wiring pass success rate. Attempts will be defined as puncture of the artery, confirmed by the back-bleeding through the needle hub but withdrawal of the needle, after failing the wiring.
2) The time to access will be measured from the point of the first application of the operator's fingers or US probe to guide access to a successful first-wiring pass success rate. For the blind puncture group: the first application of the operator's fingers on the artery to palpate it.
3) the incidence of spasm (Spasm was defined and identified by the operator as any significant resistance or patient pain with catheter manipulation)
4) Puncture site bleeding according to EASY criteria
5) Overall bleeding according to BARC criteria
6) Successful sheath insertion
7) Crossover to US guidance
8) Access site cross-over
9) Vascular access-site complication
10) Distal radial artery occlusion (at discharge , clinical examination and pulse presence)
11) Hemostasis time
12) Pain associated with the procedure

6. STUDY DESIGN

In this multicentre, prospective, randomized, controlled open-label pilot study we will include all consecutive patients that are scheduled for an invasive coronary angiogram or PCI fulfilling in- and exclusion criteria. A first ultrasound examination will be performed in all patients, followed by 1:1 randomization to a conventional Seldinger based puncture technique for obtaining a dTRA or a second group where the puncture will be guided by ultrasound (US) using a pre-defined protocol.

Protocols for blind distal radial puncture

For each procedure, we will start by carefully positioning the hand before getting proximal radial artery. Specifically, we settle the hand palm in a supine position to achieve hyperextension of the wrist. Then, a standard single anterior vessel wall puncture technique will be performed without ultrasound guidance. We perform the puncture in the portion of the distal radial artery at the anatomical snuffbox (Figure 1A), in the dorsal side of the wrist (fovea radialis), limited posteriorly by the edge of the extensor pollicis longus tendon, and anteriorly by the extensor pollicis brevis and abductor pollicis longus tendons. Local anesthesia will be performed using a mix of 3 mg of mepivacaine hydrochloride and 1 mg of isosorbide dinitrate injected subcutaneously. The access site puncture will be performed using a 21-gauge bare needle from lateral to medial with an angle of around 35°. After achieving radial artery access, a 5 Fr sheath (Radifocus, Terumo, Japan) will be inserted for the diagnostic angiogram or a 6 Fr sheath for coronary angioplasty. All the patients will receive a low dose of midazolam, with additional IV morphine in case of discomfort. An intra-arterial spasmolytic cocktail with 2 mg of verapamil and 100 µg of nitroglycerin will be administered routinely following sheath insertion. A second cocktail with verapamil and nitroglycerine will be administered in case of pain during advancement of the catheters. All patients will receive unfractionated heparin at doses of 50 U/kg for diagnostic catheterization and 100 U/kg for coronary angioplasty. A conventional 0.035˝ J tip Emerald Wire (Cordis, Johnson and Johnson, USA) will be positioned in the ascending aorta. In case of difficulties in moving the guide catheter forward, the operator will have different alternatives: downsizing the guide catheter, increasing patient sedation, further antispasmolytic mix, or using the railway technique or a ballon-tracking technique. The selection and use of one or more of the mentioned strategies depended on operator choice. At the end of the procedure, we will use dedicated devices for achieving artery hemostasis through artery external compression for two hours: the TR Band (Terumo, Japan) for proximal radial artery and the Prelude SYNC (Merit, USA) for distal radial access site.

Protocols for ultrasound (US) echography guided distal radial puncture

The region around the anatomical snuffbox will be prepped and covered as standard with a sterile drape.
The position of the arm: in a pronated position and the patient will be asked to bring the thumb to touch the base of the little finger (Figure bring the thumb to touch the base of the little finger) which makes us puncture easily under ultrasound guidance. In the case of left radial access, the arm is naturally placed over the patient's abdomen, and the hand is positioned over the right groin.

A detailed US analysis of the surrounding structure will be performed, and the proper puncture site of the DRA will be chosen accordingly to

- The distance between the skin and the artery (the most superficial trajectory possible)
- The floor of the anatomical snuffbox (AS) . (The DRA need to be closed to a bone structure, too secure the compression and the anastomosis
- The surrounding structure: to avoid puncturing the cephalic vein (CV), superficial branch of radial nerve, or the extensors tendons
- The tortuosity of the artery: see the curvilinear trajectory of the DRA in long axis

The local anesthesia around the puncture site will NOT BE administered before the puncture, in order to avoid the spasm of the DRA or the decrease in identifying the structures on the US image and knowing also that the anesthetic can push/compress the artery.
The DRA will be punctured by the conventional method, the Seldinger technique, with a 20-gauge (G) puncture needle under the short axis view. The hand of the operator held the ultrasound transducer, which will be placed first inside a sterile sheath, while the dominant handheld the 20G needle. A stable US image with the DRA clearly identify in the SOX view in the middle of the screen is needed. The needle will puncture 2 cm far from the middle of the probe at an angle of 30–45° to the skin and will be advanced under ultrasound guidance until its entry into the distal radial artery. The tip of the needle will be difficult to visualize in some cases, therefore the movements of the surrounding tissue by « shaking the needle » could be helpful. The tenting of the anterior wall of the DRA is the last US detail that needs to be detected before the needle puncture the artery. Other solutions could be to tilt the probe on either its long (heel-toe movement) or short axis (toggle movement) to locate the needle tip. A tactile feeling of release will be perceived by the operator and the appearance of the back-flow bleeding through the needle hub will be perceived. Sometimes we don't see the tip of the needle at the superior mid part of the DRA, with a tenting of the artery also, and the puncture still not correct when we advanced. The explanations could be related to the fact that we are not seeing exactly the puncture site and therefore after changing the angulation of the needle we can adjust the position, avoiding touching other structures or the periost that trigger an acute pain.
The needle can be inclined more than 45 degrees. In some cases the guidewire may encounter resistance due to tortuosity; leaving the needle free rather than fixing it with the hand may help overcome the acute angles, or even coronary guidewires may be used.

After a successful puncture, a 0.021-inch plastic-type mini guidewire attached to the Terumo sheath (Terumo, Tokyo, Japan) will be inserted. A 4, 5, or 6 Fr sheath will be inserted over the guidewire after the subcutaneous injection of 1–3 mL lidocaine 2% had been administrated.
An intraarterial isosorbide dinitrate 2cc and heparin (3000 units for CAG and 5000 units for PCI) will be injected through the introducer sheets.
Following the procedure, hemostasis will be achieved with the TR Band (Terumo) or the Prelude System (Merit) or manual compression. Patent hemostasis and removal of any bands following the procedure will be according to local practice. Between 1 and 4 h following the procedure, patient pain levels at the point of radial access will be measured using a 0 to 10 visual analog scale. Screening for radial artery occlusion or vascular complications occurred per local practice, including at a minimum a pulse check.

Coronary angiogram and Percutaneous coronary intervention

Coronary angiogram and PCI will be carried out according to standard practice and will be left to the discretion of the operator.

7. INFORMED CONSENT

Informed consent should be obtained in accordance to the applicable regulations, the declaration of Helsinki and Good Clinical Practice. Patients eligible for the study will be informed according to the informed consent best practices. A copy of the Informed Consent is attached in appendix A. The patient information as well as the patient informed consent will have the approval of the institution's Review Board and/or Ethics Committee (IRB/IEC) prior to their usage.

8. SCREENING AND ENROLMENT

Screen for study eligibility : One of the investigators of the Sound Distal study will review the patient's medical and cardiac history and plan the invasive coronary procedure through dTRA. Only if all inclusion criteria are met/exclusion criteria are not met, the patient can be enrolled into the study. Randomization will be done by Interactive Voice Response System (IVRS) before starting the procedure.

9. INCLUSION CRITERIA

- Patient older than 18 years.
- The subject has stable (Anginal status according to CCS), unstable angina (Braunwald classification), acute coronary syndrome, or a positive functional study for ischemia.
- The subject is eligible for PCI.
- The subject is male, or if female, has no childbearing potential or has had a negative urine or serum pregnancy test within 7 days of the index procedure and has no intention to become pregnant within a year of the procedure.
- The subject provides consent prior to study inclusion.

10. EXCLUSION CRITERIA

- Pregnant and/or breast-feeding females or females who intend to become pregnant.
- Patients who intend to have a major surgical intervention within 6 months of enrolment in the study at the level of the vascular site access.
- Patients who previously participated in this study.
- The subject has suffered a stroke or transient ischemic neurological attack or cerebrovascular accident within the past six months, or has any known intracranial mass, arteriovenous malformation, aneurysm or other intracranial pathology.

11. RANDOMIZATION

The randomization system is a computerized on-line system working with end-to-end encryption and no access to the randomization engine. The responsible data manager overseeing the system is independent of the study organization. Investigators have no direct access to the data manager or any aspects of the randomization process. All transactions in the system are logged. There is no back-up “envelope based” randomization system. The randomization will be done after obtaining consent and before performing the distal radial puncture. Time zero is defined as the time of treatment allocation.

12. STUDY SITE INVESTIGATORS

Primary investigator site is UZA and the co-primary investigator study is CHU Helora - Hôpital de La Louvière- site Jolimont which is considered to be an appropriate clinical facility. The hospital carries out over 1100 PCI cases per year including a large volume of complex cases..

Other center : Clinique Saint Joseph Arlon, Belgium

13. PROCEDURAL DETAILS

13.1 Pre-procedural assessments :

13.1.1 Patient Characteristics

Age, years
Men
Height
Weight
Body mass index, kg/m2
Hypertension
Dyslipidemia
Diabetic mellitus
Current or former smoker
Chronic kidney disease*
- Hemodialysis

Atrial fibrillation
LV ejection fraction, %
Prior myocardial infarction
Prior PCI
Prior coronary bypass grafting
Clinical presentation
- Stable ischemic heart disease
- Unstable angina
- NSTEMI

*Values are in (%) or median (Q1, Q3). *Estimated creatinine clearance <60 mL/min using the Cockcroft-Gault formula. NSTEMI: non ST segment elevation myocardial infarction; PCI = percutaneous coronary intervention.*

13.1.2 Angiographic and Procedural Characteristics

Target vessel
- Left main
- Left anterior descending
- Left circumflex
- Right
- Multivessel disease

Lesion location
- Proximal
- Mid
- Distal

Reference vessel diameter, mm

Lesion length, mm
Minimum lumen diameter, mm
Diameter stenosis, %
Ostial location
Bifurcation
Moderate/severe tortuosity
Chronic total occlusion
Vascular access site
Distal radial
7Fr
6Fr
Proximal radial
7Fr
6Fr
Femoral
7Fr
8Fr
6Fr
Vascular access site crossover
Describe the reason and your choice
Vascular particularities

- Small radial artery (RA diameter less than 1.5 mm)
- Significant RA tortuosity
- Significant Brachial tortuosity
- Subclavian tortuosity
- Severe and resistant RA spasm
- Complex RA loops
- Subclavian stenosis

13.2 Ultrasound echoardiography methodology

The anatomy of the forearm region is complex, with several muscles and an extensive network of vessels and nerves. To guarantee the success of the evaluation by HRUS, knowledge of the normal anatomy of the region is essential.

The anatomical snuffbox (AS) is a small triangular area situated in the radial part of the wrist, laterally limited by the tendons of abductor pollicis longus and extensor pollicis brevis muscles, and medially limited by the tendon of extensor pollicis longus muscle.

The base formed by the distal margin of the retinaculum of extensor muscles and a vertex conformed by the attachment of the tendons of extensor pollicis longus and extensor pollicis brevis muscles.

The roof is formed by the skin and superficial fascia, in where we can fine the cephalic vein (CV) and superficial branch of the radial nerve (N). The terminal branches of the radial nerve has 3 terminals; one lateral branch, one intermediate and one media.

The ground is conformed by the distal radius, scaphoid, trapezium and the base of the first metacarpal bone.

Dimensions / Position / Anatomical variability

The average height of the AS was 6 cm and the average width at its base was 1.5 cm.The CV and had two branches that crossed the AS. The CV and RA almost invariably coursed through the AS and were found less than 5 mm one from one to another. The CV was found more frequently in the medial part of the AS. The base of this triangular area ranged in length from 1–22 cm (mean . 1.5 cm). The length of the TA ranged from 6–9 cm (mean . 6 cm).

AR in the AS *penetrates going deep* to the tendons of the abductor pollicis longus and extensor pollicis brevis muscles. *AR is at the bottom of this structure, onto the trapezium bone.*

AR was closely related (<2 mm) with the SBRN (superficial branches of the radial nerve), near the styloid process of radius in 48% of samples. The tendon of extensor carpi radialis brevis can also be found in the AS, depending on how distal the retinaculum of extensor muscles is, and how medial the dorsal tubercle of the radius is found.

The structures that we need to recognize when we performed US guidance

1= tendon of abductor pollicis longus muscle; 2= tendon of extensor pollicis brevis muscle; 3= tendon of extensor pollicis longus muscle; 4= cephalic vein; 5= terminal branches of the superficial branch of radial nerve; 6= radial artery; 7= superficial branch of radial nerve; 8= retinaculum of extensor muscles; 9= tendon of extensor carpi radialis longus muscle; 10= tendon of extensor carpi radialis brevis muscle. 10= styloid process of the radius

US appearance of the structures

The vessel presents a hyperechoic anterior and posterior wall on two-dimensional ultrasound imaging in the long-axis view as well as a long, black, anechoic train-track structure (figure 5) in the middle and an anechoic oval structure in the short-axis view.
The superficial branch of the radial nerve is located near the *extensor pollicis longus, which presents with small striated structures* with hypoechoic and hyperechoic lines alternating on the long-axis view and honeycomb-like structures with a mixture of hypoechoic and hyperechoic lines and annular hyperechoic wrapping on the short-axis view. (EPB APL)
The bone cortical surface shows a *strong echogenic signal with a posterior acoustic shadow:*

The superficial branches of the radial nerve (N) : hypoechoic fascicles and surrounding echo-genic epineurium
(The superficial radial nerve (SRN) is a terminal sensory branch of the radial nerve that passes along the front of the radial side of the forearm and runs beneath the tendon of the brachioradialis, piercing the deep fascia. It innervates the skin of two thirds of the dorsoradial region of the hand, including the proximal part of the dorsum of the thumb and the proximal portion of one-and-a-half or two-and-a-half adjacent fingers. Obtaining detailed knowledge on the anatomic pathway of SRN could help in approaching the radial region of the forearm and hand during treatment for De Quervain disease, nerve conduction study of the SRN, and localization of regional nerve blockades. Nerve injury may lead to neuroma formation and possible wrist and hand pain that may be difficult to treat. Thus, an understanding of the anatomic location of the SRN and CV is important for the prevention of nerve injury. However, its close proximity to the SRN increases the risk of nerve injury during CV cannulation or puncture
The retinaculum of extensor muscles: hypoechoic compared with adjacent extensor digitorum tendons (ED).
At the dorsum of the wrist, the extensor retinaculum is a fibrous band that holds the extensor tendons in place and prevents bow-stringing.

The US appearance for each of the structure:

1= tendon of abductor pollicis longus muscle;
2= tendon of extensor pollicis brevis muscle;
3= tendon of extensor pollicis longus muscle;
4= cephalic vein;
5= terminal branches of the superficial branch of radial nerve;
6= radial artery;
7= superficial branch of radial nerve;
8= retinaculum of extensor muscles;
9= tendon of extensor carpi radialis longus muscle;
10= tendon of extensor carpi radialis brevis muscle.
11= styloid process of the radius
12= first metacarpal bone
13= second metacarpal bones

DEFINITION and Methodology of US uses

How to use US probe : used to secure the ultrasound probe, with the little finger touching the patient's forearm as a support point

The short-axis (SAX) view of the vessel: the plane of the ultrasound beam intersects the target vessel in a cross-section

The long-axis (LAX) view of the vessel: the plane of the ultrasound beam intersects the vessel longitudinally. Why: for the visualization of the tortuosity of the artery / to increase the chance of easy wiring

out-of-plane, OOP : The needle tip can approach the target vessel perpendicular to the plane of the ultrasound beam

in-plane, IP : The needle tip can approach the target vessel inside the plane of the ultrasound beam.

Of the four possible needle-tip approaches to the target vessel only two are considered effective: LAX-IP and SAX-OOP. Dynamic Needle Tip Positioning (DNTP) is a new, dynamic and very useful variant of SAX-OOP vessel is approached with SAX-OOP technique just until the needle tip is displayed as a hyperechoic dot on the monitor between the skin and the vessel
While keeping the needle immobile, the probe is parallel shifted away from the operator just until the cross-sectional image of the needle tip disappears. While keeping the probe immobile, the needle is advanced until the cross-sectional image of the needle tip reappears on the monitor. The procedure is repeated until the needle tip is inserted profoundly intravascularly.
The position of the needle tip in the center of the vessel can be controlled with needle hub steering. With this technique, the operator keeps real-time track of the position of the needle tip at all times with a high degree of accuracy

The SAX-OOP seems to be the more convenient for our study and will be prose as the default strategy.

The study will use GE US machines with a high-frequency linear (flat) transducer capable of imaging and displaying at a depth of 2 mm with a screen of at least 12.1 diagonal inches. Sterile probe covers and transducer gel will be used for all US-guided DRA procedures.

Operator Training
This study will include operators experienced in distal trans-radial catheterization to minimize potential confounders. Participation in the study required a minimum of 50 previous distal radial artery catheterization procedures, with at least 25 US-guided procedures.

US use
The visualization of the vessels can be improved by adjusting the depth on the ultrasound machine to the minimum depth and adjusting the gain. The examiner's hand should rest partially on the patient, and only light pressure should be applied to the soft tissues. The vigorous pressing of the transducer leads to the compression of the artery. The artery is visualized as an anechoic or dark circle that can be distinguished from veins based on the pulsation of the vessel. Manual compression, pulsed wave Doppler, and color flow Doppler are
additional tools that ease the detection of the artery.

Protocol of US DRA puncture and cannulation

The region around the anatomical snuffbox will be prepped and covered as standard with a sterile drape.
The position of the arm: in a pronated position and the patient will be asked to bring the thumb to touch the base of the little finger which makes us puncture easily under ultrasound guidance. In the case of left radial access, the arm is naturally placed over the patient's abdomen, and the hand is positioned over the right groin
A detailed US analysis of the surrounding structure will be performed, and the proper puncture site of the DRA will be chosen accordingly to

- The distance between the skin and the artery (the most superficial trajectory possible)
- The floor of the AS (The DRA need to be closed to a bone structure, too secure the compression and the anastomosis
- The surrounding structure: to avoid puncturing the CV, N, or Extensors tendons
- The tortuosity of the artery: see the curvilinear trajectory of the DRA in long axis

The local anesthesia around the puncture site will NOT BE administered before the puncture, in order to avoid the spasm of the DRA or the decrease in identifying the structures on the US image and knowing also that the anesthetic can push/compress the artery.
The DRA will be punctured by the conventional method, the Seldinger technique, with a 20-gauge (G) puncture needle under the short axis view. The hand of the operator held the ultrasound transducer, which will be placed first inside a sterile sheath, while the dominant handheld the 20G needle. A stable US image with the DRA clearly identify in the SOX view in the middle of the screen is needed. The needle will puncture 2 cm far from the middle of the probe at an angle of 30–45° to the skin and will be advanced under ultrasound guidance until its entry into the distal radial artery. The tip of the needle will be difficult to visualize in some cases, therefore the movements of the surrounding tissue by « shaking the needle » could be helpful. The tenting of the anterior wall of the DRA is the last US detail that needs to be detected before the needle puncture the artery. Other solutions could be to tilt the probe on either its long (heel-toe movement) or short axis (toggle movement) to locate the needle tip. A tactile feeling of release will be perceived by the operator and the appearance of the back-flow bleeding through the needle hub will be perceived. Sometimes we don't see the tip of the needle at the superior mid part of the DRA, with a tenting of the artery also, and the puncture still not correct when we advanced. The explanations could be related to the fact that we are not seeing exactly the puncture site and therefore after changing the angulation of the needle we can adjust the position, avoiding touching other structures or the periost that trigger an acute pain.
The needle can be inclined more than 45 degrees. In some cases, the guidewire may encounter resistance due to tortuosity; leaving the needle free rather than fixing it with the hand may help overcome the acute angles, or even coronary guidewires may be used.

After a successful puncture, a 0.021-inch plastic-type mini guidewire attached to the Terumo sheath (Terumo, Tokyo, Japan) will be inserted. A 4, 5, or 6 Fr sheath will be inserted over the guidewire after the subcutaneous injection of 1–3 mL lidocaine 2% had been administrated.
A intraarterial isosorbide dinitrate 2cc and heparin (3000 units for CAG and 5000 units for PCI) will be injected through the introducer sheets.
Following the procedure, hemostasis will be achieved with the TR Band (Terumo) or the Prelude System (Merit) or manual compression. Patent hemostasis and removal of any bands following the procedure will be according to local practice. Between 1 and 4 h following the procedure, patient pain levels at the point of radial access will be measured using a 0 to 10 visual analog scale. Screening for radial artery occlusion or vascular complications occurred per local practice, including at a minimum a pulse check.

13.3 Coronary angiogram and Percutaneous coronary intervention

Coronary angiogram and PCI will be carried out according to standard practice and will be left to the discretion of the operator.

13.3.1 Procedural and In-Hospital Outcome

Procedural duration, min
Fluoroscopy time, min
Contrast amount, mL
Large dissection, >5 mm
Perforation
- Conservatory treatment
- Balloon inflation only
- Covered stent implantation

Pericardial effusion
No/slow flow
Final TIMI flow <III
Residual stenosis >20%
Compromised side branch
Stent failure
Death
- Cardiac death
- Noncardiac death

MI
- Target vessel MI
- Periprocedural MI
- Spontaneous MI

Target vessel re-PCI
- Clinically indicated TVR

CABG
Stent thrombosis
Access site complications

14. POST PROCEDURE FOLLOW-UP

In-hospital follow-up includes:

- A physical examination: 1 and 6 hours after procedure. All adverse events as (no radial pulse,, signs of ischemia of the hand, persistent compression/bleeding, any hematoma, any swelling) will be reported.

- A 12-lead ECG which will be completed within 24 hours post-procedure or prior to hospital discharge (whichever comes first).

- Anginal status according to CCS or Braunwald classification, adverse events, vascular complications: Puncture site bleeding according to EASY criteria ( ) Overall bleeding according to BARC criteria ( ) Vascular access-site complication. Distal radial artery occlusion. Concomitant medications, and any interventional treatment that occurred since the procedure should be recorded before discharge.

15. MEDICATION RECOMMENDATION

At least dual antiplatelet therapy (aspirin + clopidogrel or prasugrel or ticagrelor) will be prescribed according to current guidelines in case PCI was performed.1

16. TREATMENT FAILURES

Technical success of dTRA and procedural success of coronary angiography and/or PCI will be recorded (see definitions below).

17. ADVERSE EVENTS

During the course of this study adverse events might occur. These adverse events will be determined by the investigator. All serious adverse events must be reported within 24 hrs from acknowledgement. Other adverse events should only be reported whenever they affect one or more of the pre-defined endpoints of the study. These include all vascular complications . These adverse events must be reported on the respective Adverse Event (AE) Form.

Adverse events definition and classification
An AE is any untoward medical occurrence in a patient whether or not related to the investigated treatment. Any current condition that is recorded as a pre-existing condition either in the medical history of physical examination section, unless there is a change in nature, severity, or degree of incidence, is not an AE.

Serious Adverse Event
In case any of the following criteria is applicable to the Adverse Event it classifies as SAE. These include:

- results in death;
- is life threatening;
- requires patient hospitalization or prolongation of current hospitalization;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect.

This also applies to AEs that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed above.

The assessment of “seriousness” is independent from any relation to the investigational device.

Hospitalization is defined by a medical need for admitting the patient to the hospital. For procedures that are commonly performed ambulant and require inpatient hospitalization solely based on nonmedical needs (e.g. logistical reasons) this criterion could be considered not applicable by the investigator. Proper documentation of the reasons for decision is required in this case. Events that are planned (e.g. elective surgery) and documented prior to study entry will not be recorded as (serious) adverse events. Medication received during hospitalization will be recorded.

Expected adverse events

As with any invasive coronary imaging or intervention, there are possible risks and complications: Death, myocardial infarction, emergent repeat hospital intervention, bailout stenting, emergency CABG, aneurysm or pseudo aneurysm formation, distal embolization, air embolization, vessel spasm, fistulisation, haemorrhage, infection, restenosis of the vessel (greater than 50% obstruction), rupture of the vessel, stent migration/embolization, thrombosis (acute, subacute or late), failure to deliver the stent(s) to the intended site, occlusion, dissection, arrhythmias, prolonged angina, cardiac tamponade, perforation, hypotension, haematoma, allergic reaction, fever, stroke, renal failure, balloon rupture, dissection of non-treated site, retained pieces of dilatation catheter, stent compression, angina pectoris, bleeding complications, endocarditis, hemodynamic changes to flow, injury of the coronary artery, ischemia, palpitations, pulse arrhythmia, pyrogenic reaction, sepsis/infection, unstable angina, ventricular fibrillation.

WITHDRAWAL FROM STUDY/STUDY DISCONTINUATION

A patient’s participation in the trial is voluntary and the patient may refuse to participate or withdraw from the trial at any time, without penalty or loss of benefits to which the patient is otherwise entitled.

Drop outs are defined as patients who decided not to continue the study/not to perform the follow-up visits for whatever reason;

When a participant decides to withdraw from the study, follow-up by phone call will be continued, unless the patient does not provide consent to follow-up. However, all data collected prior to discontinuation from the study will be retained in the database unless the patient refuse it.

18. DATA COLLECTION

18.1 Data collection
The investigator or an individual designated by the investigator is responsible for recording all data from the study in patient's medical history and Case Report Form (CRF).

18.2 Protocol deviations
A protocol deviation is defined as an event where the clinical investigator or site personnel did not conduct the study according to the clinical investigation plan.

18.3 Record retention by study site
All study records and reports will remain in file at the study sites for a minimum of 25 years after completion of the study and will further be retained in accordance with local applicable law and guidelines.

18.4 Monitoring of data to source documents
A clinical research file (CRF) will be completed at the study site for each subject enrolled in the study. The CRFs will contain a record of the subject's eligibility to enter the study, medical history, pre procedure work up and clinical laboratory results, concurrent medications, plus a record of all devices used during the procedure, all procedural complications and adverse events, discharge, follow up, and any non-scheduled visit involving a late adverse event requiring hospitalization or additional procedures. The CRFs will be monitored at the site to verify source data accuracy and provide quality assurance.

19. STATISTICS AND ANALYSIS

19.1 Sample Size
Sample size calculation
Considering 7,4 to 10% of dTRA failure using blind puncture and 2% of dTRA failure using echo guided, 274 patients are needed per arm.
Therefore, in consideration of these statistical assumptions and practical constraints, this study will be conducted in a pilot design, enrolling 600 subjects (300 per arm) at 3 investigational centers. This provides the opportunity to reject the null hypothesis should the treatment effect be sufficiently large and provides strong estimates of key parameters of interest.

19.2 Statistical analysis
All quantitative variables will be tested for normal distribution according to the Kolmogorov-Smirnov test. Continuous variables will be expressed as mean ± SD and comparisons between both groups will be done with t test. Categorical variables will be expressed as n in % and the chi-square test will be applied. Statistical analyses will be performed applying a significance level of ≤0.05. Descriptive statistics (mean/median, standard deviation and percentiles for continuous data; percentage for categorical data) and graphical representation (boxplots, histograms and density plots) will be used to compare both groups' characteristics.

20. REGULATORY REQUIREMENTS

20.1 Institutional Review Board and Ethics Committee: IRB/IEC

The clinical investigation plan as well as other study documents required by the ethics committee will be submitted for getting approval from the IRB/IEC.

20.2 Insurance

In accordance with the Belgian Law relating to experiments on human persons dated May 7, 2004, Sponsor shall assume, even without fault, the responsibility of any damages incurred by a Study subject and linked directly or indirectly to the participation to the study and shall provide compensation therefore through its insurance.

20.3 Confidentiality

Patient confidentiality will be maintained throughout the study. It will be ensured that the information can always be tracked back to the source data, if required. Data relating to the study might be made available to regulatory authorities preconditioned the data are treated confidentially and that the patient's privacy is guaranteed.

20.4 Publication Policy

The study results will be disseminated, valorized and published via abstracts and publications in high-index, peer-reviewed journals. Also, the results will be presented at several international (EuroPCR, TCT, etc.) and national (Belgian Society of Cardiology (BSC), Belgian Working Group of Interventional Cardiology (BWGIC) congresses and symposia.

20.5 Intellectual Property

Any Intellectual Property conceived or reduced to practice under this Agreement solely by Principal Investigator, Institution (Jolimont Hospital, Belgium) or local study site employees shall be owned by the Institution ("Institution Intellectual Property"); provided, however, no Institution Intellectual Property shall include Confidential Information provided by the local study sites. To the extent permitted by the policy of a medical-professional journal, medical institution, educational institution, or medical association relating to any publication or presentation of study data or results hereunder, ownership of the copyright in any publication, abstract, or presentation approved under this section will belong to the Institution (Jolimont Hospital).

20.6 Publication

The Principal Investigator shall have the right, and shall use reasonable efforts, to publish or otherwise publicly disclose study data and results and shall have the final authority to determine the scope and content of any publications originating from the study provided that before publishing, Institution shall submit copies of any proposed publication or presentation to all co-investigators for review. Institution shall in good faith consider any comments provided by any co-investigator and shall delete any Confidential Information identified prior to submission.

21. FUNDING

No external funding is planned for this study

22. SCHEDULE

	Q3 2024	Q1 2025	Q2 2025
Procedures			
Screening	X		
Baseline	X		
Post Procedure	X		
Assess			
inclusion	X		
exclusion criteria	X		
Informed consent	X		
Enrolment	X		
Patient characteristics		X	
US echography characteristics		X	
Cannulation quality measures		X	
Adverse events	X		
Serious adverse events	X		
Objective			
Secure initial fundings			
Ethics approval	X		
Patient recruitment (200 patients per center)	X		
Analysis and reporting			X

23. REFERENCES:

1. Shinsuke Mori , Keisuke Hirano, Masahiro Yamawaki et al. A Comparative Analysis between Ultrasound-Guided and Conventional Distal Transradial Access for Coronary Angiography and Intervention. J Interv. Cardiol. 2020 Sep 8;2020:7342732.
2. A. Hadjivassiliou, F. Kiemeneij, S. Nathan, and D. Klass. Ultrasound-guided access of the distal radial artery at the anatomical snuffbox for catheter-based vascular interventions: a technical guide. Eurointervention, 2019.