COGENIUS Trial

*Comparison of **conventional** and **cooled** radiofrequency treatment of the **genicular nerves** versus **sham** procedure for patients with chronic knee pain: a multicentre, double blind, randomised controlled trial*

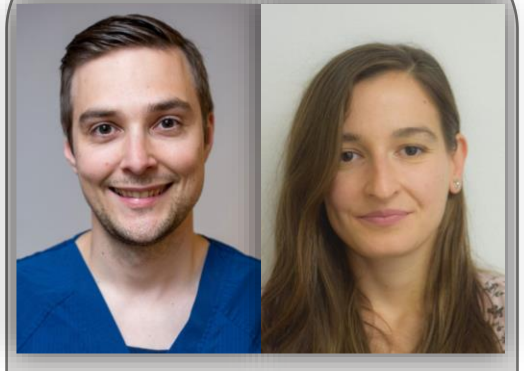
Workshop - 25 February 2022

Ziekenhuis Oost-Limburg

Trial Management Group

Chief Investigator
Co-Chief Investigator

Prof. Dr. Jan Van Zundert
Prof. Dr. Vincent Bonhomme



Scientific Team

Dr. Thibaut Vanneste
Dr. Amy Belba

ZOL CTU

Katrien Tartaglia (PM)
Charlotte Claes (PM)
Diana Clemente (CRA)
Kristof Neven (CRA)
Kimy Emonds (DM)
Marlies Dictus (DM)
Liesbet Van Brussel (DM)

Trial Funding

KCE
Belgian Health Care Knowledge Centre

COGENIUS

Ziekenhuis Oost-Limburg

Materials

Participating sites

AZ Klina
Dr. Laurence Van Gestel

UZ Antwerpen (UZA)
Dr. Babak Baheri

UZ Leuven
Prof. Dr. Bart Morlion

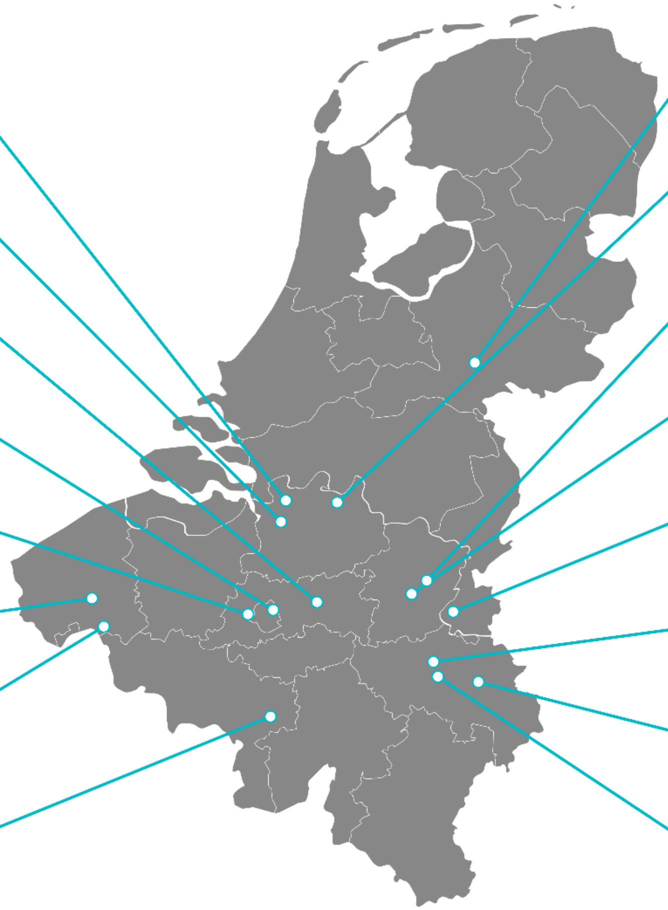
UCL Saint-Luc
Dr. Arnaud Steyaert

Hôpital Erasme - ULB
Prof. Dr. Turgay Tuna

AZ Delta
Dr. Karel Hanssens

AZ Groeninge
Dr. Bert Vanneste

CHU Charleroi
Dr. Gundula Dernedde



Rijnstate
Dr. Jan-Willem Kallewaard

AZ Turnhout
Dr. Christophe Lebrun

Ziekenhuis Oost-Limburg (ZOL)
Dr. Thibaut Vanneste

Jessa Ziekenhuis
Dr. Michiel Brands

Maastricht UMC+ (MUMC)
Dr. Micha Sommer

CHR de la Citadelle
Dr. Caroline Dresse

Clinique CHC Heusy
Dr. Frédéric Louis

CHU de Liège
Prof. Dr. Vincent Bonhomme

COGENIUS

Ziekenhuis Oost-Limburg

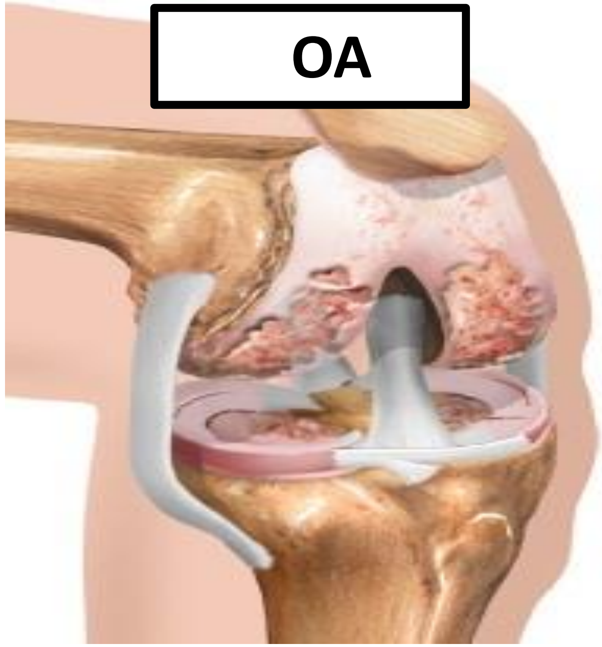
Table of Contents

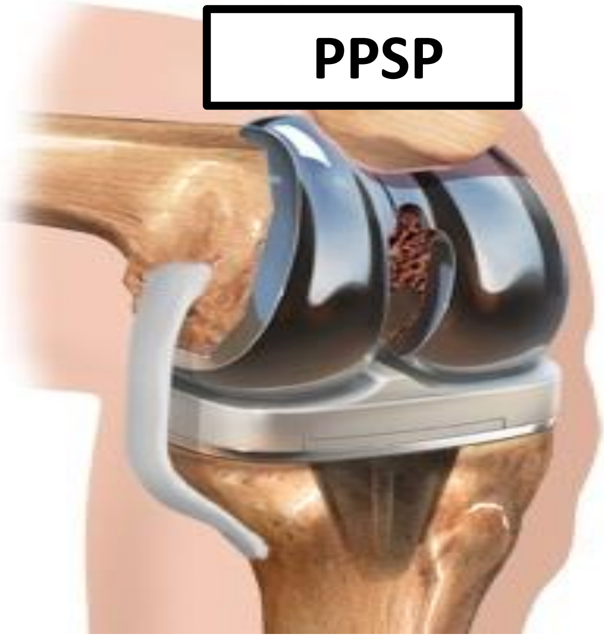
PICO of COGENIUS (1)

P Population

Therapy resistant chronic knee pain patients due to:

- Osteoarthritis of the knee (OA)
- Persistent post-surgical knee pain (PPSP) after total knee arthroplasty (TKA)





COGENIUS Ziekenhuis Oost-Limburg

PICO of COGENIUS (2)

I Intervention

- Cooled Radiofrequency ablation (RF) of genicular nerves
- Conventional Radiofrequency ablation (RF) of genicular nerves
- Sham procedure (1/5)

PICO of COGENIUS (3)

C Comparison

Comparison will be performed separately for OA and PPSP.

• Cooled RF	↔	Sham procedure
• Conventional RF	↔	Sham procedure
• Cooled RF	↔	Conventional RF

COGENIUS Ziekenhuis Oost-Limburg

PICO of COGENIUS (4)

O Objectives

Primary objective:

To compare knee pain, stiffness, and function (total WOMAC score) at 6 months between:

- Cooled RF ↔ Sham procedure
- Conventional RF ↔ Sham procedure
- Cooled RF ↔ Conventional RF

COGENIUS Ziekenhuis Oost-Limburg

PICO of COGENIUS (4)

O Objectives

Secondary objectives:

To determine the clinical effects of Cooled and Conventional RF up to 24 months.

To determine and compare health care resource use and productivity loss up to 24 months post-intervention.

COGENIUS Ziekenhuis Oost-Limburg

PICO of COGENIUS (4)

O Objectives

Exploratory objectives:

To identify the phenotype of patients suffering from PPSP.

To assess time to additional interventions after RF / sham treatment

Table of Contents

- PICO of COGENIUS trial
- **Key Inclusion/Exclusion criteria**
- Trial Procedures
- Project Timelines
- Study Intervention
- Workshop

COGENIUS Ziekenhuis Oost-Limburg

Key inclusion criteria

- **Chronic anterior knee pain** (> 12 months) that is moderate to severe (defined as NRS > 4 on most or all days for the index knee either constantly or with motion).
- **Unresponsive** (meaning insufficient pain reduction or intolerance) **to conventional treatments** ongoing for at least 12 months prior to inclusion.
- <u>OA patients</u>: **Radiologic confirmation of knee osteoarthritis** of grade 2 (mild), 3 (moderate) or 4 (severe) noted within 12 months prior to the screening for the index knee according the Kellgren Lawrence criteria diagnosed by an independent radiologist with experience in musculoskeletal imaging on Rx or MRI.
- <u>PPSP patients after TKA</u>: **No orthopaedic treatment possible**

Key exclusion criteria

- Evidence of inflammatory arthritis or an inflammatory systemic disease responsible for knee pain.
- **Intra-articular injections** (steroids, hyaluronic acid, platelet enriched plasma, …) in the index knee during the **3 months prior to procedure**.
- Allergies to products used during the procedure (lidocaine, propofol, chlorhexidine).
- Uncontrolled coagulopathy defined as supratherapeutic dose of anticoagulation medication.
- Patient is currently implanted with a neurostimulator.

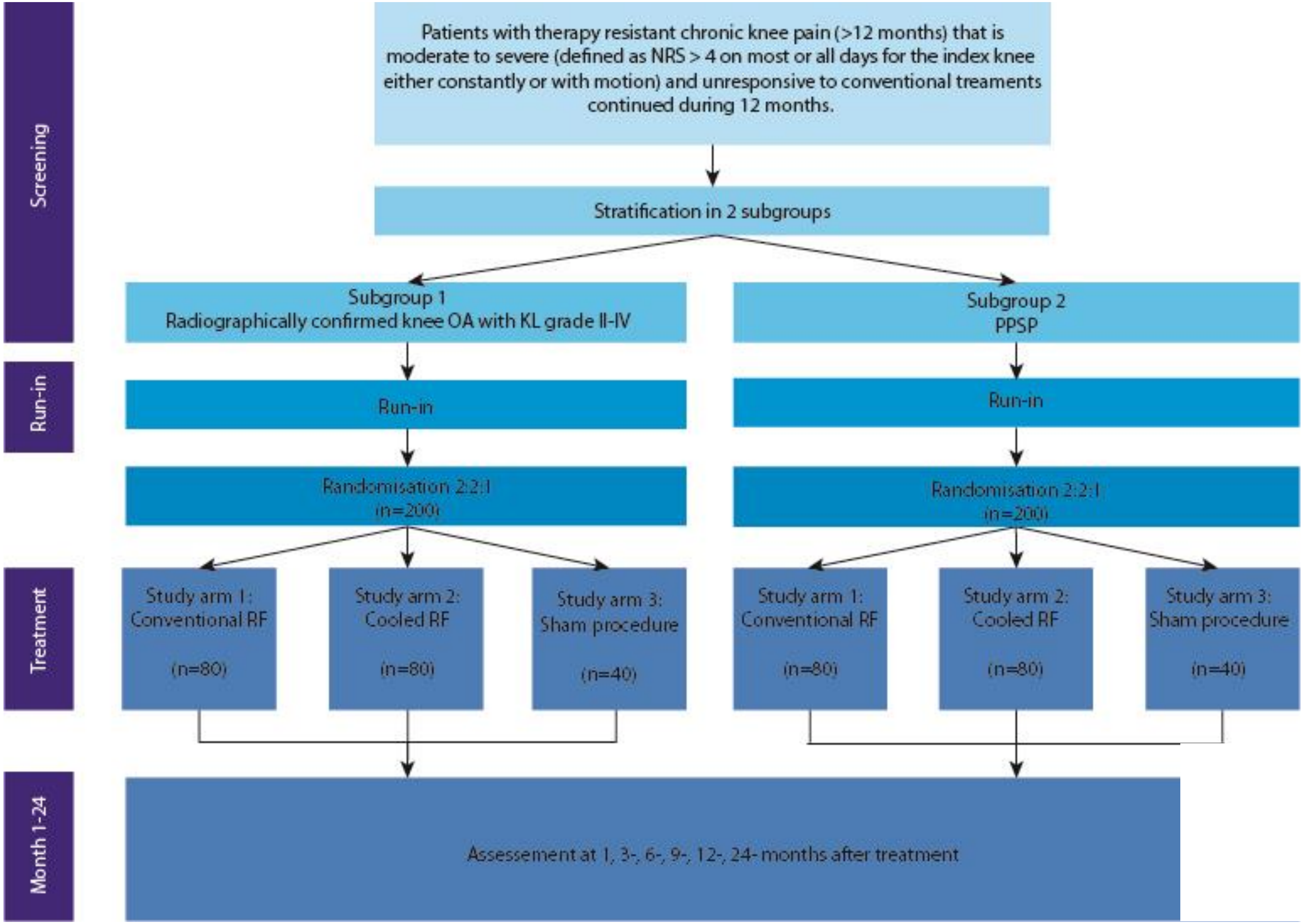
COGENIUS Ziekenhuis Oost-Limburg

Key exclusion criteria

- Current radicular pain in index leg.
- Previous conventional or cooled radiofrequency of the index knee.
- Patients with **bilateral knee pain** defined as chronic knee pain (> 12 months) in both knees that is moderate to severe (defined as NRS > 4 on most or all days for the index knee either constantly or with motion) and that is unresponsive (meaning insufficient pain reduction or intolerance) to conventional treatments ongoing for at least 12 months prior to inclusion.
- Patients who have a planned TKA in the near future defined as patients who already have agreed on a date for the TKA procedure.

Table of Contents

- PICO of COGENIUS trial
- Key Inclusion/Exclusion criteria
- **Trial Procedures**
- Project Timelines
- Study Intervention
- Workshop


Screening
Run-in
Treatment
Month 1-24
Patients with therapy resistant chronic knee pain (>12 months) that is moderate to severe (defined as NRS > 4 on most or all days for the index knee either constantly or with motion) and unresponsive to conventional treaments continued during 12 months.
Stratification in 2 subgroups
Subgroup 1
Radiographically confirmed knee OA with KL grade II-IV
Subgroup 2
PPSP
Run-in
Run-in
Randomisation 2:2:1
(n=200)
Randomisation 2:2:1
(n=200)
Study arm 1:
Conventional RF
(n=80)
Study arm 2:
Cooled RF
(n=80)
Study arm 3:
Sham procedure
(n=40)
Study arm 1:
Conventional RF
(n=80)
Study arm 2:
Cooled RF
(n=80)
Study arm 3:
Sham procedure
(n=40)
Assessement at 1, 3-, 6-, 9-, 12-, 24- months after treatment

Materials/supplies

CRK-17-75-4	PMP-18-100	PMF18-100-10	PMA-GP-BAY
COOLIEF Probe Kit: 3 Introducers, 1 Probe	Stainless Steel Probe	Straight Sharp Cannula	Split grounding pad
			
17 GA 75 mm Length 4 mm Active Tip	sterilizable, 18 GA, 100 mm Straight Probe	18 GA, 100 mm, 10 mm Active Tip Radiopaque Straight Sharp Cannula	

- ✓ Equipment use -> approved by your hospital
- ✓ Cleaning & sterilisation of conventional RF probe

COGENIUS Ziekenhuis Oost-Limburg

Unblinding vs. blinding study team

Conventional RF
Cooled RF
Sham

?

Performs the study intervention

Keeps track of the study material stock

Organizes/Performs FU visits

Data transfer (eCRF)

EPD
Blinding procedure guidelines

Table of Contents

COGENIUS

Ziekenhuis Oost-Limburg

Project Timelines

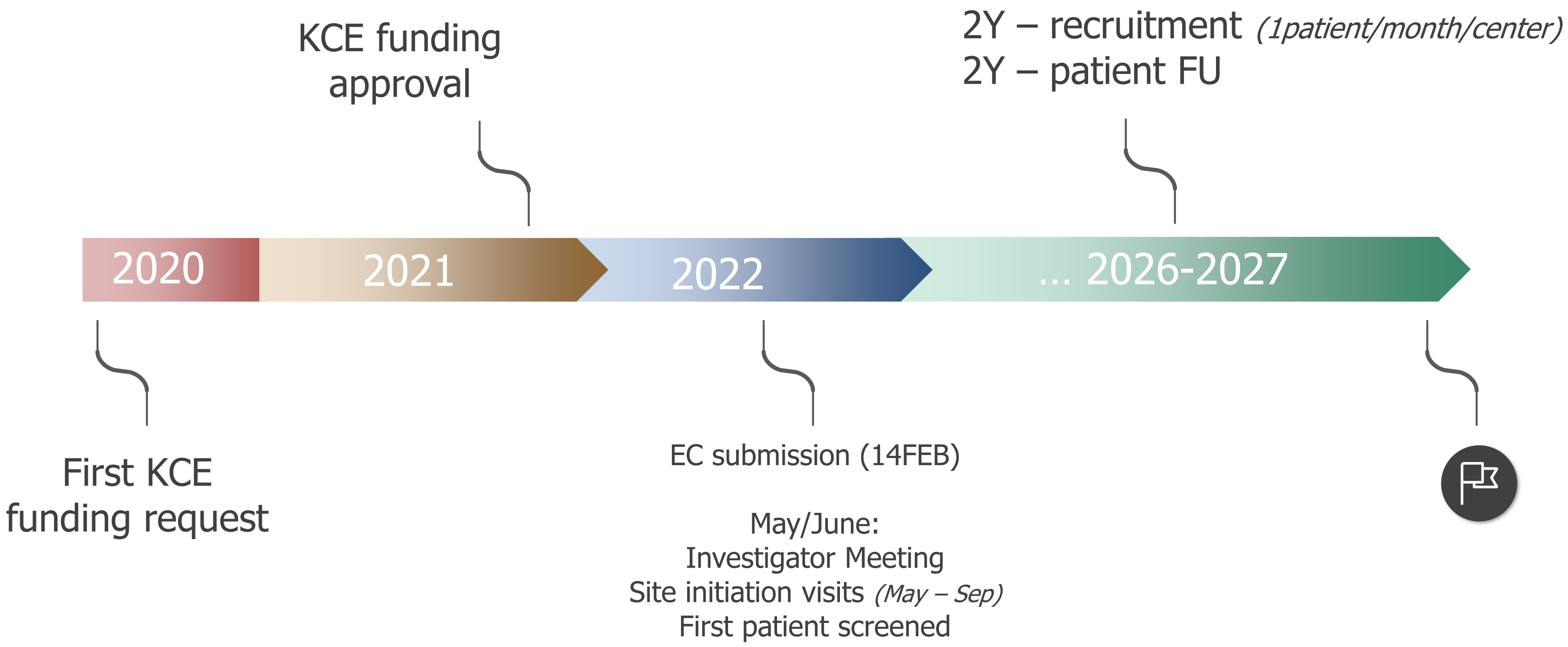
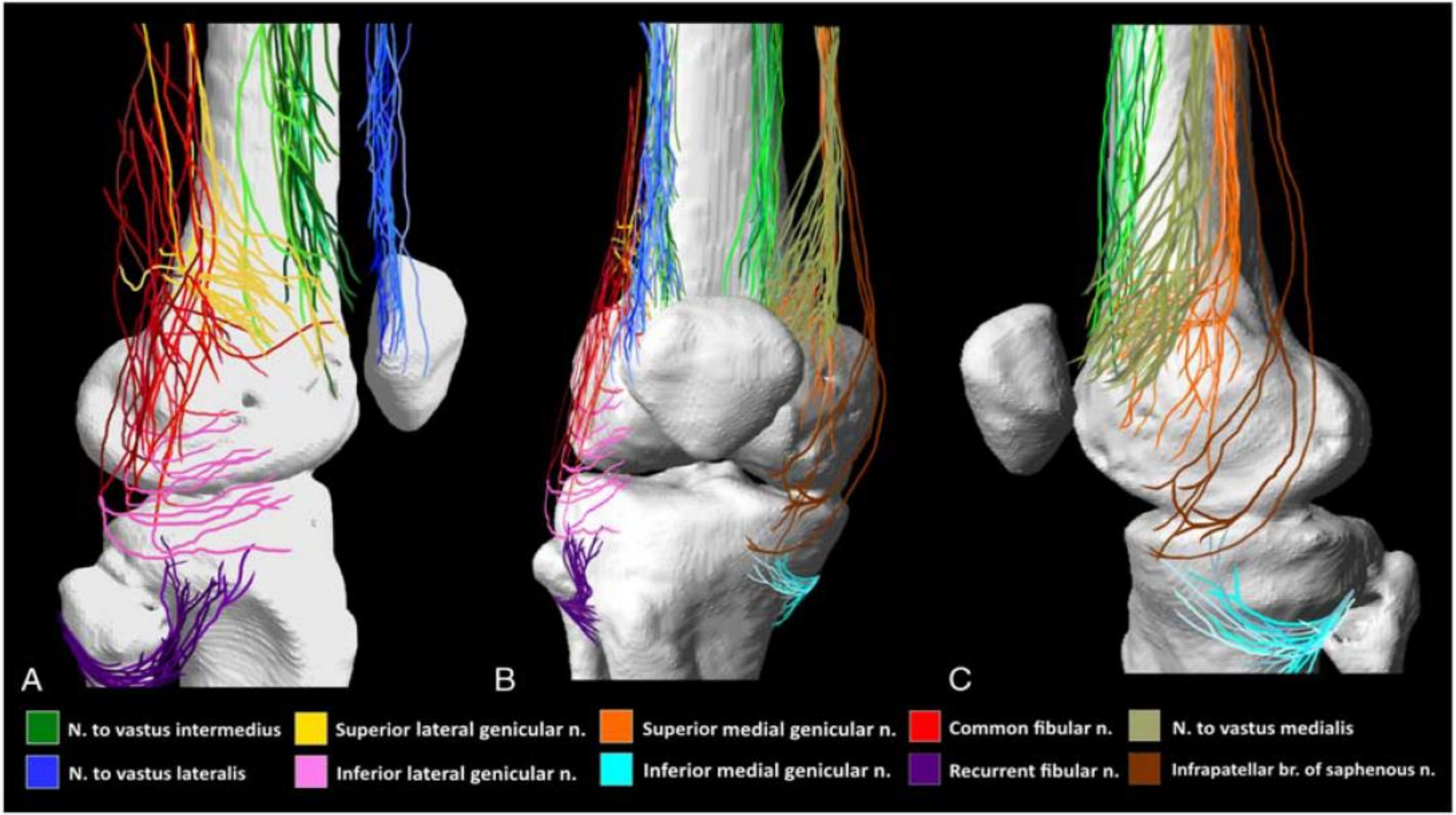
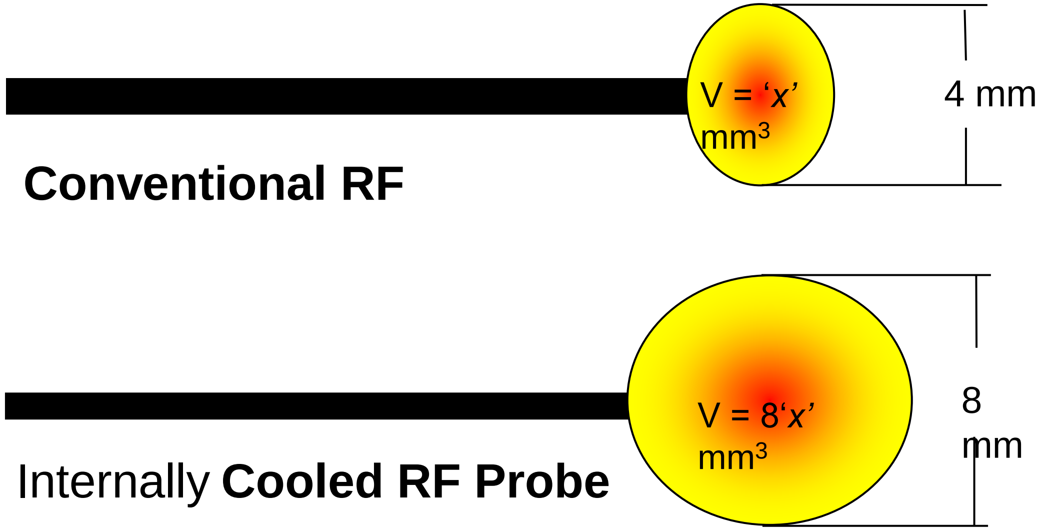


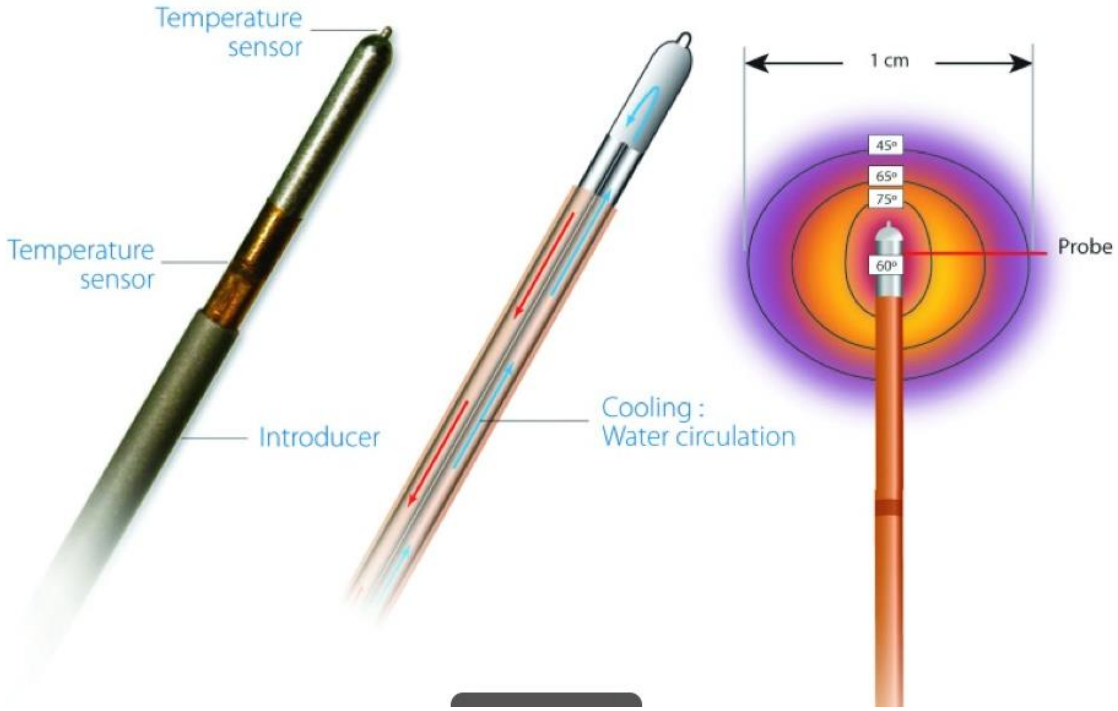
Table of Contents

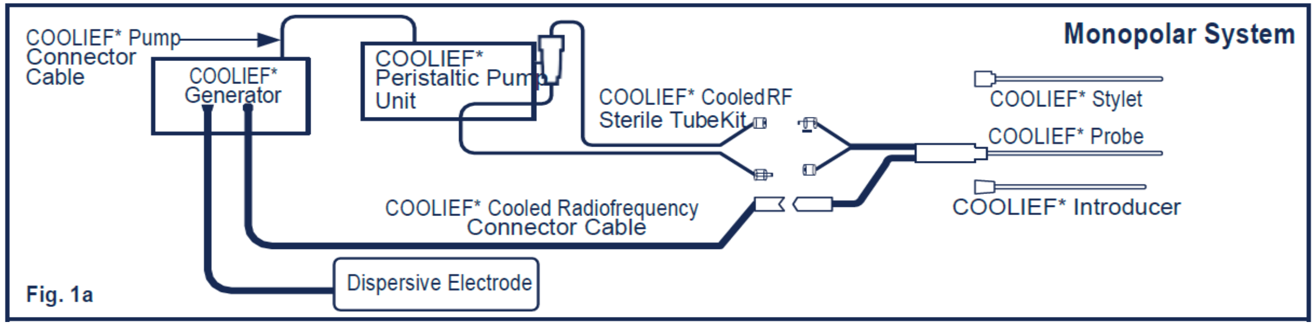
- PICO of COGENIUS trial
- Key Inclusion/Exclusion criteria
- Trial Procedures
- Project Timelines
- **Study Intervention**
- Workshop


A
B
C
N. to vastus intermedius
N. to vastus lateralis
Superior lateral genicular n.
Inferior lateral genicular n.
Superior medial genicular n.
Inferior medial genicular n.
Common fibular n.
Recurrent fibular n.
N. to vastus medialis
Infrapatellar br. of saphenous n.

RF treatment of the genicular nerves







COGENIUS

Ziekenhuis Oost-Limburg

Trial intervention

General aspects:

- Pulse oxymeter
- Sedation (propofol) if needed
- Supine, index knee flexed 10-15°
- No diagnostic block
- High frequency linear probe
- Sensory and motor stimulation
- Ultrasound placement, check fluoroscopy
- 30 minutes recovery

Trial intervention

Superomedial genicular nerve

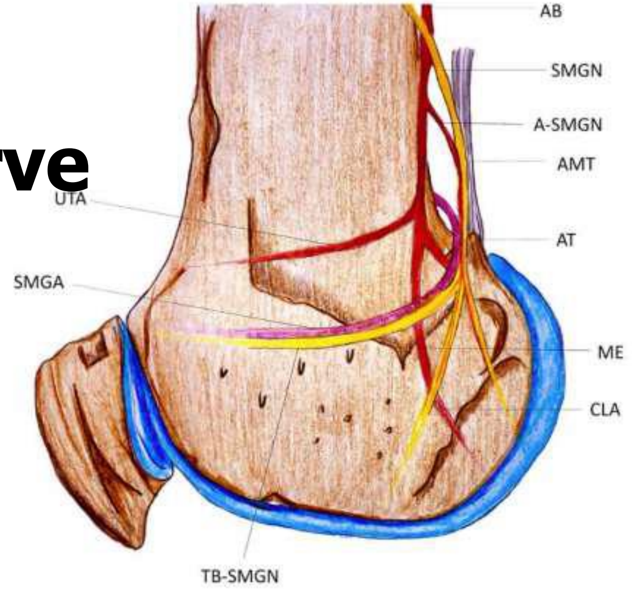


Fig. 9. Diagram of the anatomical relationships of SMGN and its terminal branches to the arteries at the superior medial aspect of the knee. The artery of the SMGN (A-SMGN) is detached from the trunk of the osteo-articular branch (AB) of the descending genicular artery, and descends with the SMGN on the adductor magnus tendon (AMT). The superior-medial genicular artery (from popliteal artery), runs alongside the transverse terminal branch of the SMGN (TB-SMGN) at the level of medial epicondyle. The upper transverse artery (UTA) runs at junction of medial femoral epiphysis and diaphysis, without a nerve branch. SMGN, superior-medial genicular nerve; AT, adductor tubercle; ME, medial femoral epicondyle; CLA, central longitudinal artery.

Ziekenhuis Oost-Limburg

Trial intervention

Superomedial genicular nerve

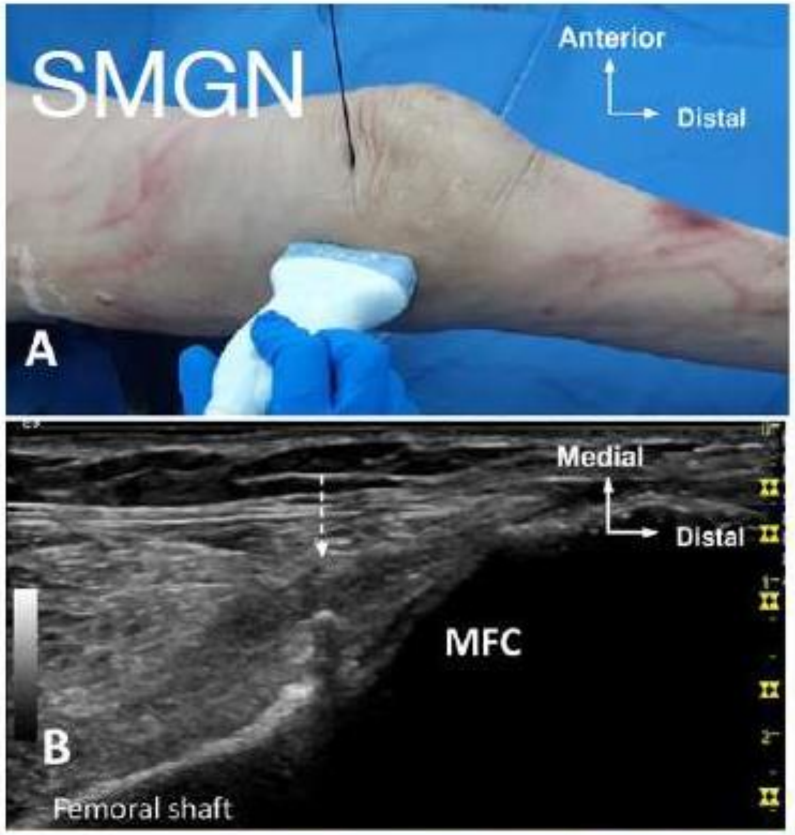
Coronal plane medial side knee

Target point at junction shaft-condyl:

- Adductor tubercle – adductor magnus
- Superomedial genicular artery?

Entry point:

- Estimated probe-to-target distance perpendicular to the center



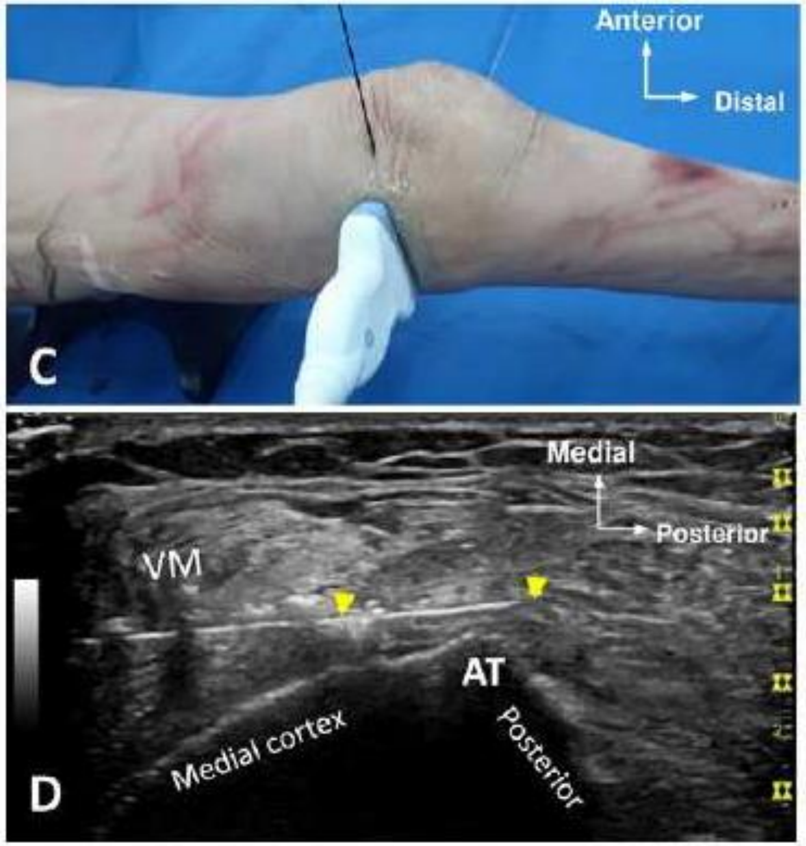
Trial intervention

Superomedial genicular nerve

Transverse plane medial side knee

Target point:

In plane posterior half femur



Ziekenhuis Oost-Limburg

Trial intervention

Inferomedial genicular nerve

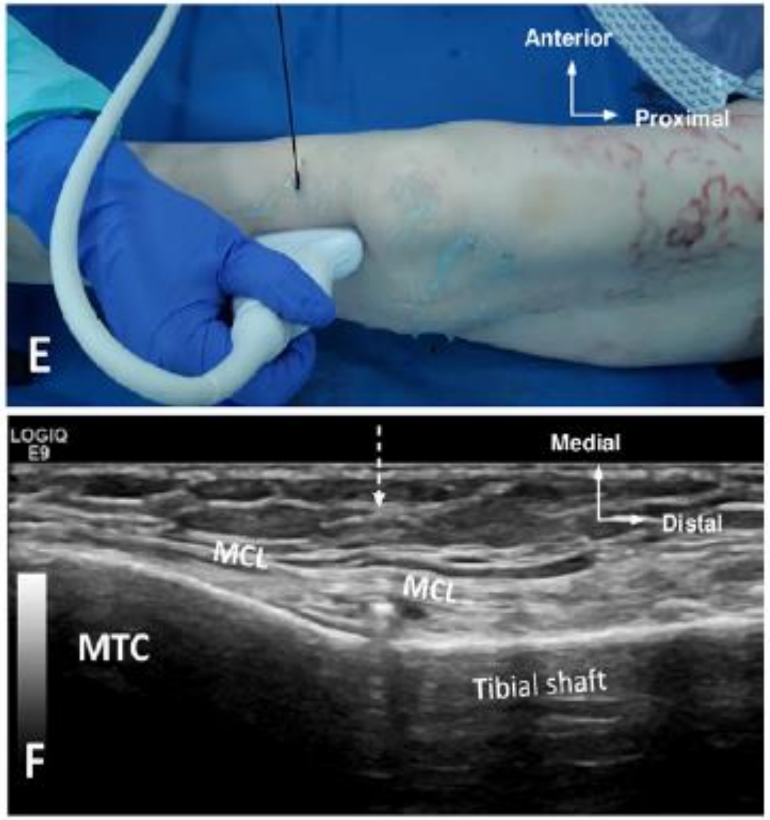
Coronal plane medial side knee

Target point at junction shaft-condyl:

- Beneath medial collateral ligament
- Midpoint tibial medial epicondyl – tibial insertion medial collateral ligament
- Inferomedial genicular artery?

Entry point:

- Estimated probe-to-target distance perpendicular to the center



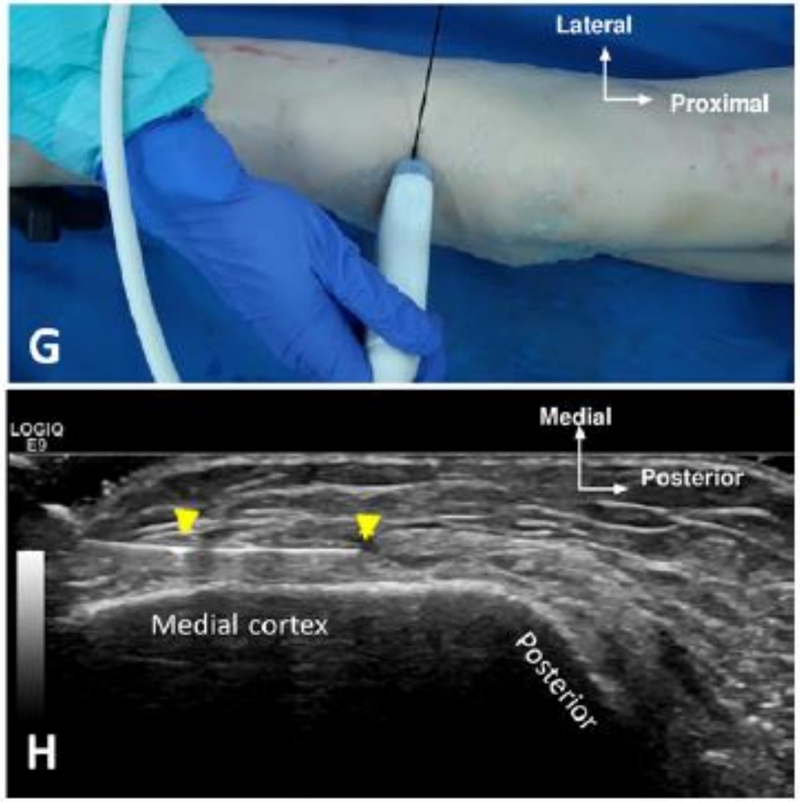
Trial intervention

Inferomedial genicular nerve

Transverse plane medial side knee

Target point:

In plane center tibia



Ziekenhuis Oost-Limburg

Trial intervention

Superolateral genicular nerve

1. Coronal plane lateral side knee

Target point:

- Junction shaft-condyl
- Superolateral genicular artery?

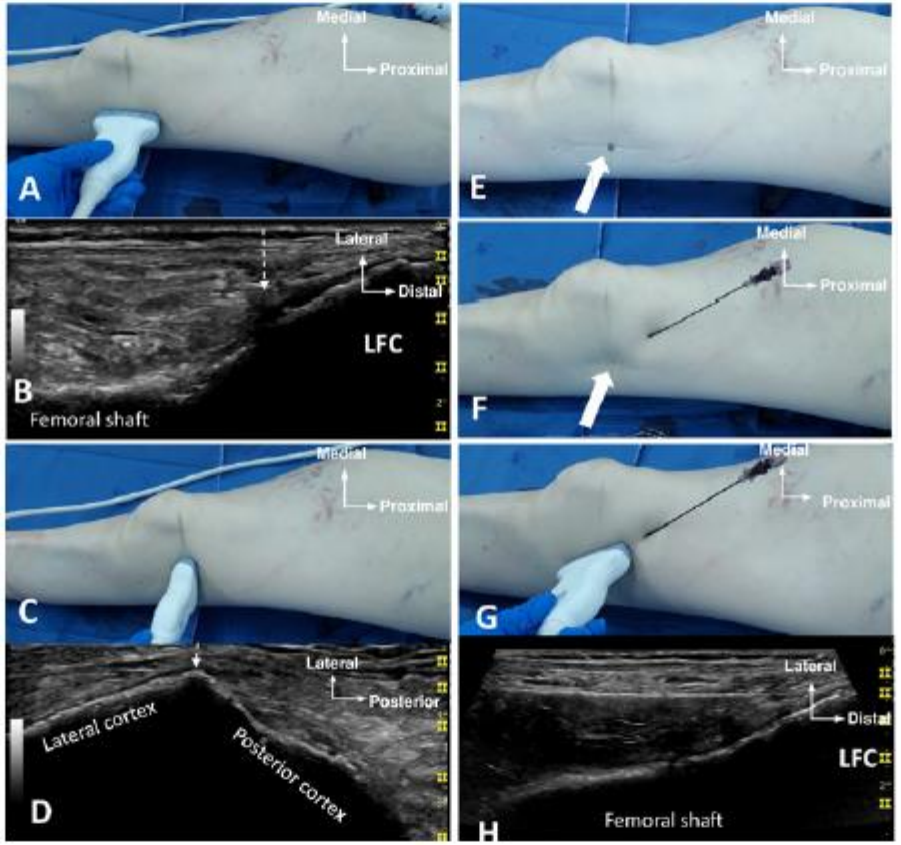
2. Transverse plane lateral side knee

Target point:

- Posterior side

3. 45° oblique plane

Entry point: 3 cm anterior, 3 cm proximal



Ziekenhuis Oost-Limburg

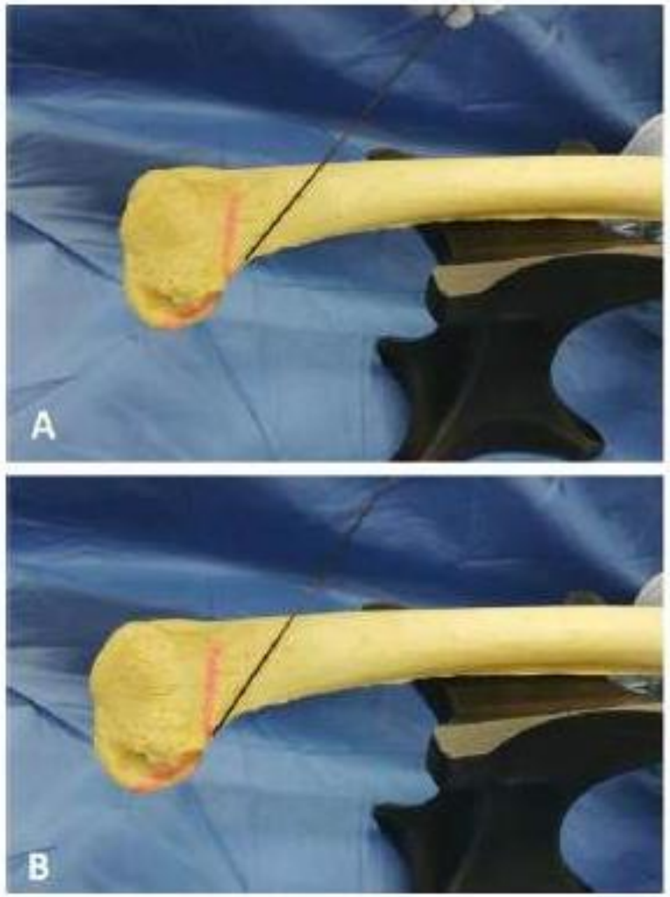
Trial intervention

Superolateral genicular nerve

Oblique plane lateral side knee

Target point:

In plane posterior side femur



Trial intervention

Sham procedure

- Standardised script – vertical drape
- Ultrasound and fluoroscopy (placement without use radiation)
- Subcutaneous local anaesthetic
- Introducer and probe placement
- Testing
- Sound recording mimicing generator 150 seconds

Ziekenhuis Oost-Limburg

Table of Contents

- PICO of COGENIUS trial
- Key Inclusion/Exclusion criteria
- Trial Procedures
- Project Timelines
- Study Intervention
- **Workshop**

Workshop

A	B
Dr. Babak Baheri (UZA)	Dr. Brice Constant (CHU Charleroi)
Dr. Jens Gios (UZA)	Dr. Caroline Dresse (CHR Citadelle)
Prof. Dr. Vincent Bonhomme (CHU Liège)	Dr. Tracy Surinder (CHR Citadelle)
Dr. Michiel Brands (Jessa)	Dr. Arnaud Steyaert (UCL Saint Luc)
C	**D**
Dr. Christophe Lebrun (AZ Turnhout)	Dr. Ionut Tabolcea (ULB Erasme)
Dr. Leen Govaers (AZ Turnhout)	Dr. Laurence Van Gestel (AZ Klina)
Dr. Frédéric Louis (CHC Heusy)	Dr. Bert Vanneste (AZ Groeninge)
Dr. Karel Hanssens (AZ Delta)	

Workshop

Station	Session 1	Session 2
Station 1 Dr. Thibaut Vanneste (ZOL)	A	C
Station 2 Dr. Micha Sommer (MUMC) Dr. Jan-Willem Kallewaard (Rijnstate)	B	D
Station 3 D.E.N. Medical	C & D	A & B

Thank you!