2024 MID-ATLANTIC CONFERENCE

12th ANNUAL CURRENT CONCEPTS IN VASCULAR THERAPIES

2024

Technological Advances in PAD: What's New

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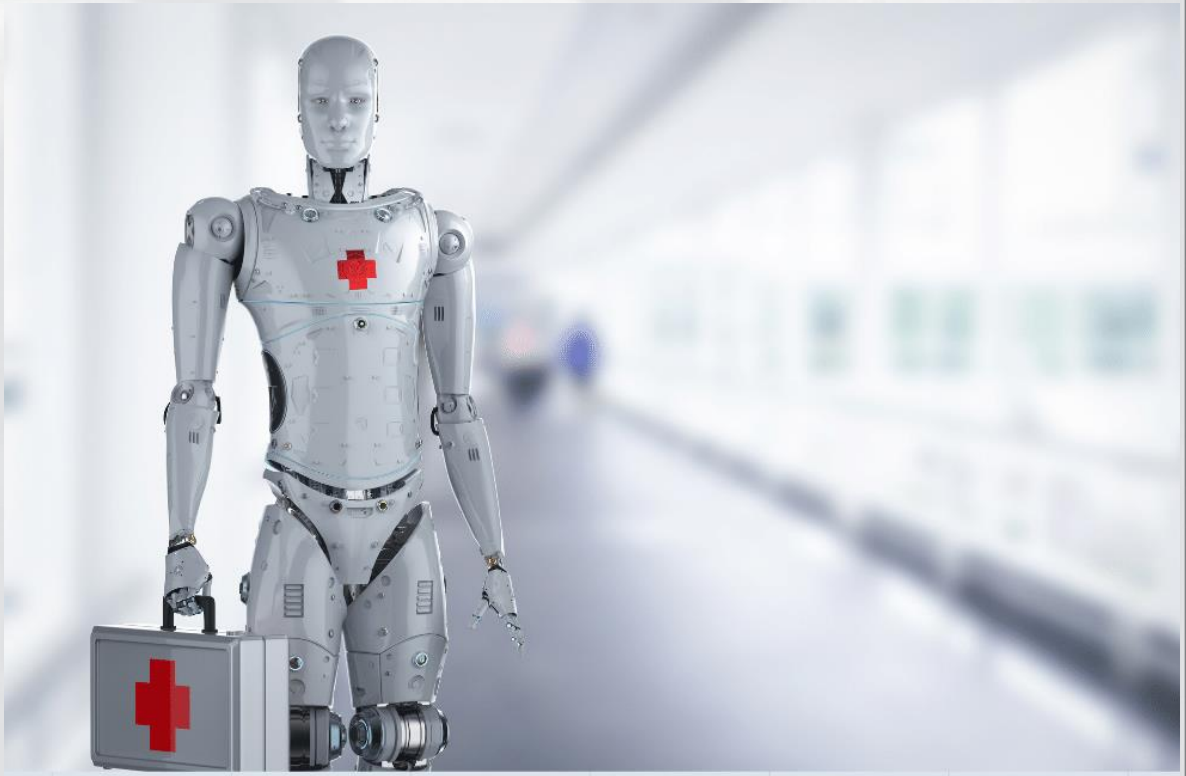
Disclosures

- Speaker
  - Medtronic, Abbott, BD, Endologix
- Consultant
  - Philips

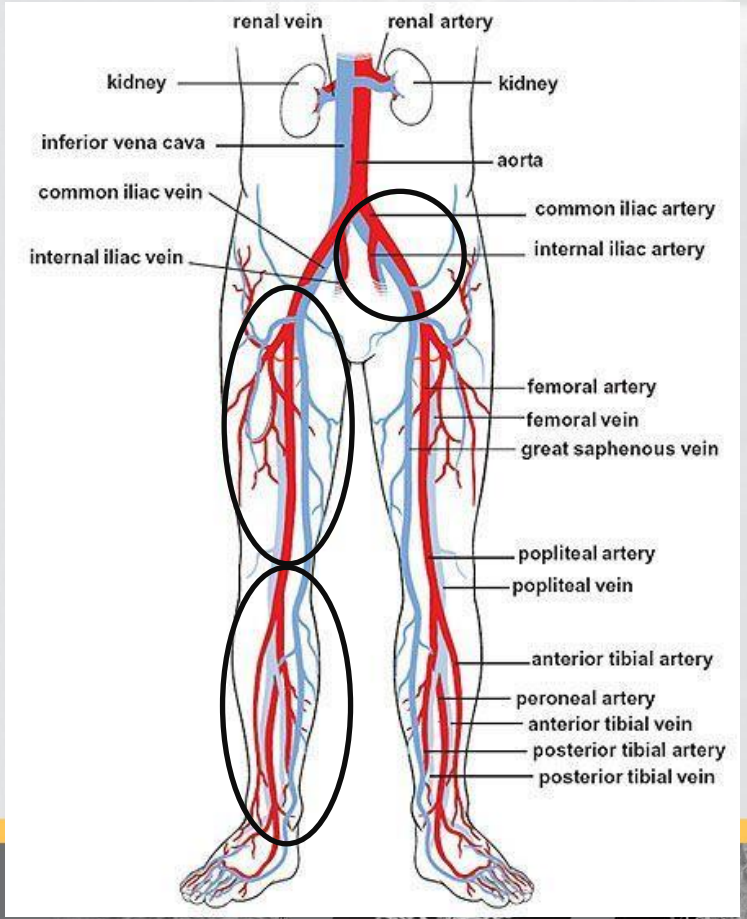
- Devices without FDA approval will be presented

Outline

- New Devices
  - Spur Stent
  - Esprit BTK
  - Bioresorbable stent
  - Vibrato Limbsonic
  - EndoNaut
- Artificial intelligence in PAD
- Developing Technology



Endovascular Devices for Infra-popliteal obstruction



- Iliac arteries – stents
- Femoral arteries – Atherectomy, drug coated balloons
- Infra-popliteal – reoccurrence is common
  - Drug delivery has not succeeded

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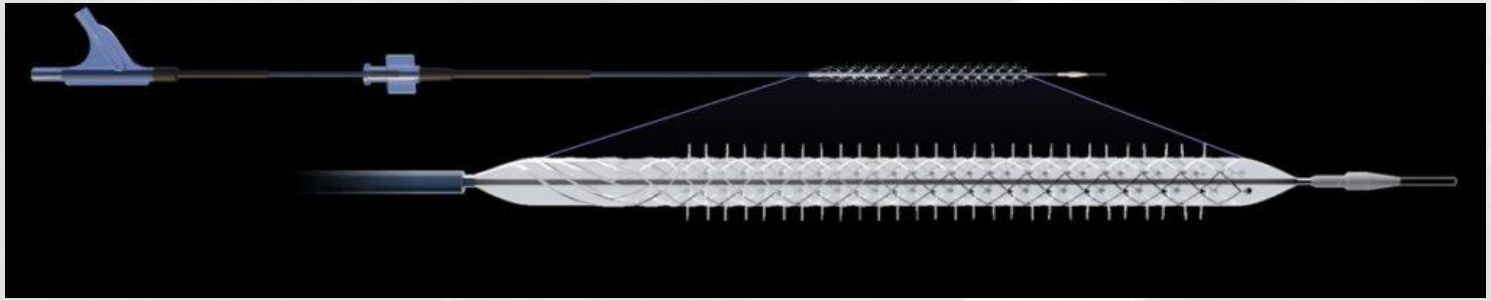
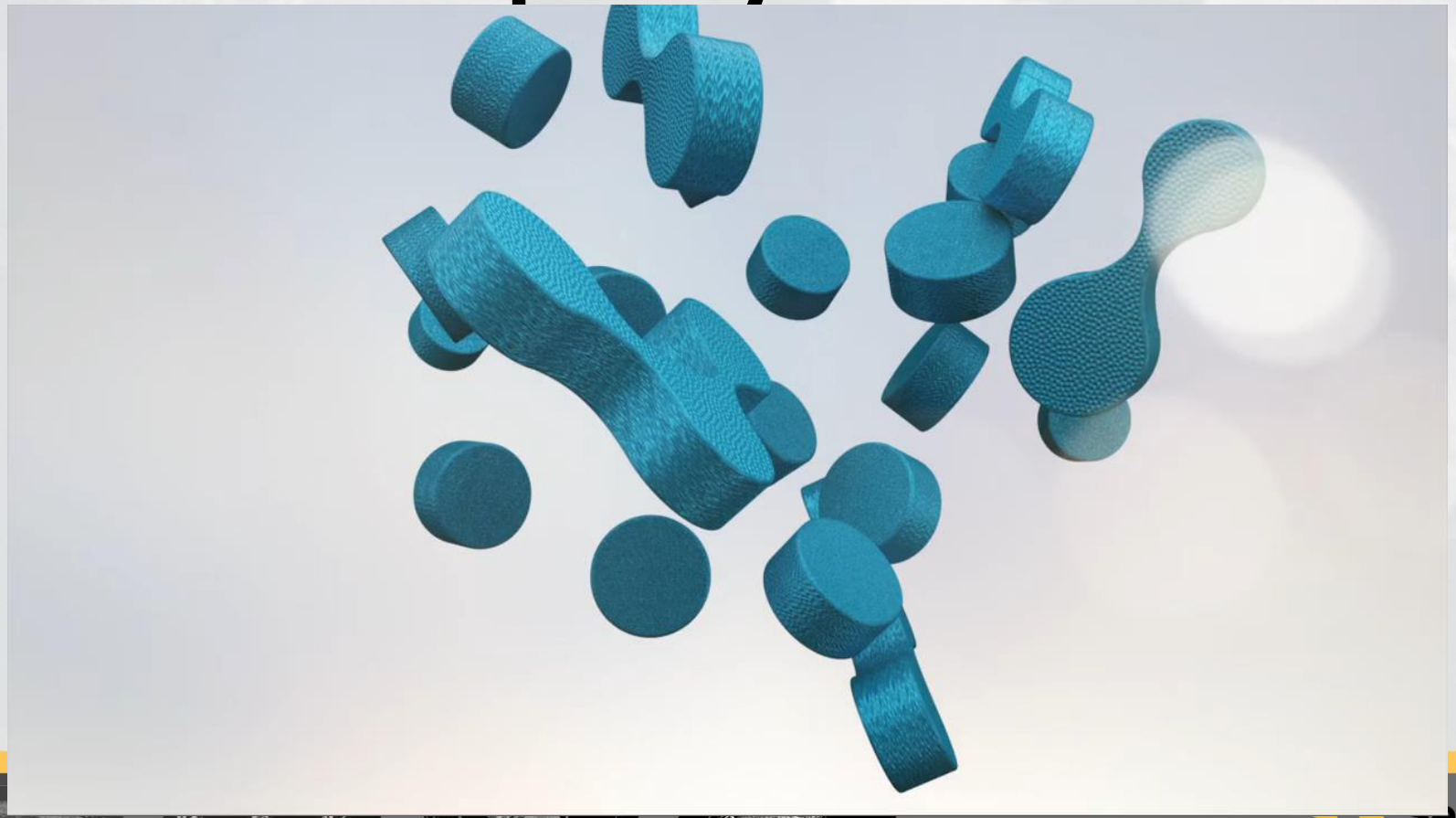
Spur Stent

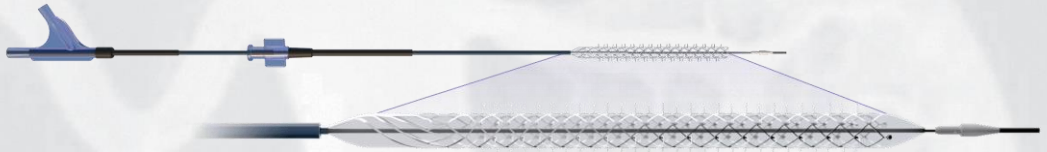
- Reflow Medical
- Designed for infra-popliteal delivery of local drug



Spur System



Spur System: Does is work?



- 1-year results from DEEPER OUS
- 107 patients enrolled
- AVG treatment length: 92.7 ± 36.63 mm
- The most commonly used Spur size was 3 X 60 mm
- 12 month outcomes:
  - Target lesion primary patency was achieved in 57/71 (79.2%)
  - Freedom from CD-TLR was achieved in 71/80 (88.8%)
  - 60% of wounds achieving total wound healing
  - freedom from major amputation of the target limb at 12 months was 78/78 (100%)

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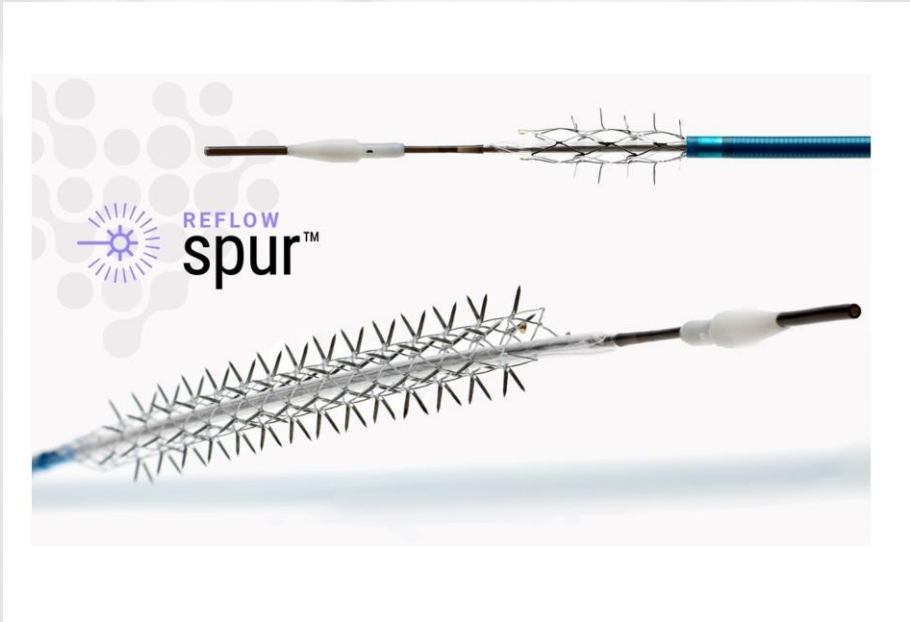
Next Steps

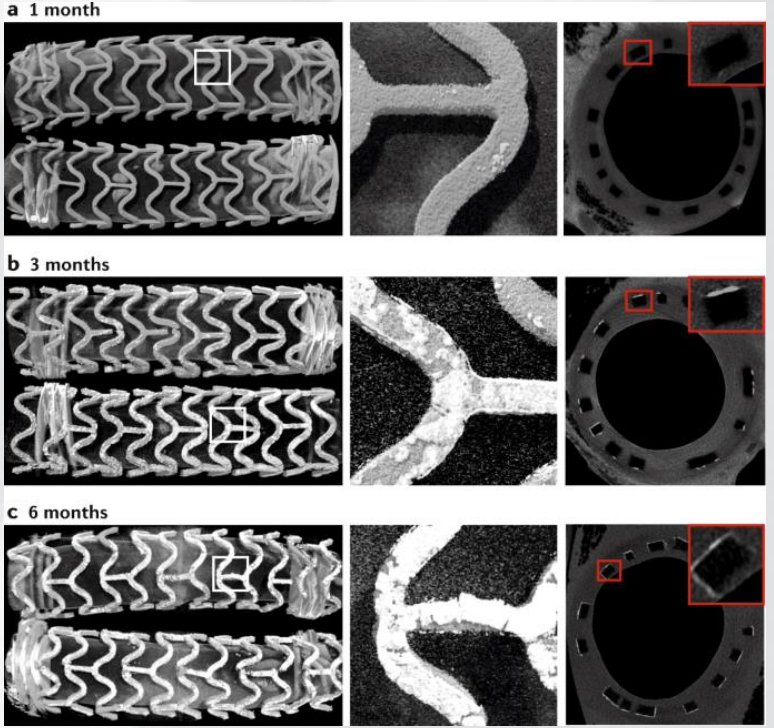
- Received CE mark – Jan 2024
- Planning 5 year follow up for DEEPER OUS
- Determine ideal antiproliferative drug to use
  - DEEPER LIMUS
- Study use in preventing vessel recoil after angioplasty



Fully bioresorbable vascular scaffolds: lessons learned and future directions

Key Points

- Bioresorbable scaffolds (BRS) were designed to overcome the limitations of metallic stents, such as vessel caging with a lack of coronary vasomotion and preclusion of bypass surgery in stented segments.
- The most advanced fully BRS is the Absorb Bioresorbable Vascular Scaffold (BVS; Abbott Vascular); however, clinical trials have shown higher rates of target-vessel myocardial infarction and stent thrombosis with the Absorb BVS than with current-generation metallic drug-eluting stents.
- These studies have taught us about the limitations of animal models in predicting the clinical safety of devices in humans.
- The Absorb BVS has also provided important information about strut thickness, vessel wall coverage and their influence on thrombosis induced by shear forces.
- The timing of scaffold degradation and its relationship to healing in humans must be better understood before this technology can become mainstream.
- Newer-generation BRS are being developed with thinner struts, but most have not been examined in large-scale clinical trials or real-world registries; the technology must be rigorously tested before initiating trials in humans.



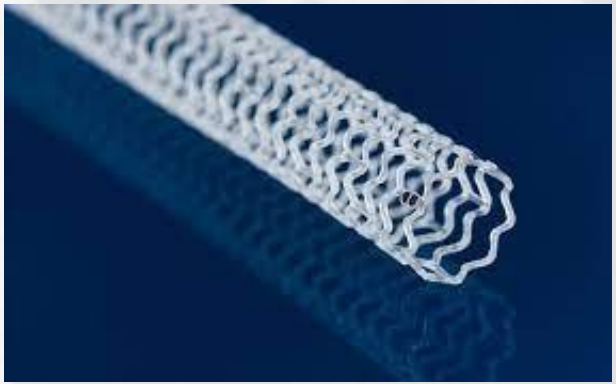
Jinnouchi, H., Torii, S., Sakamoto, A. et al. Fully bioresorbable vascular scaffolds: lessons learned and future directions. Nat Rev Cardiol 16, 286–304 (2019). https://doi.org/10.1038/s41569-018-0124-7

nature reviews cardiology

Esprit BTK

Drug-Eluting Resorbable Scaffold

- There are currently no drug-eluting stents, drug-coated balloons or bare-metal stents approved for below the knee (BTK) use in the U.S
- Thin strutted scaffold made from poly-L-lactide (PLLA), a semi-crystalline bioresorbable polymer engineered to resist vessel recoil and provide a platform for drug delivery. The scaffold is uniformly coated with poly-D, L-lactide (PDLLA) and the cytostatic drug, everolimus. PDLLA is an amorphous bioresorbable polymer coating designed to allow controlled drug release.



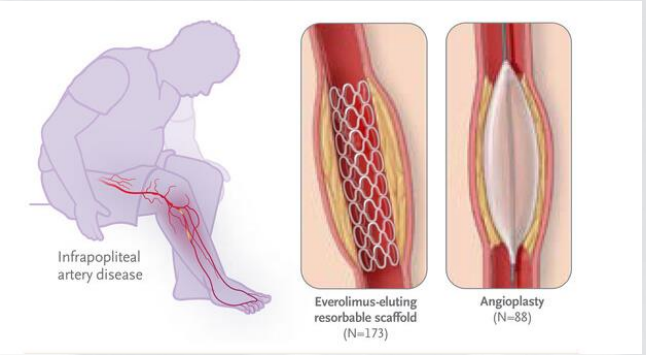
Esprit BTK: Does it work?

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

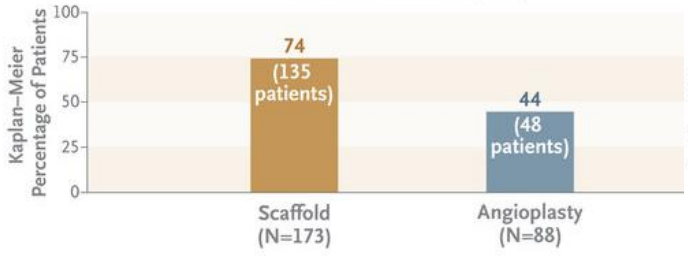
Drug-Eluting Resorbable Scaffold versus Angioplasty for Infrapopliteal Artery Disease

Varcoe RL et al. DOI: 10.1056/NEJMoa2305637



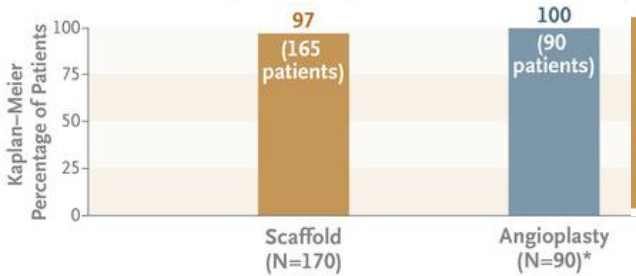
Freedom from Amputation, Total Occlusion of Target Vessel, Revascularization of Target Lesion, and Binary Restenosis at 1 Yr

Absolute difference, 30 percentage points (95% CI, 15 to 46); one-sided P<0.001 for superiority



Freedom from Major Adverse Limb Events at 6 Mo and from Perioperative Death

Absolute difference, −3 percentage points (95% CI, −6 to 0); one-sided P<0.001 for noninferiority



*2 patients crossed over from scaffold to angioplasty

CONCLUSIONS

Among patients with CLTI due to infrapopliteal artery disease, treatment with a new everolimus-eluting resorbable scaffold was superior to angioplasty in reducing reintervention and maintaining patency at 1 year.

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N Engl J Med 2024;390:9-19

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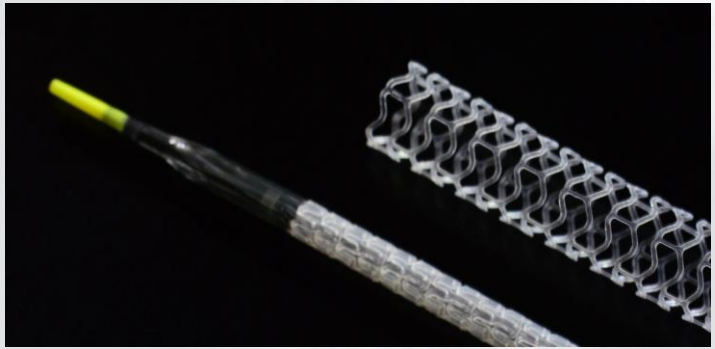
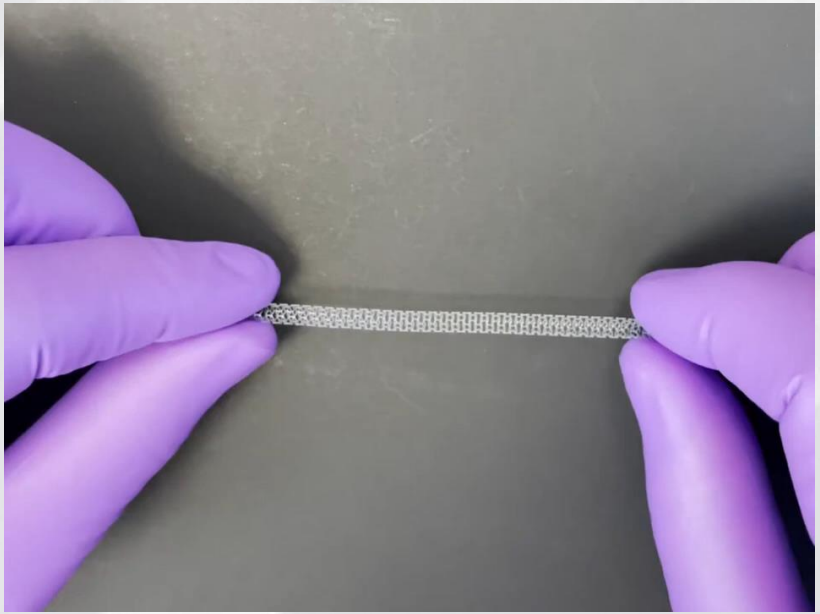
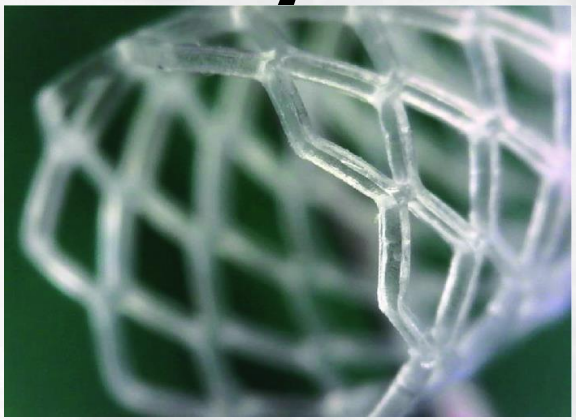
Resorbable stent competitor



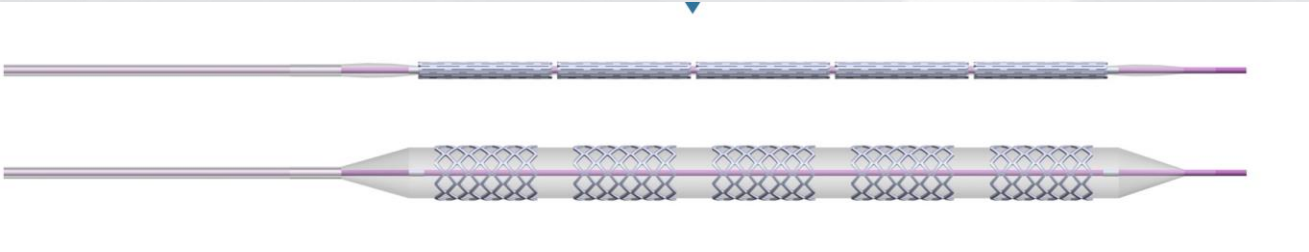


- **R3 Vascular's Magnitude Bioresorbable Scaffold**
- **FIH - 6-month results for 30 patients in an ongoing study**

Efemoral Vascular Scaffold System



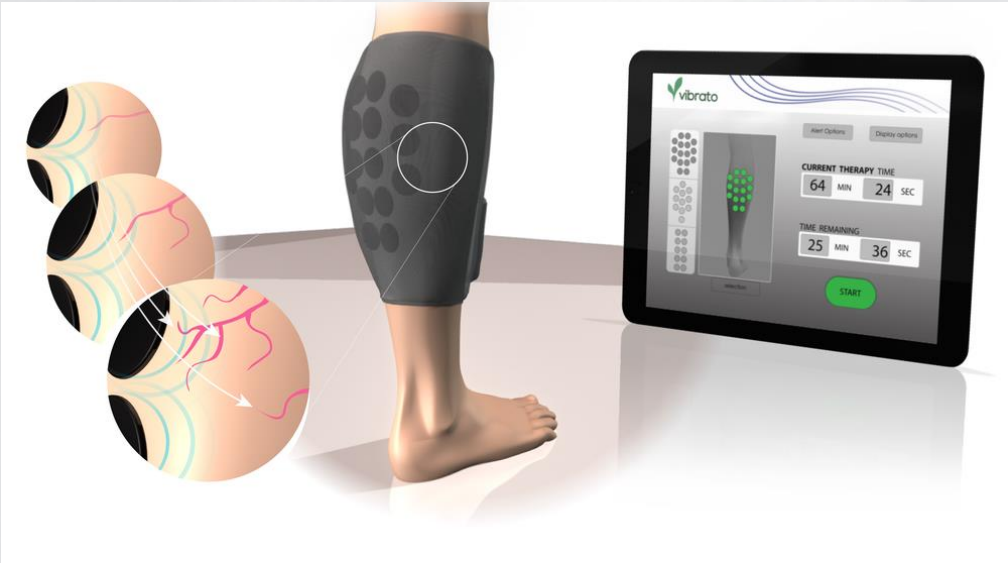
- Sirolimus-eluting bioresorbable platform using multiple, serial intravascular scaffolds
- Granted FDA Breakthrough Device status
- Femoropopliteal iteration is currently in a first-in-human study in New Zealand and Australia
- Device in development for infrapopliteal arteries



Limbsonic by Vibrato

- Noninvasive treatment for Critical Limb Ischemia and Peripheral Arterial Disease
- First wearable therapeutic ultrasound
- Therapeutic ultrasound has been seen in animal and clinical studies
  - Vasodilation
  - collateral vessel growth
  - angiogenesis

Prelude study



- 12-patients
- 30-40 TUS treatment sessions over 2 months
- Toe perfusion increased acutely by 180% ($p<0.001$)
- Tissue oxygenation increased by 17% ($p=.02$)

- Generate panoramic views of PAD combined with the precision of the dedicated image fusion help significantly reduce:
- X-ray dose
- contrast media volume

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Generate preoperative panoramas

- **Easily create comprehensive pre-operative panoramas,** by stitching both fluoroscopic and angiographic limb images
- **Display automatically a mixed panorama,** getting a detailed view of the entire lower limb

Identify and mark all the lesions

- **Mark thrombotic and stenotic areas within the panorama** to get a clear picture of the required treatment approach
- **Make a calibration to easily get** lesion cues and length measurement
- **Use the measurements** to optimize the choice of balloons and stents, resulting in improved procedural outcomes

EndoNaut two-dimensional fusion imaging with a mobile C-arm for endovascular treatment of occlusive peripheral arterial disease

Caroline Caradu, MD, PhD,[a] Katherine Stenson, MD,[b] Hassan Houmaïda, MD,[c] Julie Le Ny, MS,[d] Florent Lalys, PhD,[d] Eric Ducasse, MD, PhD,[a] *and* Benoit Gheysens, MD,[c] *Bordeaux, Libourne, and Rennes, France; and London, UK*

ABSTRACT

Background: Endovascular treatment has become the first-line strategy for peripheral arterial disease (PAD). Given the number of procedures required, any technology associated with a reduction in radiation exposure and contrast volume is highly relevant. In the present study, we evaluated whether two-dimensional (2D) fusion imaging could reduce the radiation exposure and contrast volume during endovascular treatment of occlusive PAD.

Methods: Our consecutive, retrospective, single-center, nonrandomized comparative trial included patients with PAD at the femoral, popliteal, and/or tibial level, at any clinical stage, if they were candidates for endovascular revascularization. Patients were treated with or without the EndoNaut 2D fusion imaging system (Therenva, Rennes, France) in a nonhybrid room with the same Cios Alpha mobile C-arm (Siemens, Munich, Germany). The indirect dose-area product and contrast medium volume were recorded.

Results: Between March 2018 and April 2020, 255 patients underwent endovascular femoropopliteal revascularization with (n = 124) or without (n = 131) 2D fusion imaging. The volume of injected contrast medium (34.7 ± 13.8 mL vs 51.3 ± 26.7 mL; $P < .001$) and dose-area product (8.9 ± 9.9 Gy/cm^2 vs 13.5 ± 14.0 Gy/cm^2; $P = .003$) were significantly lower for the 2D fusion imaging group than for the control group. A subgroup analysis of complex (TransAtlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease C/D) lesions showed similar results. Stratification of the fusion imaging group into three subgroups, according to the procedure dates, showed no effect of a potential learning curve on the operative parameters.

Conclusions: The results from the present study showed a significant reduction in the contrast volume and radiation dose for endovascular treatment of PAD when applying 2D fusion imaging technology. Overall, a reduction of >30% was observed for both operative parameters, without excessive training requirements, highlighting the potential benefits of using 2D fusion imaging when performing endovascular revascularization for PAD. (J Vasc Surg 2022;75:651-9.)

Keywords: Artificial intelligence; Contrast agent; Flat panel; Fusion imaging; Hybrid room; Peripheral artery disease; Radiation protection

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Podimetrics SmartMat

remote temperature monitoring

Monitor foot temperature over time

Alert to early signs of inflammation

Rapidly respond to help reduce inflammation before complications start

Support patients and their providers, every step of the way

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Elastomeric Surgical Sealant

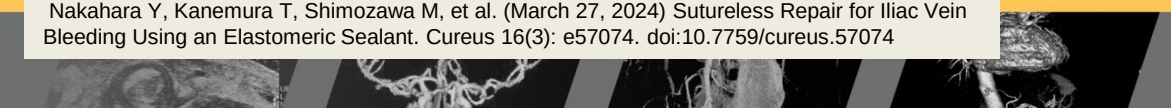
- Hydrofit (Aquabrid) is a sealant comprised of reactive isocyanate groups and a fluorine-containing polyether polyurethane prepolymer
- It reacts rapidly with tissue water to form a robust adhesive film
- Hydrofit thrives in moist environments and boasts precise application thanks to its viscosity, preventing unwanted spread into vessels

Sutureless repair for iliac vein bleeding using an elastomeric sealant

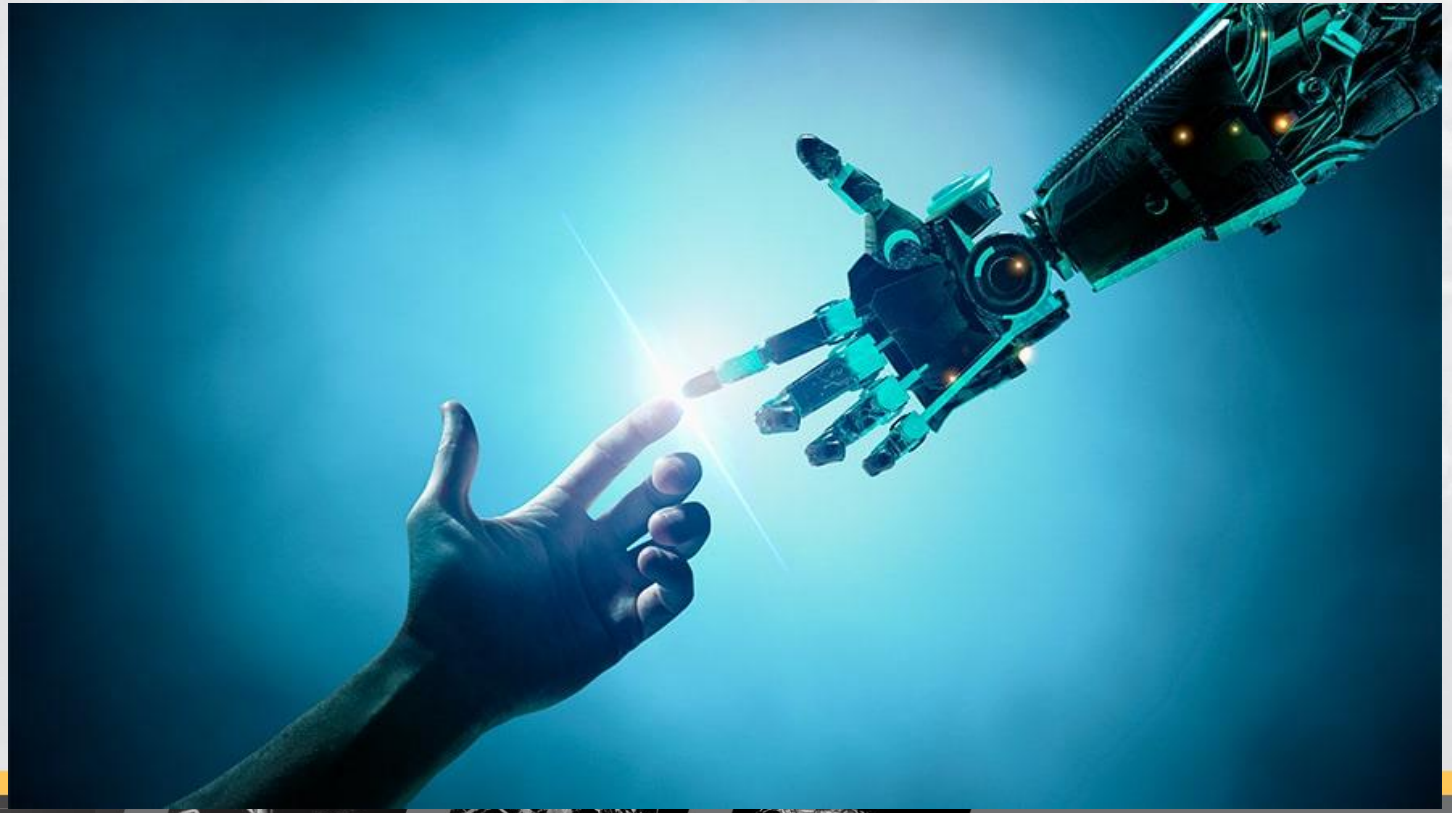
Yoshinori Nakahara

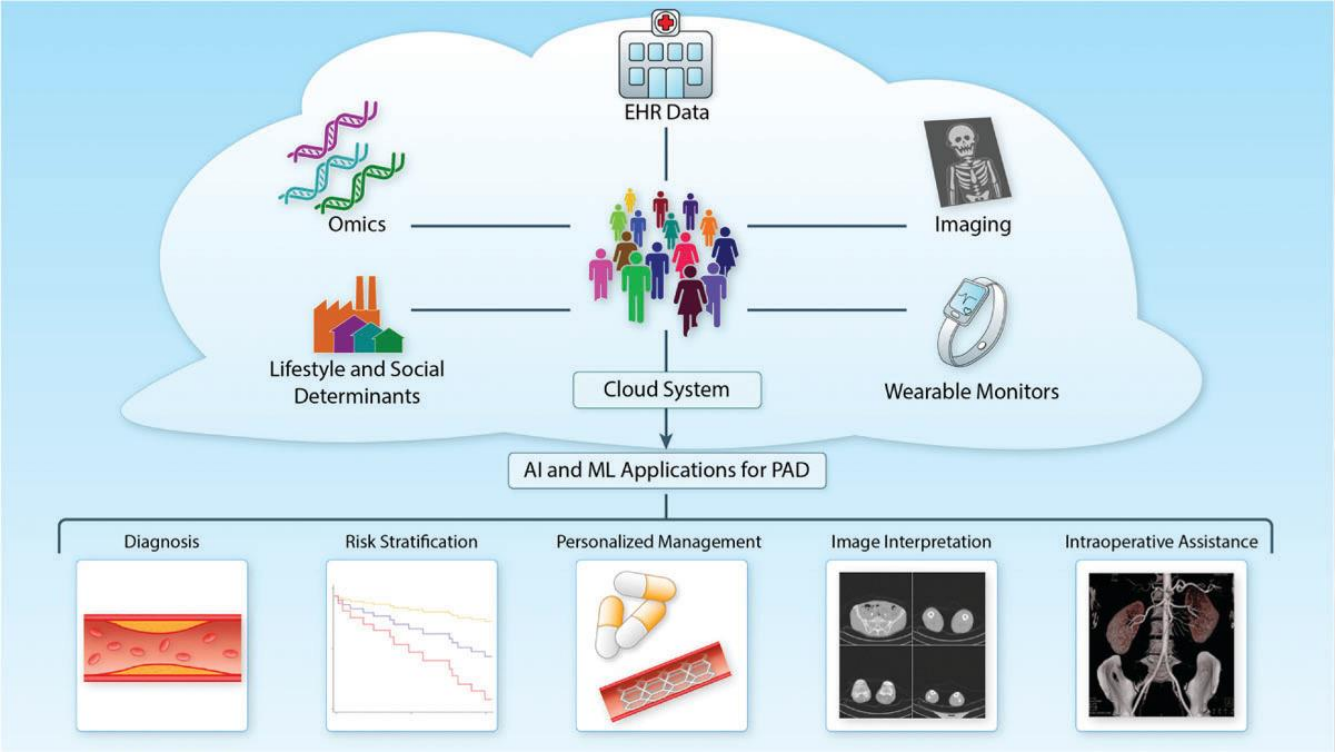
Department of Cardiovascular surgery,
IMS Katsushika Heart Center

Nakahara Y, Kanemura T, Shimozawa M, et al. (March 27, 2024) Sutureless Repair for Iliac Vein Bleeding Using an Elastomeric Sealant. Cureus 16(3): e57074. doi:10.7759/cureus.57074

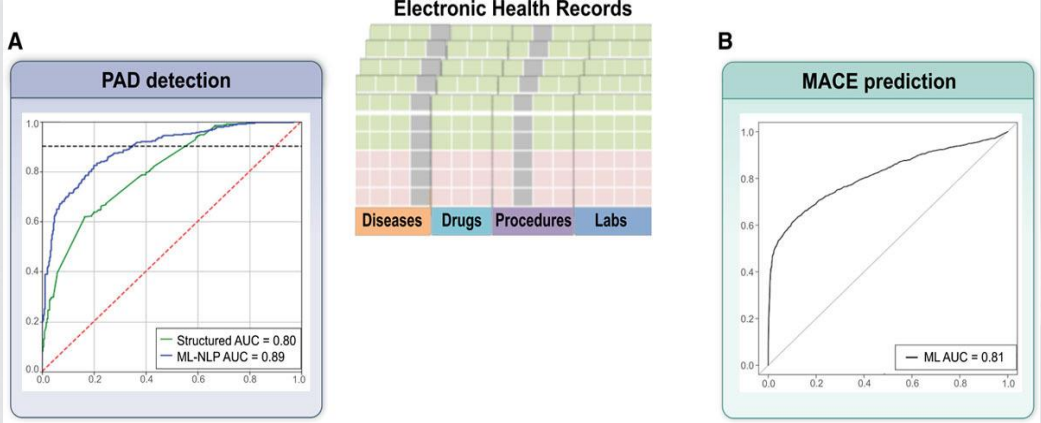


Artificial Intelligence in PAD



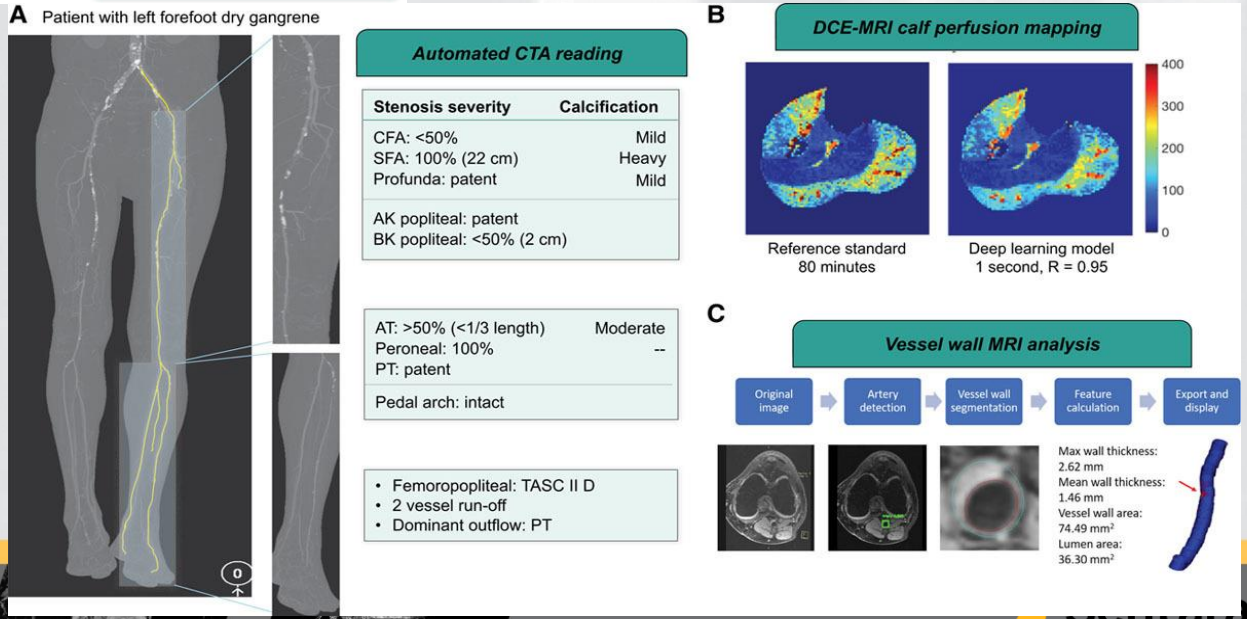


Alyssa M. Flores. Circulation Research. Leveraging Machine Learning and Artificial Intelligence to Improve Peripheral Artery Disease Detection, Treatment, and Outcomes, Volume: 128, Issue: 12, Pages: 1833-1850, DOI: (10.1161/CIRCRESAHA.121.318224)



When applied to the electronic health record (HER), machine learning models reliably identify peripheral artery disease (PAD) and predict future cardiovascular events

Computer vision for peripheral artery disease imaging interpretation



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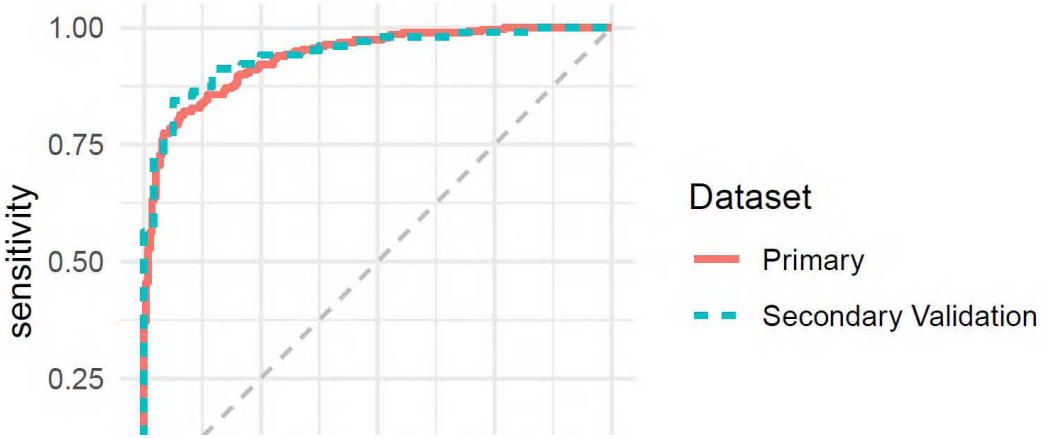
Volume 79, Issue 9, suppl A

Vascular Medicine

ARTIFICIAL INTELLIGENCE FOR PERIPHERAL ARTERY DISEASE DETECTION USING ARTERIAL DOPPLER WAVEFORM ANALYSIS

- 1,941 patients with PAD and 1,491 without PAD were included
- Deep neural networks were trained on resting posterior tibial arterial Doppler waveforms to predict normal (>0.9) or PAD (≤0.9) post-exercise ABI
- The predictive model identified PAD with an AUC 0.94 (CI = 0.92-0.96), sensitivity 0.83 specificity 0.88, accuracy 0.85 and positive predictive value (PPV) 0.90



An artificial intelligence enabled analysis of a resting Doppler arterial waveform permits identification of PAD at a clinically relevant performance level

Artificial intelligence of arterial Doppler waveforms to predict major adverse outcomes among patients with diabetes mellitus

Robert D. McBane II, MD,[a,b] Dennis H. Murphree, PhD,[c] David Liedl, RN,[a] Francisco Lopez-Jimenez, MD, MSc, MBA,[b,c] Adelaide Arruda-Olson, MD, PhD,[b] Christopher G. Scott, MS,[d] Naresh Prodduturi, MS,[d] Steve E. Nowakowski, MS,[e] Thom W. Rooke, MD,[a,b] Ana I. Casanegra, MD,[a,b] Waldemar E. Wysokinski, MD,[a,b] Damon E. Houghton, MD,[a,b] Kalpana Muthusamy, MBBS, MD,[f] *and* Paul W. Wennberg, MD,[a,b] *Rochester, Minnesota*

ABSTRACT

Objective: Patients with diabetes mellitus (DM) are at increased risk for peripheral artery disease (PAD) and its complications. Arterial calcification and non-compressibility may limit test interpretation in this population. Developing tools capable of identifying PAD and predicting major adverse cardiac event (MACE) and limb event (MALE) outcomes among patients with DM would be clinically useful. Deep neural network analysis of resting Doppler arterial waveforms was used to detect PAD among patients with DM and to identify those at greatest risk for major adverse outcome events.

Methods: Consecutive patients with DM undergoing lower limb arterial testing (April 1, 2015-December 30, 2020) were randomly allocated to training, validation, and testing subsets (60%, 20%, and 20%). Deep neural networks were trained on resting posterior tibial arterial Doppler waveforms to predict all-cause mortality, MACE, and MALE at 5 years using quartiles based on the distribution of the prediction score.

Results: Among 11,384 total patients, 4211 patients with DM met study criteria (mean age, 68.6 ± 11.9 years; 32.0% female). After allocating the training and validation subsets, the final test subset included 856 patients. During follow-up, there were 262 deaths, 319 MACE, and 99 MALE. Patients in the upper quartile of prediction based on deep neural network analysis of the posterior tibial artery waveform provided independent prediction of death (hazard ratio [HR], 3.58; 95% confidence interval [CI], 2.31-5.56), MACE (HR, 2.06; 95% CI, 1.49-2.91), and MALE (HR, 13.50; 95% CI, 5.83-31.27).

Conclusions: An artificial intelligence enabled analysis of a resting Doppler arterial waveform permits identification of major adverse outcomes including all-cause mortality, MACE, and MALE among patients with DM. (J Vasc Surg 2024;■:1-9.)

Keywords: Artificial intelligence; Diabetes mellitus; Doppler waveform; Major adverse cardiac events; Major adverse limb events; Peripheral artery disease

JVS Journal of Vascular Surgery

Applications of artificial intelligence for patients with peripheral artery disease

Fabien Lareyre, MD, PhD,[a,b] Christian-Alexander Behrendt, MD, PhD,[c] Arindam Chaudhuri, MD,[d] Regent Lee, MD, PhD,[e] Marion Carrier, PhD,[f] Cédric Adam, PhD,[f] Cong Duy Lê, MD,[a,b] *and* Juliette Raffort, MD, PhD,[b,g,h] *Antibes, and Nice, France; Hamburg, Germany; Bedford, and Oxford, UK; Paris, and Côte d'Azur, France*

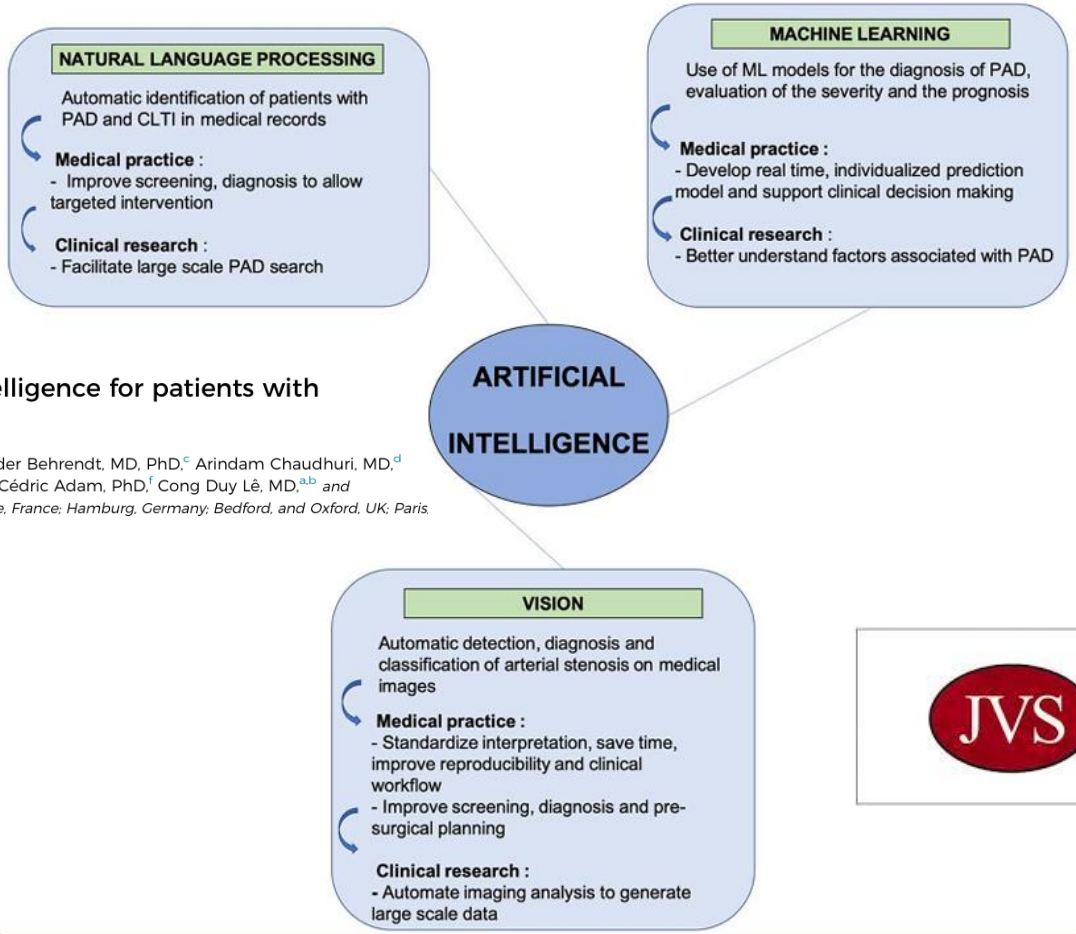


Fig. Main applications of artificial intelligence (AI) for patients with PAD. *CLTI*, Critical limb-threatening ischemia; *ML*, machine learning; *PAD*, peripheral artery disease.

JVS Journal of Vascular Surgery

Developing Technology

Table 1

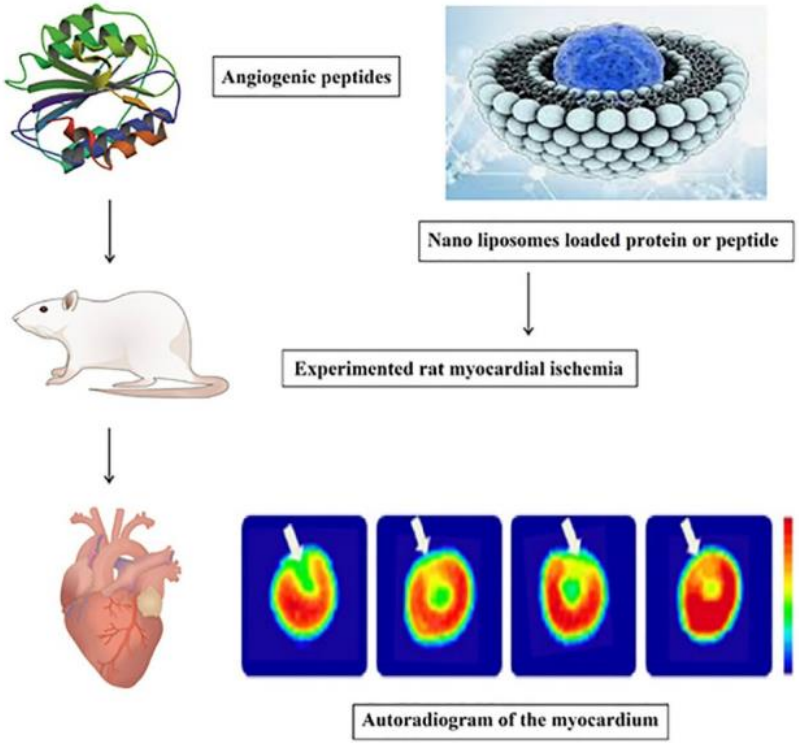
Randomized controlled trials of stem cells for critical limb ischemia

Arabzadeh A, Faghfuri E, Razi Soofiyani S, Dalir Abdolahinia E, Siapush S, Nejati-Koshki K, Shahrami B, Asghariazar V, Pahlavan Y. Current and Novel Emerging Medical Therapies for Peripheral Artery Disease: A Literature Review. Adv Pharm Bull. 2023 Mar;13(2):259-268. doi: 10.34172/apb.2023.025. Epub 2022 Apr 4. PMID: 37342373; PMCID: PMC10278215.

N	Cell type(s)	Route	Outcomes associated with treatment	Ref
41	BMCs	IM/ IA	Improved TcO2, pain scale, EQ5D and significant reduction in the Rutherford category of CLI (no differences among functional parameters in patients undergoing IM versus IA delivery	48
28	BM-MSC	IM	Increase in ABPI & ankle pressure, improved rest pain	49
81	BMSC	sham injection/ IA	Reduction in ulcer size and improvement in pain-free walking distance	50
62	BMCs	local IM/IA	Improved TcpO2, pain scale, quality of life, wound healing, IA and Rutherford category	51
48	BMAC	IM	Improved pain rest	52
40	G-CSF mobilized peripheral blood (PBMNCs)	SQ	Improved pain score, amputation rates, collateral vessel development, and number of healed limb ulcers	53

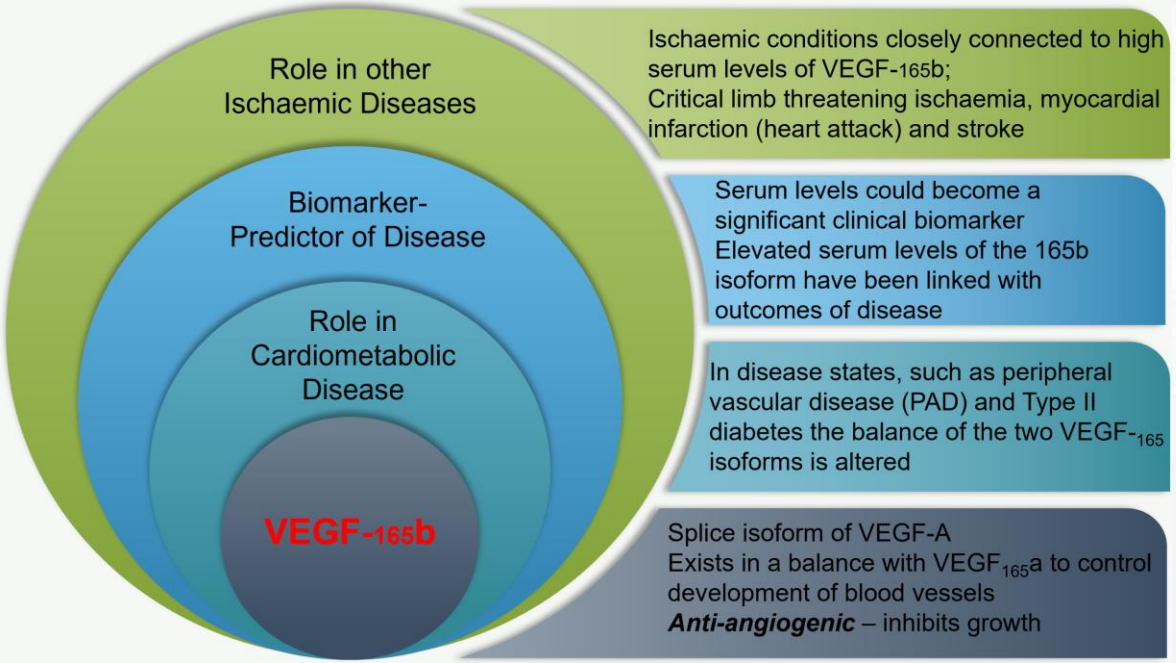
BMCs, bone marrow cells; TcO2, total carbon dioxide; TRC, tissue repair cell; EQ5D, quality-of-life questionnaire; CLI, critical limb ischemia; IA, intra-arterial; IM, intramuscular; BM-MSC, Bone marrow derived mesenchymal stem cells; ABPI, ankle brachial pressure index; PBMNC, peripheral blood mononuclear cells; GCSF, granulocyte colony-stimulating factor; SQ, subcutaneous injection.

Nano-technology and nanoparticles (NPs)



The therapeutic effects of angiogenic peptides loaded in PEGylated Nano liposomes improve perfusion defects. Reperfusion was administered after 30 minutes of rat myocardial ischemia followed by treatment with angiogenic peptides.

IsomAb



- IsomAb is developing isoform specific disease-modifying antibodies and it has identified, ISM-001 which specifically inhibits the VEGF-A165b isoform of Vascular Endothelial Growth Factor-A (VEGF-A, the evidence shows reducing serum levels of VEGF-A165b is key to ensuring new blood vessel formation in patients with ischemic disease.
- Novel approach to regulate the control switch of angiogenesis – the pro- and anti-angiogenesis VEGF balance

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Conclusions

- Mechanical technology is often merging with local drug delivery for PAD
- Imaging is undergoing a revolution for diagnosis and treatment of PAD
- Upcoming advances will involve AI, nanotechnology and promoting angiogenesis at the subcellular level