


New advanced management of chronic leg ulcer






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Role of Stem cells ??



Stem cell

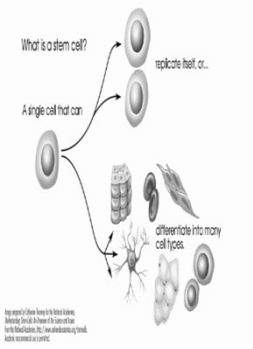
- Potential to develop into many different cell types
- Internal repair system
- Dividing essentially without limit

What's a stem cell?

A single cell that can

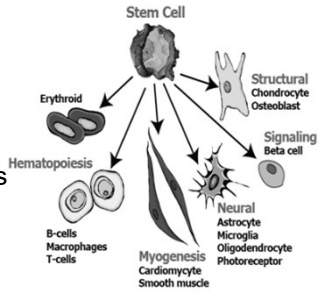
replicate itself, or...

differentiate into many cell types.



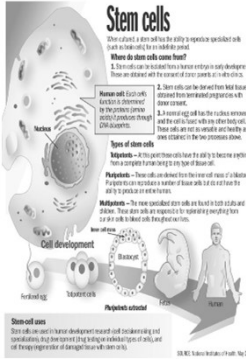
Stem cells

- Serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive



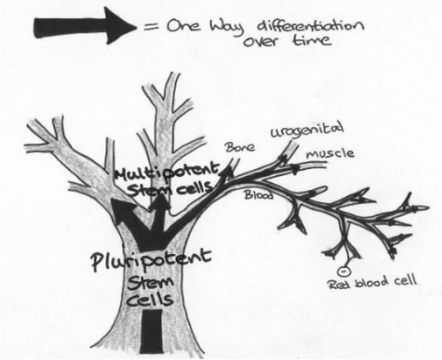
Differentiation potential of Stem cells

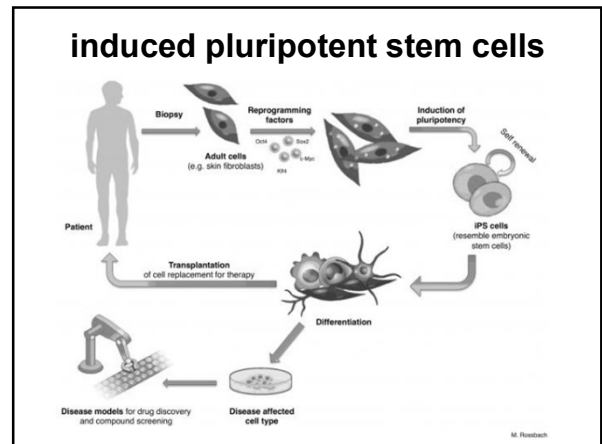
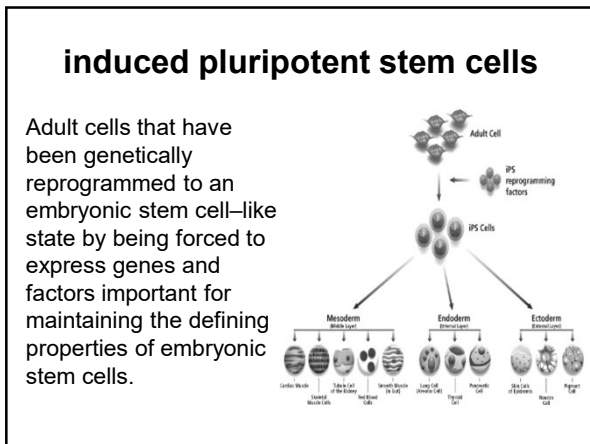
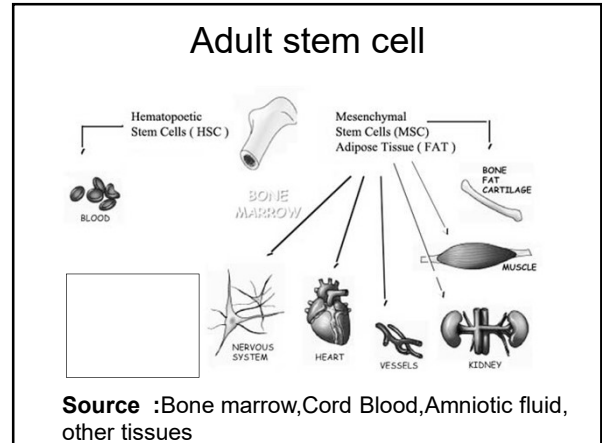
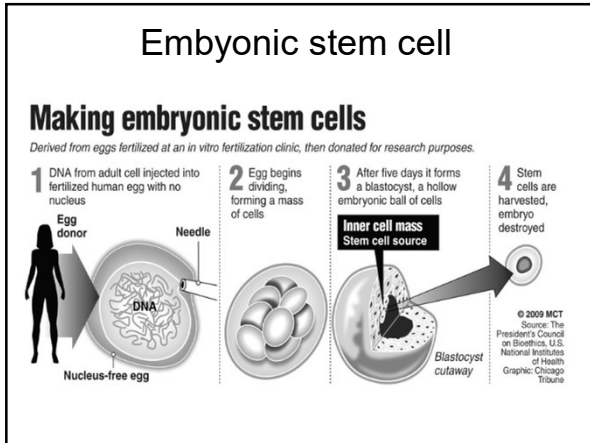
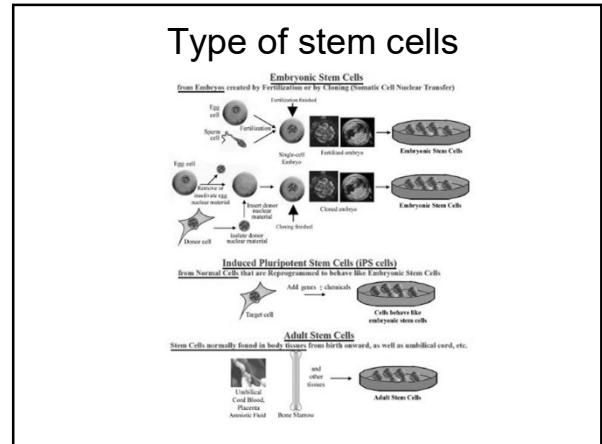
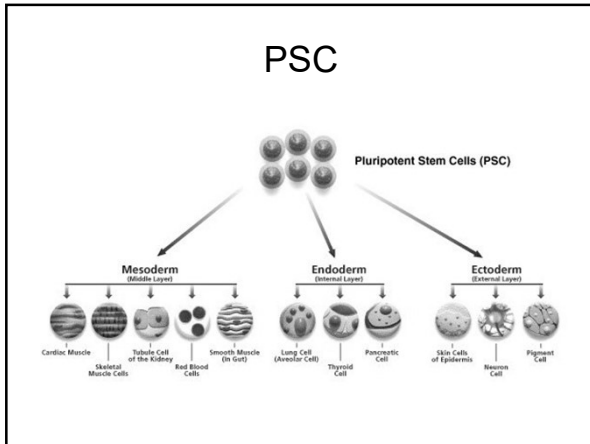
- Totipotent :
 - Generate all cells and tissues
 - Can construct a complete entire human
- Pluripotent :
 - Can differentiate into all 3 germ layer: : endoderm,mesoderm and ectoderm
- Multipotent :
 - Can differentiate into a number of cells ,but only those of closely related family of cells
- Unipotent :
 - Can produce only one cell type

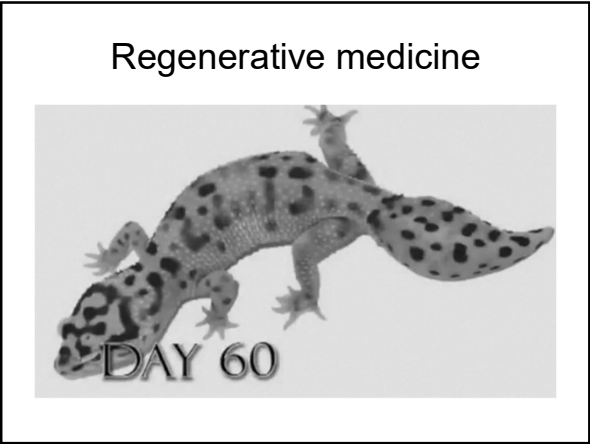
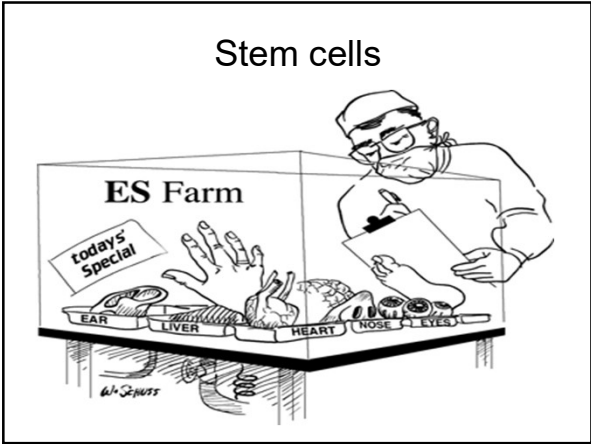
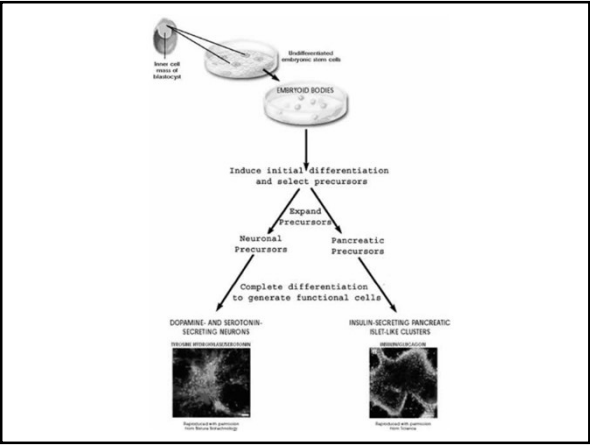
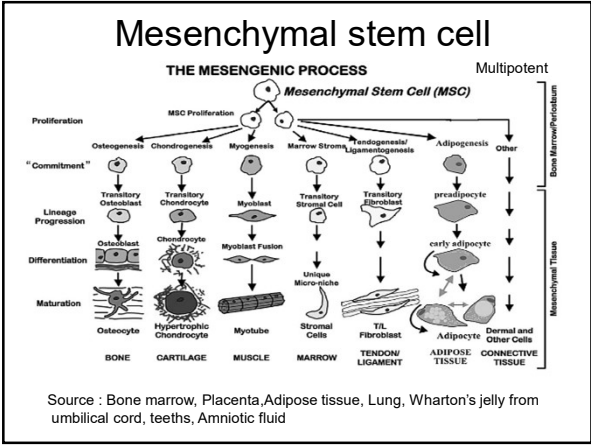
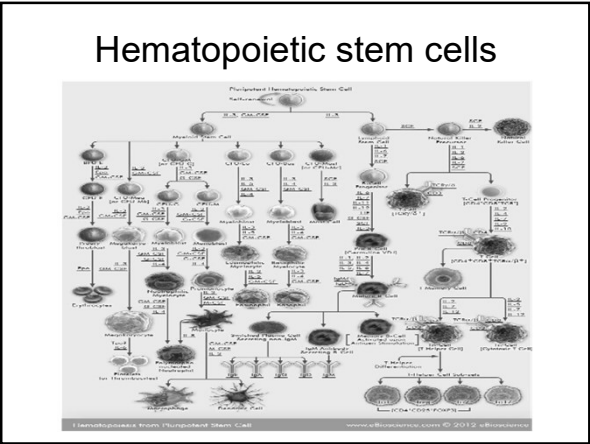
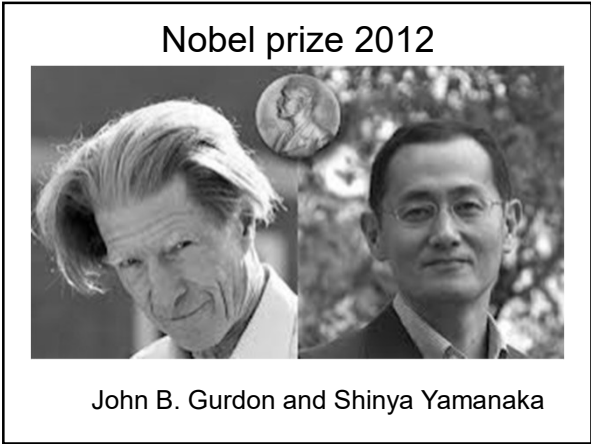


Differentiation potential of Stem cells

➔ = One Way differentiation over time



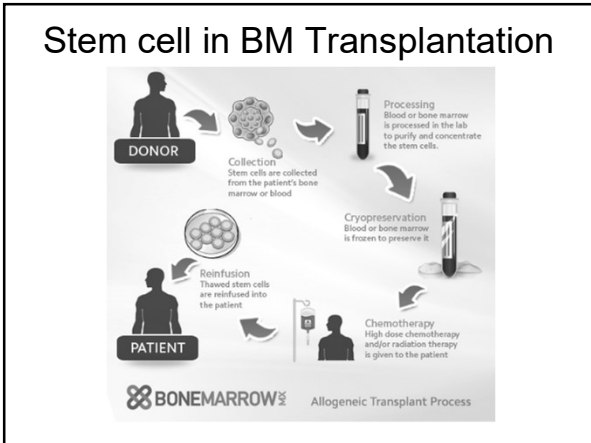




Clinical Application

- การนำสเต็มเซลล์มาใช้รักษาโรคมะเร็ง 3 แนวทาง
- 1. ปลูกถ่ายสเต็มเซลล์เข้าไปแทนที่สเต็มเซลล์ที่ไม่ทำงานในอวัยวะที่ต้องการสร้างเซลล์อย่างสม่ำเสมอ
 - Leukemia, Lymphoma
 - 2. การนำเซลล์ไปสร้างเซลล์ชนิดจำเพาะก่อนนำมาปลูกถ่าย
 - Parkinson, DM
 - 3. การปลูกเซลล์หวังให้เกิดการกระตุ้นการซ่อมแซมอวัยวะต่างๆในร่างกาย
 - Cytokine

- ### แพทยสภา
- โรคทางระบบโลหิตวิทยา 5 โรค คือ
 - 1. โรคมะเร็งโลหิตขาว (Leukemia)
 - 2. โรคมะเร็งต่อมน้ำเหลือง (Lymphoma)
 - 3. โรคไขกระดูกฝ่อ (Aplastic anemia)
 - 4. โรคมะเร็งมัลติเพิลไมyeloma (Multiple myeloma)
 - 5. โรคโลหิตจางพันธุกรรมธาลัสซีเมีย (Thalassemia)



หน้า ๕๖
เริ่ม ๑๒๑ ตอนพิเศษ ๓ ง ราชกิจจานุเบกษา ๑๑ มกราคม ๒๕๕๑

ข้อบังคับแพทยสภา
ว่าด้วยการรักษาจริยธรรมแห่งวิชาชีพเวชกรรม
เรื่อง การปลูกถ่ายเซลล์ต้นกำเนิดเพื่อการรักษา พ.ศ. ๒๕๕๒

ออกตามความในมาตรา ๒๑ (๓) (ข) มาตรา ๒๕ แห่งพระราชบัญญัติวิชาชีพเวชกรรม พ.ศ. ๒๕๒๕ ด้วยความเห็นชอบของสภานายกพิเศษ คณะกรรมการแพทยสภาจึงออกข้อบังคับไว้ดังต่อไปนี้

ข้อ ๑ ใบข้อบังคับนี้

“การปลูกถ่ายเซลล์ต้นกำเนิดเพื่อการรักษา” หมายความว่า การประกอบวิชาชีพเวชกรรมที่เกี่ยวข้องกับการปลูกถ่ายเซลล์ต้นกำเนิดซึ่งเป็นเซลล์ต้นกำเนิด หรือ โปรเจเนเตอร์เซลล์ (progenitor cell) หรือเซลล์ที่เจริญมาจากภาวะเสถียรเซลล์ต้นกำเนิด เพื่อการรักษาโรคในคน แต่ไม่หมายความรวมถึงการปลูกถ่ายเซลล์ต้นกำเนิดเม็ดโลหิตในการรักษาโรคโลหิตวิทยา จึงเป็นไปตามข้อบังคับว่าด้วยการนั้น”

ข้อ ๒ การปลูกถ่ายเซลล์ต้นกำเนิดเพื่อการรักษาจะกระทำได้ในกรณีดังต่อไปนี้

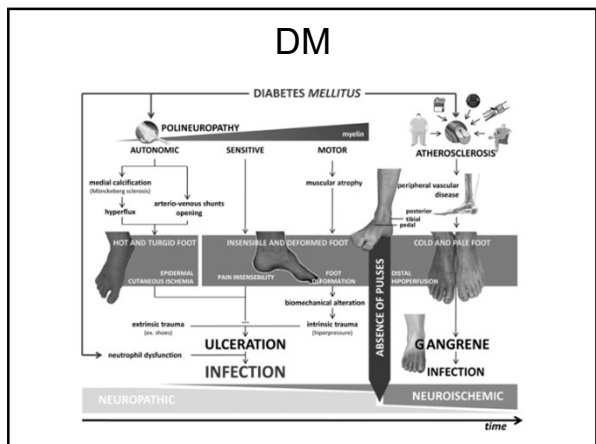
๒.๑ เป็นการปลูกถ่ายเซลล์ต้นกำเนิดเพื่อการรักษาที่มีกรทำวิจัยมาแล้ว จนเป็นที่ยอมรับว่าเป็นวิธีการรักษาที่เป็นมาตรฐานและแพทยสภามั่นใจชอบ

๒.๒ ในกรณีที่เป็นการปลูกถ่ายเซลล์ต้นกำเนิดเพื่อการรักษาโรคในคนที่ตั้งอยู่ในระหว่างการทำวิจัย โครงการวิจัยนั้นต้องได้รับการอนุมัติจาก

๒.๒.๑ คณะกรรมการจริยธรรมการทำวิจัยในคนของสถาบันที่ผู้ทำวิจัยสังกัด

และ

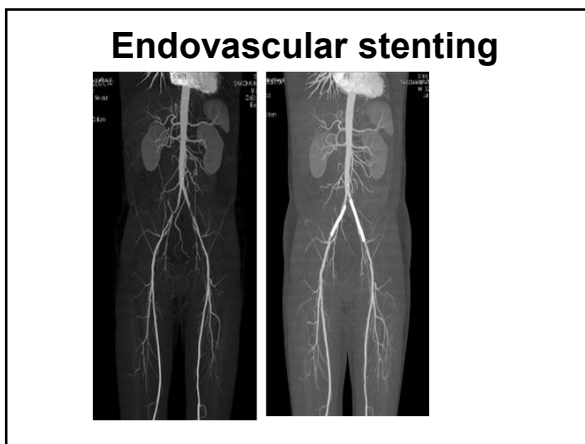
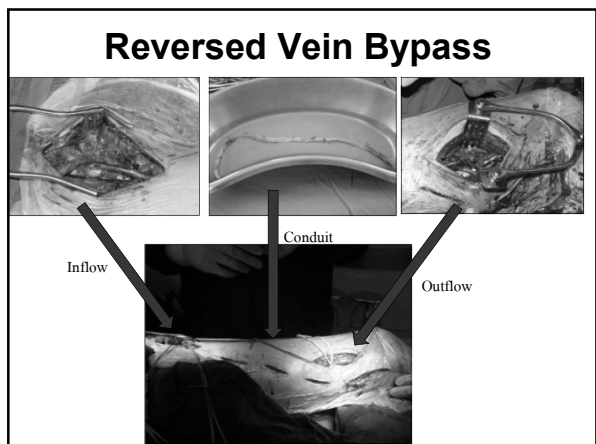
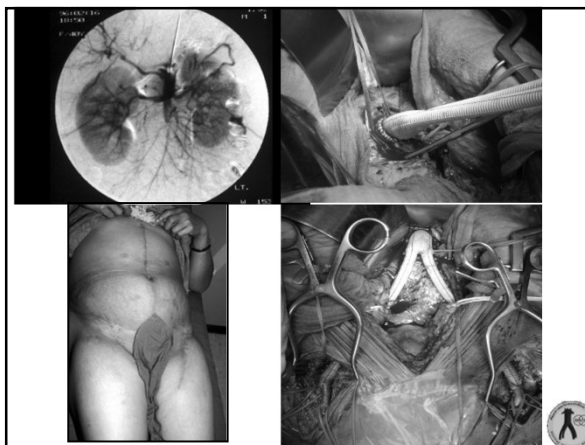
๒.๒.๒ คณะกรรมการวิชาการและจริยธรรมการทำวิจัยในคนด้านเซลล์ต้นกำเนิดของแพทยสภา



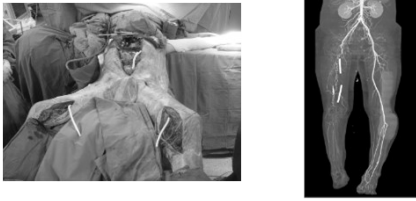
Important of DFU

- 15 to 20% of all individuals with diabetes
- The 5 year re-ulceration 70%
- Chance of losing the remaining limb within 3 years 50%
- The 5-year mortality rate for bilateral amputees is high

Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD005082.



No-option CLI

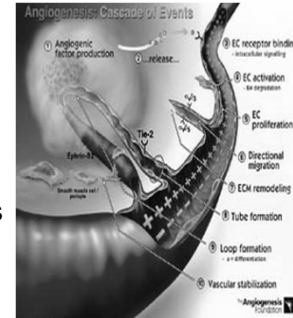


- Despite these advances in surgical and endovascular techniques, approximately 20% to 40% of patients with CLI will not be candidates for either of these approaches

Semin Vasc Surg 1999;12:142-7.

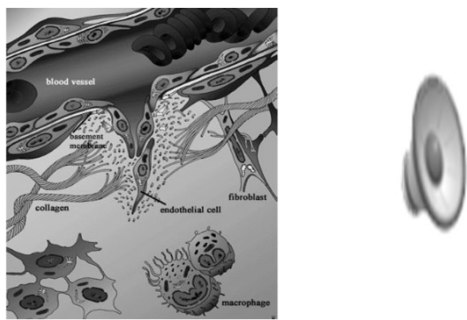
Mechanisms of new blood vessel growth in adults

- Angiogenesis
- Arteriogenesis
- Vasculogenesis

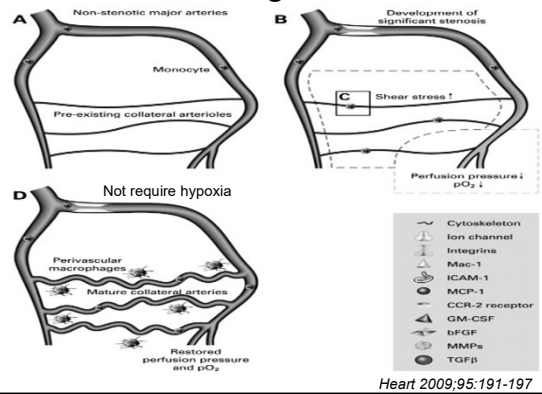


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Angiogenesis

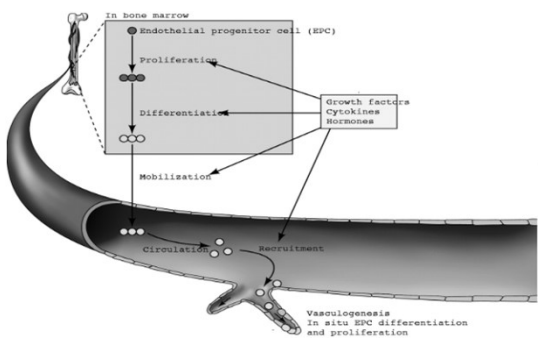


Arteriogenesis



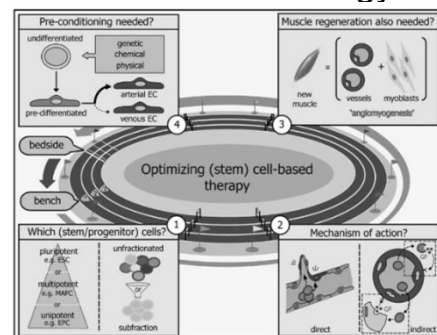
Heart 2009;95:191-197

Vasculogenesis



Physiology February 2005 vol. 20 no. 1 36-42

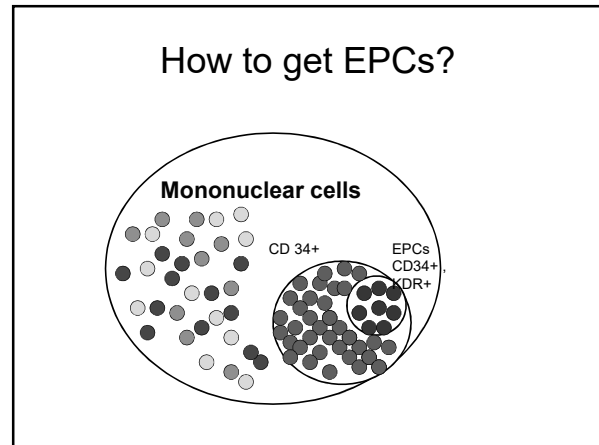
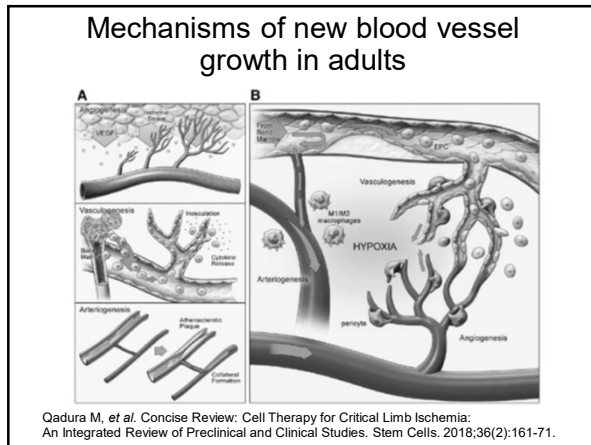
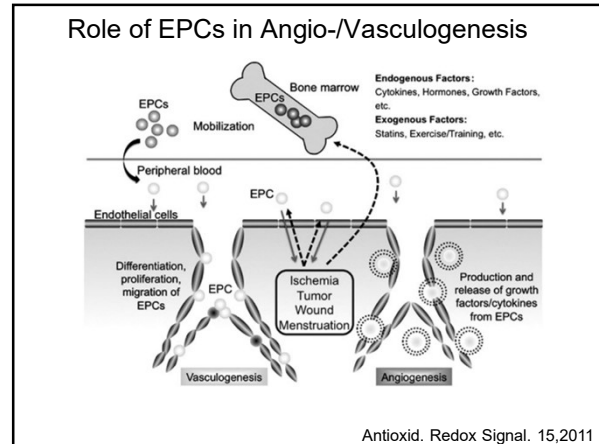
Cell-based strategy



J Mol Med (2009) 87:3-16

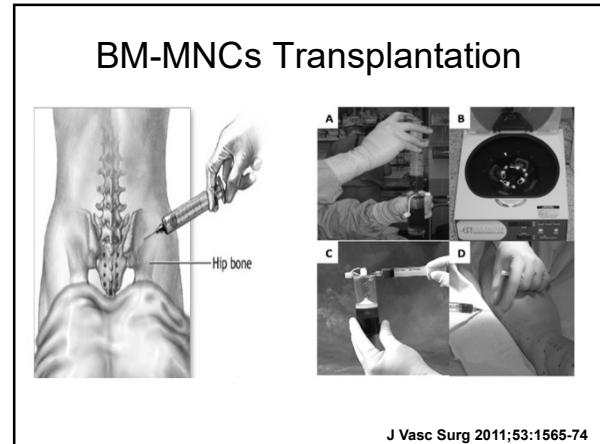
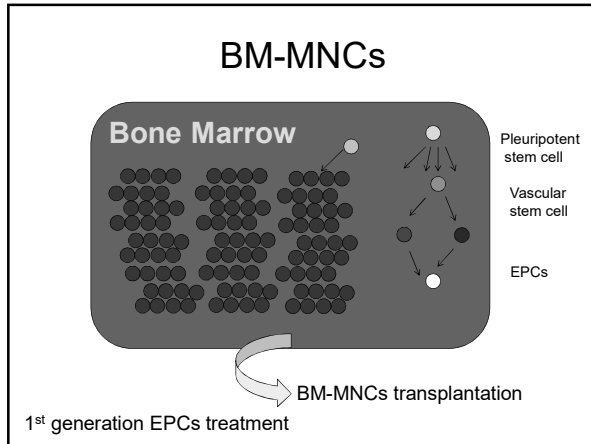
Endothelial Progenitor Cells (EPCs)

Asahara, T., et al (1997) Science 275: 964-7.



G1-EPC Tx	G2-EPC Tx	G3-EPC Tx	G4 EPC Tx
BM/PB Mononuclear Cell Transplantation	CD34/CD133+ cell Transplantation	Cultured CD34/CD133+ cells Transplantation	Cultured Mononuclear Cells Transplantation
↓	GCSF+ apheresis+ magnetic isolation	↓	↓
Mononuclear Cell Isolation	EPC Isolation following in vivo Expansion	Quantity and Quality Control of EPCs	Quantity and Quality Control of EPCs and Lympho-Monocytes
↓	↓	↓	↓
Angiogenesis (+) Vasculogenesis (+/-)	Angiogenesis (+) Vasculogenesis (+) Anti-inflammation (+) Anti-fibrosis (+)	Angiogenesis (++) Vasculogenesis (++) Anti-inflammation (+) Anti-fibrosis (++)	Angiogenesis (++) Vasculogenesis (++) Anti-inflammation (++) Anti-fibrosis (++)
Simple Technics Economical Medicine	Complicated Technics Not Economical Medicine	Complicated Technics Not Economical Medicine Need Culture Regulations	Simple Technics Economical Medicine Need Culture Regulations
Developed Clinical Treatment	Physician-Lead Clinical Research	Planning Clinical Trial	Planning Clinical Trial

- ### 1st generation of EPCs treatment
- Direct Intramuscular Injection of Bone Marrow Mononuclear Cells (BM-MNC)
 - Direct Intramuscular Injection of Cytokine Mobilized and Apheresed Mononuclear Cells (PB-MNC)



Therapeutic Angiogenesis using Cell Transplantation(TACT) trial

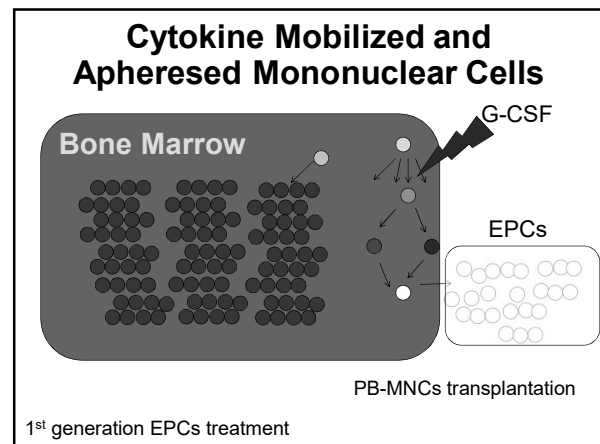
Variable (mean (SD))	Group A (unmasked, n=25)				Group B (randomised, double-blind, n=20)			
	Change from baseline		Difference (95% CI)	p	Change from baseline		Difference (95% CI)	p
	BM-MNC	Saline			BM-MNC	PB-MNC		
ABI								
4 weeks	0.13 (0.1)	0.01 (0.02)	0.12 (0.09 to 0.16)	<0.0001	0.1 (0.05)	0.02 (0.02)	0.09 (0.06 to 0.11)	<0.0001
24 weeks	0.11 (0.1)	-0.01 (0.02)	0.11 (0.07 to 0.15)	<0.0001	0.1 (0.05)	0.02 (0.03)	0.09 (0.06 to 0.12)	<0.0001
ToD ₅₀ (mm Hg)								
4 weeks	19 (12)	0.5 (1.4)	17 (12 to 22)	<0.0001	17.4 (9.5)	4.8 (3.5)	13 (8 to 17)	<0.0001
24 weeks	18 (11)	1.1 (2.6)	16 (11 to 21)	<0.0001	16.6 (9.9)	4.8 (2.8)	12 (7 to 16)	<0.0001
Rest pain (+4 to 0)*								
4 weeks	-2.6 (1.1)	-0.23 (0.7)	-2.3 (-3 to -1.6)	<0.0001	-2.2 (1.1)	-1.4 (0.7)	-0.85 (-1.6 to -0.12)	0.025
24 weeks	-2.6 (0.9)	+0.23 (0.7)	-2.8 (-3 to -2)	<0.0001	-2.4 (0.8)	-1.4 (1.1)	-1.0 (-1.7 to -0.32)	0.0061
New collateral (+3 to 0)†								
4 weeks	1 (1)	0 (0)	1 (0.6 to 1.5)	<0.0001	1.1 (1)	0.3 (0.6)	0.85 (0.3 to 1.4)	0.0025
Pain-free walking time (min)								
4 weeks	3.4 (2.7 to 4.2)	<0.0001	1.2 (0.7 to 1.7)	0.0001
24 weeks	3.5 (3.0 to 4.2)	<0.0001	1.4 (0.9 to 1.8)	<0.0001

Lancet. 2002 Aug 10;360(9331):427-35

Bone marrow-derived mononuclear cells

	Study level	# Subjects	ABI	TcPO ₂	Pain	Amp.	±†
2002 Teneishi-Yuyama (59)	1b	45, PAD, DM	↑	↑	↓	↓	+
2002 Esato (128)	4	8, PAD, TAO	↑	→	↓	↓	+
2004 Saigusa (128)	4	8, PAD, DM	↑	↑	↓	↓	+
2004 Higashi (130)	4	8, PAD	↑	↑	↓	↓	+
2004 Miyamoto (131)	4	12, PAD, CLI	↑	→	↓	→	+
2005 Nizankowski (132)	4	10, TAO, CLI	↑	↑	↓	↓	+
2006 Darbu (133)	1b	28, TAO	↑	↑	↓	↓	+
2006 Bartsch (134)	4	10, PAD, CLI	↑	↑	→	→	+
2006 Miyamoto (138)	4	8, TAO, CLI	→	→	↓	→	+
2007 Kajiguchi (135)	4	7, CLI, TAO	→	(↑)	↓	?	±†
2007 Huang (136)	2	74, PAD, DM	↑	↑	↓	→	+
2007 Hernandez (137)	4	12, PAD, DM	↑	↑	↓	↓	+
2008 Gu (138)	4	16, PAD/CLI	↑	↑	↓	↓	+
2008 Chochola (139)	4	28, CLI, PAD	↑	↑	↓	↓	+
2008 Wester (140)		8, CLI	→	→	↓	↓	+
2008 Van Tongeren (141)	4	27, PAD	↑	↑	↓	?	+
2008 De Vriese (142)	4	16, PAD	→	↑	↓	?	±†
2009 Amann (143)	4	51, CLI	↑	↑	↓	↓	+
2009 Prohaska (150)	4	37, CLI, DM	↑	↑	↓	→	+

Thromb Haemost 2010; 103: 696-709

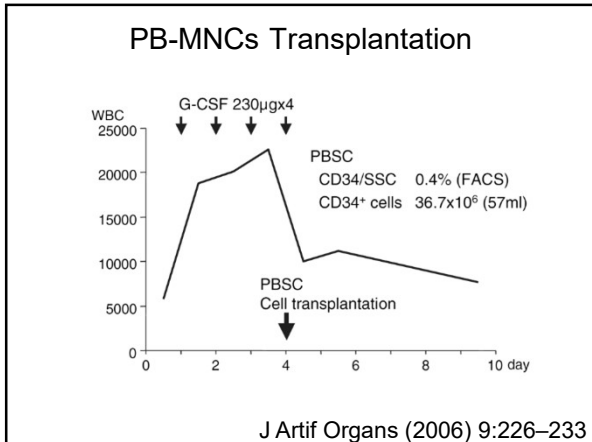
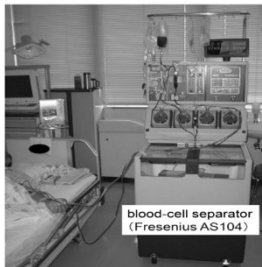


Cytokine Mobilized and Apheresed Mononuclear Cells

After 4-5 days of G-CSF 5-10 µg/Kg/day SC
When the white blood cell count reached 20,000–40,000/mm³,

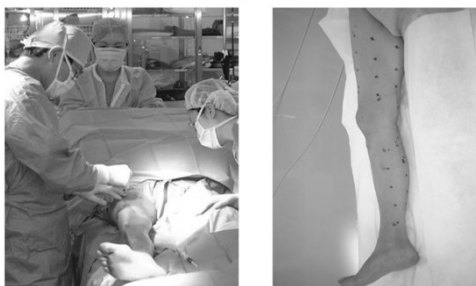
Collection of peripheral-blood mononuclear cells (PBMCs)

Ten liters of peripheral blood was processed and 180 ml of cell suspension was collected. Then further concentrated to 20ml.

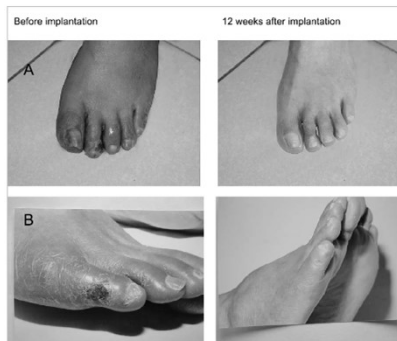


PB-MNCs IMPLANTATION

Cell Transplant (0.5ml X40 sites)



PB-MNCs Transplantation



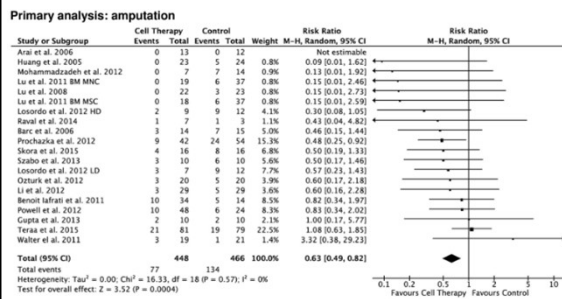
Thromb Haemost 2007; 98: 1335–1342

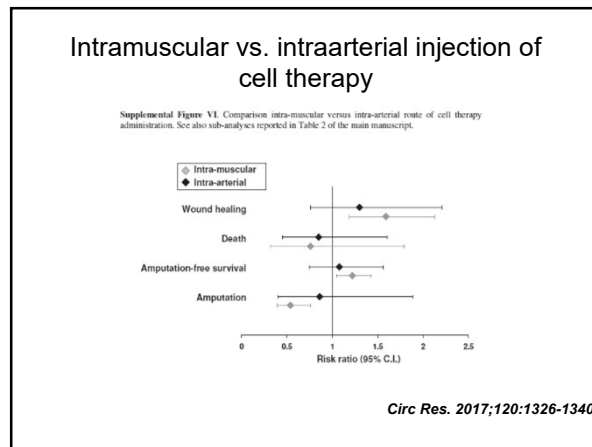
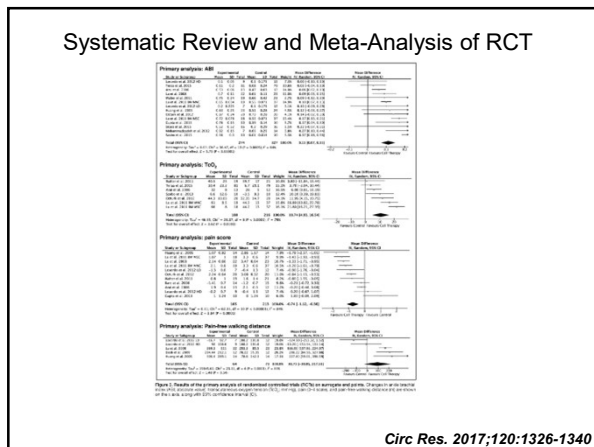
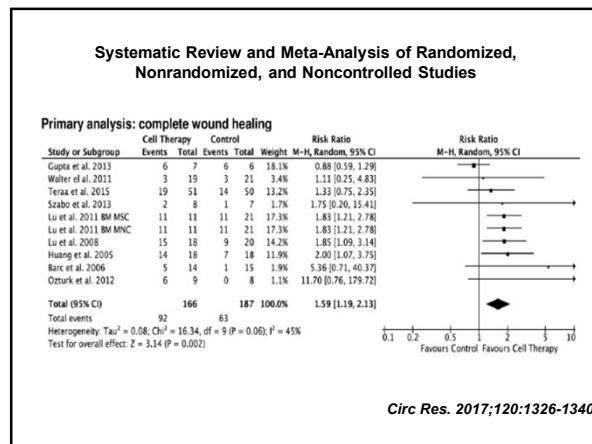
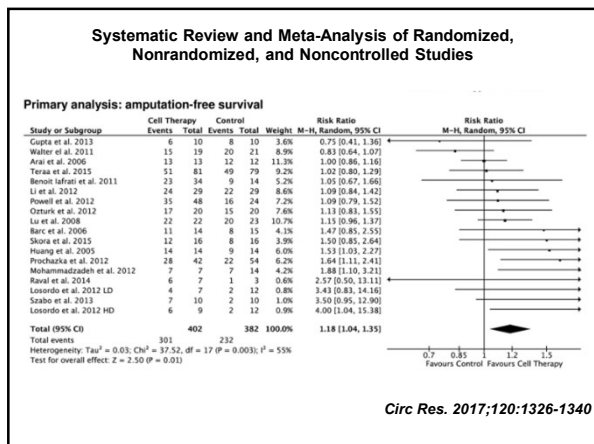
Mobilised peripheral blood mononuclear cells (PBMNC)

Study level	# Subjects	ABI	TcPO ₂	Pain	Amp.	+/-
2004 Huang (144)	4, PAD	→	↑	↓	?	+
2005 Kawamura (145)	30, PAD, CLI	↑	↑	↓	↓	+
2005 Lenk (146)	4, 7, CLI	↑	↑	↓	?	+
2005 Huang (147)	2, 28, CLI, DM	↑	↑	↓	↓	+
2005 Ishida (148)	4, 6, TAO	↑	↑	↓	?	+
2006 Kawamura (149)	4, 75, CLI	↑	↑	↓	↓	+
2007 Huang (136)	2, 76, PAD	↑	↑	↓	?	+

Thromb Haemost 2010; 103: 696–709

Systematic Review and Meta-Analysis of Randomized, Nonrandomized, and Noncontrolled Studies





Intramuscular vs. intraarterial injection of cell therapy

Table 2. Sensitivity Subanalyses

Study Design and Quality	Amputation (RR)	Amputation-Free Survival (RR)	Death (RR)	Complete Wound Healing (RR)	ABI	TO ₂ (mmHg)	Pain Score (0-4)	Pain-Free Walking Distance (m)
Nonrandomized	0.17 (0.08-0.34)	2.12 (1.49-3.03)	0.77 (0.36-1.64)	3.36 (1.13-9.99)	0.15 (0.08-0.21)	20.8 (16.4-25.2)	-2.12 (-3.64 to -0.60)	418.7 (194.3-643.1)
Randomized versus standard of care	0.47 (0.31-0.71)	1.31 (1.04-1.64)	0.69 (0.26-1.83)	2.05 (1.40-3.02)	0.12 (0.06-0.19)	8.22 (4.27-12.2)	-0.83 (-1.36 to -0.30)	178.2 (126.2-228.3)
Randomized versus placebo	0.76 (0.55-1.05)	1.10 (0.95-1.35)	0.65 (0.47-1.14)	1.39 (0.98-1.99)	0.11 (0.06-0.16)	11.6 (2.11-21)	-0.63 (-1.24 to -0.02)	-71.5 (-183.6 to 40.6)
Low risk of bias	1.00 (0.64-1.56)	0.99 (0.81-1.21)	0.66 (0.40-1.04)	1.05 (0.61-1.78)	0.09 (-0.05 to 0.22)	3.7 (-3.0 to 10.4)	1.00 (-0.09 to 2.09)	N/A
Route (RCTs)	Intramuscular: 0.54 (0.39-0.76)	Intramuscular: 1.22 (1.05-1.42)	Intramuscular: 0.76 (0.32-1.79)	Intramuscular: 1.59 (1.19-2.13)	Intramuscular: 0.12 (0.06-0.16)	Intramuscular: 13.5 (7.2-19.8)	Intramuscular: -0.74 (-1.14 to -0.33)	N/A
	Intra-arterial: 0.86 (0.40-1.88)	Intra-arterial: 1.08 (0.75-1.56)	Intra-arterial: 0.65 (0.45-1.00)	Intra-arterial: 1.30 (0.76-2.21)	Intra-arterial: 0.04 (-0.03 to 0.10)	Intra-arterial: 3.1 (-2.90 to 9.00)	Intra-arterial: -0.8 (-1.55 to -1.55)	N/A

Circ Res. 2017;120:1326-1340

Circulation

ORIGINAL ARTICLE

Effect of Repetitive Intra-Arterial Infusion of Bone Marrow Mononuclear Cells in Patients With No-Option Limb Ischemia: The Randomized, Double-Blind, Placebo-Controlled JUVENTAS Trial

Markus Treier, Ralf H. Springer, Roger C. Schlegel, Ineke C.H. Sieper, Christoph Vlachopoulos, Volker von der Gröben, Alex Algra, Ingrid Isaksson, Peter A. van der Wal, Frank J. W. van't Hof, Frank J. W. van't Hof, Marianne C. Verhaar

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Article Supplemental Materials Info & Metrics eLetters

Abstract

Background—Patients with severe limb ischemia may not be eligible for conventional revascularization. Preparing clinical trials to support that bone marrow (BM)-derived cell therapy enhances revascularization, improves tissue perfusion, and prevents amputation. The objective of this trial was to determine whether repetitive intra-arterial infusion of BM mononuclear cells (BMNCs) in patients with severe, non-revascularizable limb ischemia can prevent major amputation.

Methods and Results—The JUVENTAS trial is a randomized, double-blind, placebo-controlled clinical trial in 102 patients with severe, non-revascularizable limb ischemia. Patients were

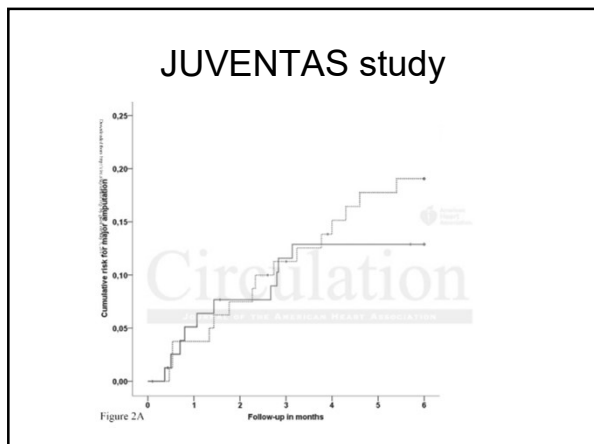
Current Issue

Circulation
July 4, 2017, Volume 135, Issue 1

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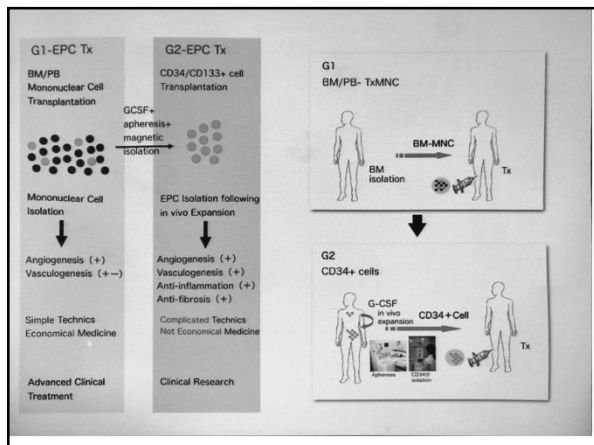
Jump to



BM-MNCs vs PB-MNCs

Study design and quality	Amputation (RR)	Amputation-Free Survival (RR)	Death (RR)	Completes Wound Healing (RR)	ABI	TcD ₂ mmHg	Pain Score (0-4)	Pain-Free Walking Distance, m
Nonrandomized	0.17 (0.08-0.34)	2.12 (1.48-3.03)	0.77 (0.36-1.64)	3.36 (1.13-9.99)	0.15 (0.08-0.21)	20.8 (16.4-25.2)	-2.12 (-3.64 to -0.60)	418.7 (194.3-643.1)
Randomized versus standard of care	0.47 (0.31-0.71)	1.31 (1.04-1.64)	0.69 (0.26-1.83)	2.05 (1.40-3.02)	0.12 (0.06-0.19)	8.22 (4.27-12.2)	-0.83 (-1.36 to -0.30)	178.2 (128.2-228.3)
Randomized versus placebo	0.76 (0.55-1.05)	1.10 (0.95-1.35)	0.85 (0.47-1.54)	1.39 (0.98-1.99)	0.11 (0.06-0.16)	11.6 (2.11-21.1)	-0.83 (-1.24 to -0.02)	-71.5 (-183.6 to 40.6)
Low risk of bias	1.00 (0.64-1.56)	0.99 (0.81-1.21)	0.86 (0.40-1.84)	1.05 (0.61-1.78)	0.09 (-0.05 to 0.22)	3.7 (-3.0 to 10.4)	1.00 (-0.09 to 2.09)	N/A
Route (RCTs)	0.54 (0.39-0.76)	1.22 (1.05-0.42)	0.76 (0.32-1.79)	1.59 (1.19-2.13)	0.12 (0.06-0.16)	13.5 (7.2-19.8)	-0.74 (-1.14 to -0.33)	N/A
Intra-arterial	0.66 (0.40-1.08)	1.08 (0.75-1.56)	0.85 (0.45-1.60)	1.30 (0.76-2.21)	0.04 (-0.03 to 0.13)	-3.1 (-2.90 to 9.00)	-0.8 (-1.55 to -1.55)	N/A
Cell type (RCTs)	BM-MNCs 0.68 (0.46-1.01)	1.11 (0.93-1.32)	0.83 (0.46-1.49)	1.66 (1.20-2.29)	0.09 (0.04-0.13)	7.57 (0.66-14.5)	-0.75 (-1.40 to -0.09)	N/A
BM-MSCs	0.43 (0.11-1.79)	1.00 (0.83-1.57)	0.90 (0.27-3.08)	1.42 (0.82-2.46)	0.14 (0.06-0.20)	21.9 (8.2-37.6)	-0.59 (-1.43 to 0.24)	173.5 (121.1-225.9)
PB-MNCs	0.42 (0.23-0.78)	1.02 (1.11-2.34)	0.91 (0.12-6.74)	3.22 (0.57-18.2)	0.11 (0.02-0.21)	12.0 (4.2-19.8)	-0.85 (-1.50 to -0.36)	N/A

Circ Res. 2017;120:1326-1340



- ### At Siriraj Hospital
- Direct Intramuscular Injection of Cytokine Mobilized and Apheresed Mononuclear Cells (PBMNC)
 - Pilot Study (under Thai Medical Association)
 - 8 cases



- ### Case no.1
-
- Female 70 year old.
 - Rest pain/ Gangrene
 - Bilateral femoropopliteal occlusive disease
 - Failed bypass surgery
 - Gangrene extend to forefoot area
 - HT, DM, Dyslipidemia

PBMNCs



PBMNC volume 60 cc.
CD34+ cells 1.16×10^6 / cc

PBMNC injection



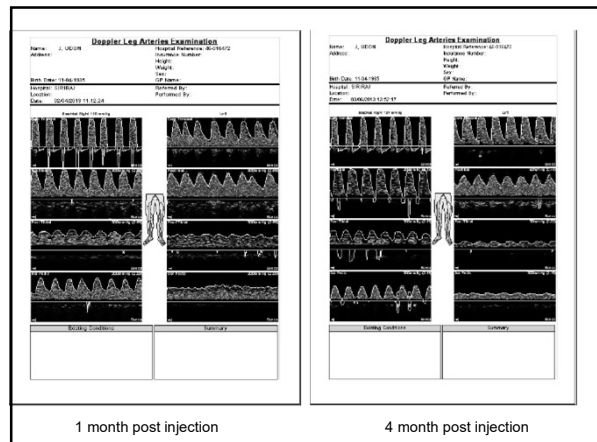
PBMNC injection



Post injection Day 1 (Feb 16 2013)



2 month after injection



Before-After Injection

Transcutaneous Oximetry Report

LEFT LEG	20 min Supine	5 min Erect/Lean	5 min Supine	15 min O ₂ 100%	5 min Supine
Electrode 1	42	33	37	42	33
Electrode 2	32	23	27	32	23
Electrode 3	32	23	27	32	23
Electrode 4	32	23	27	32	23
Mean S.T.	34	25	29	34	25
Electrode 5	23	4	7	41	23
Electrode 6	24	0.6	0.10	0.05	0.6
Electrode 7	2	0.1	0.01	0.01	0.1
Electrode 8	2	0.1	0.01	0.01	0.1
Mean S.T.	0.22	0.08	0.06	0.23	0.11

Electrode Sites:

Tekscan's comment: Before injection

Transcutaneous Oximetry Report

LEFT LEG	20 min Supine	5 min Erect/Lean	5 min Supine	15 min O ₂ 100%	5 min Supine
Electrode 1	39	42	44	39	40
Electrode 2	32	32	32	32	32
Electrode 3	42	32	42	40	36
Mean S.T.	37	35	39	38	36
Electrode 4	27	7	27	28	42
Electrode 5	0.08	0.06	0.03	0.11	0.23
Electrode 6	2	0.1	0.01	0.01	0.1
Electrode 7	2	0.1	0.01	0.01	0.1
Electrode 8	2	0.1	0.01	0.01	0.1
Mean S.T.	2	0.1	0.01	0.01	0.1

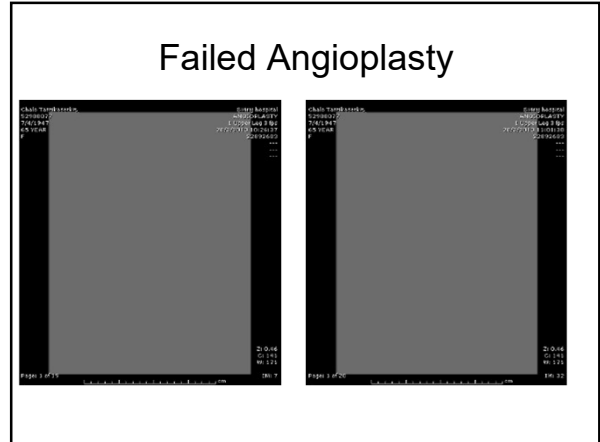
Electrode Sites:

Tekscan's comment: 4 month post injection



Case 2

- Female 66 year old
- Non healing mixed venous ulcer+ ischemic ulcer 5 month
- Bilateral tibioperoneal occlusive disease
- HT, Dyslipidemia
- Failed Angioplasty



Before injection

Diaplex Leg Arterial Examination

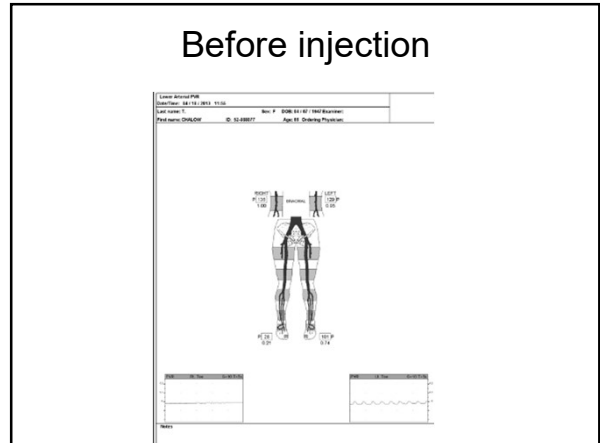
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 Patient: S. D. MURKIN
 Referral: Vascular Medicine
 Referral Date: 08/09/07
 Referral Ref: 08/09/07

Exam: 08/09/07
 Exam Ref: 08/09/07
 Exam Ref: 08/09/07

Diaplex Leg Arterial Examination

Ref: 1-144-08
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 Referral Ref: 08/09/07

Exam: 08/09/07
 Exam Ref: 08/09/07
 Exam Ref: 08/09/07



Before injection

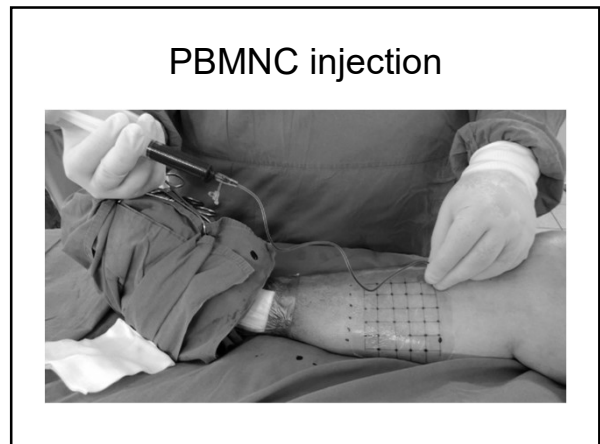
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 DEPARTMENT OF SURGERY
 FACULTY OF MEDICINE, SHERAT HOSPITAL
 MAHMOUD UNIVERSITY

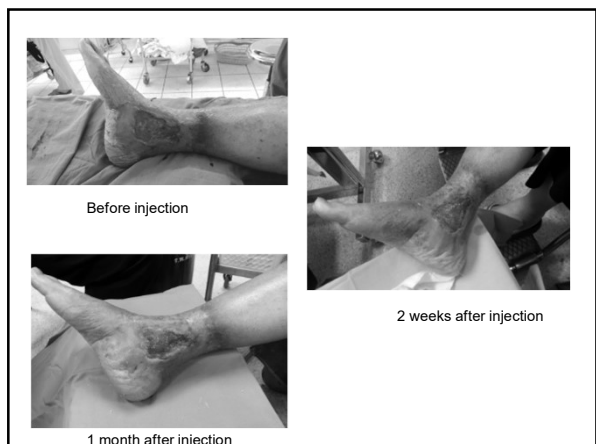
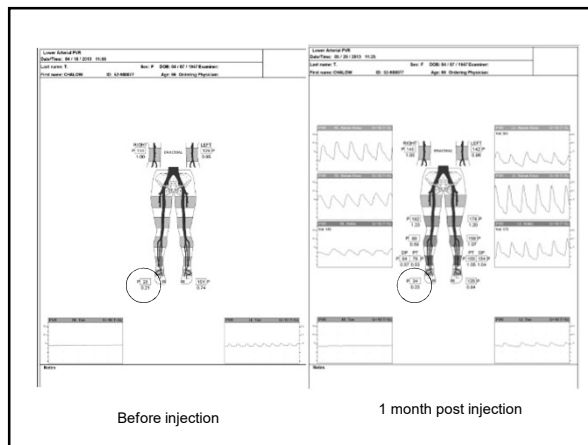
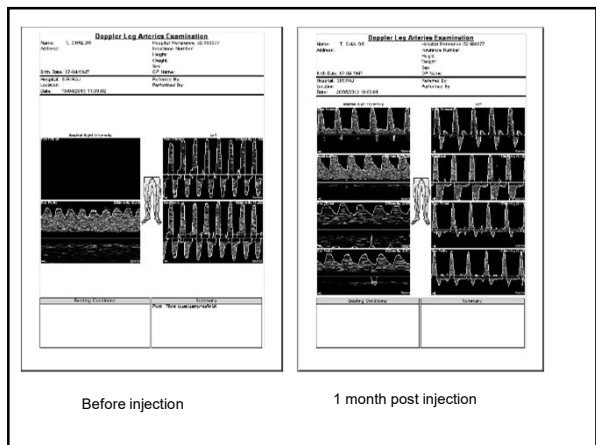
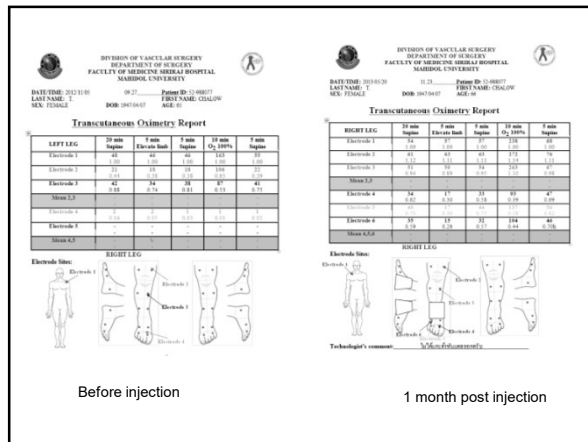
DATE/TIME: 26/12/11 05:09:27 Patient ID: 12 08077
 LAST NAME: T FIRST NAME: CHALOPH
 SEX: FEMALE DOB: 10/1/04/07 AGE: 65

Transcutaneous Oximetry Report

	LEFT LEG		RIGHT LEG	
	20 min Supine	5 min Elevate limb	5 min Supine	10 min O ₂ 100%
Electrode 1	43	46	40	35
Electrode 2	1.00	1.00	1.00	1.00
Electrode 3	0.24	0.15	0.21	0.19
Mean S.T.	0.55	0.74	0.51	0.71
Electrode 4	-	-	-	-
Electrode 5	0.24	0.05	0.05	0.52
Mean S.T.	-	-	-	-

Electrode Sites:





Case No.3



1 year later

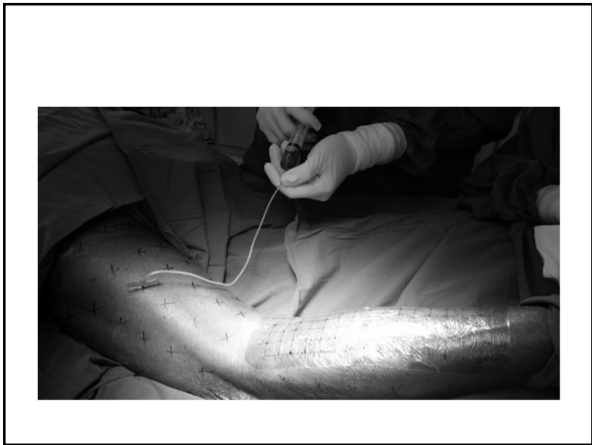


1 year later



After 2nd stem cell injection







Case no.6





Patients characteristic

Case No.	Age	Sex	HT	Smoking	DM	Dyslipidaemia	Presenting symptom
1	77	F	Yes	No	Yes	Yes	Gangrene
2	66	F	Yes	No	No	Yes	Non-Healing Ulcer
3	62	M	Yes	No	Yes	Yes	Non-Healing Ulcer
4	71	M	No	Yes	No	No	Gangrene
5	62	M	Yes	No	Yes	Yes	Non-Healing Ulcer
6	71	F	Yes	Yes	Yes	Yes	Rest-Pain
7	72	F	Yes	No	No	Yes	Gangrene
8	66	M	Yes	Yes	Yes	Yes	Rest-Pain

Patients characteristic

Case No.	Age	Sex	HT	Smoking	DM	Dyslipidaemia	Site	arterial occlusion
1	77	F	Yes	No	Yes	Yes	Lt	Bilat FPOD
2	66	F	Yes	No	No	Yes	Rt	Bilat TPOD
3	62	M	Yes	No	Yes	Yes	Rt	Bilat TPOD
4	71	M	No	Yes	No	No	Lt	Lt FPOD
5	62	M	Yes	No	Yes	Yes	Rt	Bilat TPOD
6	71	F	Yes	Yes	Yes	Yes	Both	AIOD
7	72	F	Yes	No	No	Yes	Lt	RT TPOD Left FPOD
8	66	M	Yes	Yes	Yes	Yes	Lt	Rt FPOD Lt IFOD

Patients characteristic

Case No.	Age	Sex	HT	Smoking	DM	Dyslipidemia	Site					
								PBSC (ml) (X10 ⁶ /ml)	CD34+ (X10 ⁶ /kg)	CD34+ (X10 ⁶ /kg)	CD34+/KDR+ (X10 ⁶ /ml)	CD34+/KDR+ (X10 ⁶ /kg)
1	77	F	Yes	No	Yes	Yes	Lt	60	1.12	1.34	0.44	0.52
2	66	F	Yes	No	No	Yes	Rt	105	1.28	2.53	0.68	1.35
3	62	M	Yes	No	Yes	Yes	Rt	120	2.80	4.34	0.13	0.20
4	71	M	No	Yes	No	No	Lt	120	2.97	6.24	0.70	1.56
5	62	M	Yes	No	Yes	Yes	Rt	128	7.57	12.52	3.31	5.47
6	71	F	Yes	Yes	Yes	Yes	Both	123	9.91	23.91	NA	NA
7	72	F	Yes	No	No	Yes	Lt	123	3.19	6.97	0.80	1.74
8	66	M	Yes	Yes	Yes	Yes	Lt	120	2.47	4.97	2.18	4.21

Patients characteristic : DM

Case No.	Age	Sex	HT	Smoking	DM	Dyslipidemia	Site					
								PBSC (ml) (X10 ⁶ /ml)	CD34+ (X10 ⁶ /kg)	CD34+ (X10 ⁶ /kg)	CD34+/KDR+ (X10 ⁶ /ml)	CD34+/KDR+ (X10 ⁶ /kg)
1	77	F	Yes	No	Yes	Yes	Lt	60	1.12	1.34	0.44	0.52
2	66	F	Yes	No	No	Yes	Rt	105	1.28	2.53	0.68	1.35
3	62	M	Yes	No	Yes	Yes	Rt	120	2.80	4.34	0.13	0.20
4	71	M	No	Yes	No	No	Lt	120	2.97	6.24	0.70	1.56
5	62	M	Yes	No	Yes	Yes	Rt	128	7.57	12.52	3.31	5.47
6	71	F	Yes	Yes	Yes	Yes	Both	123	9.91	23.91	NA	NA
7	72	F	Yes	No	No	Yes	Lt	123	3.19	6.97	0.80	1.74
8	66	M	Yes	Yes	Yes	Yes	Lt	120	2.47	4.97	2.18	4.21

Patients characteristic: Smoking

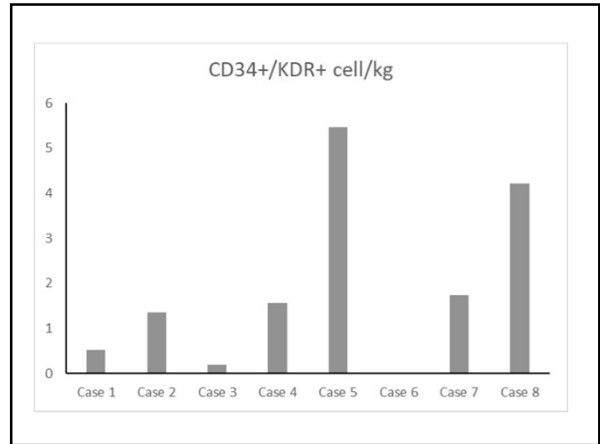
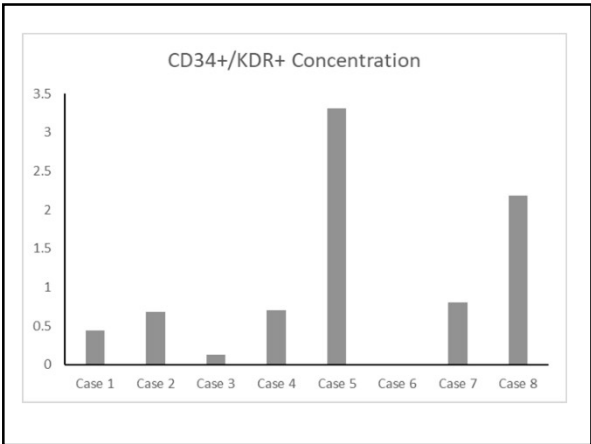
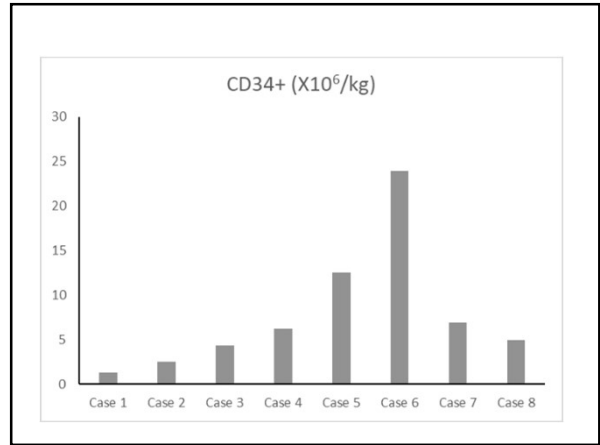
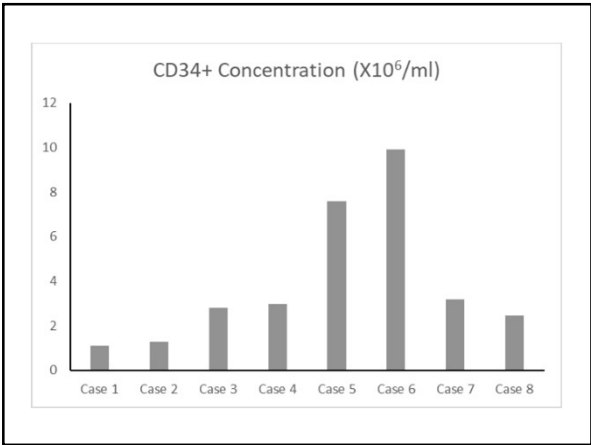
Case No.	Age	Sex	HT	Smoking	DM	Dyslipidemia	Site					
								PBSC (ml) (X10 ⁶ /ml)	CD34+ (X10 ⁶ /kg)	CD34+ (X10 ⁶ /kg)	CD34+/KDR+ (X10 ⁶ /ml)	CD34+/KDR+ (X10 ⁶ /kg)
1	77	F	Yes	No	Yes	Yes	Lt	60	1.12	1.34	0.44	0.52
2	66	F	Yes	No	No	Yes	Rt	105	1.28	2.53	0.68	1.35
3	62	M	Yes	No	Yes	Yes	Rt	120	2.80	4.34	0.13	0.20
4	71	M	No	Yes	No	No	Lt	120	2.97	6.24	0.70	1.56
5	62	M	Yes	No	Yes	Yes	Rt	128	7.57	12.52	3.31	5.47
6	71	F	Yes	Yes	Yes	Yes	Both	123	9.91	23.91	NA	NA
7	72	F	Yes	No	No	Yes	Lt	123	3.19	6.97	0.80	1.74
8	66	M	Yes	Yes	Yes	Yes	Lt	120	2.47	4.97	2.18	4.21

Patients characteristic : DM+Smoking

Case No.	Age	Sex	HT	Smoking	DM	Dyslipidemia	Site	PBSC (ml) (X10 ⁶ /ml)	CD34+ (X10 ⁶ /kg)	CD34+/KDR+ (X10 ⁶ /ml)	CD34+/KDR+ (X10 ⁶ /kg)	
1	77	F	Yes	No	Yes	Yes	Lt	60	1.12	1.34	0.44	0.52
2	66	F	Yes	No	No	Yes	Rt	105	1.28	2.53	0.68	1.35
3	62	M	Yes	No	Yes	Yes	Rt	120	2.80	4.34	0.13	0.20
4	71	M	No	Yes	No	No	Lt	120	2.97	6.24	0.70	1.56
5	62	M	Yes	No	Yes	Yes	Rt	128	7.57	12.52	3.31	5.47
6	71	F	Yes	Yes	Yes	Yes	Both	123	9.91	23.91	NA	NA
7	72	F	Yes	No	No	Yes	Lt	123	3.19	6.97	0.80	1.74
8	66	M	Yes	Yes	Yes	Yes	Lt	120	2.47	4.97	2.18	4.21

Patients characteristic :

Case No.	Age	Sex	Presenting symptom	PBSC (ml) (X10 ⁶ /ml)	CD34+ (X10 ⁶ /kg)	CD34+/KDR+ (X10 ⁶ /ml)	CD34+/KDR+ (X10 ⁶ /kg)
1	77	F	Gangrene	60	1.12	1.34	0.44
2	66	F	Non-Healing Ulcer	105	1.28	2.53	0.68
3	62	M	Non-Healing Ulcer	120	2.80	4.34	0.13
4	71	M	Gangrene	120	2.97	6.24	0.70
5	62	M	Non-Healing Ulcer	128	7.57	12.52	3.31
6	71	F	Rest-Pain	123	9.91	23.91	NA
7	72	F	Gangrene	123	3.19	6.97	0.80
8	66	M	Rest-Pain	120	2.47	4.97	2.18



Outcomes

Case No.	Age	Sex	Presenting symptom	Outcomes
1	77	F	Gangrene	Healed ulcer
2	66	F	Non-Healing Ulcer	Healed ulcer
3	62	M	Non-Healing Ulcer	Healed ulcer
4	71	M	Gangrene	Healed ulcer
5	62	M	Non-Healing Ulcer	Healed ulcer
6	71	F	Rest-Pain	No rest pain
7	72	F	Gangrene	No progression of gangrene
8	66	M	Rest-Pain	No rest pain

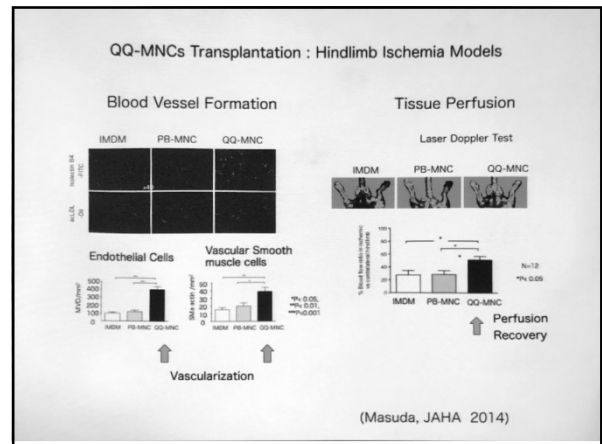
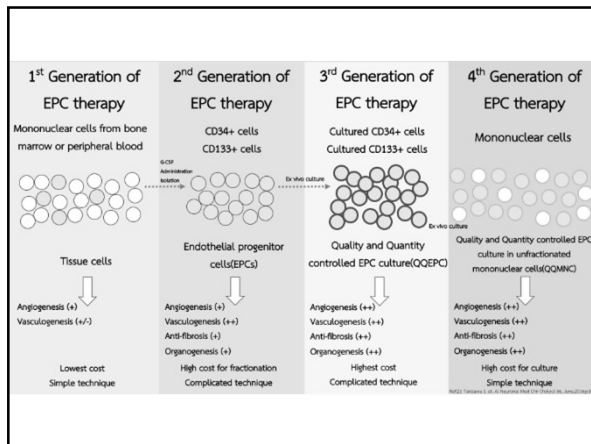
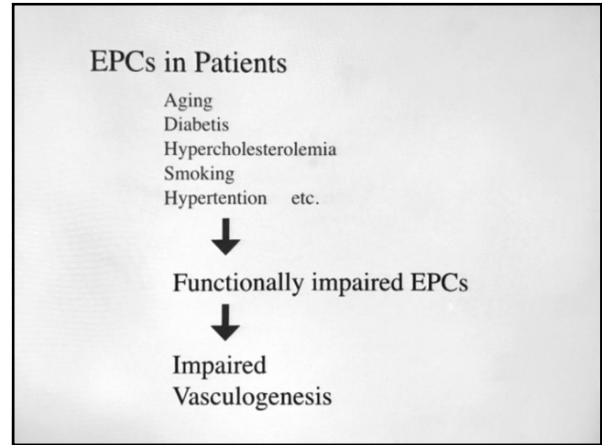
Outcomes

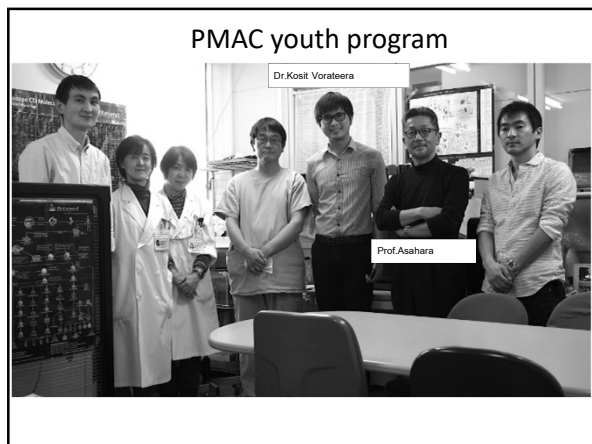
Case No.	Age	Sex	Presenting symptom	Outcomes	Current status
1	77	F	Gangrene	Healed ulcer	Death from other side of leg infection 1 year after stem cell
2	66	F	Non-Healing Ulcer	Healed ulcer	Recurrent mixed arterial and venous ulcer 1 year
3	62	M	Non-Healing Ulcer	Healed ulcer	Well being
4	71	M	Gangrene	Healed ulcer	Well being
5	62	M	Non-Healing Ulcer	Healed ulcer	Well being
6	71	F	Rest-Pain	No rest pain	Death from aspiration pneumonia from leg fracture
7	72	F	Gangrene	No progression of gangrene	Keep clean and dry of toe gangrene
8	66	M	Rest-Pain	No rest pain	Well being

research

Peripheral blood mononuclear cell transplantation to treat no-option critical limb ischaemia: effectiveness and safety

Abstract: This study evaluated the effectiveness and safety of peripheral blood mononuclear cell (PBMC) transplantation in patients with critical limb ischaemia (CLI) who were not candidates for revascularization. The study included 10 patients who received PBMC transplantation and 10 who received a placebo. The primary endpoint was the proportion of patients who were free from major adverse limb events (MALE) at 12 months. The secondary endpoints were the proportion of patients who were free from major adverse cardiovascular events (MAACE) and the proportion of patients who were free from major adverse events (MAE). The results showed that PBMC transplantation was effective in reducing the risk of MALE and MAACE compared with placebo. The study was limited by its small size and the lack of a control group.

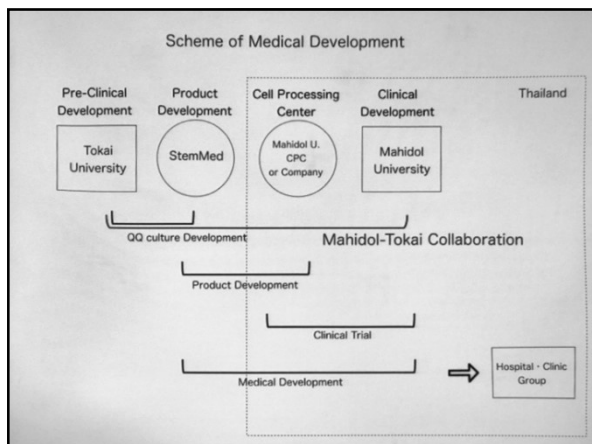
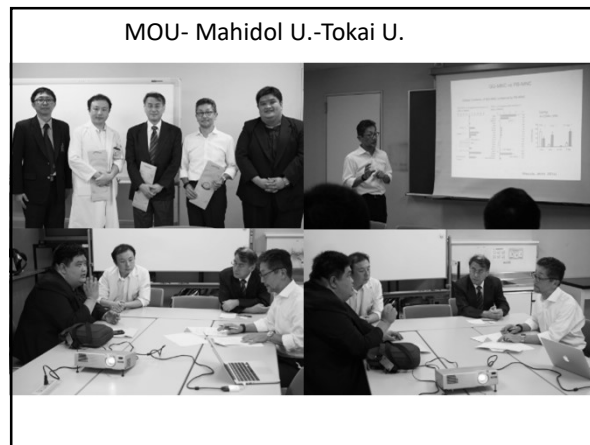
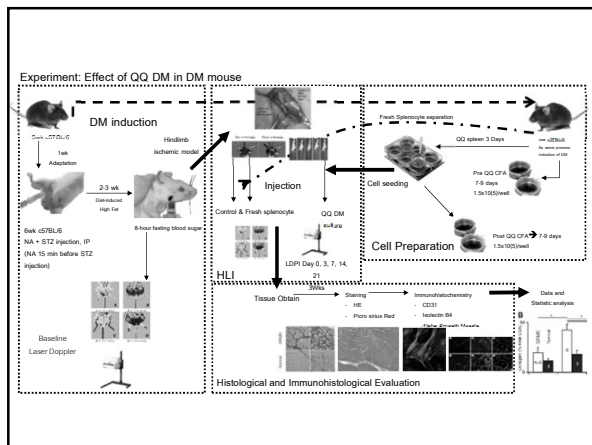




REASSURE Study: Revascularization and Angiogenesis
Effect of Quality and Quantity Culture System
in Hindlimb Ischemia of Diabetic Mice

Kosit Vorateera, MD; Amankeki Salybekov, MD
 International Mentor: Takayuki Asahara, MD, PhD; Haruchika Masuda, MD, PhD
 Thai Mentor: Nuttawat Sermsthanasawadi, MD, PhD

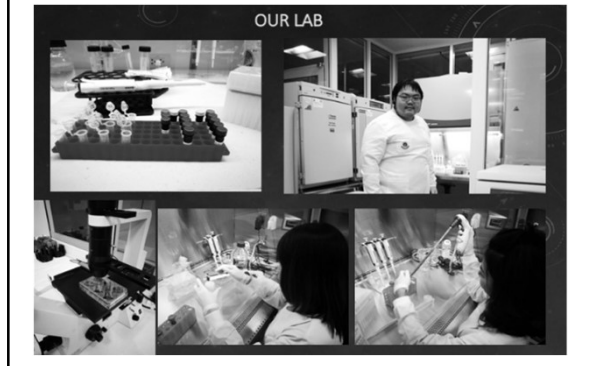
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Siriraj Stem cell and Applied Vascular and Endovascular Research **SISAVER**

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Siriraj Stem cell and Advanced Vascular and Endovascular Research (SiSAVER)



SiSAVER's Laboratory

Primary Lab Space

Clean cell culture room



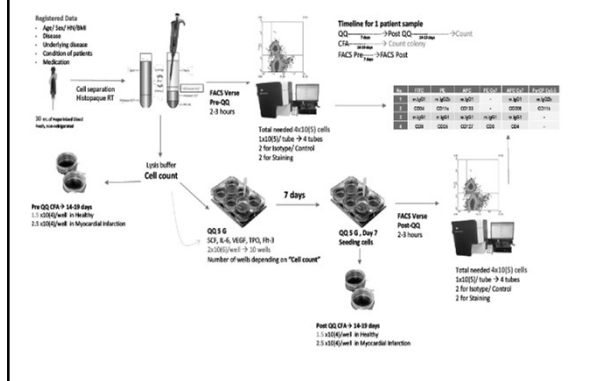
Siriraj Core Research Facility 1 SIMR Building
5th Floor



Siriraj's Clean Room Class 100

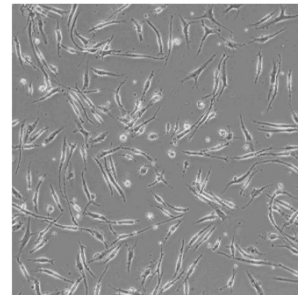


QQ-MNC



Siriraj Stem cell and Advanced Vascular and Endovascular Research (SiSAVER)

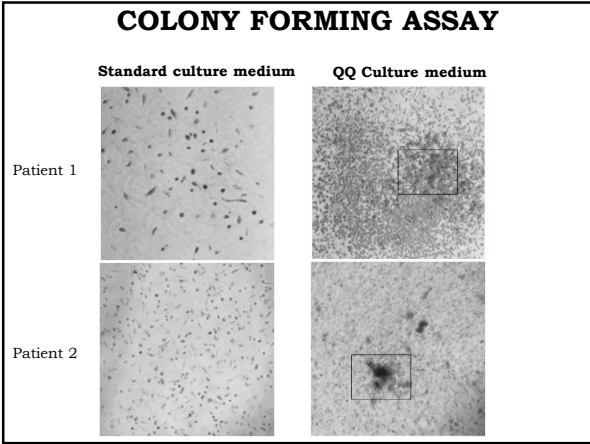
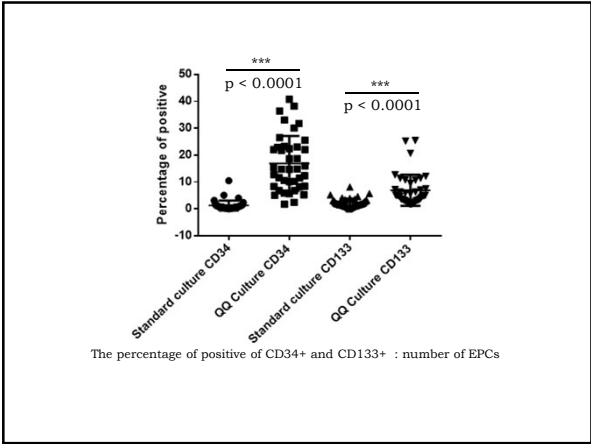
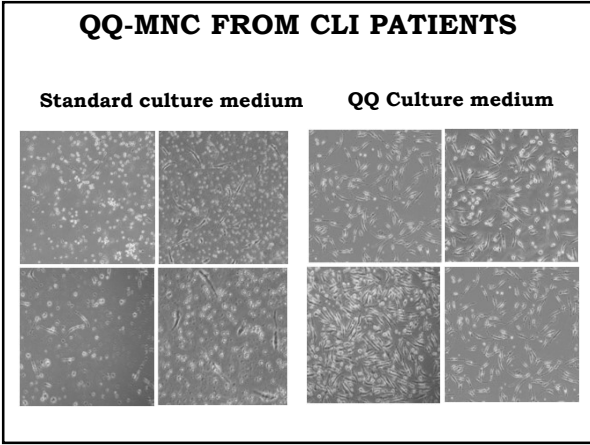
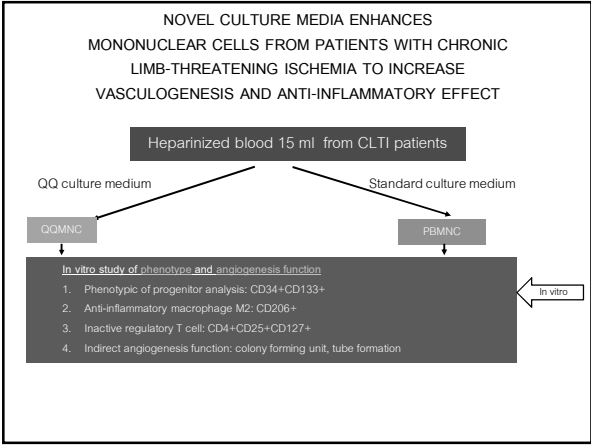
- "QQ-MNC" The new stem cell for no-option critical limb ischemia

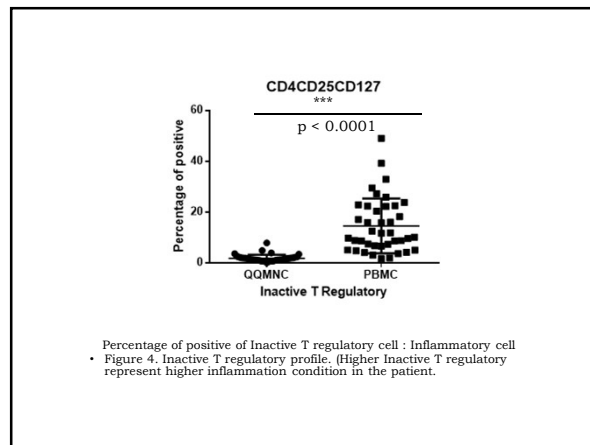
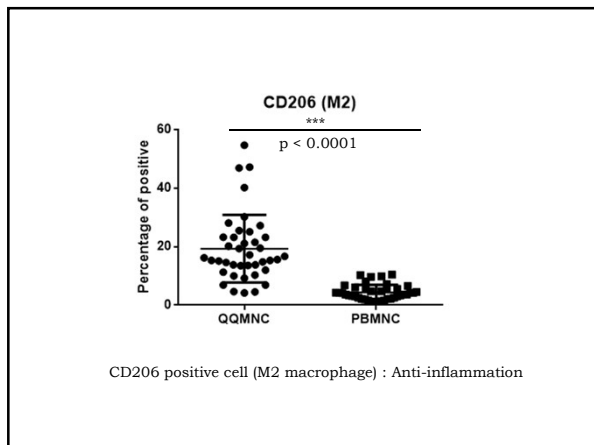
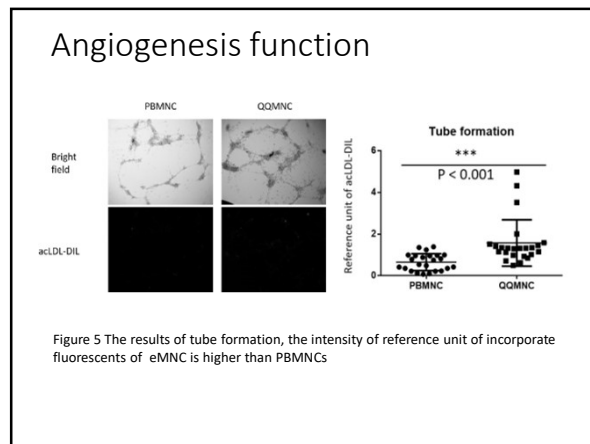
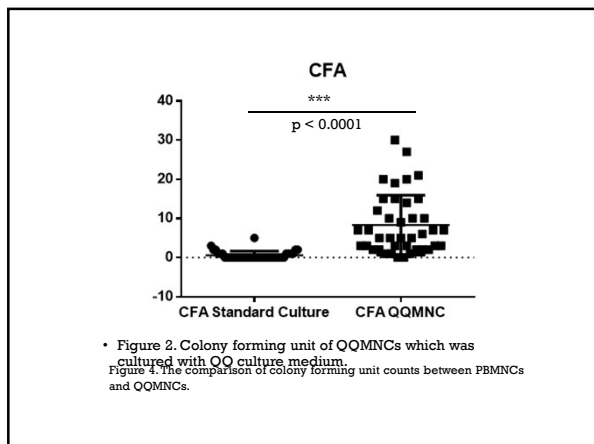


- ### QQ-MNC from CLI patients
- To study the efficacy of QQMNC from critical limb ischemic patient
 - To study the safety of QQMNC in animal model
 - The ultimate goal of this study is to find the efficacy and safety evidence *in vivo*, in order to pave the way to the clinical trial of using autologous QQMNC in human as a next step.

Study populations

Number of cases	22
Ages	65 +/-8
Male (n)	19
Female (n)	3
Gangrene (n)	13
Non-healing ulcer (n)	9
Diabetes mellitus type II (n)	14





QQ-MNC in CLI patients

- More number of EPCs
- More angiogenesis function
- Lower inflammatory effect

Open Access

Novel culture media enhances mononuclear cells from patients with chronic limb-threatening ischemia to increase vasculogenesis and anti-inflammatory effect

Background: Limb-threatening ischemia (LTI) is a severe vascular disease. The aim of this study was to evaluate the effect of novel culture media on mononuclear cells (MNC) from patients with LTI. Methods: MNCs were cultured in standard culture media and novel culture media. Results: The novel culture media significantly increased the number of MNCs and enhanced their angiogenic and anti-inflammatory functions. Conclusion: The novel culture media may be a promising approach to improve the therapeutic efficacy of MNCs in LTI patients.

BMC

EFFICACY AND SAFETY STUDY OF QQ-MNC IN CRITICAL LIMB ISCHEMIC ANIMAL MODEL


Wanchai Chinchalongporn, M.D.
Nuttapol Chruengkamlow, Ph.D.
Assoc. Prof. Dr. Nuttawut Sermasathanasawadi, M.D., Ph.D.

IN VIVO STUDY


Pilot cross-sectional study

Nude mice with limb ischemia (n =40)

IM injection of
QQMNC (n=20)




IM injection of
PBMNC (n=20)



Efficacy outcome : Limb viability/ blood circulation
Safety outcome : Survival/ infection

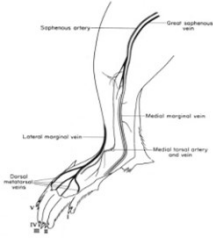
QQ-MNC injection in Animal ischemic model

- Nude mice
 - BALB/cAJcl-nu/nu
 - Lacking of T cell
 - Proper for Xeno-transplantation




Ischemic mice model

Laser Doppler Imager:
MOORLDI2-IR

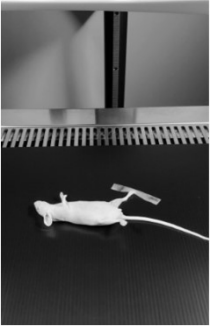
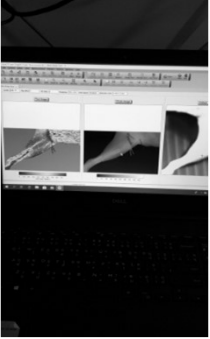


QQMNC
Or PBMNC
injection

5000
cell/20µl/position




Blood flow measurement





The comparison of blood flow :PBMNC vs QQMNC

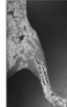
Initial D1 No operation




Initial D1 After operation




D12 After operation



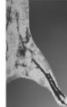
Initial D12 No operation



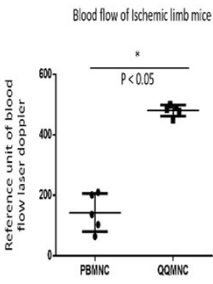
Initial D12 After operation



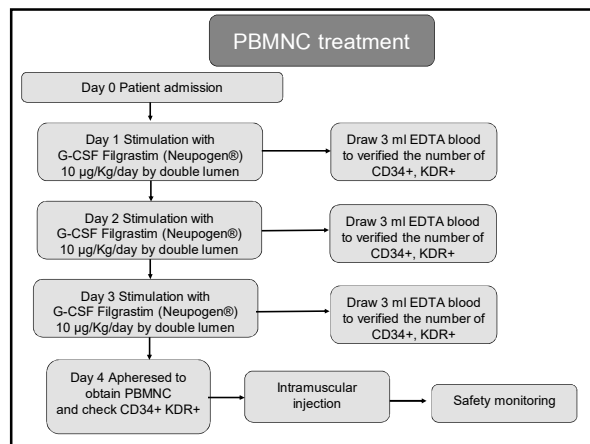
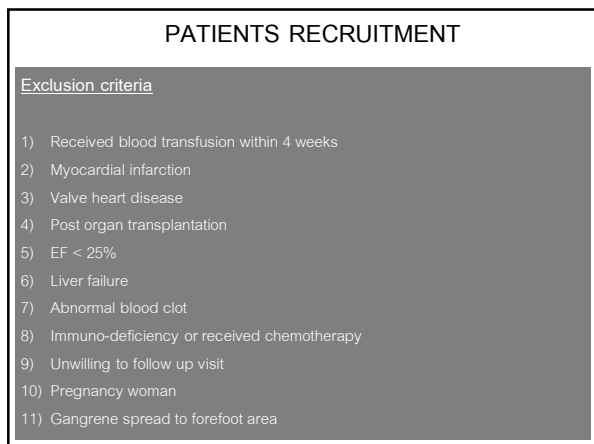
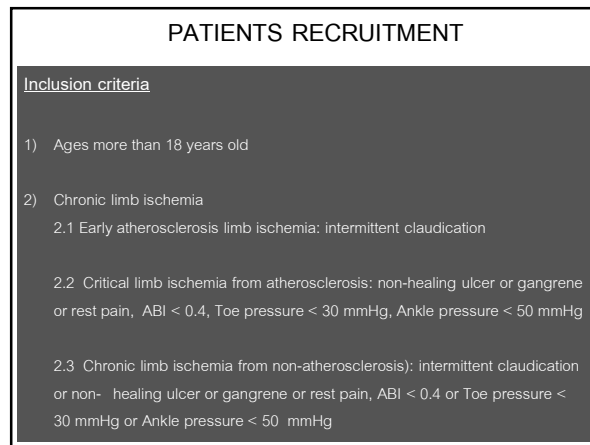
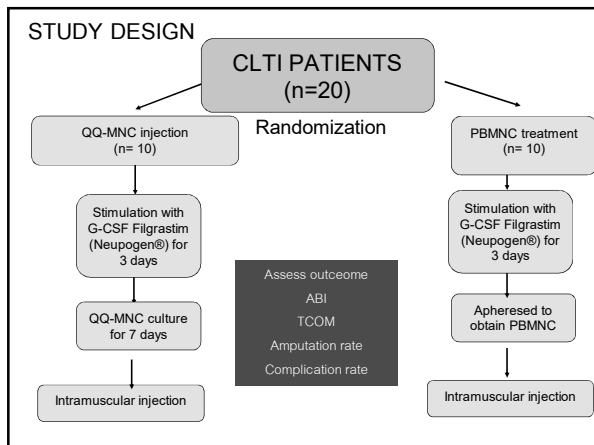
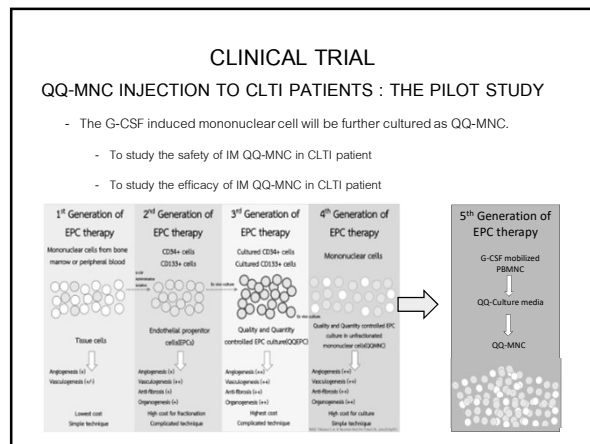
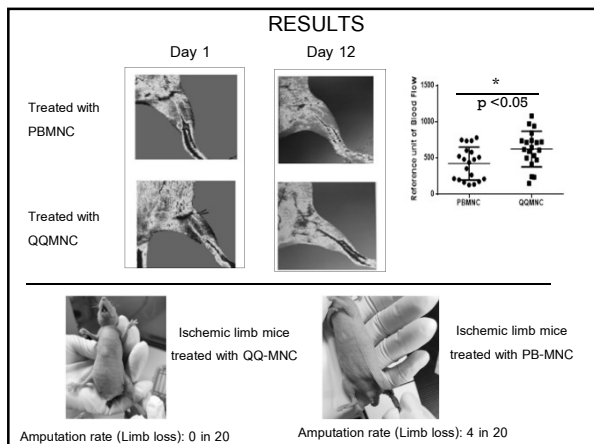
D12 After operation



Blood flow of Ischemic limb mice



Group	Reference unit of blood flow laser doppler
PBMNC	~150
QQMNC	~500

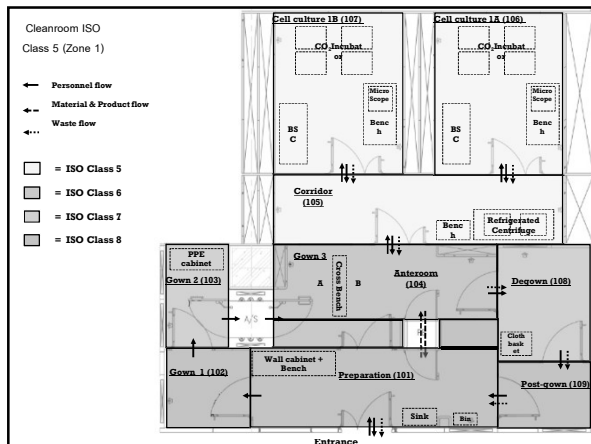
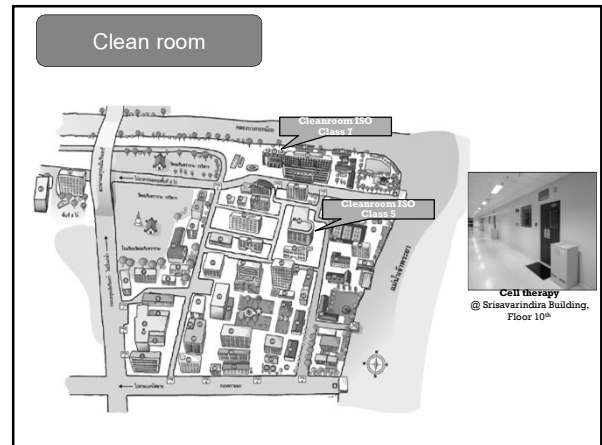
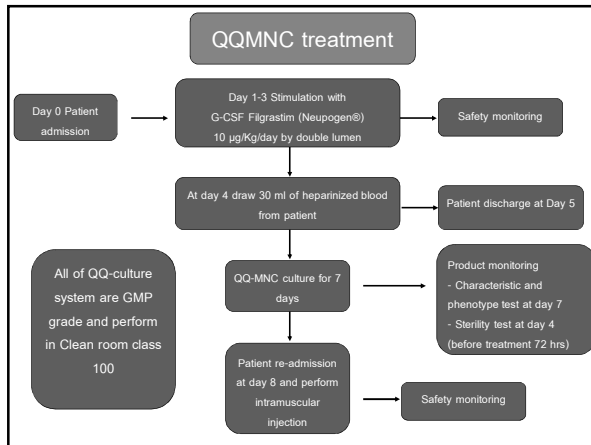


POSSIBLE COMPLICATION

- 1) Edema, swelling, diarrhea, oral pain, vomiting as complication of Neupogen.
- 2) Pneumonia hemothorax as possible complication from double lumen method.
- 3) Infection at injection site.

SAFETY MONITORING

- 1) Injection location (Bruise, infection)
- 2) Blood test
 - 2.1 Hematology: RBC, Hemoglobin, Hematocrit, WBC, ESR, Neutrophils, Lymphocytes, Monocytes, Platelet count, Blood clotting test (PT, PTT, INR)
 - 2.2 Chemistry: Glucose, Blood Urea Nitrogen (BUN), Serum Creatinine, Serum Chloride, Serum Potassium, Serum Sodium, Serum Albumin, Total Serum Proteins, SGOT/AST, SGPT/ALT, Alkaline Phosphatase, Total Bilirubin, Creatinine phosphokinase (CPK), HbA1C
- 3) Vital sign



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- 1) Edema, swelling, diarrhea, oral pain, vomiting as complication of Neupogen.
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- 3) Vital sign

PHENOTYPE AND STERILITY MONITORING

Phenotypic monitoring

- 1) CD34+, CD133+
- 2) CD206+
- 3) CD3+CD4+CD25+CD127

Sterility monitoring

Contamination	Method	Frequency/timing	Assessor	Reference
Microorganism contamination negative	Microscopy observation	Every day	in house	Masuda, et al.
	Culture supernatant with Agar test plate	Day 4 (72 hrs before injection)	Department of Microbiology Faculty of Medicine Siriraj	USP <T1>
	Real time PCR	Day 4 (72 hrs before injection)		ISO 17025
Mycoplasma contamination negative		Day 4 (72 hrs before injection)	Division of Research Faculty of Medicine Siriraj	USP <BS>,<I81>
	Culture supernatant with LAL Assay		Division of Research Faculty of Medicine Siriraj	

Endotoxin level < 0.2 EU/ml

OUTCOME MEASUREMENT

Efficacy

- ABI, TCOM
- Amputation rate
- Monitor at 1, 3, 6, 12 month

Safety

- Infection rate
- Complication rate
- Monitor at 1, 3, 6, 12 month



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หน้าหลัก | เกี่ยวกับเรา | กิจกรรม | ผลงาน | ร่วมบริจาค | ติดต่อเรา

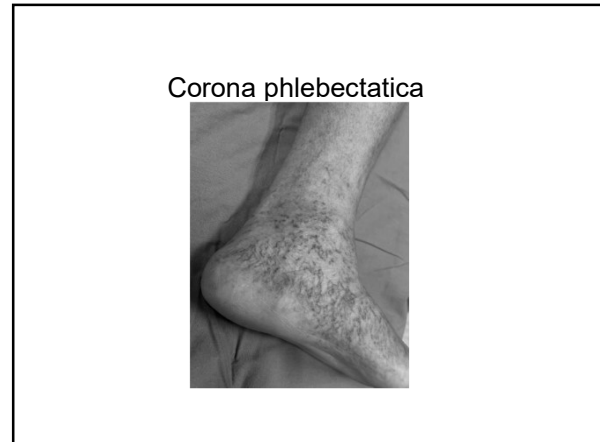
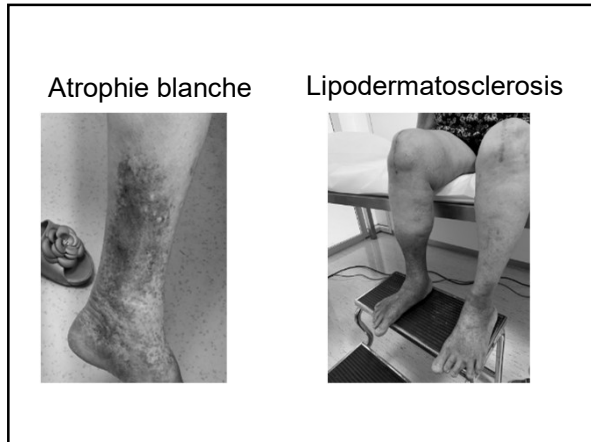
ศิริราชมูลนิธิ



D003835

พัฒนาเซลล์ต้นกำเนิด และโรคหลอดเลือดส่วนปลาย





Management of C_{6,S}

- Arterial pulse examination and measurement of ankle-brachial index
- Color duplex ultrasonography
 - assess for venous reflux and obstruction

Am Fam Physician. 2019; 100(5):298-305.

Management of C_{6,S}

- Color duplex ultrasonography
 - assess for venous reflux and obstruction

Am Fam Physician. 2019; 100(5):298-305.

Management of C_{6,S}

- Compression 30-40 mmHg and wound care
- Medication for healing ulcer: MPFF ; Pentoxifylline, Sulodexide
- Surgery
 - Correct ICVO
 - Superficial vein : Ablation to aid healing and prevent recurrence
 - HUS ; UGFS
 - Thermal ablation : RFA; Laser
 - NTNT : MOCA; Glue
 - Pathologic perforating vein ; concomitant with superficial vein ablation
 - UGFS/ RFA
 - Deep vein reflux : Axillary vein transfer
 - In case of nonhealing ulcer after superficial, perforator ablation
- Recalcitrant VLU
 - IPC
 - Growth factor
 - Hb spray

Compression therapy in Thailand

- Single component bandaging (elastic bandage)
- Multicomponent bandaging
- Elastic compression stockings

Velcro Compression Stocking

Spiral elastic bandaging technique

Stretch 50%, Overlapp 50%

Adequate target sub bandage pressure
 Resident 25%
 Patient (self performed) 33 %

Sermathanasawadi et al. Int Wound J 2017; 14:636-640
 Sermathanasawadi et al. Phlebology 2018, Vol. 33(9) 627-635

CPG-EB

- CPG-EB
 - improve efficacy of compression bandaging
 - Reusable
 - Cheap
 - Adjust desired sub-bandage pressure

Sermathanasawadi et al. Int Wound J 2017; 14:636-640
 Sermathanasawadi et al. Phlebology 2018, Vol. 33(9) 627-635

CPG-EB

Sermathanasawadi et al. Int Wound J 2017; 14:636-640
 Sermathanasawadi et al. Phlebology 2018, Vol. 33(9) 627-635

CPG-EB

Sermathanasawadi et al. Int Wound J 2017; 14:636-640
 Sermathanasawadi et al. Phlebology 2018, Vol. 33(9) 627-635


Compression for treatment of venous ulcers

- Intermittent pneumatic pressure (IPC)
- in patients who cannot or will not use an adequate compression dressing system (Level I)

Wound Rep Reg (2006) 14 649-662

Dressings applied to venous ulcers in addition to compression

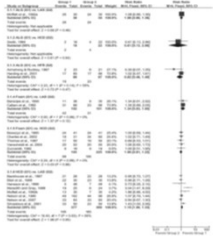
- Dressings promote moist wound healing



BMJ 2007;335:244
Am Fam Physician. 2019; 100(5):298-305

Dressings applied to venous ulcers in addition to compression


- No one dressing type has been shown to be superior when used with appropriate compression therapy
- Consider dressing based on
 - Wound characteristic
 - Dressing property



Dermatol Online J. 2016 Aug

Selection of wound dressing


- Manage venous leg ulcer exudate
 - Absorb wound exudate produced by the ulcer
 - Protect the periwound skin.
 - Maintain a moist, warm wound bed
- Based on wound location, size, depth, moisture balance, presence of infection, allergies, comfort, odor management, ease and frequency of dressing changes, cost, and availability



J Vasc Surg 2014;60:3

Selection of wound dressing

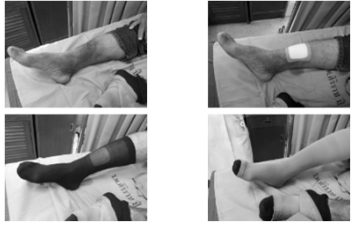
- Depend on compression method
 - Multilayered wrapped dressings
 - Can change wound dressing every 7 days
 - *Foam*
 - Compression Stocking/ Customized Bandage/EB/Velcro Stocking
 - Can change wound dressing any time
 - *Any wound dressing depend on wound characteristic*



Selection of wound dressing

	No infection	Infection
No exudate	Film	-
Low Exudate	Hydrogel Hydrocolloid	Ag paste/ SZD/ cadexomer Iodine
Moderate exudate	Hydrofiber	Hydrofiber/alginate /foam + Ag
High exudate	Alginate/ Foam	Alginate + Ag Foam + Ag

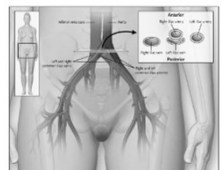
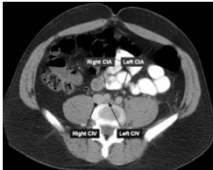
Foam Hydrofiber +GCS



Management of C_{6,S}

- Compression 30-40 mmHg and wound care
- Medication for healing ulcer: MPFF ; Pentoxifylline, Sulodexide
- Surgery
 - Correct ICVO
 - Superficial vein : Ablation to aid healing and prevent recurrence
 - HLS ; UGFS
 - Thermal ablation : RFA: Laser
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 - Pathologic perforating vein : concomitant with superficial vein ablation
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 - Deep vein reflux : Axillary vein transfer
 - In case of nonhealing ulcer after superficial, perforator ablation
- Recalcitrant VLU
 - IPC
 - Growth factor
 - Hb spray

May-Thurner syndrome

Rt common iliac artery === Lt common iliac vein

Residence risk factors and evaluation of iliacal obstruction in advanced chronic venous insufficiency

Abstract

Background: Iliac vein obstruction (ICVO) is a common cause of advanced chronic venous insufficiency (CVI). The purpose of this study was to evaluate the prevalence of ICVO in patients with CEAP C4b-C6 and to identify risk factors for ICVO.

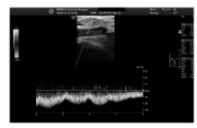
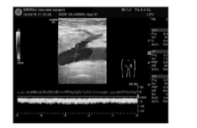
Methods: A retrospective analysis of 100 patients with CEAP C4b-C6 was performed. All patients underwent a common iliac vein ultrasound (CTV) to evaluate for ICVO. The prevalence of ICVO was determined, and risk factors for ICVO were identified.

Results: The prevalence of ICVO in patients with CEAP C4b-C6 was 28.1%. Risk factors for ICVO included age, gender, and history of deep vein thrombosis (DVT).

Patients with CEAP C4b C5 and C6 : >50% ICVO by CTV 28.1%

Semsathanasawadi et al .J Vasc Surg Venous Lymphat Dis

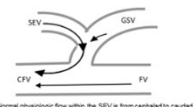
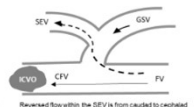
Loss of resp variation in CFV






Sensitivity 23.7%
Specificity 100%

Semsathanasawadi et al .J Vasc Surg Venous Lymphat Dis

Reversed flow in SEV

Sensitivity 7.9 %
Specificity 100 %

Semsathanasawadi et al .J Vasc Surg Venous Lymphat Dis

ICVO algorithms

```

    graph TD
      A[Limbs with lipodermatosclerosis, healed, active venous ulcer] --> B[Duplex ultrasound  
- Respiratory variation of CFV  
- Reversed flow in SEV]
      B --> C{Loss of respiratory variation in CFV  
Reversed flow in SEV}
      B --> D{Normal respiratory variation in CFV  
No reversed flow in SEV}
      C --> E[Venous intervention]
      D --> F[CTV especially in high risk (left leg, previous history of DVT)]
      F --> G{Venous obstruction}
      F --> H{No venous obstruction}
      G --> I[Venous obstruction]
      H --> J[No further investigation]
    
```

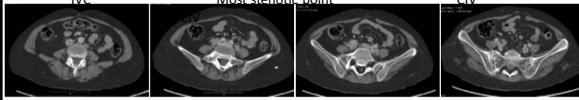
Semsathanasawadi et al .J Vasc Surg Venous Lymphat Dis

CTV: Measurement of % ICVO

IVC

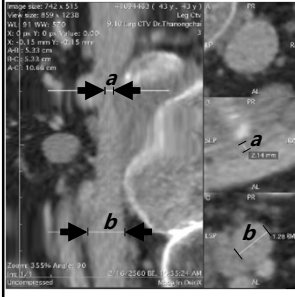
Most stenotic point

CIV



Centerline Reconstruction

J Vasc Surg Venous Lymphat Disord. 20



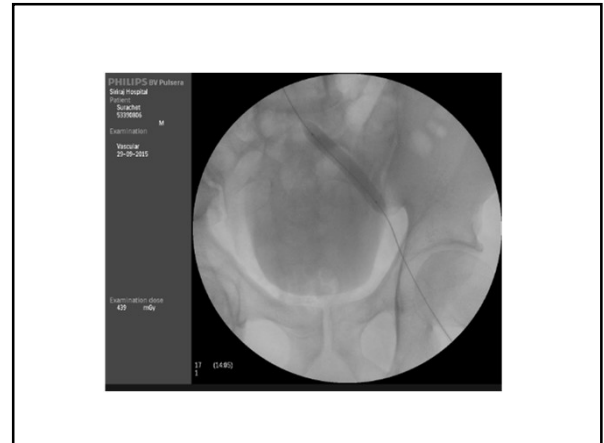
Percentage of ICVO = $(1 - \frac{a}{b}) \times 100$

The area of maximal compression was identified and the smallest diameter of the vein was compared to the diameter of the normal-appearing vein caudal to the area of obstruction



If the entire external or common iliac vein was affected, the diameter in the stenotic segment was compared to the diameter of the contralateral vein if this seemed to be free from obstruction.

Venous stenosis > 50%
 ↓
 >50% ICVO

J Vasc Surg Venous Lymphat Disord. 20



IVUS

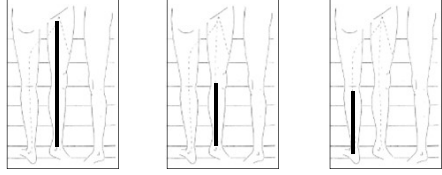


Iliac vein or IVC stenting for obstructive disease without superficial truncal reflux as first-line treatment in a symptomatic patient with skin or subcutaneous changes, healed or active ulcers

Appropriate (see Section 6 discussion)

J Vasc Surg: Venous and Lym Dis 2020;8:5

Saphenous ablation



CEAP C4-C6
G
Appropriate

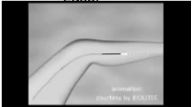


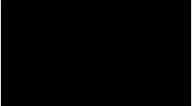
CEAP C4-C6
G
Appropriate

CEAP C4-C6
SS
Appropriate

* Correct all saphenous reflux and pathologic perforating vein related to VLU *

J Vasc Surg: Venous and Lym Dis 2020;8:5


Endovenous treatment

<p>Laser</p> 	<p>RFA</p> 
<p>MOCA</p> 	<p>GLUE</p> 

High ligation+ Venous stripping

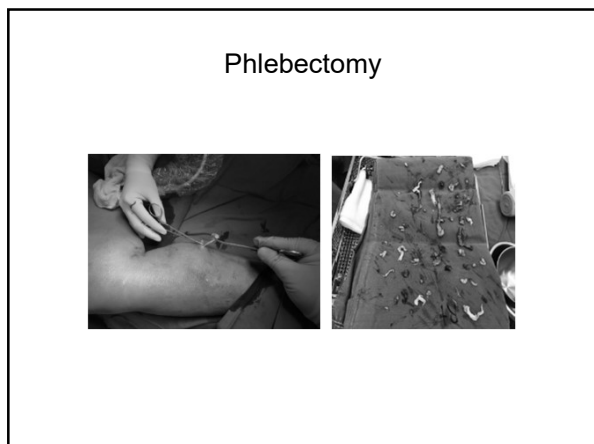
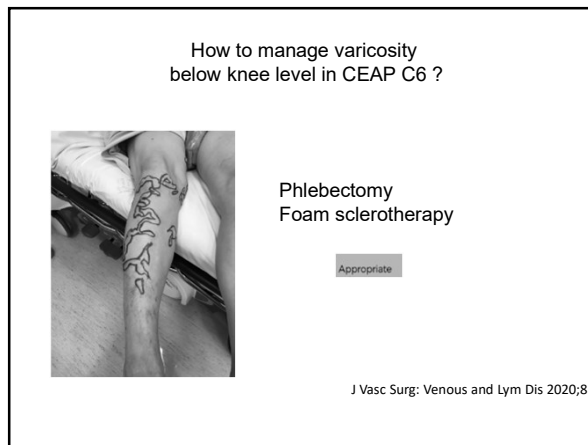
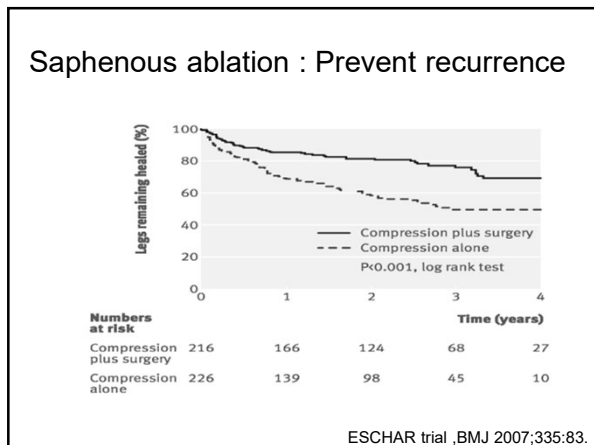
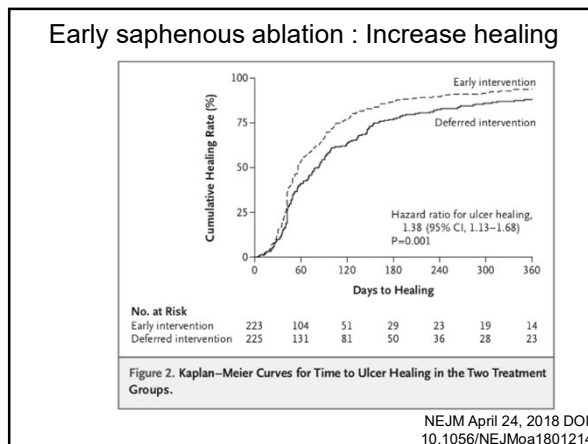
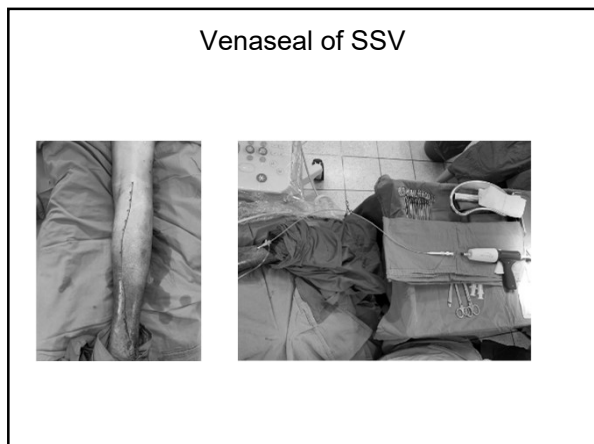


Thermal ablation : RFA




Venaseal for GSV :VLU





- ### Venous reflux surgery
- **Superficial vein surgery**
 - High ligation+ Venous stripping
 - Ambulatory phlebectomy
 - UGFS
 - Ablation: radiofrequency, laser/MOCA/ GLUE
 - **Perforator veins surgery**
 - Perforator ligation
 - UGFS
 - LASER/RFA
 - **Deep vein surgery**
 - Axillary valve transplantation
 - Valve repair (Vulvuloplasty)

Perforator incompetence



Perforator vein treatment of veins with high outward flow and large diameter directed toward affected area in a symptomatic patient with skin or subcutaneous changes, healed or active ulcers (CEAP classes 4-6)

Appropriate see Section 5 (discussion)

Pathologic perforating vein

J Vasc Surg: Venous and Lym Dis 2020;8:5

Factors that influence venous leg ulcer healing and recurrence rate after endovenous radiofrequency ablation of incompetent saphenous vein


• RFA of GSV reflux + UGFS of the pathologic perforating vein was the factor significantly associated with VLU healing (HR 2.84; 95% CI, 1.07-7.55)

• Deep vein reflux was the risk factor for VLU recurrence.

Sermathanasawadi et al. J Vasc Surg: Venous and Lym Dis 2020

Infrainguinal deep venous reflux

- C4b,C5,C6
 - Primary valve repair [GRADE - 2C]
 - Valve transposition or transplantation [GRADE - 2C]
 - Autogenous valve substitute [GRADE - 2C]
 - Don't ligation of the femoral or popliteal veins as routine [GRADE - 2C]

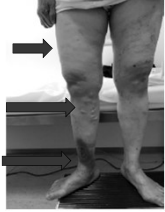


J Vasc Surg 2014;60:3S-59S

VLU and Venous surgery

Looking for ICVO and treat first in C4b, C5 ,C6

- GSV reflux
 - For C2,C3,C4a : Above knee GSV ablation is enough
 - For C4b,C5,C6 : To lowest part of GSV reflux
- Branch varicosity : UGFS/Phlebectomy
- Pathologic perforator reflux: UGFS/RFA/Laser



Treat deep vein reflux if other causes were corrected (C5,C6 only)



