Blood Flow Restriction Training In the Upper Extremity Practical Application

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The Structured Process of BFR Implementation

Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Screening	Cuff Application	Cuff Pressure	Exercise Stimulus	Exercise Parameters	Monitoring & Progression
Precautions & Contraindications	Location & Cuff Properties	Specific & Individualized Pressures	Type of Exercise	Dosage of Exercise	When & How to Progress

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Safety & Side Effects – Basic BFR Principles

Best Practices are as follows:

- **1. Confirm No Contraindications** for 'normal exercise' → PAR-Q
- **2. Hemodynamically Unstable Patients** (slide 62, 63) should NOT partake in BFR Training
 - Exception: 'expert' clearance has been provided
- 3. Thrombotic Diseased Patients are Contraindicated
 - Believed to be reason why serious complications have been seldom occurred until now
 - Rheomatologic investigations after BFR have shown NO evidence for increased risk of thrombosis⁸³
- 4. Explain **Petechial Hemorrhage Risk –** prior to initiation of training (especially UE)
- 5. Individualize training to subjects' physical capacity & condition
- 6. Build Relationship & Trust with Patient

Nakajima 2011⁸⁸

Safety & Side Effects – Basic BFR Principles

- 7. Pay Attention to Prodromal Symptoms (syncopy)
 - faintness, dizziness, or light-headedness
- 8. Caution: Older (>65), Bedridden, Postoperative Patients (DVT risk)
- 9. AED Available

10. SHORT Term and LOW intensity Loads

- High Intensity Loads has little effect, but is may be rather dangerous
- Long duration (UE: >15 min, LE: >30 min) blood flow restriction should be avoided

11. If unsure about medical condition seek specialist consult



Nakajima 2011⁸⁸

Practical Application – When to deflate?

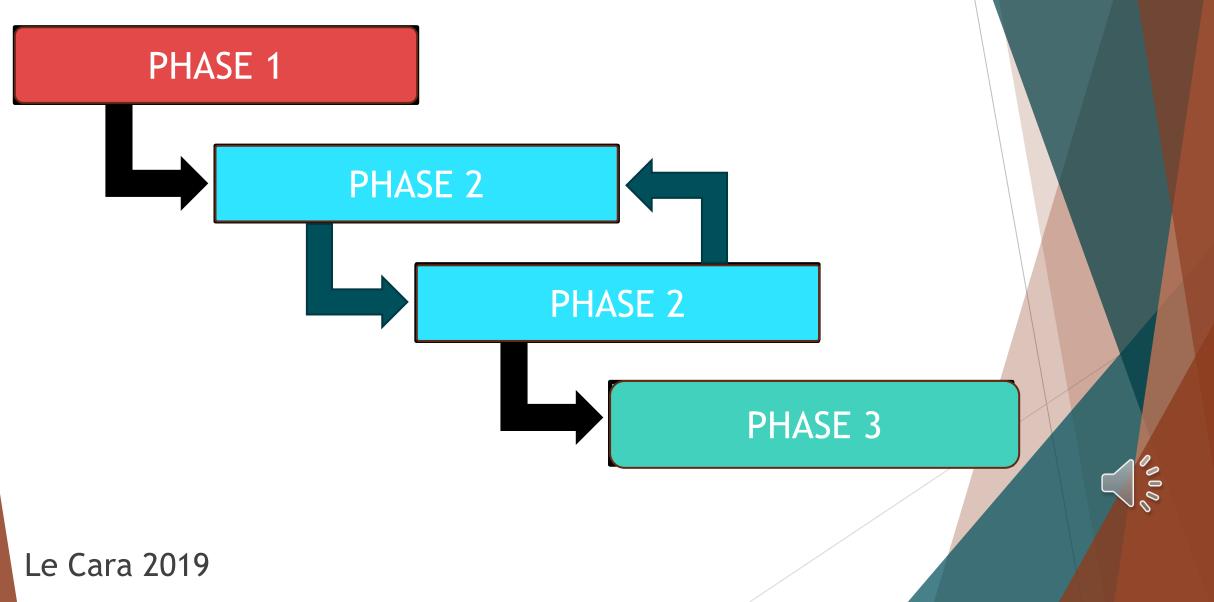
- Development of ventricular or atrial arrhythmias.
- Onset of chest pain/discomfort, or other symptoms, suggestive of myocardial ischemia.
- Dizziness, confusion, deteriorating balance, or other significant neurological symptoms.
- □ Paleness or cyanosis.
- □ Vomiting, nausea, or feeling generally unwell.
- □ SBP ≥ 250 mmHg &/or DBP ≥ 115 mmHg.

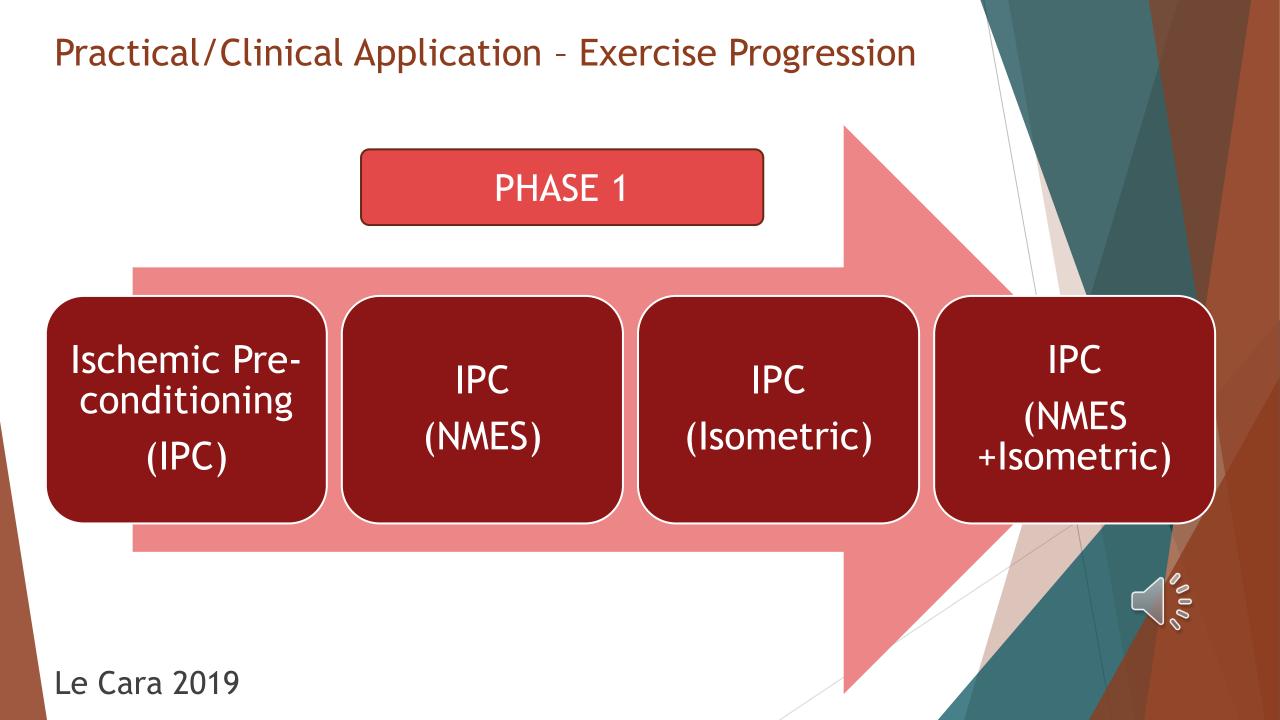
- Exhaustion or fatigue (malaise), sometimes persisting for days, that is out of keeping with the person's usual response to exercise at a given intensity.
- □ Swelling and shortness of breath.
- Skin of the affected limb that is too hot or cold to touch.
- □ Increased/excessive pain in the affected limb.
- □ Excessive discoloration of the affected limb.
- □ Subject requests to stop.



Nascimento 2022

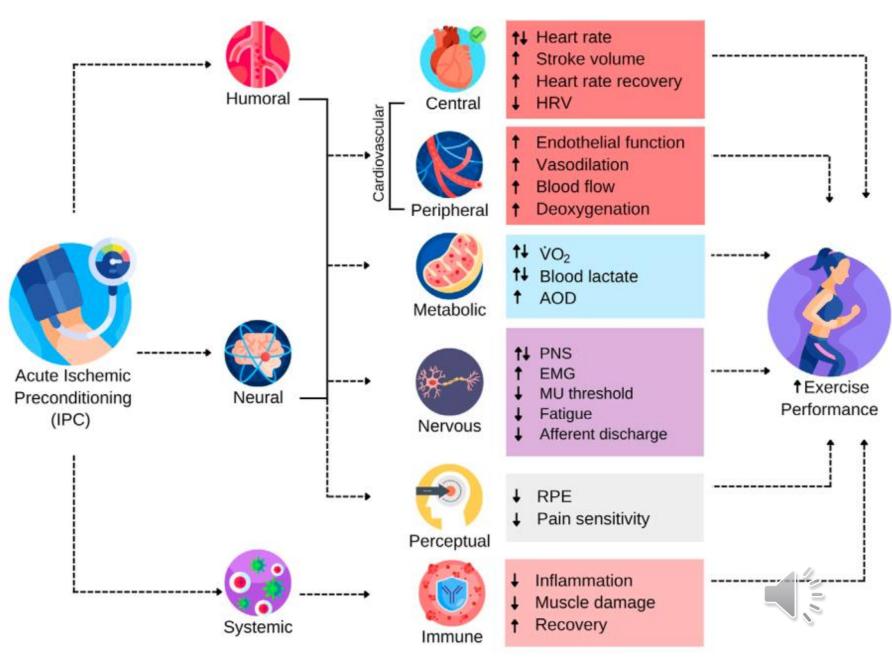
Practical/Clinical Application - Exercise Specifications (cont'd)



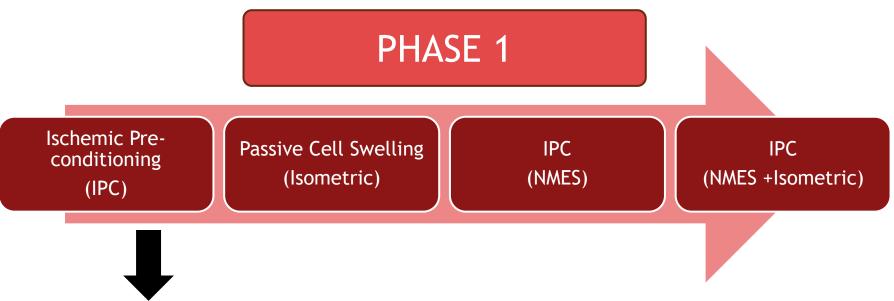


Ischemic Preconditioning

- The Range of Reported Potential Triggers and Subsequent Responses Contributing to Ergogenic Effects of IPC.¹
- Arrows indicate directionality of documented changes in the literature
- Muscle damage following exercise & recovery²
- Preservation of lean tissue during immobilization⁴
- Improves maximal performance in highly trained swimmers³



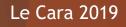
O'Brien 2022¹, Franz 2018², Jean-St-Michel 2011³, Kubota 2008⁴



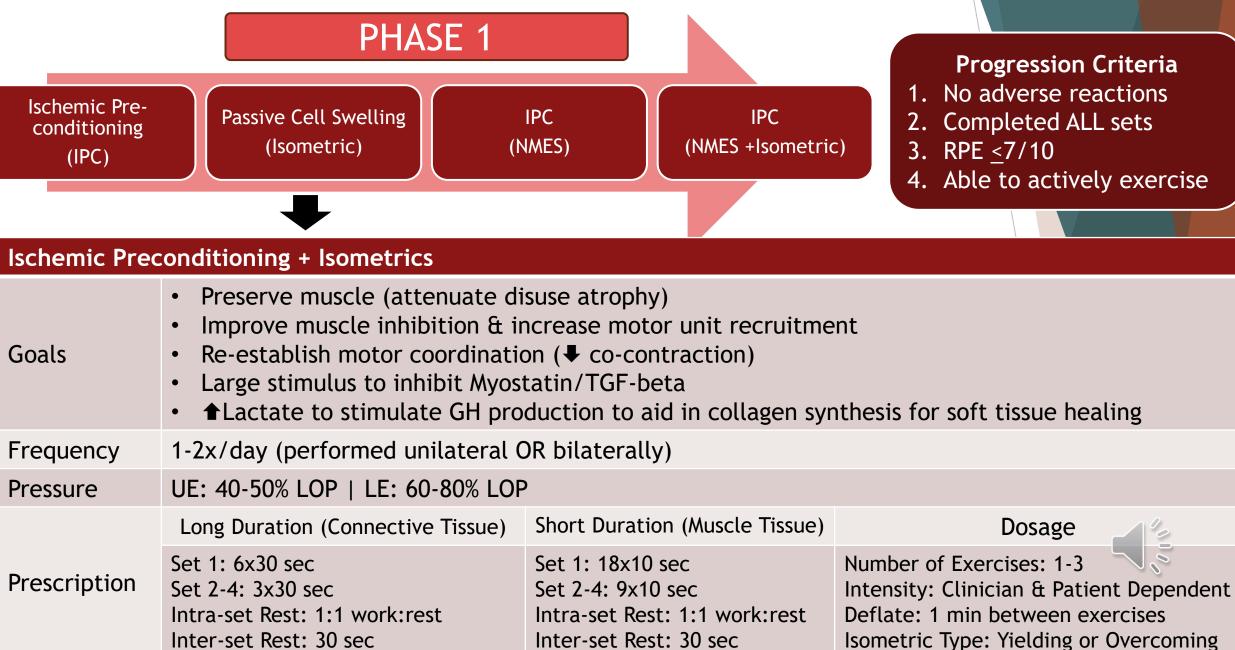
Progression Criteria

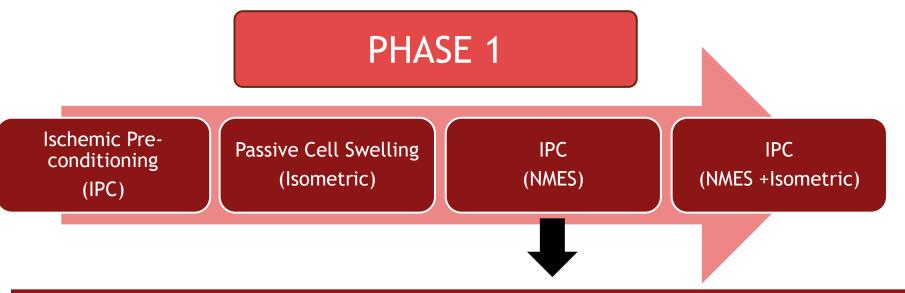
- 1. No adverse reactions
- 2. Completed ALL sets
- 3. RPE <7/10
- 4. Able to actively exercise

Ischemic Preconditioning		
Goals	 Acclimate patient to BFR Preserve muscle (
Frequency	Perform bilateral 2x/day	
Limb Pressure	100% LOP	
Prescription	5x5 min Set Rests: 3 min (Soft Tissue & PROM)	



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Progression Criteria

- 1. No adverse reactions
- 2. Completed ALL sets
- 3. RPE <7/10
- 4. Able to actively exercise

Ischemic Preconditioning + NMES

Goals	 Preserve muscle (attenuate disuse atrophy) Large NMES stimulus to inhibit Myostatin/TGF-beta Lactate to stimulate GH production to aid in collagen synthesis for soft tissue healing 	
Frequency	1-2x/day (performed unilateral OR bilaterally) 3-5 d/week	
Limb Pressure	UE: 40-50% LOP LE: 60-80% LOP	
Prescription	5x5 min Rest: 3 min (soft tissue, manual, &/or prom)	Le Cara 2019
NMES ²	Frequency: 35-50 Hz Pulse Duration: 400 ms Work:Rest 3:1	Nussbaum 2017

PHASE 1

Progression Criteria

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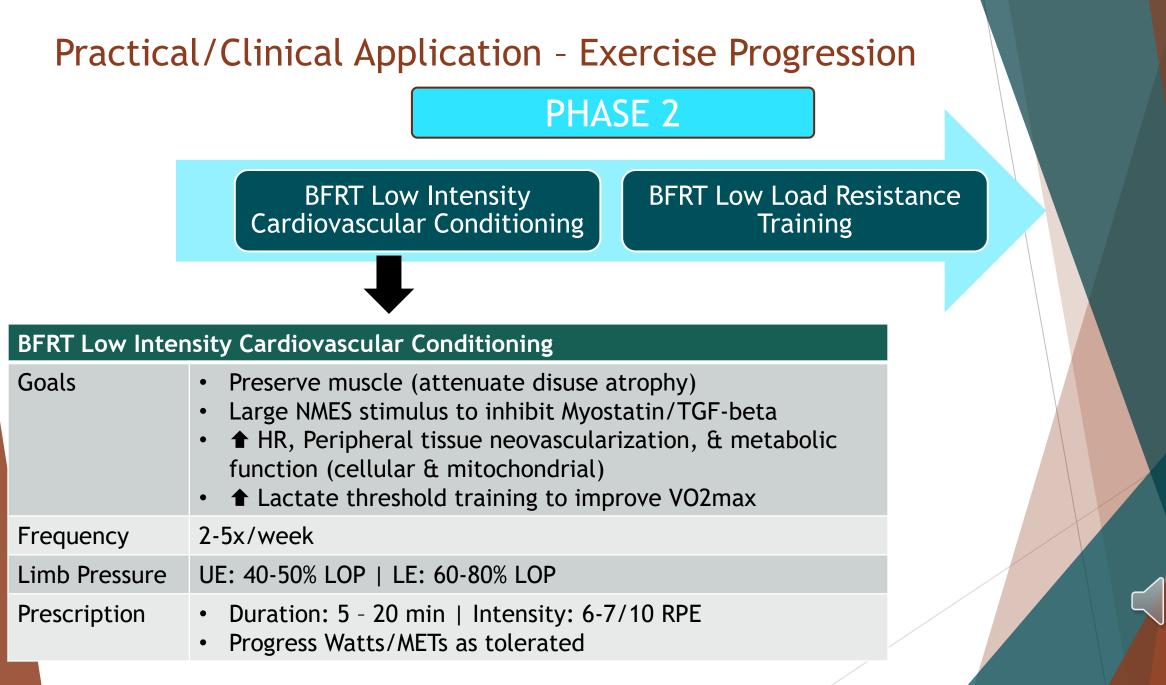
No adverse reactions
 Able to complete ALL sets/reps
 RPE <7/10
 Able to actively exercise

PHASE 2

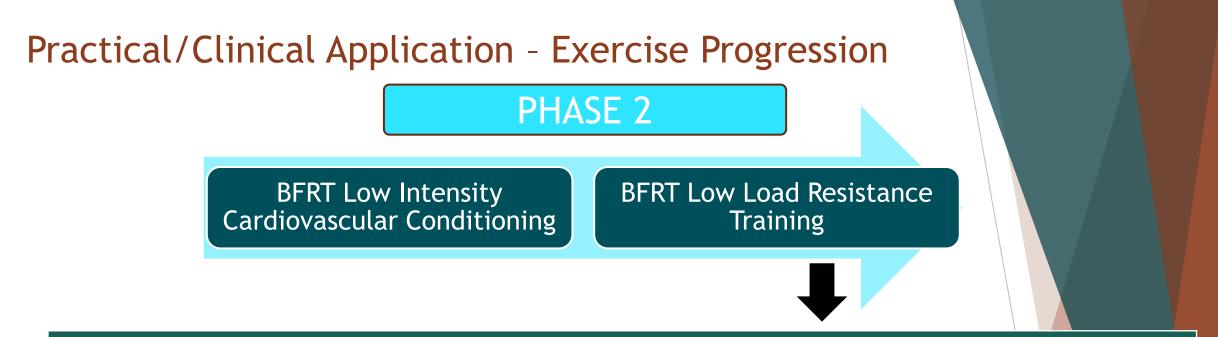
BFRT Low Intensity Cardiovascular Conditioning

BFRT Low Load Resistance Training

Le Cara 2019



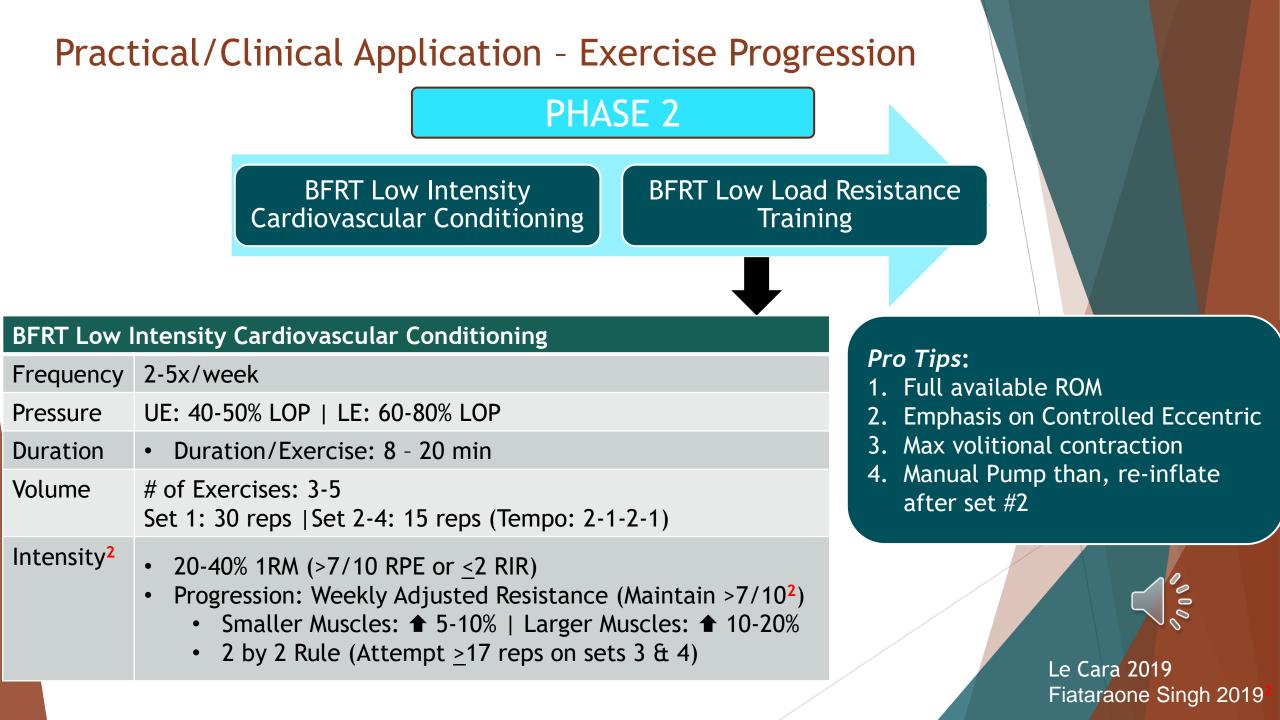
Le Cara 2019

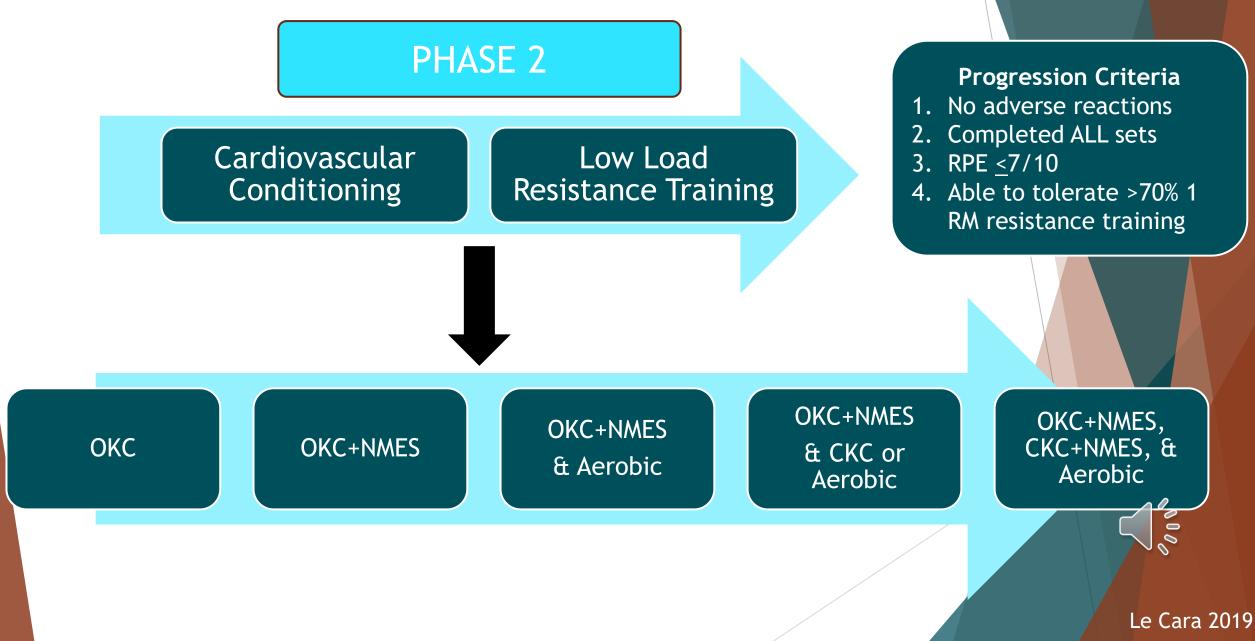


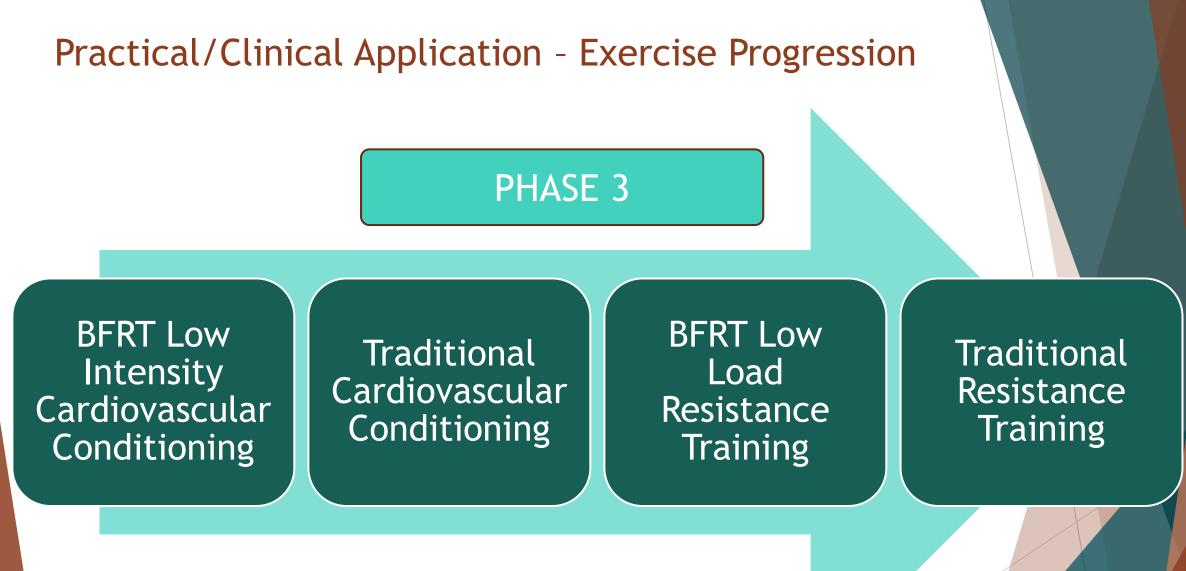
Goals: BFRT Low Intensity Resistance Training

- Preserve muscle (attenuate disuse atrophy)
- Auscle inhibition & Amotor unit recruitment
- Large stimulus to inhibit Myostatin/TGF-beta
- 1 Lactate to stimulate GH production to aid in collagen synthesis for soft tissue healing
- 1 Tolerance to active ROM, internal load, & external resistance

Le Cara 2019

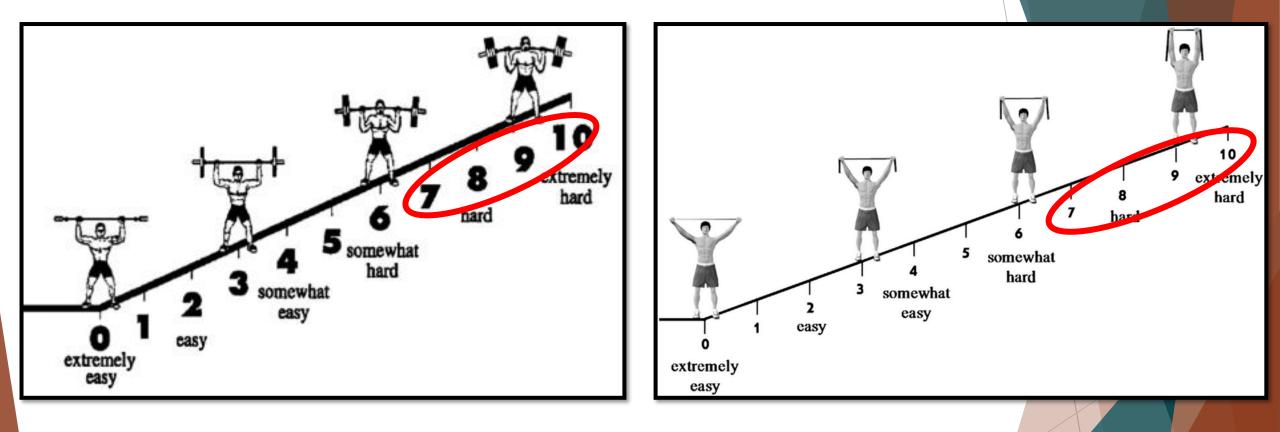






Le Cara 2019

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Robertson 2001, Colado 2012, Colado 2014, Morishita 2018

RPE*	What it feels like	Repetitions in reserve**	Actual RPE	Assigned RPE range 6–8
10	Your absolute limit	0	1	Increase load by 20%
9.5	You could maybe add a couple pounds to the bar	0	2	Increase load by 16%
9	Very close to your max	1	3	Increase load by 12%
	Where you typically end a set			Increase load by 8%
8.5 when you're pushin hard	when you're pushing yourself hard	f 1-2 5	5	Increase load by 4%
8	Where you typically end a set	2	6	Participant choice
•	when you're feeling strong		7	Participant choice
_	Where you end a set when you're trying to leave some-	0	7.5	Participant choice
7	thing in the tank (or when you just don't have it that day)	you 3 8	8	Participant choice
5-6	Warmup sets	4-6	8.5	Decrease load by 2%
3-4	General warmup	Too many	9	Decrease load by 4%
		to count	9.5	Decrease load by 6%
1-2	Anything more strenuous than watching TV	Infinite	10	Decrease load by 8%

Zourdos 2016

Helms 2018

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IF: patient exceeds target rep by 2 reps on final set on 2 consecutive exercise bouts

THEN: progress resistance

Description of the athlete*	Body area exercise	Estimated load increase [†]
Smaller, weaker, less trained	Upper body	2.5-5 pounds (1-2 kg)
	Lower body	5-10 pounds (2-4 kg)
Larger, stronger, more trained	Upper body	5-10+ pounds (2-4+ kg)
	Lower body	10-15+ pounds (4-7+ kg)

*The strength and conditioning professional will need to determine which of these two subjective categories applies to a specific athlete.

[†]These load increases are appropriate for training programs with loadvolumes of approximately three sets of 5 to 10 repetitions. Note that the goal repetitions per set remain constant as the loads are increased.

		Resistance in	n Pounds at:	1
Thera-Band® Band/Tubing Color	Increase from Preceding Color at 100% Elongation	100% Elongation	200% Elongation	9122
Thera-Band Tan		2.4	3.4	BEGI
Thera-Band Yellow	25%	3.0	4.3	BEGINNER
Thera-Band Red	25%	3.7	5.5	
Thera-Band Green	25%	4.6	6.7	
Thera-Band Blue	25%	5.8	8.6	
Thera-Band Black	25%	7.3	10.2	A
Thera-Band Silver	40%	10.2	15.3	ADVANCED
Thera-Band Gold	40%	14.2	21.3	
	Band/Tubing Color Thera-Band Tan Thera-Band Yellow Thera-Band Red Thera-Band Green Thera-Band Blue Thera-Band Black Thera-Band Silver	Band/Tubing ColorColor at 100% ElongationThera-Band Tan-Thera-Band Yellow25%Thera-Band Red25%Thera-Band Green25%Thera-Band Blue25%Thera-Band Black25%Thera-Band Silver40%	Thera-Band® Band/Tubing ColorIncrease from Preceding Color at 100% Elongation100% ElongationThera-Band Tan-2.4Thera-Band Yellow25%3.0Thera-Band Red25%3.7Thera-Band Green25%4.6Thera-Band Blue25%5.8Thera-Band Black25%7.3Thera-Band Silver40%10.2	Band/Tubing ColorColor at 100% ElongationElongationElongationThera-Band Tan-2.43.4Thera-Band Yellow25%3.04.3Thera-Band Red25%3.75.5Thera-Band Green25%4.66.7Thera-Band Blue25%5.88.6Thera-Band Black25%7.310.2Thera-Band Silver40%10.215.3

Represents typical values. All products not available in all colors.

Baechle 2008

Number of Repetitions Performed	Percent of 1-Repetition Maximum	Multiply Weight Lifted By:
1	100	1.00
2	95	1.05
3	93	1.08
4	90	1.11
5	87	1.15
6	85	1.18
7	83	1.20
8	80	1.25
9	77	1.30
10	75	1.33
11	70	1.43
12	67	1.49
15	65	1.54

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Haff 2015

Practical/Clinical Application - RPE Adaptation

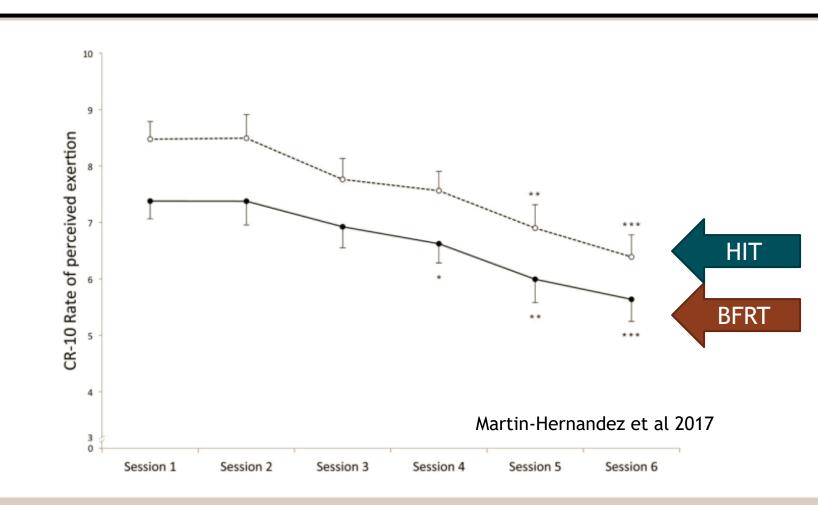


Figure 1. Ratings of perceived exertion (RPE) values after each session of blood flow restriction training (BFF and high-intensity training (HIT). Each session RPE is expressed as the average RPE of all sets. Values are mean *SE*. *, **, *** significantly different from session 1 ($p \le 0.05$, p < 0.01, p < 0.001, respectively).

High Intensity Training:

- Sets: 3
- Reps: 8
- Intensity: 85% 1RM
- Leg Extension

BFR Training (BFRT):

- Sets: 4
- Reps: 30/15/15/15
- Intensity: 20% 1RM
- Leg Extension

Conclusion:

- BFRT induces a marked RPE to training, vs HIT
- may not limit the application of BFRT to highly motivated individuals

Practical/Clinical Application

Clinical Outcomes

- Circumference of thickest portion of limb segment
- Force production (i.e. strength)
- Work Capacity (i.e., total work via fatigue assessments)
- Rate of force development (i.e., isometric strength)
- Biofeedback / Surface EMG
- Serial imaging
- Patient specific physical performance measure
- Functional Outcome Measures

The Limitations of BFR

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Limitations of BFR

- 1. NOT superior to Heavy Load Resistance Training
- 2. Use of non-FDA Regulated Cuffs
- 3. Poor prescription practices
- 4. Effects of chronic BFR utilization unknown
- 5. Methodology of study design (risk of bias & conflicts of interest)



The Limitations of BFR: BFR Cuff Selection

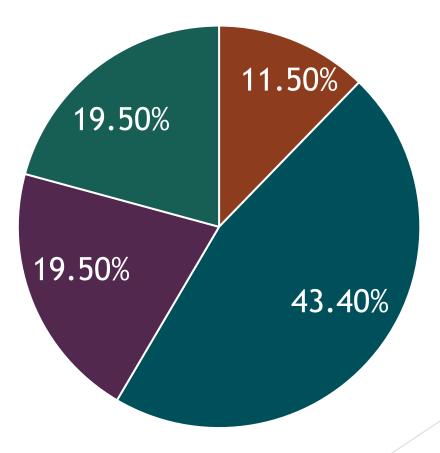


The Limitations of BFR: Poor Prescription

N = 250

- Strength & Conditioning Coaches
- Sports Scientists
- Physiotherapists
- Researchers
- Doctors

Factors Determining BFR Cuff Press



- Limb Occlusion Pressure
- Literature Values
- Limb Circumference
- Patients Brachial Blood Pressure

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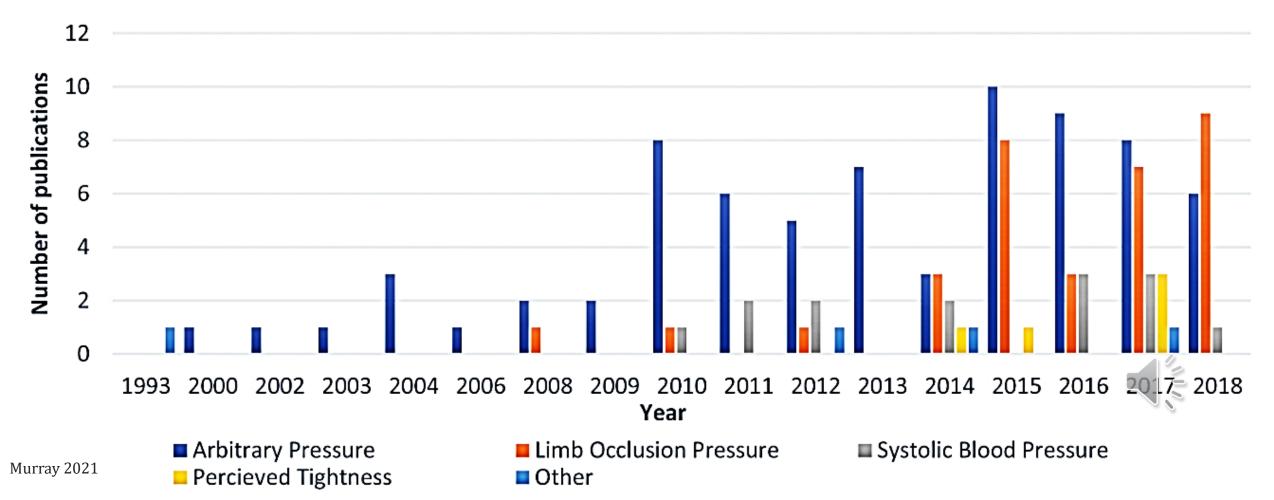
Patterson 2018

Practical Application – Cuff Pressure

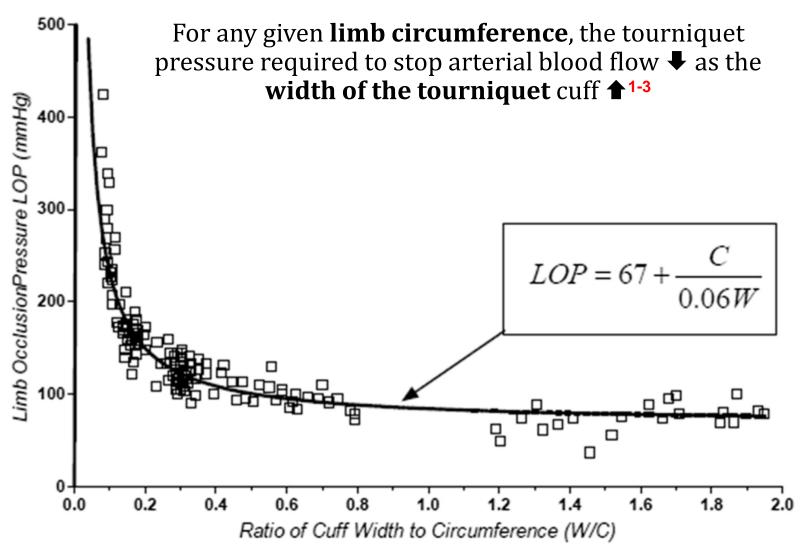
Approaches to determining occlusion pressure for blood flow restricted exercise training: Systematic review

James Murray 🕞^{a,b}, Hunter Bennett 🕞^{a,b}, Terry Boyle 🕞^{a,c}, Marie Williams 🕞^{a,d} and Kade Davison 🕞^{a,b}

Number of studies published each year for each calculation method



Practical/Clinical Application – Cuff Specifications



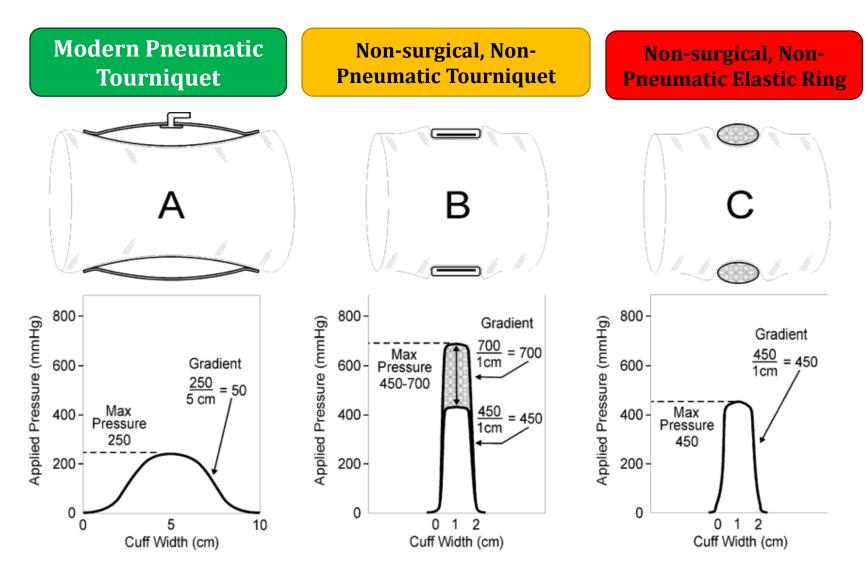
Additional variables that can influence limb occlusion pressures:

- Systolic Blood Pressure⁷
- Body position⁴
- Sex/Race⁵
- Limb Density
- Laterality⁶



McEwen 2019¹, Graham 1993², Weatherholt 2019³, Leonneke 2015, Hughes 2018⁴, Jessee 2016⁵, Evin 2020⁶, Leonneke 2015⁷

Practical/Clinical Application – Cuff Specifications



- Each tourniquet was selected and applied as recommended by the respective manufacturer to stop arterial blood flow in an upper limb.
- Higher levels of pressure and higher-pressure gradients are associated with higher probabilities of patient injuries.
- Risk of nerve related injuries increase with pressure gradients
- Higher demand pressures associated with higher CV demand
- Complete arterial flow effectiveness of BFR

McEwen 2019, Graham 1993





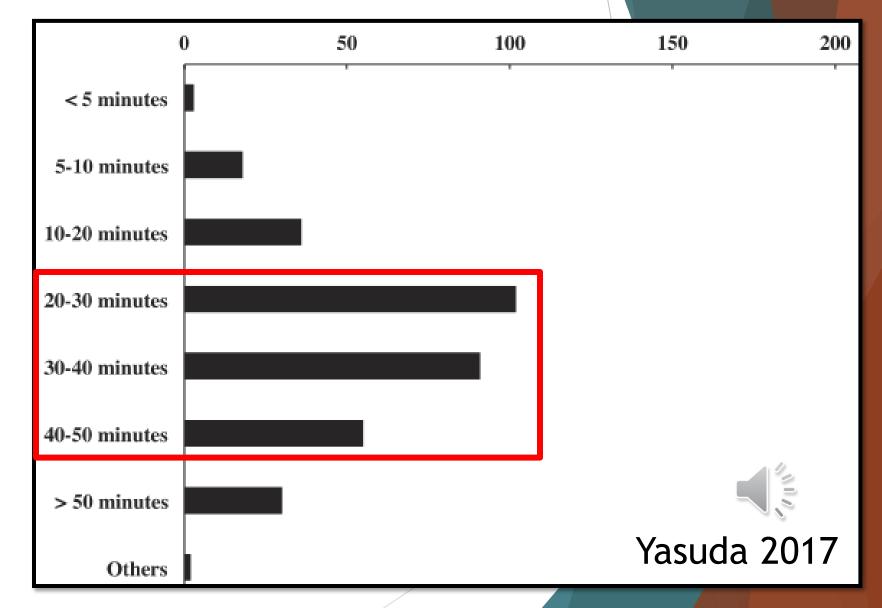
Summary of Cuff Selection

- The cuff always goes on the most proximal location of the limb:
 - Lower Extremity: as close to the groin as possible
 - Upper Extremity: as close to the axilla as possible
- FDA Registered (C.Y.A.)
- Pneumatic tourniquet, single chamber, circumferential bladder, curved cuff
- Sufficient width Legs (9 -18.5 cm), Arms (5-12 cm)¹
 - wider cuffs (13.5 cm) restrict blood at lower pressures vs narrow cuffs $(5 \text{ cm})^2$
 - Arms: narrow cuffs may limit normal/required ROM & muscle hypertrophy stimulus may be attenuated directly below the cuff³
 - Legs: wider cuffs some individuals did NOT reach arterial occlusion using narrow cuffs on Legs at pressure up to 300 mmHg²
- Autoregulation a nice to have but not a need to have if pressures are assessed post sets.



Limitations of BFR: Poor Prescription

 Occlusion pressure, intensity of training, number of sets and duration of a training unit remain unclear (Heitkamp 2015)



Limitations of BFR (cont'd)

- 4. Effects of chronic BFR utilization unknown
- 5. Methodology of study design

(risk of bias & conflicts of interest)



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BFR Legislation & Logistics



Blood Flow Restriction Training & Scope of Practice

- **APTA Positional Statement:** <u>What to Know About Blood Flow Restriction Training 2018</u>³
 - "BFRT is part of the professional scope of practice for physical therapists."
- The <u>Scope of Practice of Physical Therapy</u> has 3 components³
 - **Professional:** the unique body of knowledge, supported by educational preparation, based on a body of evidence, and linked to existing or emerging practice frameworks
 - **Jurisdiction (legal):** is established by a state's practice act governing the specific physical therapist's license, and the rules adopted pursuant to that act
 - **Personal:** consists of activities for which an individual physical therapist is educated and trained and their competence to perform
- **BFR became part of OT & PT scope of practice in 2018⁴** & CEU Credit available for³
 - OT, PT, ATC
- Licensed medical healthcare providers able to purchase medical grade pneumatic tourniquet system¹
 - Physician (MD, DO)
 - Athletic Trainers
 - Physical Therapists/Occupational Therapists
 - Chiropractors

Owens Recovery Science¹, MedBridge, APTA website³, <u>CAOperformanceandtherapy.com</u>⁴

Practical Implications – Legislation

• BFR Training Scope of Practice

• APTA: "BFRT is part of the professional scope of practice for physical therapists."

State Legislation

- 1. Check State's Practice Act
 - May be silent in regard to BFRT
- 2. Check State's Laws for Confirmation

• CAPTA Practice Act Silent on BFR & No laws prohibiting use of BFRT

Blood Flow Restriction Training & Billing

CPT Code Number	Title	
97110	Therapeutic Exercise	
97112	Neuromuscular Re-education	
97116	Gait Training	
97530	Therapeutic Activities	
9140	Manual Therapy	





Practical Implications – Legislation & Billing

FDA Regulation

- Pneumatic Tourniquets are Class 1 FDA regulated products
- Ensure that product is registered and approved by the FDA when practicing in the United States

Billing

 Billed under the standard physical therapy codes depending on the activity that the patient is performing

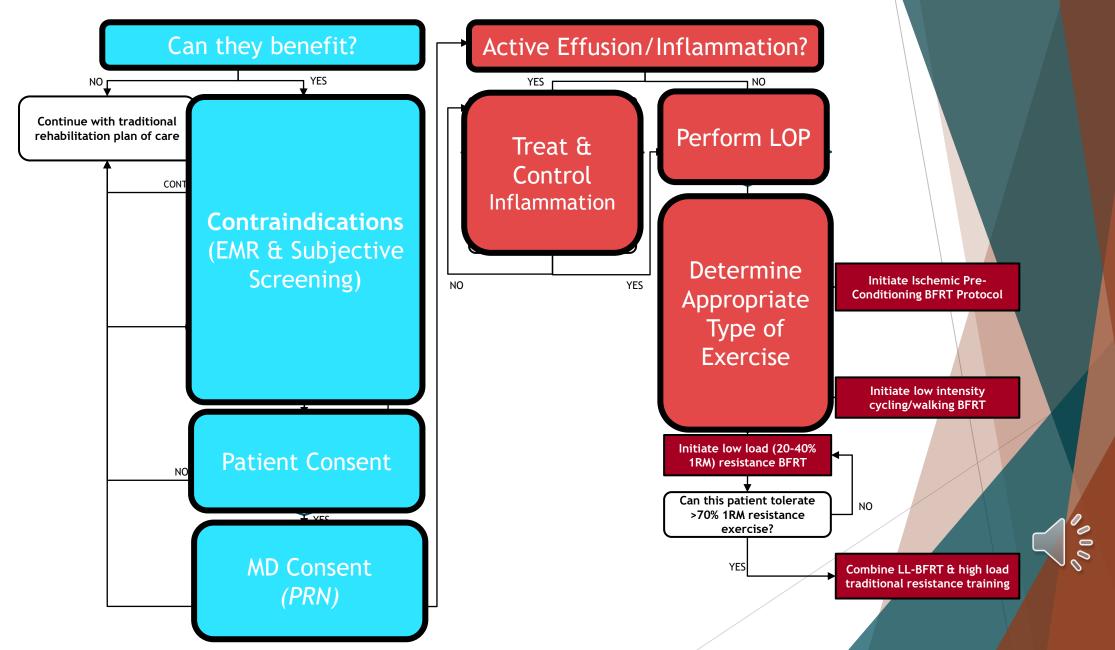


Summary & Conclusion

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- 1. Summary Slides
- 2. Review Objectives
- 3. Lab

Blood Flow Restriction Training Screening Algorithm



Practical/Clinical Application - Exercise Specifications¹

Variable	Passive Exercise	Aerobic Exercise	Resistance Exercise
Type of Exercise			
Frequency		PF	HASE 2
Exercise Intensity			
Volume	PHASE 1		
Rest ²		PF	HASE 3
Duration			
Tempo			

Scott 2014¹, Heitkamp 2015², Loenneke 2012³, Slyzs 2016⁴, Inagaki 2011⁵

Objectives

The Background & Science

What is blood flow restriction training (BFR)?

How does it actually produce said adaptations? (Pre-material)

Why would I consider using BFR? AND Who can benefit from BFR?

What does the evidence say about the effectiveness of BFR? (*Pre-material*)

How do I safely apply BFR in the clinical setting?

- 1. Is it *truly* safe? And for who?
- 2. What are the risks & side effects?
- 3. How do I know if my patient is appropriate?

Practical/Clinical Application



Questions, Comments, Feedback, Discussion...



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- Colado JC, Garcia-Masso X, Triplett TN, Flandez J, Borreani S, Tella V. <u>Concurrent validation of the OMNI-resistance exercise scale</u> of perceived exertion with Thera-band resistance bands. The Journal of Strength & Conditioning Research. 2012 Nov 1;26(11):3018-24.
- 2. Colado JC, Garcia-Masso X, Triplett NT, Calatayud J, Flandez J, Behm D, Rogers ME. <u>Construct and concurrent validation of a new</u> resistance intensity scale for exercise with thera-band® elastic bands. Journal of sports science & medicine. 2014 Dec;13(4):758.
- 3. Baechle TR, Earle RW, editors. Essentials of strength training and conditioning 3rd edition. Human kinetics; 2008.
- 4. Bamigboye AA, Smyth RM. Interventions for varicose veins and leg oedema in pregnancy. Cochrane Database of Systematic Reviews. 2007(1).
- 5. Bennett, H., & Slattery, F. (2019). Effects of Blood Flow Restriction Training on Aerobic Capacity and Performance: A Systematic Review. The Journal of Strength & Conditioning Research, 33(2), 572-583
- 6. Ediz L, Ceylan MF, Turktas U, Yanmis I, Hiz O. <u>A randomized controlled trial of electrostimulation effects on effussion, swelling and pain recovery after anterior cruciate ligament reconstruction: a pilot study</u>. Clinical rehabilitation. 2012 May;26(5):413-22.
- 7. Gorman WP, Davis KR, Donnelly R. <u>ABC of arterial and venous disease: Swollen lower limb–1: General assessment and deep vein</u> <u>thrombosis.</u> BMJ: British Medical Journal. 2000 May 27;320(7247):1453.
- 8. Haff GG, Triplett NT, editors. Essentials of strength training and conditioning 4th edition. Human kinetics; 2015 Sep 23.
- 9. Heitkamp, H. C. "<u>Training with blood flow restriction. Mechanisms, gain in strength and safety</u>." The Journal of sports medicine and physical fitness 55.5 (2015): 446-456.
- 10. Helms ER, Byrnes RK, Cooke DM, Haischer MH, Carzoli JP, Johnson TK, Cross MR, Cronin JB, Storey AG, Zourdos MC. RPE vs. <u>Percentage 1RM loading in periodized programs matched for sets and repetitions</u>. Frontiers in physiology. 2018 Mar 21;9:247.
- 11. Inagaki Y, Madarame H, Neya M, Ishii N<u>. Increase in serum growth hormone induced by electrical stimulation of muscle combined</u> with blood flow restriction. European journal of applied physiology. 2011 Nov 1;111(11):2715-21.
- 12. Le Cara E, Novo M, Rolnick N, Ascanio Y. Blood Flow Restriction Level 1 Manual. Smart Tools Plus. 2019.
- Lixandrao, Manoel E., et al. "Magnitude of muscle strength and mass adaptations between high-load resistance training versus lowload resistance training associated with blood-flow restriction: a systematic review and meta-analysis." Sports medicine 48.2 (2018): 361-378.

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14. Loenneke, J. P., R. S. Thiebaud, and T. Abe. "Does blood flow restriction result in skeletal muscle damage? A critical review of available evidence." Scandinavian journal of medicine & science in sports 24.6 (2014): e415-422.

- 13. Macedo CS, Alonso CS, Liporaci RF, Vieira F, Guirro RR. <u>Cold water immersion of the ankle decreases neuromuscular response of</u> <u>lower limb after inversion movement</u>. Brazilian journal of physical therapy. 2014 Feb;18(1):93-7.
- 14. Martín-Hernández, Juan, et al. "<u>Adaptation of perceptual responses to low-load blood flow restriction training</u>." Journal of strength and conditioning research 31.3 (2017): 765-772.
- 15. Mooventhan A, Nivethitha L. Scientific evidence-based effects of hydrotherapy on various systems of the body. North American journal of medical sciences. 2014 May;6(5):199.J, ANDREACCI J. <u>Concurrent validation of the OMNI perceived exertion scale for resistance exercise.</u> Medicine & Science in Sports & Exercise. 2003 Feb 1;35(2):333-41.
- 16. Morishita S, Tsubaki A, Takabayashi T, Fu JB. <u>Relationship between the rating of perceived exertion scale and the load intensity</u> of resistance training. Strength and conditioning journal. 2018 Apr;40(2):94-109.
- 17. Nakajima, T., Morita, T., Sato Y. "Key Considerations when conducting KAATSU training." Int. J KAATSU Training Res. 2011; 7:1-6.
- 18. Owens J, Personalized Blood Flow Restriction Rehabilitation Course Manual. Owens Recovery Science Inc. 2015.
- 19. Patterson, S. D., & Brandner, C. R. (2018). <u>The role of blood flow restriction training for applied practitioners: A questionnaire-based survey</u>. Journal of sports sciences, 36(2), 123-130.
- Robertson RJ, GOSS FL, RUTKOWSKI J, LENZ B, DIXON C, TIMMER J, FRAZEE K, DUBE J, ANDREACCI J. <u>Concurrent</u> validation of the OMNI perceived exertion scale for resistance exercise. Medicine & Science in Sports & Exercise. 2003 Feb 1;35(2):333-41.
- 21. Sari Z, Aydoğdu O, Demirbüken İ, Yurdalan SU, Polat MG<u>. A Better Way to Decrease Knee Swelling in Patients with Knee</u> Osteoarthritis: A Single-Blind Randomised Controlled Trial. Pain Research and Management. 2019;2019.
- 22. Scott, Brendan R., et al. <u>"Exercise with blood flow restriction: an updated evidence-based approach for enhanced muscular</u> <u>development</u>." Sports medicine 45.3 (2015): 313-325.

- 22. Slysz, Joshua, Jack Stultz, and Jamie F. Burr. <u>"The efficacy of blood flow restricted exercise: A systematic review & meta-analysis."</u> Journal of science and medicine in sport 19.8 (2016): 669-675.
- 23. Su EP, Perna M, Boettner F, Mayman DJ, Gerlinger T, Barsoum W, Randolph J, Lee G. <u>A prospective, multi-center,</u> <u>randomised trial to evaluate the efficacy of a cryopneumatic device on total knee arthroplasty recovery.</u> The Journal of bone and joint surgery. British volume. 2012 Nov;94(11_Supple_A):153-6.
- 24. Tamir L, Hendel D, Neyman C, Eshkenazi AU, Ben-Zvi Y, Zomer R<u>. Sequential foot compression reduces lower limb</u> swelling and pain after total knee arthroplasty. The Journal of arthroplasty. 1999 Apr 1;14(3):333-8.
- 25. Tischer TS, Oye S, Lenz R, Kreuz P, Mittelmeier W, Bader R, Tischer T. <u>Impact of compression stockings on leg swelling</u> <u>after arthroscopy-a prospective randomised pilot study</u>. BMC musculoskeletal disorders. 2019 Dec;20(1):161.
- 26. Wainwright TW, Burgess LC, Middleton RG. <u>Does Neuromuscular Electrical Stimulation Improve Recovery Following</u> <u>Acute Ankle Sprain? A Pilot Randomised Controlled Trial</u>. Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders. 2019 May;12:1179544119849024.
- 27. Yasuda, T, Meguro M, Sato, Y, Nakajima T. "Use and safety of KAATSU training: results of national survey in 2016." Int. J KAATSU Training Res. 2017; 13:1-9.
- 28. Zourdos MC, Klemp A, Dolan C, Quiles JM, Schau KA, Jo E, Helms E, Esgro B, Duncan S, Merino SG, Blanco R. <u>Novel</u> <u>resistance training-specific rating of perceived exertion scale measuring repetitions in reserve.</u> The Journal of Strength & Conditioning Research. 2016 Jan 1;30(1):267-75.

- 1. Loenneke, Jeremy P., et al. "<u>Blood flow restriction: how does it work?</u>." *Frontiers in physiology* 3 (2012): 392.
- 2. Takarada, Y., Takazawa, H., and Ishii, N. (2000a). Applications of vascular occlusion diminish disuse atrophy of knee extensor muscles. *Med. Sci. Sports Exerc.* 32, 2035–2039.
- 3. Takarada, Y., Takazawa, H., Sato, Y., Takebayashi, S., Tanaka, Y., and Ishii, N. (2000b). Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. *J. Appl. Physiol.* 88, 2097–2106.
- 4. Yasuda, T., Brechue, W. F., Fujita, T., Shirakawa, J., Sato, Y., and Abe, T. (2009). Muscle activation during low- intensity muscle contractions with restricted blood flow. *J. Sports Sci.* 27, 479–489.
- 5. Ozaki, H., Sakamaki, M., Yasuda, T., Fujita, S., Ogasawara, R., Sugaya, M., et al. (2011). Increases in thigh muscle volume and strength by walk training with leg blood flow reduction in older participants. *J. Gerontol. A Biol. Sci. Med. Sci.* 66, 257–263.
- 6. Schliess, F., Richter, L., Vom Dahl, S., and Haussinger, D. (2006). Cell hydration and mTOR-dependent signal- ling. *Acta Physiol. (Oxf.)* 187, 223–229.
- 7. Suga, T., Okita, K., Morita, N., Yokota, T., Hirabayashi, K., Horiuchi, M., et al. (2010). Dose effect on intramuscular metabolic stress during low-intensity resistance exercise with blood flow restriction. *J. Appl. Physiol.* 108, 1563–1567.
- 8. Loenneke, J. P., Fahs, C. A., Rossow, L. M., Abe, T., and Bemben, M. G. (2012a). The anabolic benefits of venous blood flow restriction training may be induced by muscle cell swelling. *Med. Hypotheses* 78, 151–154.
- 9. Loenneke, J. P., Wilson, J. M., Marin, P. J., Zourdos, M. C., and Bemben, M. G. (2012b). Low intensity blood flow restriction training: a meta-analysis. *Eur. J. Appl. Physiol.* 112, 1849–1859.
- 10. Fry, C. S., Glynn, E. L., Drummond, M. J., Timmerman, K. L., Fujita, S., Abe, T., et al. (2010). Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men. *J. Appl. Physiol.* 108, 1199–1209.

- 11. Manini, T. M., Vincent, K. R., Leeuwenburgh, C. L., Lees, H. A., Kavazis, A. N., Borst, S. E., et al. (2011). Myogenic and proteolytic mRNA expression follow- ing blood flow restricted exercise. *Acta Physiol. (Oxf.)* 201, 255–263
- 12. Kubota, A., Sakuraba, K., Koh, S., Ogura, Y., and Tamura, Y. (2011). Blood flow restriction by low compressive force prevents disuse muscular weakness. *J. Sci. Med. Sport.* 14, 95–99.
- 13. Kubota, A., Sakuraba, K., Sawaki, K., Sumide, T., and Tamura, Y. (2008). Prevention of disuse muscular weakness by restriction of blood flow. *Med. Sci. Sports Exerc.* 40, 529–534.
- 14. Laurentino, G. C., Ugrinowitsch, C., Roschel, H., Aoki, M. S., Soares, A. G., Neves, M. Jr. et al. (2012). Strength training with blood flow restriction diminishes myostatin gene expression. *Med. Sci. Sports Exerc.* 44, 406–412.
- 15. Abe, T., Kearns, C. F., and Sato, Y. (2006). Muscle size and strength are increased following walk training with restricted venous blood flow from the leg muscle, Kaatsu-walk training. *J. Appl. Physiol.* 100, 1460–1466.
- 16. VanWye, William R., Alyssa M. Weatherholt, and Alan E. Mikesky. <u>"Blood Flow Restriction Training: Implementation into Clinical Practice."</u> International journal of exercise science 10.5 (2017): 649.
- 17. Martín-Hernández, Juan, et al. <u>"Adaptation of Perceptual Responses to Low-Load Blood Flow Restriction Training."</u> Journal of strength and conditioning research 31.3 (2017): 765-772.
- 18. Kumagai, K., et al. <u>"Cardiovascular drift during low intensity exercise with leg blood flow restriction.</u>" Acta Physiologica Hungarica 99.4 (2012): 392-399.
- 19. Kaufman, Kenton R., et al. <u>"Physiological prediction of muscle forces—I. Theoretical formulation."</u> Neuroscience 40.3 (1991): 781-792.
- 20. de Freitas, Marcelo Conrado, et al. "Role of metabolic stress for enhancing muscle adaptations: practical applications." World journal of methodology 7.2 (2017): 46.

- 21. Goldberg AL, Etlinger JD, Goldspink DF, et al. Mechanism of work-induced hypertrophy of skeletal muscle. Med Sci Sports. 1975;7(3):185–98.
- 22. Spangenburg EE, Le Roith D, Ward CW, et al. A functional insulin-like growth factor receptor is not necessary for loadinduced skeletal muscle hypertrophy. J Physiol. 2008;586(1): 283–91. 38.
- 23. Vandenburgh H, Kaufman S. In vitro model for stretch-induced hypertrophy of skeletal muscle. Science. 1979;203(4377):265–8.
- 24. Manini TM, Clark BC. Blood flow restricted exercise and skeletal muscle health. Exerc Sports Sci Rev. 2009;37(2):78–85.
- 25. Suga T, Okita K, Morita N, et al. Intramuscular metabolism during low-intensity resistance exercise with blood flow restriction. J Appl Physiol. 2009;106(4):1119–24.
- 26. Cook SB, Murphy BG, Labarbera KE. Neuromuscular function after a bout of low-load blood flow-restricted exercise. Med Sci Sports Exerc. 2013;45(1):67–74.
- 27. Schoenfeld BJ. Potential mechanisms for a role of metabolic stress in hypertrophic adaptations to resistance training. Sports Med. 2013;43(3):179–94.
- 28. Schoenfeld BJ. The mechanisms of muscle hypertrophy and their application to resistance training. J Strength Cond Res. 2010;24(10):2857–72.
- 29. Goldspink G. Cellular and molecular aspects of muscle growth, adaptation and ageing. Gerodontology. 1998;15(1):35–43.
- 30. Zou K, Meador BM, Johnson B, et al. The a7b1-integrin increases muscle hypertrophy following multiple bouts of eccentric exercise. J Appl Physiol. 2011;111(4):1134–41.
- 31. Adams GR. Invited review: autocrine/paracrine IGF-I and skeletal muscle adaptation. J Appl Physiol. 2002;93(3):1159–67.
- 32. Tatsumi R, Liu X, Pulido A, et al. Satellite cell activation in stretched skeletal muscle and the role of nitric oxide and hepatocyte growth factor. An 1 Physiol Cell Physiol. 2006;290(6):C1487–94.

- 33. Uchiyama S, Tsukamoto H, Yoshimura S, et al. Relationship between oxidative stress in muscle tissue and weight-liftinginduced muscle damage. Pflugers Arch. 2006;452(1):109–16.
- 34. Takarada Y, Nakamura Y, Aruga S, et al. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol. 2000;88(1):61–5.
- 35. Takarada Y, Takazawa H, Sato Y, et al. Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. J Appl Physiol. 2000;88(6): 2097–106. 7.
- 36. Takarada Y, Sato Y, Ishii N. Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. Eur J Appl Physiol. 2002;86(4):308–14
- 37. Loenneke JP, Fahs CA, Rossow LM, et al. The anabolic benefits of venous blood flow restriction training may be induced by muscle cell swelling. Med Hypotheses. 2012;78(1):151–4
- 38. Febbraio MA, Pedersen BK. Contraction-induced myokine production and release: is skeletal muscle an endocrine organ? Exerc Sport Sci Rev. 2005;33(3):114–9
- 39. Schiaffino S, Dyar KA, Ciciliot S, et al. Mechanisms regulating skeletal muscle growth and atrophy. FEBS J. 2013;280(17): 4292–314.
- 40. Kawada S, Ishii N. Skeletal muscle hypertrophy after chronic restriction of venous blood flow in rats. Med Sci Sports Exerc. 2005;37(7):1144–50.
- 41. Pope ZK, Willardson JM, Schoenfeld BJ. A brief review: exercise and blood flow restriction. J Strength Cond Res. 2013;27(10):2914–26.

- 43. Pearson, Stephen John, and Syed Robiul Hussain. <u>"A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy.</u>" Sports Medicine 45.2 (2015): 187-200.
- 44. Queme, Luis F., Jessica L. Ross, and Michael P. Jankowski. "Peripheral mechanisms of ischemic myalgia." Frontiers in cellular neuroscience 11 (2017): 419.
- 45. Ehrnborg C, Rosen T. Physiological and pharmacological basis for the ergogenic effects of growth hormone in elite sports. Asian J Androl 2008; 10: 373–383
- 46. Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, Ishii N. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol 2000; 88:61–65
- 47. Kawada S, Ishii N. Skeletal muscle hypertrophy after chronic restriction of venous blood flow in rats. Med Sci Sports Exerc 2005; 37: 1144–1150
- 48. Takano H, Morita T, Iida H, Asada K, Kato M, Uno K, Hirose K, Matsumoto A, Takenaka K, Hirata Y, Eto F, Nagai R, Sato Y, Nakajima T. Hemodynamic and hormonal responses to a short-term low-intensity resistance exercise with the reduction of muscle blood flow. Eur J Appl Physiol 2005; 95: 65–73
- 49. Anderson JE, Wozniak AC. Satellite cell activation on fibers: modeling events in vivo an invited review. Can J Physiol Pharmacol 2004; 82: 300–310.
- 50. Uematsu M, Ohara Y, Navas JP, Nishida K, Murphy TJ, Alexander RW, Nerem RM, Harrison DG. Regulation of endothelial cell nitric oxide synthase mRNA expression by shear stress. Am J Physiol 1995; 269:C1371–C1378

- 51. Reid MB. Role of nitric oxide in skeletal muscle: synthesis, distribution and functional importance. Acta Physiol Scand 1998; 162: 401–409
- 52. Snijders, Tim, et al. "Satellite cells in human skeletal muscle plasticity." Frontiers in physiology 6 (2015): 283.
- 53. Anderson JE. A role for nitric oxide in muscle repair: Nitric oxide-mediated activation of muscle satellite cells. Mol Biol Cell 2000; 11:1859–1874
- 54. Kraemer, William J., and David P. Looney. <u>"Underlying mechanisms and physiology of muscular power."</u> Strength & Conditioning Journal 34.6 (2012): 13-19.
- 55. Moritani T, Sherman WM, Shibata M, Matsumoto T, Shinohara M. Oxygen availability and motor unit activity in humans. Eur J Appl Physiol 1992; 64: 552–556
- 56. Idstrom JP, Subramanian VH, Chance B, Schersten T, Bylund-Fellenius AC. Energy metabolism in relation to oxygen supply in contracting rat skeletal muscle. Fed Proc 1986; 45: 2937–2941
- 57. Katz A, Sahlin K. Effect of decreased oxygen availability on NADH and lactate contents in human skeletal muscle during exercise. Acta Physiol Scand 1987; 131: 119–127
- 58. Moritani T, Muro M, Nagata A. Intramuscular and surface electromyogram changes during muscle fatigue . J Appl Physiol 1986 ; 60:1179–1185
- 59. Takarada Y,Nakamura Y, Aruga S,Onda T, Miyazaki S, Ishii N. Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol 2000; 88:61–65
- 60. Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, Ishii N. Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. J Appl Physiol 2000; 88:2097–2106
- 61. Takarada Y, Takazawa H, Ishii N. Application of vascular occlusion diminsh disuse atrophy of knee extensor muscles. Med Sci Sports Exerc 2000; 32: 2035–2039

- 62. Wang X, Proud CG. <u>The mTOR pathway in the control of protein synthesis</u>. Physiology (Bethesda) 2006; 21: 362–369
- 63. Fujita S, Abe T, Drummond MJ, Cadenas JG, Dreyer HC, Sato Y, Volpi E, Rasmussen BB. Blood flow restriction during low-intensity resistance exercise increases S6K1 phosphorylation and muscle protein synthesis. J Appl Physiol 2007; 103: 903–910
- 64. Drummond MJ, Fujita S, Takashi A, Dreyer HC, Volpi E, Rasmussen BB. Human muscle gene expression following resistance exercise and blood flow restriction. Med Sci Sports Exerc 2008; 40: 691–698
- 65. McPherron AC, Lawler AM, Lee SJ. Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member. Nature 1997; 387: 83–90
- 66. McPherron AC, Lee SJ. Double muscling in cattle due to mutations in the myostatin gene. Proc Natl Acad Sci USA 1997; 94: 12457–12461
- 67. Schuelke M, Wagner KR, Stolz LE, Hubner C, Riebel T, Komen W, Braun T, Tobin JF, Lee SJ. Myostatin mutation associated with gross muscle hypertrophy in a child. N Engl J Med 2004; 350:2682–2688
- 68. Mesires NT, Doumit ME. Satellite cell proliferation and differentiation during postnatal growth of porcine skeletal muscle. Am J Physiol Cell Physiol 2002; 282: C899–9
- 69. McCroskery S, Thomas M, Maxwell L, Sharma M, Kambadur R. Myostatin negatively regulates satellite cell activation and self-renewal. J Cell Biol 2003; 162: 1135–1147
- 70. Grounds MD, Yablonka-Reuveni Z. Molecular and cell biology of skeletal muscle regeneration. Mol Cell Biol Hum Dis Ser 1993; 3: 210–256

- 71. Dodd S, Hain B, Judge A. Hsp70 prevents disuse muscle atrophy in senescent rats. Biogerontology 2008
- 72. Senf SM, Dodd SL, McClung JM, Judge AR. Hsp70 overexpression inhibits NF-kappaB and Foxo3a transcriptional activities and prevents skeletal muscle atrophy. FASEB J 2008; 22: 3836–3845
- 73. Naito H, Powers SK, Demirel HA, Sugiura T, Dodd SL, Aoki J. Heat stress attenuates skeletal muscle atrophy in hindlimb-unweighted rats. J Appl Physiol 2000 ; 88 : 359 363
- 74. Takarada Y, Takazawa H, Ishii N. Application of vascular occlusion diminsh disuse atrophy of knee extensor muscles. Med Sci Sports Exerc 2000; 32: 2035–2039
- 75. Takarada Y, Tsuruta T, Ishii N. Cooperative effects of exercise and occlusive stimuli on muscular function in low-intensity resistance exercise with moderate vascular occlusion. Jpn J Physiol. 2004;54(6):585–92.
- 76. Takada S, Okita K, Suga T, et al. Low-intensity exercise canincrease muscle mass and strength proportionally to enhanced metabolic stress under ischemic conditions. J Appl Physiol.2012;113(2):199–205.
- 77. Sumide T, Sakuraba K, Sawaki K, et al. Effect of resistance exercise training combined with relatively low vascular occlusion. J Sci Med Sport. 2009;12(1):107–12.
- 78. Loenneke JP, Pujol TJ. The use of occlusion training to produce muscle hypertrophy. Strength Cond J. 2009;31(3):77–84.
- 79. Moore DR, Burgomaster KA, Schofield LM, et al. Neuromuscular adaptations in human muscle following low intensity resistance training with vascular occlusion. Eur J Appl Physiol. 2004;92(4–5):399–406.
- 80. Kaijser L, Sundberg CJ, Eiken O, et al. Muscle oxidative capacity and work performance after training under local leg ischemia. J Appl Physiol. 1990;69(2):785–7.

- 81. Shinohara M, Kouzaki M, Yoshihisa T, et al. Efficacy of tourniquet ischemia for strength training with low resistance. Eur JAppl Physiol Occup Physiol. 1998;77(1–2):189–91
- 82. Loenneke JP, Kearney ML, Thrower AD, et al. The acute response of practical occlusion in the knee extensors. J Strength Cond Res. 2010;24(10):2831–4.
- 83. Heitkamp, H. C. "<u>Training with blood flow restriction. Mechanisms, gain in strength and safety</u>." The Journal of sports medicine and physical fitness 55.5 (2015): 446-456.
- 84. Loenneke, J. P., R. S. Thiebaud, and T. Abe. "Does blood flow restriction result in skeletal muscle damage? A critical review of available evidence." Scandinavian journal of medicine & science in sports 24.6 (2014): e415-422.
- 85. Slysz, Joshua, Jack Stultz, and Jamie F. Burr. <u>"The efficacy of blood flow restricted exercise: A systematic review & meta-analysis."</u> Journal of science and medicine in sport 19.8 (2016): 669-675.
- 86. Loenneke, Jeremy P., et al. "Low intensity blood flow restriction training: a meta-analysis." European journal of applied physiology 112.5 (2012): 1849-1859.
- 87. Scott, Brendan R., et al. <u>"Exercise with blood flow restriction: an updated evidence-based approach for enhanced muscular development</u>." Sports medicine 45.3 (2015): 313-325.
- 88. Nakajima, T., Morita, T., Sato Y. "Key Considerations when conducting KAATSU training." Int. J KAATSU Training Res. 2011; 7:1-6.
- 89. Yasuda, T, Meguro M, Sato, Y, Nakajima T. "Use and safety of KAATSU training: results of national survey in 2016." Int. J KAATSU Training Res. 2017; 13:1-9.



- 90. Loenneke JP, Fahs CA, Rossow LM, et al. Effects of cuff width on arterial occlusion: implications for blood flow restricted exercise. Eur J Appl Physiol. 2012;112(8):2903–12.
- 91. Cook SB, Clark BC, Ploutz-Snyder LL. Effects of exercise load and blood-flow restriction on skeletal muscle function. Med Sci Sports Exerc. 2007;39(10):1708–13.
- 92. Loenneke JP, Kim D, Fahs CA, et al. Effects of exercise with and without different degrees of blood flow restriction on torque and muscle activation. Muscle Nerve. Epub 2014 Sep 3. doi:10.1002/mus.24448.
- 93. Wilson JM, Lowery RP, Joy JM, et al. Practical blood flow restriction training increases acute determinants of hypertrophy without increasing indices of muscle damage. J Strength Cond Res. 2013;27(11):3068–75.
- 94. Loenneke JP, Thiebaud RS, Fahs CA, et al. Effect of cuff type on arterial occlusion. Clin Physiol Funct Imaging. 2013;33(4):325–7
- 95. Loenneke JP, Thiebaud RS, Fahs CA, et al. Blood flow restriction: Effects of cuff type on fatigue and perceptual responses to resistance exercise. Acta Physiol Hung. 2014;101(2):158–66.
- 96. Kacin A, Strazar K. Frequent low-load ischemic resistanceexercise to failure enhances muscle oxygen delivery and endur-ance capacity. Scand J Med Sci Sports. 2011;21(6):e231–41.
- 97. Spranger, Marty D., et al. "Blood flow restriction training and the exercise pressor reflex: a call for concern." American Journal of Physiology-Heart and Circulatory Physiology 309.9 (2015): H1440-H1452.
- 98. Patterson, Stephen D., and Richard A. Ferguson. "Increase in calf post-occlusive blood flow and strength following short-term resistance exercise training with blood flow restriction in young women." European journal of applied physiology 108.5 (2010): 1025-1033.



- 99. MacDougall JD, Tuxen D, Sale DG, Moroz JR, Sutton JR. Arterial blood pressure response to heavy resistance exercise. J Appl Physiol 58:785–790, 1985
- 100. Loenneke, J. P., et al. "Potential safety issues with blood flow restriction training." Scandinavian journal of medicine & science in sports 21.4 (2011): 510-518.
- 101. Mattar, Melina Andrade, et al. <u>"Safety and possible effects of low-intensity resistance training associated with partial blood flow restriction in polymyositis and dermatomyositis.</u>" Arthritis research & therapy 16.5 (2014): 473.
- 102. Douris, Peter C., et al. <u>"THE EFFECTS OF BLOOD FLOW RESTRICTION TRAINING ON FUNCTIONAL IMPROVEMENTS IN AN ACTIVE SINGLE SUBJECT WITH PARKINSON DISEASE.</u> International Journal of Sports Physical Therapy 13.2 (2018).
- 103. Tennent, David J., et al. <u>"Blood flow restriction training after knee arthroscopy: a randomized controlled pilot study."</u> Clinical Journal of Sport Medicine 27.3 (2017): 245-252.
- 104. Iida, Haruko, et al. "Effects of walking with blood flow restriction on limb venous compliance in elderly subjects." Clinical physiology and functional imaging 31.6 (2011): 472-476.
- 105. Luebbers, Paul E., Emily V. Witte, and Johnathan Q. Oshel. <u>"The Effects Of Practical Blood Flow Restriction Training On Adolescent Lower Body</u> <u>Strength.</u>" Journal of strength and conditioning research (2017).
- 106. Ozaki, Hayao, et al. "Increases in thigh muscle volume and strength by walk training with leg blood flow reduction in older participants." Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences 66.3 (2010): 257-263.
- 107. Ozaki, Hayao, et al. <u>"Effects of 10 weeks walk training with leg blood flow reduction on carotid arterial compliance and muscle size in the elderly adults.</u>" Angiology 62.1 (2011): 81-86.



- 108. Jørgensen, A. N., et al. "<u>Blood-flow restricted resistance training in patients with sporadic inclusion body myositis: a randomized controlled trial.</u>" Scandinavian journal of rheumatology (2018): 1-10.
- 109. Libardi, C. A., et al. "Effect of concurrent training with blood flow restriction in the elderly." International journal of sports medicine (2015).
- 110. Hackney, Kyle J., et al. "Blood flow-restricted exercise in space." Extreme physiology & medicine 1.1 (2012): 12.
- 111. Pinto, Roberta R., et al. "Acute resistance exercise with blood flow restriction in elderly hypertensive women: haemodynamic, rating of perceived exertion and blood lactate." Clinical physiology and functional imaging 38.1 (2018): 17-24.
- 112. Takarada, Yudai, Haruo Takazawa, and Naokata Ishii. "<u>Applications of vascular occlusions diminish disuse atrophy of knee extensor muscles</u>." Medicine and science in sports and exercise 32.12 (2000): 2035-2039.
- 113. Iversen, Erik, Vibeke Røstad, and Arne Larmo. <u>"Intermittent blood flow restriction does not reduce atrophy following anterior cruciate ligament reconstruction</u>." Journal of Sport and Health Science 5.1 (2016): 115-118.
- 114. Ohta, Haruyasu, et al. <u>"Low-load resistance muscular training with moderate restriction of blood flow after anterior cruciate ligament reconstruction.</u>" Acta Orthopaedica Scandinavica 74.1 (2003): 62-68.
- 115. Slysz, Joshua T., and Jamie F. Burr. <u>"The effects of blood flow restricted electrostimulation on strength and hypertrophy."</u> Journal of sport rehabilitation 27.3 (2018): 257-262.
- 116. Bittar, S. T., et al. "Effects of blood flow restriction exercises on bone metabolism: a systematic review." Clinical physiology and functional imaging (2018).