REDUCTION OF LOWER LIMB OEDEMA BY GRADIENT COMPRESSION STOCKINGS WITH PHYSICAL MOVEMENTS: MECHANISM, MODELLING, AND EVALUATION

PIAO JINLI

PhD

The Hong Kong Polytechnic University

2025

The Hong Kong Polytechnic University

School of Fashion and Textiles

Reduction of Lower Limb Oedema by Gradient Compression Stockings with Physical Movements: Mechanism, Modelling, and Evaluation

Piao Jinli

A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy

August 2024

CERTIFICATE OF ORIGINALITY

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it reproduces no material previously published or written, nor material that has been accepted for the award of any other degree or diploma, except where due acknowledgement has been made in the text.

___________________________(Signed)

PIAO JINLI

___________________________(Name of student)

ABSTRACT

Lower limb oedema is common, especially among imbalanced diet and nutrition, prolonged walking, standing, and sedentariness, pregnancy, obese individuals, venous insufficiency, and lymphatic obstruction can also be associated with the oedema generation. Without proper treatment, it can develop into chronic venous disease. Treatment options include medication, leg elevation, compression therapy, manual lymphatic massage, electrical stimulation, and surgery, depending on the symptoms. Because of the side effects of medication, risks of surgery, and inconvenience of other treatments, compression therapy has become a promising long-term solution. Skeletal muscle movement also helps improve blood circulation and reduce oedema. Recent studies have shown that applying compression to the lower limbs can effectively reduce oedema. However, there are still some limitations in current research. Many numerical models only consider limb deformation under pressure and ignore the fluid exchange among blood vessels, tissues, and lymph. They also often overlook the physiological factors of blood and interstitial fluid. Moreover, there are not enough practical trials combining compression methods with physical movements in the treatment of lower limb oedema.

To address these challenges, this thesis focuses on the reduction of lower limb oedema through the integration of gradient compression stockings with physical movements. At first, a new simplified capillary-blood-tissue model is proposed based on the computational fluid dynamics (CFD) method to analyse fluid exchange between blood and interstitial fluid and determine critical pressures. Then, various physiological parameters, including capillary and tissue porosity, blood viscosity, and inlet velocity, are studied to investigate their effects on compression treatment for oedema reduction. Lastly, three-phase trial tests are designed and conducted to validate the numerical results and statistically evaluate the efficacy of the compression methods. Furthermore, considering that skeletal muscle movement can enhance

blood circulation and contribute to oedema mitigation, specifically dedicated designed lower limb movements (LLMs) are incorporated into these trial tests to accelerate the oedema reduction process.

In the numerical study chapter, we developed a two-dimensional numerical model of the capillary-blood-tissue system using the porous media model. This simplified model improves upon previous models by more effectively simulating fluid exchange between blood and interstitial fluid, thus offering a more accurate representation of oedema generation and reduction. In the simulation, a filtration indicator (equal to 90% reabsorption and 10% lymphatic flow) is utilized to evaluate the reduction of oedema. It suggests that oedema reduction is expected if reabsorption exceeds 90%. Conversely, if reabsorption is less than 90%, oedema may persist. Correspondingly, when reabsorption is at 90%, the pressure differential between the blood vessel and the applied pressure is referred to as the "critical pressure". And then, these critical pressures were determined under varying physiological parameters, including capillary and tissue porosity, blood viscosity, and inlet velocity. Our results demonstrated that oedema reduction is directly proportional to the applied constant compression pressure. Additionally, capillary and tissue porosity, along with inlet velocity, significantly influence oedema reduction under constant compression pressure, whereas blood viscosity has a minor effect. Furthermore, constant and harmonic pressures produce similar effects on the percentage of venous outflow at the same pressure amplitude, and harmonic frequency shows no significant sensitivity to the percentage of venous outflow.

To validate the numerical results, the three-phase trial tests were conducted to evaluate the efficacy of lower limb oedema reduction. The design of these trial tests integrated gradient compression stockings with LLMs in each phase, aiming to facilitate subsequent trial tests by identifying the most effective approaches: **Phase 1:** This trial involved young healthy subjects and examined the effectiveness of Class I level gradient medical compression stockings (MCS), non-stretchable WRAP, and bare leg, with and without LLMs. The evaluation was based on volume and circumference measurements. **Phase 2:** In this phase, elderly subjects with mild oedema were tested to evaluate the efficacy of oedema reduction using Class I level gradient WRAP and MCS, with and without LLMs. The evaluation focused on circumference measurements. **Phase 3:** The final phase involved a larger group of elderly subjects with mild oedema to evaluate the efficacy and compliance of low-pressure gradient MCS with and without LLMs. This phase also assessed the acceptance of the designed LLMs among the elderly subjects. The study statistically analysed the impact of various wearing conditions, the effect of incorporating LLMs, differences between legs, gender, BMI, and the relationship between dynamic compression pressure during LLMs and the reduction rate in lower limb circumference.

The trial tests results demonstrated that regards to young healthy subjects, WRAP (Mean: -66.3 cm^3 SD: 51.0 cm^3) was bigger than MCS (Mean: -58.5 cm^3 SD: 42.0 cm^3) and bare leg (Mean: -63.5 cm^3 SD: 50.5 cm^3) in lower limb volume reduction within the group conducting LLMs, while MCS (Mean: -51.2 cm^3 SD: 46.8 cm^3) had more volume reduction than WRAP (Mean: -41.9 cm^3 SD: 35.6cm^3) and bare leg (Mean: -42.4 cm^3 SD: 57.6 cm^3) in the group without LLMs, as evaluated through water displacement volumetry. There were no significant statistical differences observed among wearing conditions within each group. However, significant circumference reductions were observed in young healthy subjects who conducted LLMs, and applying compression was more effective than bare leg for oedema reduction. MCS with LLMs (Mean: -1.3% SD: 0.8%) had more circumference reduction than WRAP with LLMs (Mean: -0.9% SD: 0.7%) at point C, the WRAP with LLMs (Mean: -1.1% SD: 0.7%) was more effective than bare leg with LLMs (Mean: -0.6% SD: 0.6%) at point D. Furthermore, males showed an extremely significant circumference reduction compared to females when

applying MCS at point C, either with or without conducting LLMs ($p < 0.001$). Regarding elderly subjects with mild oedema, MCS was better than WRAP in oedema reduction when applying compression alone, and the integration of MCS and LLMs consistently achieved oedema reduction compared to utilizing MCS alone. In addition, MCS with 2 sets of LLMs significantly had circumference reduction at various lower limb points. Subjects with a BMI $\leq$ 24.9 performed a more significant circumference reduction rate at certain points than those with a BMI >24.9, regardless of whether LLMs were conducted ($p < 0.05$).

The dynamic mean pressure declined and fluctuated during LLMs. The young healthy group showed dynamic mean pressures of 13.3 mmHg in WRAP and 10.5 mmHg in MCS at point C. The elderly group revealed dynamic mean pressures of 5.1 mmHg (=679.9 Pa) in WRAP and 6.5 mmHg (=866.6 Pa) in MCS at point C. These dynamic mean pressures containing compression stockings and muscles' contraction were higher than the critical pressure threshold of 550 Pa with normal physiological parameters in the numerical simulation. Furthermore, more than half of young subjects preferred WRAP due to its convenience in wearing. However, integrating the LLMs with low-pressure MCS performed a more stable quality of life (QoL) score than without LLMs and it was better received in terms of exercise intensity preference among the elderly population.

In summary, this thesis comprehensively studied integrating low-pressure compression stockings with physical movements on oedema reduction through numerical simulation and practical trials and provides valuable insights into its potential application in promoting active health.

LIST OF PUBLICATIONS

Publications arising from the thesis

(* corresponding author)

1. **Jinli PIAO**, Ying XIONG, Bao YANG, Manyui LEUNG, Chunmin LI, and Xiaoming TAO*, Reduction of Lower Limb Oedema by Low-Pressure Dynamic Compression Above the Critical Pressure Threshold, *Scientific Reports*, **Under review.**

2. **Jinli PIAO**, Bao YANG, Manyui LEUNG, Chunmin LI, Xiaoming TAO*, Review on Oedema Reduction by Gradient Compression Stockings and Skeletal Muscle Movement: Materials, Constructions and Effect, *iScience,* **Under review.**

Conference presentations

(* corresponding author)

1. **Jinli PIAO,** Ying XIONG, Chunmin LI, and Xiaoming Tao*, "Reduction of Lower Limb Oedema by Low-Pressure Dynamic Compression Above the Critical Pressure Threshold", Poster and Oral Presentations, **Best Poster Presentation Award,** The Symposium on Sports Science & Technology 2024, Hong Kong, China, November 2024.
2. **Jinli PIAO,** Ying XIONG, Bao YANG, Chunmin LI, and Xiaoming TAO*, " Investigation of the Synergistic Effects and Mechanisms of Low-Pressure Gradient

Compression Stockings and Lower Limb Movement Interventions in Oedema Alleviation(低压梯度压力袜与下肢运动干预在水肿缓解中的联合效应与机制研究)", Oral Presentation (in Chinese), The 17th National Experimental Mechanics Conference, Zhuhai, China, December 2024.

Publications during the PhD study but not included in this thesis

(* corresponding author)

1. Jing Yang, Ying Xiong, **Jinli Piao**, Manyui Leung, Guosai Liu, Mingyue Zhu, Shengyang Tang, Lisha Zhang, Xiaoming Tao*. (2024). Wearable Fluidic Fabric with Excellent Heat Transfer Performance for Sports Recovery. *Advanced Science*, 2411691.

2. Fang Bo, Jianmin Yan, Dan Chang, **Jinli Piao**, Kit Ming Ma, Qiao Gu, Ping Gao, Yang Chai, and Xiaoming Tao*. (2022). Scalable Production of Ultrafine Polyaniline Fibres for Tactile Organic Electrochemical Transistors. *Nature communications*, 13(1), 2101.

3. **Patent:** Xiaoming Tao, **Jinli Piao**, Bao Yang, Fiber Optic Sensor and Method for Measurement of Friction Coefficient(光纤传感器及摩擦系数的测量方法), China National Invention Patent, Application number: 202211491815.5, **Under review.**

ACKNOWLEDGEMENTS

The 3-year duration of my PhD programme has presented a valuable opportunity for significant professional and personal growth. During PhD study in the School of Fashion and Textiles at The Hong Kong Polytechnic University, I would like to express my gratitude to the many people who have supported and assisted me in my research.

My greatest appreciation is to my chief supervisor Professor Tao Xiaoming, director of Research Institute for Intelligent Wearable Systems and Vincent and Lily Woo Professor in Textile Technology. She is a professional scientist, expert, and good mentor. For me who had come to the present through the tortuous research process, she gave me many opportunities, encouraged me, and guided me to enter the PhD study smoothly. She taught me how to think about scientific problems, how to find problems, and how to finish good academic work rigorously. Through every group meeting, every project meeting, and 1 vs 1 personal meeting, she guided me in my research progress, discussed difficulties, corrected wrong ideas, and developed new thinking. These have inspired and helped me a lot as an interdisciplinary study student. Once again, I thank Professor Tao for her professional guidance and the best concern for my studies and life, and sincerely appreciative of the stipend and research fund provided for my PhD studies.

I would like to thank the co-supervisor Professor Li Chunmin, the doctor at Beijing Chao-Yang Hospital, Capital Medical University. Although he is far away, Professor Li Chunmin takes time out of his busy clinic schedule to discuss with me, listen to my progress, discuss research directions with the chief supervisor, and share his clinical experience on compression therapy. Because of his guidance, I have a clear research direction for my research.

In addition, I especially thank a former groupmate in our ream, Dr. Yang Bao, the associate professor at the South China University of Technology. He is a very rigorous scientific researcher. He helped me adapt to the new environment when I first came to the group, taught me the experimental equipment, and helped me effectively complete the project and research.

I would like to sincerely thank the panels for their dedication to the review process.

I am grateful to The Hong Kong Polytechnic University and the School of Fashion and Textile for their support. I also want to express my appreciation for the hard work of the general officers in SFT.

Thanks to Dr. Tang Hui's group at the Department of Mechanical Engineering for generously providing access to the physical experiment platform in the Water Tunnel Laboratory.

Additionally, I extend my thanks to the Innovation and Technology Fund project, the Government of the Hong Kong Special Administrative Region.

Thank you to all the participants in the trial test from Helping Hand – Po Lam Jockey Club Housing for the Elderly and The Hong Kong Polytechnic University. I also want to express my gratitude to our group members for their help in the trial project. Sincere thanks to Ms. Yang Jing and Dr. Xiong Ying, as well as Ms. Ma Kitming, Ms. Li Ke, Ms. Li Wenbo, Ms. Wong Huang Man Huen Nicole, Mr. Tang Shengyang, Ms. Liu Tongyao, Ms. Zhu Mingyue, Mr. Wang Shuo, Mr. Luo Yonghui, and Ms. Kelly.

Besides, thank you for the help from all our group members both in study and life: Dr. Fang Bo, Dr. Lin Shuping, Dr. Zhang Lisha, Dr. Zhang Ziheng, Dr.Pu Junhong, Dr. Liu Su, Dr. Li Jun, Dr. Qi Bao, Ms WANG Can, Savannah, Ms. Li Ying, Ms. Leung Manyui, Ms. Ma Linlin, Mr. Liu Shirui, Dr. Liu Jin, Dr.Yang Su, Dr Ding Xujiao, Mr. Wu Jingyang, Mr. Balilonda Andrew, Mr. Chen Xiaobin, Mr. Jin Dian, and Mr. Luo Heng.

Thank you for the scientific discussion and valuable suggestions during the meeting with old friends in ME, including Dr. Wang Zhaokun, Dr. Wang Wei, Dr. Zeng Lingwei, Dr. Wen Fuzhen, Dr. Zhou Tong, Dr. Jiang Qian, Mr. Deng Fang, Mr. Yuen Tsz Wai, and Mr. Wang Yanqi.

Finally, I attribute all the glory to my parents, who support me with their unspoken strength. I am grateful to my husband, Dr. ZHAO Fuwang, for giving me so much courage. He has provided me with countless moments of peace of mind and has been the driving force that allows me to complete my PhD without losing sight of my original intention. He has helped me maintain a positive outlook and put endless effort into my academic future.

Thank you, Hong Kong, where I have worked and studied for 8 years.

Thanks for everything in the past and I want to acknowledge all the challenges in the future.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF GENERAL SYMBOLS

Symbol	Structural parameters	Unit
ρ	density	kg/m^3
$\boldsymbol{r}$	radius	m
μ	fluid viscosity	kg/(m·s)
$\boldsymbol{M}$	momentum	Nm
$\boldsymbol{Q}$	fluid flow	m^3/s
α	permeability	
$\|\Delta p\|$	pressure difference	Pa
L	length	m
ε	porosity	
$\boldsymbol{v_m}$	mean velocity	m/s
G	shear module	N/m^2
d	diameter (d=2r)	m

LIST OF ABBREVIATIONS

Definitions	Abbreviations
Body Mass Index	BMI
Computational Fluid Dynamics	CFD
Circumference Change	CC
Finite Element Method	FEM
Deep Vein Thrombosis	DVT
Interface Pressure	IP
Lower Limb Movements	LLMs
Magnetic Resonance Imaging	MRI
Medical Compression Stocking	MCS
Quality of Life	QoL
Preference for and Tolerance of the Intensity of Exercise Questionnaire	PRETIE-Q
Standard Deviation	SD
Volume Change	VC
p-value in the statistical significance analysis of elderly subjects after completing 1 set of lower limb movements/15 minutes of sitting in the second and third trial tests	p_{1st}
p-value in the statistical significance analysis of elderly subjects after completing 2 sets of lower limb movements/30 minutes of sitting in the second and third trial tests	P_{2nd}
Mean circumference reduction percentage in statistical analysis of elderly subjects' data after completing 1 set of lower limb	$Mean_{1st}$

movements/15 minutes of sitting in the second and third trial tests	
Mean circumference reduction percentage in statistical analysis of elderly subjects' data after completing 2 sets of lower limb movements/30 minutes of sitting in the second and third trial tests	$Mean_{2nd}$
Standard deviation of circumference reduction percentage in statistical analysis of elderly subjects' data after completing 1 set of lower limb movements/15 minutes of sitting in the second and third trial tests	SD_{1st}
Standard deviation of circumference reduction percentage in statistical analysis of elderly subjects' data after completing 2 sets of lower limb movements/30 minutes of sitting in the second and third trial tests	SD_{2nd}

CHAPTER 1

INTRODUCTION

1.1 Background

Oedema, characterized by the accumulation of excess fluid in bodily tissues, can manifest in various forms such as cerebral, pulmonary, and ocular oedema. Peripheral oedema specifically refers to swelling in the limbs and is common in contemporary health, often affecting the upper or lower limbs. In the United States, the prevalence of lower limb oedema among older adults ranged from 19% to 20% between 2000 and 2016 [1]. If untreated, it can progress into a chronic condition, causing lower limb pain and itching. Those with lower limb oedema may also experience functional and cosmetic impairments, requiring ongoing treatment and psychological support [2]. Physiologically, imbalances in diet and nutrition, as well as factors like physical activity, posture (e.g., prolonged walking, standing, or sitting [3-5]), and pregnancy, obesity, can contribute to oedema. Additionally, conditions such as heart failure, hepatic cirrhosis, renal or thyroid disease, certain medications, venous insufficiency, and lymphatic obstruction are also associated with oedema. Till now, various therapies are available for lower limb oedema, including leg elevation [2, 6, 7], compression stockings and pneumatic compression [2, 6-10], manual lymphatic drainage [2, 7, 11], electrical stimulation, and surgery [8, 11]. Among these, compression stockings are widely favoured for oedema patients due to its high patient satisfaction, accessibility, and minimal side effects. The detailed therapy, advantages, and disadvantages are outlined in Chapter 2. Additionally, lower limb movements have been recognized as exerting compression effective in oedema reduction. The primary challenge in compression therapy is selecting appropriate pressure values for individual patients and effectively combining compression with beneficial movements.

To determine the optimal compression treatment threshold pressure or its range, it is essential to understand the principle of oedema reduction through a numerical model that accurately represents fluid exchange under compression pressure. Additionally, the impact of different physiological parameters on oedema reduction must be investigated, as varying physiological causes can lead to imbalances in fluid filtration and reabsorption [2, 12]. It is also important to design various compression stockings and external pressure methods to enhance the effectiveness and acceptance of oedema reduction or prevention among patients. External pressure can be applied through skeletal muscle movement in the lower limb. Conducting practical trials and efficacy analyses of these movements can provide valuable insights for clinical staff regarding compression therapy. Furthermore, examining factors that influence oedema reduction based on individual conditions can improve treatment efficacy.

1.2 Problem Statement

Current research indicates that compression therapy has shown positive results in clinical settings for oedema reduction. Therefore, understanding the mechanism of oedema reduction using suitable compression methods and conducting substantial practical experiments to evaluate their efficacy among subjects is essential for achieving the best outcomes. However, many issues need to be addressed systematically.

1) The Windkessel Model [13-15] describes the cardiovascular system as a closed hydraulic circuit, including the heart and systemic arterial system, simplifying many complex factors. However, it does not account for fluid exchange between blood vessels and tissues, or the hemodynamic responses related to spatial considerations. Additionally, while the model

simulates fluid balance at the capillary level based on experimental data on capillary permeability and hydrostatic pressures[16, 17], it does not address fluid exchange imbalances, which are crucial for understanding and reducing lower limb oedema. Therefore, developing a model that integrates both tissue and blood vessels to represent fluid exchange between blood and interstitial fluid is essential for accurately predicting the required pressure values in compression treatment.

2) The physiological mechanisms behind lower limb oedema [1, 6, 18, 19] are well understood, and varying physiological parameters result in different pressure drops in blood vessels. Consequently, predicting how the required compression pressure value will vary for oedema cases with different physiological parameters is still an open question.

3) Compression stockings effectively reduce oedema, and skeletal muscle movement stimulates the vascular and lymphatic systems through muscle contraction, helping to reduce lower limb volume in healthy individuals [20-22]. Integrating compression therapy with physical movements enhances oedema relief. However, the effects of changing compression pressure during movement and the relationship between dynamic compression pressure change and oedema reduction rate have not been thoroughly explored. Understanding these factors is crucial for optimizing clinical approaches to oedema reduction through lower limb movements.

4) Once the integration of compression pressure and physical movements for oedema reduction is established, a substantial number of subjects need to be recruited for group trial tests to validate efficacy and compliance. Selecting the optimal method through these trials is crucial. However, there is a lack of practical trials examining the efficacy of different compression stockings combined with lower limb movements on oedema

reduction. Additionally, the impact of factors such as left or right legs, gender, and BMI on oedema reduction efficacy remains unresolved.

5) The effects of compression treatment can vary across different age groups due to changes in physiological parameters, and differing muscle conditions can lead to varied exercise outcomes. Currently, there is a lack of comparative studies on the same compression treatment across different age groups.

1.3 Research Objectives

To address the deficiencies and solve the currently existing research problems, the primary research objectives of this study are as follows:

1) Develop a 2D simplified numerical model of capillary-blood-tissue to simulate fluid exchange between blood and interstitial fluid using the porous media model, to reduce oedema and uncover the mechanism of compression treatment on swelling.

2) Identify a critical indicator in the numerical simulation that can confirm and predict the oedema reduction. Calculate the critical pressure values required to reduce oedema under compression pressure on tissue, considering different physiological parameters and clinical scenarios.

3) Design trial protocols for different age groups to investigate the optimal method of integrating the wearable compression approach or bare leg and skeletal muscle movement in the lower limb. Based on the exploring results, conduct a substantial group trial to evaluate the efficacy of the optimal integrating compression and lower limb movements for oedema reduction and its compliance.

4) Statistically analyse the efficacy of reducing lower limb oedema using volume and circumference measurements, comparing the young and elderly age groups and considering factors such as leg or right lower limb, gender, and BMI.

5) Evaluate the effect of skeletal muscle movement on applying compression treatment, find out the relationship between the dynamic external compression pressure on the lower limb and circumference reduction rate, and compare different types of compression in relieving lower limb oedema.

1.4 Methodology

1.4.1 Computational fluid dynamics (CFD)

In the bio-medical research field, CFD is a useful method for the investigation of hemodynamics, the detailed information of the cardiovascular system can be obtained through it [23]. In addition, CFD has been widely used for the quantitative assessment of the hemodynamics of cardiovascular diseases to guide individualized risk-tailored treatment strategies [24]. Furthermore, the CFD method has been utilized to assess particular parameters in the body such as wall shear stress (WSS) and blood velocity in the vessel stream, which have complexity to obtain from vivo experiment [25]. Therefore, CFD is the indispensable research method in fluid mechanics and medical–industrial interdisciplinary study.

Describing every component in the numerical model will be extremely complex and it requires a vast amount of calculation time even if using the high-performance computers. Therefore, simplifying the numerical model according to the physical characteristics is essential. The flow dynamics are governed by the continuity equation and incompressible Navier–Stokes equation.

However, these equations are highly nonlinear partial differential equations, it is difficult to solve the analytical solutions.

Therefore, the Computational fluid dynamics (CFD) method is adopted to obtain the numerical result. CFD is to solve the smooth variable value at a given space and time discrete point. It reveals the point-to-point data, for example, fluid flow, velocity, pressure from the veins with small diameters, as obtaining such data is almost impossible using current medical devices [23]. CFD is the process of mathematically modelling about physical phenomena involving fluid flow and numerically solving them [26]. The basic CFD solver employs a finite volume discretization of the fluid domain.

Finally, the CFD numerical simulation results should be validated the accuracy of the modelling through physical experiments.

1.4.2 Design movements for stimulating skeletal muscle

By conducting a comprehensive review of existing literature on exercise/movement interventions for reducing lower limb oedema, an analysis of the distribution of lower limb muscles, in conjunction with sports anatomy [19, 27-29], is performed to identify effective lower limb movements for mitigating lower limb oedema. Subsequently, lower limb movements are designed based on these findings.

1.4.3 Trial tests

The trial test methods are as follows:

1) Based on the numerical simulation study, the evaluation of the simulation results through practical trials is critical. Consequently, the design of the trial tests is necessary, encompassing the determination of the trials' objectives, following the ethical

principles for non-clinic research, the design of the trials' procedures, the selection of various combinations of compression stockings and movements for oedema reduction, the establishment of conditions for the experimental and control groups, and the determination of experimental precautions.

2) The measurement methods, their robustness analysis, and repeatability verification of the measurement methods should be determined.

3) Eligible subjects with mild oedema should be recruited for the trial tests.

4) The trial tests should be conducted in three stages. The first trial test involves the elimination of the worst effective integration among medical compression stocking (MCS) and movements, non-stretchable WRAP and movements, bare leg and movements, and their corresponding control groups on oedema reduction. The second trial test is carried out using selected integration from the first trial test, and the most effective combination approach on oedema relief is selected for the third substantial large-scale group trial test.

5) Following the completion of each trial test, the statistical significance analysis should be conducted in mitigating oedema efficacy, including the identification of other factors influencing oedema reduction, and a comparative analysis of the results.

6) Finally, the quality of life (QoL) satisfaction evaluation of compression stockings with or without lower limb movements and the acceptance of designed lower limb movements should be assessed using questionnaires: VEINES-QOL/Sym questionnaire and the Preference for and Tolerance of the Intensity of Exercise Questionnaire (PRETIE-Q).

1.5 Research Significance

The novelties and significances of this thesis are shown in the following aspects:

1) Establishing the numerical model of capillary-blood-tissue using the porous media model. The critical pressure threshold obtained in the numerical simulation effectively illustrates the principle of oedema reduction through compression treatment.

2) The calculation of the critical pressure values under different physiological parameters reflects the magnitude of change of compression values for oedema reduction under different physiological scenarios.

3) A set of lower limb movements programme, designed to effectively reduce lower limb oedema within a short timeframe, has been developed.

4) The trial test is conducted with three-phases, representing a significant advancement in practical trials. Through an extensive array of trial tests, the efficacy of low-pressure compression integrated with lower limb movements in reducing lower limb oedema is effectively presented, revealing the positive impact of lower limb movements on compression treatment.

5) Trial tests are carried out on different cohorts of young and elderly subjects, the extent of the lower limb oedema reduction across different age groups is achieved by utilizing different compression stockings integrated with lower limb movements.

6) This study presents the critical pressure threshold obtained in the numerical simulation and the efficacy evaluation results from a substantial number of trial tests, which can provide valuable reference points for clinicians.

1.6 Structure of the Thesis

This thesis contains establishing numerical modelling for finding critical pressure thresholds in different pathological parameters and practical trials for selecting the optimal approach of integrating compression pressure and lower limb movements in six chapters. The main contents are as follows in six chapters.

Chapter 1 is the introduction, encompassing the background of the research, the current problem statement, research objectives, the methodology employed, and the significance of the research.

Chapter 2 is the literature review. First is the specific explanation the causes, treatment, and assessment of oedema. Second is the current study on the effect of applying compression on lower limbs and blood vessels using modelling and numerical simulation methods. Third is the review of the compression stockings' effect on oedema reduction including medical compression stockings and non-stretchable bandages. Fourth, lower limb muscle movement's effect on the relief of oedema is reviewed. They are specific elaborated advantages and limitations of utilising compression stockings and lower limb movements in the oedema treatments. Finally, it summarizes the current research progress and research gap and issues.

Chapter 3 is the research on the mechanism of the fluid exchange in blood vessel and tissue. 2D simplified numerical modelling is established which can represent fluid exchange in blood vessel and tissue using the porous media model. In addition, the assumptions and description equations employed in the numerical simulation are revealed. Then, the critical pressures of oedema reduction are calculated under different physiological parameters are presented. The physiological parameters studied are porosity, blood viscosity, inlet velocity, heart rate, and different types of compression pressure effects. Finally, the physical experimental verification is performed to ensure simplified model validity containing experiment setup and comparison of numerical simulation and physical experiment results.

Chapter 4 is the trial tests for investigating the efficacy evaluation of lower limb oedema reduction using integration compression with physical movements. The method of the trial tests, trial tests design, measurement method, and lower limb movements are designed first. It is divided into the first trial test for young healthy subjects and the second trial test for elderly mild oedema subjects. The first trial test investigates the integration of Class I level gradient MCS, non-stretchable WRAP and bare leg with/without lower limb movements on reducing lower limb oedema using the measuring volume and circumference methods. Then, selecting the better integration approach to conduct the second trial test. The second trial test used the measuring circumference method to study the efficacy of reducing lower limb oedema by integrating Class I level gradient WRAP, MCS, with/without lower limb movements. In addition, the dynamic compression pressures of subjects are measured during the lower limb movements. The statistical significance analysis of different wearing conditions and comparison between adding lower limb movements and not adding them on the calf volume change (only in the first trial test) and calf circumference change are performed in both trial tests. The efficacy of oedema reduction is also statistically analysed concerning the factors of right or left legs and gender. Then, it shows the analysis results of efficacy in minimizing lower limb oedema in the different age groups, the relationship between dynamic compression pressure and lower limb circumference reduction rate, and the comparison of different results utilizing the gradient pressure and uniform pressure of WRAP. Finally, a discussion of the whole result is revealed.

Chapter 5 is the third trial test for investigating the efficacy and compliance evaluation of low-pressure gradient compression stockings with/without lower limb movements on minimizing lower limb oedema in substantial groups. The application of low-pressure gradient MCS with lower limb movements is considered the optimal approach to reduction in calf circumference among elderly mild oedema subjects based on the second trial test. The method of the third trial test, design, measurement method are introduced first. After that, statistical significance analysis of low-pressure MCS with lower limb movements and without lower limb movements on the oedema mitigation efficacy is performed. In addition, the right or left legs, gender, and BMI factors are analysed for their effect on reliving lower limb oedema. Finally, the Quality of Life (QoL) scores are compared for their compliance between WRAP and MCS in the second trial test and MCS in the third trial tests. Furthermore, the Preference for and Tolerance of the Intensity of Exercise Questionnaire (PRETIE-Q) is used to evaluate whether the designed lower limb movements are acceptable among subjects.

Chapter 6 provides the conclusions, limitations, and outlines future research directions.

Reference

[1] S. Besharat, H. Grol-Prokopczyk, S. Gao, C. Feng, F. Akwaa, and J. S. Gewandter, "Peripheral edema: A common and persistent health problem for older Americans," *PloS one,* vol. 16, no. 12, pp. e0260742-e0260742, 2021, doi: 10.1371/journal.pone.0260742.

[2] S. K. Tiwary, *Approach to Lower Limb Oedema*, 1st ed. 2022. ed. Singapore: Springer Singapore, 2022.

[3] J. Wou, K. J. Williams, and A. H. Davies, "Compression Stockings versus Neuromuscular Electrical Stimulation Devices in the Management of Occupational Leg Swelling," *The International journal of angiology,* vol. 25, no. 2, pp. 104-109, 2016, doi: 10.1055/s-0035-1558646.

[4] G. Mosti and H. Partsch, "Occupational Leg Oedema is More Reduced by Antigraduated than by Graduated Stockings," *European journal of vascular and endovascular surgery,* vol. 45, no. 5, pp. 523-527, 2013, doi: 10.1016/j.ejvs.2013.01.032.

[5] C. Belczak, J. de Godoy, R. Ramos, M. De Oliveira, S. Belczak, and R. Caffaro, "Rate of occupational leg swelling is greater in the morning than in the afternoon," *Phlebology,* vol. 24, no. 1, pp. 21-25, 2009, doi: 10.1258/phleb.2008.008042.

[6] K. P. M. D. Trayes, J. S. M. D. Studdiford, S. M. D. Pickle, and A. S. M. D. Tully, "Edema: Diagnosis and Management," *American family physician,* vol. 88, no. 2, pp. 102-110B, 2013.

[7] J. P. O. T. R. L. C. H. T. M. Villeco, "Edema: A Silent but Important Factor," *Journal of hand therapy,* vol. 25, no. 2, pp. 153-162, 2012, doi: 10.1016/j.jht.2011.09.008.

[8] F. Pomero *et al.*, "Approach to leg Edema," *Italian Journal of Medicine,* vol. 11, p. 267, 09/11 2017, doi: 10.4081/itjm.2017.771.

[9] A. P. Gasparis, P. S. Kim, S. M. Dean, N. M. Khilnani, and N. Labropoulos, "Diagnostic approach to lower limb edema," *Phlebology,* vol. 35, no. 9, pp. 650-655, 2020, doi: 10.1177/0268355520938283.

[10] G. Cooper-Stanton, "Chronic oedema and lymphoedema: what is the difference?," *British Journal of Community Nursing,* vol. 25, pp. S31-S35, 04/01 2020, doi: 10.12968/bjcn.2020.25.Sup4.S31.

[11] E. J. Topham and P. S. Mortimer, "Chronic lower limb oedema," *Clinical Medicine,* vol. 2, no. 1, p. 28, 2002.

[12] R. Garza, R. Skoracki, K. Hock, and S. P. Povoski, "A comprehensive overview on the surgical management of secondary lymphedema of the upper and lower extremities related to prior oncologic therapies," *BMC cancer,* vol. 17, no. 1, pp. 468-468, 2017, doi: 10.1186/s12885-017-3444-9.

[13] M. Catanho, M. Sinha, and V. Vijayan, "Model of aortic blood flow using the Windkessel effect," *University of California of San Diago, San Diago,* 2012.

[14] T. M. Lassila, A. C. I. Malossi, M. Astorino, and S. Deparis, "Geometrical multiscale model of an idealized left ventricle with fluid-structure interaction effects coupled to a one-dimensional viscoelastic arterial network," in *Proceedings of the ECCOMAS*

Thematic International Conference on Simulation and Modeling of Biological Flows (SIMBIO 2011), 2011.

[15] A. L. Marsden and M. Esmaily-Moghadam, "Multiscale Modeling of Cardiovascular Flows for Clinical Decision Support," *Applied mechanics reviews*, vol. 67, no. 3, 2015, doi: 10.1115/1.4029909.

[16] C. A. Wiederhielm, "Dynamics of transcapillary fluid exchange," *The Journal of general physiology*, vol. 52, no. 1, p. 29, 1968, doi: 10.1085/jgp.52.1.29.

[17] L. Possenti *et al.*, "A computational model for microcirculation including Fahraeus-Lindqvist effect, plasma skimming and fluid exchange with the tissue interstitium," *International journal for numerical methods in biomedical engineering*, vol. 35, no. 3, pp. e3165-n/a, 2019, doi: 10.1002/cnm.3165.

[18] S. Cho and J. E. Atwood, "Peripheral edema," *The American journal of medicine*, vol. 113, no. 7, pp. 580-586, 2002, doi: 10.1016/s0002-9343(02)01322-0.

[19] E. Johnson, J. G. Betts, and P. DeSaix, *Anatomy and Physiology*. Open Textbook Library, 2013.

[20] W. Olszewski and S. A. Slavin, "Lymph Stasis: Pathophysiology, Diagnosis and Treatment," *Plastic and reconstructive surgery (1963)*, vol. 90, no. 3, p. 533, 1992, doi: 10.1097/00006534-199209000-00035.

[21] W. L. Olszewski, "Contractility Patterns of Human Leg Lymphatics in Various Stages of Obstructive Lymphedema," *ANN NY ACAD SCI*, vol. 1131, no. 1, pp. 110-118, 2008, doi: 10.1196/annals.1413.010.

[22] Y.-H. Lin, C.-Y. Chen, and M.-H. Cho, "Effectiveness of leg movement in reducing leg swelling and discomfort in lower extremities," *Applied ergonomics,* vol. 43, no. 6, pp. 1033-1037, 2012, doi: 10.1016/j.apergo.2012.03.002.

[23] Z. Hajati, F. S. Moghanlou, M. Vajdi, S. E. Razavi, and S. Matin, "Fluid-structure interaction of blood flow around a vein valve," *Bioimpacts,* vol. 10, no. 3, pp. 169-175, 2020, doi: 10.34172/bi.2020.21.

[24] Z. Xiong, D. Yuan, J. Wang, T. Zheng, and Y. Fan, "Influence of renal artery stenosis morphology on hemodynamics," *Comput Methods Biomech Biomed Engin,* pp. 1-19, Feb 10 2021, doi: 10.1080/10255842.2021.1883592.

[25] Y. Tokuda *et al.*, "Three-dimensional numerical simulation of blood flow in the aortic arch during cardiopulmonary bypass," *Eur J Cardiothorac Surg,* vol. 33, no. 2, pp. 164-7, Feb 2008, doi: 10.1016/j.ejcts.2007.11.021.

[26] R. Löhner, *Applied computational fluid dynamics techniques: an introduction based on finite element methods*. John Wiley & Sons, 2008.

[27] A. M. Gilroy, B. R. MacPherson, and L. M. Ross, *Atlas of anatomy*. Stuttgart ;: Thieme, 2008.

[28] J. E. Muscolino, *Kinesiology : the skeletal system and muscle function,* 2nd ed. ed. St. Louis, Mo: Mosby/Elsevier, 2011.

[29] M. Schünke, E. Schulte, and U. Schumacher, *Thieme atlas of anatomy : general anatomy and musculoskeletal system* (Atlas of anatomy : general anatomy and musculoskeletal system.). Stuttgart ;: Thieme, 2006.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Lower limb oedema is particularly prevalent in contemporary society. Even individuals who are in relatively sound health can easily experience lower limb oedema in their daily lives, such as supermarket checkout employees, quality control workers, physicians, nurses, and others [1-5]. The reason is that gravity is attributed to a notable increase in the volume of the lower limb. Gravity can contribute to potential overload on the vascular walls over extended periods, spanning days, months, and years. Therefore, the longtime gravitational exposure has the potential to induce lower limb oedema for individuals without cardiovascular or kidney disorders diseases.

Apparently, the lower limb oedema is a physiological phenomenon occurring after long periods of sitting and standing [6-8]. **Figure 2.1** directly revels the physicians and nurses' substantial increased lower limbs volume change after 8 hours of prolonged standing (from 7:00 am to 3:00 pm). Such individuals may exhibit venous symptoms in their lower limb, such as heaviness or pain, and are more susceptible to developing varicose vein, swelling, skin changes and ulcer [9, 10]. Moreover, prolonged lower limb oedema predisposes individuals to chronic disease, including heart failure, venous disease, obesity, kidney disease [5, 11]. Therefore, lower limb oedema should be addressed promptly using appropriate interventions.

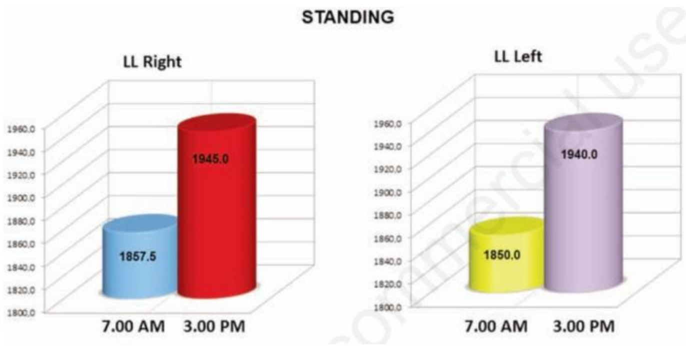

Figure 2. 1 Lower limbs volume significant increase after 8 hours of prolonged standing without wearing any elastic stocking, both the leg and foot volumetric changes [5].

For current methods for reducing or relieving oedema problems, a diversity of compression treatments and management methods for lower limb oedema have been made available with a lot of clinical result on their efficacy. However, due to different physiological conditions and lower limb shape for every individual, the identification of the most suitable pressure range for effectively reducing lower limb oedema is still a significant challenge. Furthermore, regarding the method of oedema reduction combined with muscle movements, there is currently no systematic movement programme, and it is also a big challenge for quantitative analysis of muscle movement intensity and frequency.

In this chapter, the literature review contains an overview of the danger and causes underlying lower limb oedema in section 2.2, while including various treatment options and assessment methods. Additionally, the literature review about progressive advances in lower limbs and blood vessels' compression effect research concerning modelling and numerical simulation is in section 2.3. Furthermore, a comprehensive exploration of the effects observed in clinical and experimental studies about medical compression stockings and non-stretchable bandages on oedema reduction is presented in section 2.4. The lower limb muscle movement which contributes to lower limb oedema management is investigated in section 2.5. Finally, section 2.6 summarises the currently existing problems and challenges of applying compression stockings and muscle movement in lower limb oedema reduction.

2.2 Causes, treatment, and assessment of oedema

2.2.1 Blood circulation and causes of oedema

In our body system, the blood is transported from the heart to diverse organs and tissues through the arterial system, then fluid exchange take place across numerous capillaries situated within various organs. Subsequently, the blood after completing fluid exchange returns to the heart through the venous system, this is a closed loop called cardiovascular circulation. In parallel, the lymphatic circulation is not a closed circuit. Lymphatic vessels uptake macromolecules and cells from the interstitial fluid and subsequently traverse a sequence of lymph nodes, which finally converge into the vena cava via the thoracic duct, as shown in **Figure 2.2.**

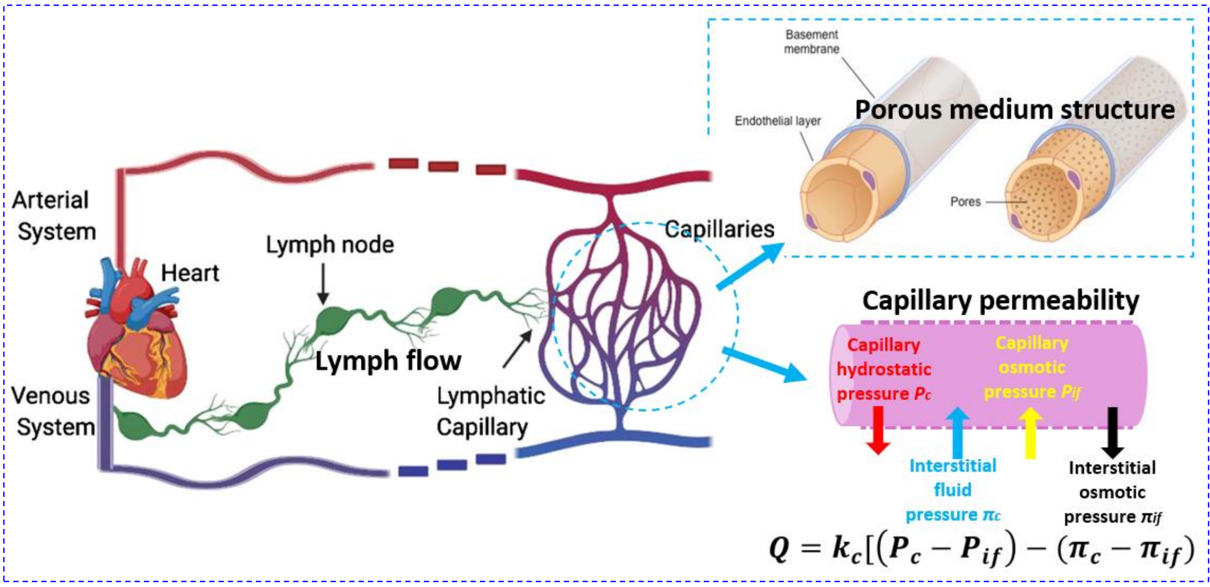

Figure 2. 2 The blood circulatory system, lymphatic system, and common causes of lower limb oedema [12, 13].

Among blood vessels, the capillary is a porous medium structure. According to the mechanism of the fluid exchange between the capillaries blood and interstitial fluid thorough this porous structure, the cause of the oedema is that the fluid filtration is not equal to the fluid reabsorption and lymphatic flow. The mechanism of the fluid exchange balance in the capillary bed is that fluid filtration is equal to the total amount of fluid reabsorption and lymphatic flow [14]. The net fluid flow between capillaries blood and interstitial fluid can be described using the starling equation [15, 16], as shown in equation (2-2).

$$Q = k_c[(P_c - P_{if}) - (\pi_c - \pi_{if})] \tag{2-2}$$

In which,

Q: Net flow, when Q >0 is filtration, when Q <0 is reabsorption.

k_c : Permeability coefficient of the capillary walls.

P_c : Hydrostatic pressure in blood.

P_{if} : Interstitial hydrostatic pressure.

π_c : Osmotic pressure in blood.

π_{if} : Interstitial osmotic pressure.

Filtration is the movement of fluid out of the arterial end of the capillary. Filtration is enhanced when the capillary hydrostatic pressure is increased, the interstitial osmotic pressure is increased, or the capillary permeability is increased. Reabsorption is the movement of fluid into the venous end of the capillary. Reabsorption is heightened in situations where the conditions contrary to the filtration promotion, or the capillary osmotic pressure is decreased.

The filtered fluids process a reabsorption at the venous end of the capillary, and a portion of fluid is reabsorbed in the lymphatic circulation. Typically, a daily 20 Liters of fluid leaves the capillaries, approximately 18 Liters (constituting 90%) is reabsorbed, while around 2 Liters (constituting 10%) are removed via lymphatic vessels [12, 14].

Therefore, the common causes of the lower limb oedema are summarised [7, 15-18]: The first one is the increased capillary hydrostatic pressure, which is the driving force of fluid exchange in the capillary bed, it can be caused by local metabolites or frequently occurs in the impairment of venous valve functionality. The second one is decreased oncotic pressure, involving liver diseases, nephrotic syndrome, malnutrition and protein-losing enteropathy. The third cause is decreased interstitial hydrostatic pressure such as burns, and the fourth one is increased interstitial osmotic pressure if capillary endothelial damage or infections occur. The fifth cause is inadequate lymph flow, which occurs when there is failure of the lymphatic system or lymphatic obstruction. The last one is the increased capillary permeability.

Overall, in pathophysiology, the imbalance of the fluid exchange between the interstitial fluid and blood causes the oedema. According to the mechanism of the fluid exchange between the capillaries blood and interstitial fluid, oedema results from that the fluid filtration is bigger than the total amount of fluid reabsorption and lymphatic flow.

2.2.2 Diagnosis and treatment methods

Currently, there is an established systematic diagnostic procedure for lower limb oedema in the clinic, as shown in literature [19], including unilateral lower limb oedema or anasarca. One diagnostic method is clinical diagnosis according to oedema features, as shown in **Figure 2.3**. In details, pitting on the skin whose examination focus on the medial malleolus, the bony portion of the tibia and the dorsum of the foot; checking skin change, containing skin colour, texture, infection, erythema and temperature; and oedema part is accompanied by pain [19-23]. The other method is diagnosis using medical equipment. For example, duplex ultrasonography is toward chronic venous insufficiency and suspected deep vein thrombosis (DVT); MRI is toward high DVT and that cannot be detected by duplex ultrasonography. Besides, venography with intravascular ultrasound for lower limb oedema, lymphoscintigraphy (lymph flow cannot be detected with ultrasonography) and so on [19, 20].

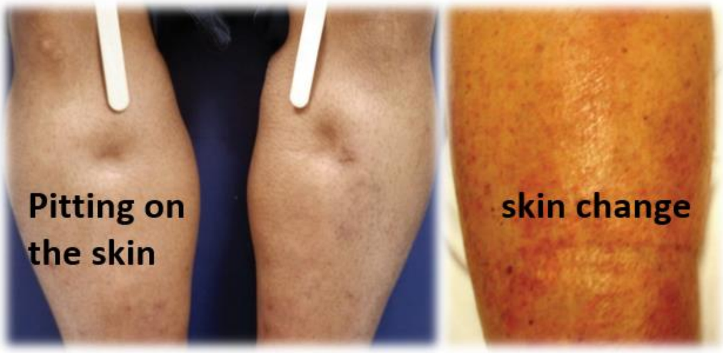

Figure 2. 3 Oedema features: pitting on the skin and checking skin change, containing skin colour, texture, infection, erythema, and temperature [19].

According to different oedema symptoms, there are suitable treatments for lower limb oedema including taking medicine [7, 24, 25], leg elevation [7, 19, 26], compression therapy [7, 24, 26], manual lymphatic massage [7, 26, 27], surgery [24, 27] and so on.

However, the limitations of above different treatment methods are summarised as follows. Firstly, taking medicine treatment, for example flavonoids, benzopyrones is not available for every having oedema individual. Because most of them abandoned due to adverse effects [7, 24, 25]. Secondly, leg elevation is conducive to the return of blood from the leg, however, it is inconvenient during working periods or outside. Moreover, elevation is particularly beneficial in the early-stage oedema when oedema is easily mobilized [7, 19, 26]. Thirdly, the manual lymphatic massage cannot be accepted in infected areas because it facilitates the dissemination of infection [7, 26, 27]. In addition, the surgery is of value only in a few patients in whom other therapies have shown not to be effective, or the dimensions and mass of the limb impose limitations on effects on post physical treatment mobility [24, 27]. And there is lack of a clearly defined selection method to determine which oedema patients may benefit from surgery [28]. Regards to the compression treatment method [7, 19, 20, 29], it can contribute to reabsorb oedema into the veins and lymphatic system [30] and it is presently recognized as the most conventional therapeutic method for lower limb oedema, containing compression stocking, non-stretchable bandage, and pneumatic compression and so on.

Compared with other treatment methods, compression therapy is suitable for long-term oedema management. It is currently accepted as the most main treatment choice for lower limb oedema to reduce the limb circumference, volume, and shape in the clinic. Although prolonged pressure on the skin can cause itching, compression applied to the lower limb can enhance the velocity of venous blood flow and mitigate lower limb oedema when patients are walking or prolonged standing.

2.2.3 Assessment methods

Several methods can be utilized to assess the extent of oedema reduction, including water displacement volumetry, measuring the maximum calf circumference, measuring muscle stiffness and skin thickness and so on. There is main clinical measure metrics employed to assess improvements in oedema following treatment.

For intuitive measurement metrics, the first metric involves the assessing the volume of the lower limbs using the water displacement volumetry [6, 7, 9, 31-37]. The second metric entails measuring circumferences at standardized points on the lower limb, a widely adopted method in both clinic and research [10, 31, 32, 35, 36, 38-41]. Measurements are taken using a metric tape at locations such as point B, B1, C, D, F and G in accordance with international guidelines. The rate of change of circumferences can be determined by theoretical formular (2-1) [32]. The third encompasses measurement the subcutaneous thickness of the lower limbs using the high-resolution ultrasound [31, 35]. Besides, for the compliance metrics, the questionnaire-based assessment of Quality of life (QoL) is essential in investigate the subjective perceptions of users or patients following relevant treatment. Typically, the QoL questionnaire employs a scale ranging from 0 to 100 to gauge physical and emotional well-being, with higher scores representing a better perceived health status [31, 32, 42-44]. **Table 2.1** summaries the different types and characteristics associated with these measure metrics.

$$\Delta C\% = \{(C_{\mathrm{A}} - C_0)/C_0\} \cdot 100\% \qquad (2\text{-}1)$$

In which,

C_0: Initial circumference (cm).

C_{A}: Circumference at time A (cm).

Table 2. 1 Measurement types and characteristics.

Measure metrics	Measurement method	Advantages	Disadvantages	Reference
Volume of the lower limbs	Measured by a water displacement volumetry, as shown in **Figure 2.4(a).**	1)Easy to measure. 2) Intuitive measurement.	1)Requires large space devices, water tanks, etc. 2)Require considering the volume exclusion of the feet if only need the volume of the lower limb.	[6, 7, 9, 31-37]
Circumferences of the lower limbs	Measured with a metric tape at standardized	1)Easy to measure.	When the change is uneven, it can be	[10, 31, 32, 35, 36, 38-41].

	points of the lower limb according to international guidelines, as shown in **Figure 2.4(b).**	2) Intuitive measurement.	measured only local changes.	
Subcutaneous thickness of the lower limbs	Measured by high-resolution ultrasound	Professional medical examination.	Require specific medical equipment and demands professional medical guidance.	[31, 35]
Quality of life (QoL)	Measured by questionnaire	Compliance index	Subjective opinions.	[31, 32, 42-44]

Figure 2. 4 Measurement methods: (a) is measuring volume of the calf using the water displacement volumetry, (b) is measuring circumferences of the calf using the soft tape.

2.3 Mechanism study of applying compression on lower limbs and blood vessels

To proficiently predict and assess the impact of compression therapy on oedema and human tissues, numerical modelling and simulation methods are employed to prognosticate the deformation and associated parameter effects induced by the application of compression to the lower limbs, encompassing blood vessels and muscular tissues.

From the microscopic perspective on the principle of fluid filtration and reabsorption, the first consideration of the numerical modelling pertains to the capillaries, arterial and venous modelling. Modelling the blood vessels, particularly the capillaries, presents significant challenges due to the variability in vessel diameters and the dynamic nature of blood flow velocity at various locations within the blood vessels. The capillary bed holds significant research value in the context of oedema reduction. Capillaries, responsible for nutrient, gas, and fluid exchange, consist of thin permeable walls composed of endothelial cells and basal membranes [45]. However, capillaries are fragile and can break under high blood pressure or impact. About the model of blood vessel, the Windkessel Model, designed by German physiologist Otto Frank in the late 1800s, described the heart and systemic arterial system as a closed hydraulic circuit [46]. This three-element RCR (capacitor and two resistors) model is used in arterial network, however, it cannot achieve fluid exchange and space-related hemodynamic response [47, 48]. The physiological mechanism causing lower limb oedema is already clear. C. A. Wiederhielm [49] and L. Possenti et al. [50] conducted the simulation of fluid balance at the capillary level utilizing experimental data pertaining to regional differences in capillary permeability and hydrostatic pressures. In which [50], capillaries are depicted as 1D channels to account for fluctuations in flow rate and pressure along the capillary axis. In addition, D. Notaro et al. [51] proposed the model in which a 1D domain is embedded into a 3D porous medium for the coupled incompressible flow. A. Coccarelli et al. [52] proposed 1D arterial blood flow porous models that the vascular embedded in the solid tissue is equivalent poroelastic material model, enabling the expression of fluid exchange through the porosity of the porous media.

Regards to the numerical simulation, a clear understanding venous hemodynamics in the lower limbs is essential for designing effectively applying compression for clinic patients [53-57]. Therefore, the numerical simulation methods like the finite element method (FEM) and computational fluid dynamics (CFD) method are used to study hemodynamics, sometimes combined with certain models assisted by medical apparatus such as Magnetic Resonance Imaging (MRI) [56, 58-62]. These numerical methods can intuitively simulate various possibilities during applying compression force and analyse related parameters on blood vessels such as pressure, vessel wall shear stress, blood flow velocity, viscosity, and peripheral vascular resistance and so on [61, 63-66]. Due to the complex interplay among actual human lower limb tissues, blood vessels, lymphatic vessels, and blood and interstitial fluids, numerical simulations often adopt the truncation of blood vessels to simplify the interdependencies of physiological parameters. For example, C. P. Y. Rohan et al. [56] developed human limb with varicose veins using the 2D patient-specific finite element model to calculate the stress distribution in and around the vein wall and to evaluate the efficacy of medical compression stockings in reducing trans-mural pressure and narrowing leg veins. Also, this study contributed to the influence of compression therapy on the local pressure on the soft tissues.

Furthermore, a macroscopic perspective is conducted to investigate the pressure effect on the human body using numerical simulation. R. Liu [67] analysed the interface pressure between the medical compression stocking and the limb, and the stress distribution of the medical compression stocking with 3D modelling using FEM, including medical compression stocking stress changes over time, and the comfort assessment. In addition, Chongyang Ye et al. [68] developed a 3D lower limb FE model and fluid-structure interaction model to simulate the interface pressure, stress transmission, and venous blood flow dynamics associated with the application of elastic compression stockings. After then, Chongyang Ye et al. [69] developed and validated the compression stocking model considering the 3D material mechanical properties, and combined the 3D solid lower limb model to process simulation using FEM. This new model significantly improved the precision of predicting the interface pressure between elastic compression stockings and the contact surface compared with the model using 2D mechanical properties.

2.4 Effect of compression stockings on oedema

2.4.1 Medical compression stockings

Applying compression on the lower limb oedema is to mitigate the effects of gravity upon the venous lymphatic circulation. By exerting pressure on an area of the body's surface using elastic or inelastic textile materials, compression therapy effectively decrease ambulatory venous hypertension and interstitial pressures, thereby preventing venous and lymphatic disorders [70]. Therefore, applied compression on the lower limb leads to improve capillary resorption and restrict capillary filtration. Specifically, the compression pressure on the tissues, firstly works to prevent filtration, secondly to prevent reflux of fluid, thirdly to promote resorption of excess fluid from the interstitial space. In other way, compression method can promote venous blood return, the features of the blood vessels can also explain the reasons. When blood vessels are constricted, there are changes in resistance, blood pressure, and blood flow. In case of artery or arteriole constriction, the radius decreases, leading to increased resistance, increased pressure, and decreased blood flow. However, veins demonstrate different outcomes. Due to their thin and irregular wall, when the smooth muscle in those walls constricts, the lumen becomes more rounded [13]. This more rounded lumen results in reduced surface area for blood contact, leading to increased pressure but decreased resistance, ultimately increased blood flow within the veins. These blood vessel parameters changed are listed in **Table 2.2**.

Table 2. 2 Blood vessel parameters change when constriction.

Blood vessels	Radius	Resistance	Pressure	Blood flow
Artery or arteriole	↓	↑	↑	↓
Vein	↓	↓	↑	↑

Extensive research has been conducted on compression stockings and their clinical applications [71-74]. The medical compression stocking can decrease volume of lower limb and decrease the pain associated with lower limb oedema [75, 76]. Nearly 20 years ago, M. Hirai et al. [77] processed the effect of the elastic compression stockings on varicose veins patients employing strain gauge plethysmography, it demonstrated that elastic compression stockings with pressure levels of 22 mmHg and 30 ~ 40 mmHg are highly effective in preventing foot oedema for those group in 2002. In 2004, HUGO PARTSCH et al. [78] advocated that individuals engaged in prolonged periods of standing or sitting should wear medical compression stockings (calf-length) against oedema. By conducting four days of experiments, they demonstrated that compression stockings exerting a pressure range of 11 to 21 mmHg were effective in mitigating or completely preventing evening oedema. In 2008, it observed that calf-length compression stockings exerting the pressure range between 11~21 mmHg can reduce or completely prevent evening oedema in workers who engage in prolonged sitting or standing tasks [9, 40]. In 2010 C.E.Q. Belczak et al. [9], revealed that the effect of wearing time of elastic compression stockings on the change of lower limb volume, it shows that wearing compression stockings (20 ~ 30 mmHg) for half a day is more effective than not wearing them, and wearing them for a whole day is more effective than wearing them only for half a day. In 2011, [79] expounded that applications of compression garments include long-term management, prevention, and initial treatment of lymphedema during the maintenance phase. They may also be used as the sole form of compression in time-consuming controlled compression therapy, most patients wore compression garments during their waking hours, including during exercise. In 2015, M.

Zaleska et al. [80] researched intermittent pneumatic compression which is employed for lower limbs obstructive lymphedema patients. It expressed that a high-pressure intermittent compression device was designed to apply compression to the tissues affected by lymphedema, leading to the formation of tissue channels that serve as pathways for the evacuation of oedema fluid. Obviously, not only for oedema patients, but also for healthy people, compression stockings have proven to be an effective approach for alleviating lower limb oedema during extended working hours with the same posture [35, 38, 41, 81]. In 2015, M. Tessari et al. [6] investigated the compression stockings can effectively reduce the lower limb volume in individuals working for 8 hours with standing posture through comparing of lower limbs volume change after a working day with and without elastic compression stockings, **Table 2.3** shows the detailed data of lower limbs volume change after a working day with and without elastic compression stockings. In 2018, I. Sugahara et al. [35] illustrated the impact of calf graduated compression stockings on lower limb oedema for healthy individuals when rested in a seated position for 30 minutes. The result indicated a significant decrease in maximum calf circumference, and the lower limb volume and the shear modulus of muscles tended to decrease when graduated compression stockings are used. Moreover, the size for the specific pressure level of the commercial medical compression stockings have been determined. However, for the different lower limb shape individuals, their requirements of compression stockings are different. As previously indicated, G. Mosti et al. [36] researched that compression stockings exhibit considerable efficacy in reducing lower limb oedema, continuing to readjust compression stocking size in accordance with the diminished lower limb volume subsequent to oedema reduction. Therefore, the customized medical compression stockings have been proposed. In 2022, Xiong [82] studied a customized medical compression stockings prototype which was fabricated with the help of computer aided design (CAD) and computer integrated manufacturing (CIM). These customized medical compression stockings can predict the pressure distribution for the requirements, and they can achieve pressure management by taking advantage of the fabric-based pressure sensors adhered. Furthermore, in 2023, Yang and Xiong et al. [83] conducted the comparative analysis between standard graduated elastic compression stockings (s-GECSs) and customized graduated elastic compression stockings (c-GECSs) worn by patients with the chronic venous disease over the course of one month, three months, and six months revealed that both types of stockings effectively reduced lower limb oedema. It observed no significant disparity was observed between the two in terms of lower limb volume reduction, however, c-GECSs exhibited superior patient compliance in relation to fit and comfort.

Table 2. 3 Comparison of the volume change in the lower limbs after a working day with and without elastic stockings[6].

Unit: mL	**Without elastic stocking**		**With elastic stocking**	
	Right leg	Left leg	Right leg	Left leg
7:00 am	1857.5±196.9	1850±194.7	1970±221	1965±233.5
3:00 pm	1945±209.6	1940±216.2	1962.5±220	1957.5±239.7

2.4.2 Non-stretchable bandage

Non-stretchable bandages are extensively utilized in management of oedema, including the treatment of severe unilateral lymphedema, breast cancer-related lymphedema (BCRL), post-total knee arthroplasty oedema, and primary lymphoedema after liposuction.

In 2011, D. A. Lamprou et al. [84] examined the effectiveness of the two-component compression (2CC) system compared with the conventional inelastic multicomponent compression bandages (IMC) on the treatment of hospitalized patients with moderate to severe unilateral lymphedema (stage II–III) from September 2008 to April 2009. These two systems demonstrated high stiffness. The results presented that after using the 2CC system for 2 hours, there was a decrease of 2.9% in median lower limb volume, while the IMC system resulted in a decrease of 1.8%. Furthermore, after 24 hours, they revealed reductions of 8.4% and 4.4% in lower limb volume for the 2CC and IMC systems, respectively. Another study [85] conducted in 2015 focused on the patients undergoing post-total knee arthroplasty who received the inelastic, short-stretch compression bandage. This technique was considered safe due to the advantage of the low resting pressure but ability to produce high pressure during movement, thereby improving the efficacy of the calf muscle pump. In 2020, M. Karafa et al. [86] studied that the patient with long-standing primary lymphoedema of the right lower limb benefited from non-elastic leg binders, such as the Circaid device which provided greater stiffness, while one class of compression garment is not always sufficient for effective management. A recent study published in 2021 [87] revealed the effect of the self-adaptive IC device (Circaid®, Medi GmbH & Co. KG, Bayreuth, Germany), and conclude that it could be considered as safe, well-tolerated, and effective tool in the rehabilitative management of BCRL patients.

Comparing with compression stockings, during movement such as dorsiflexion in the sitting position and tip-toeing in the standing position or while walking, it has been observed that pressure fluctuations perform significantly greater magnitudes when non-stretchable bandage (e.g. augmentation 23 mmHg) compared to an elastic bandage (e.g. augmentation 8 mmHg) at medial aspect of the leg [88]. Due to low elasticity, non-stretchable bandage provides greater pressure to the human body during movement. G. Mosti et al. [36] conducted a comparative analysis of the impacts of strong inelastic bandages and compression stockings on chronic lower limb oedema. The findings indicated that an increase in pressure exerted by both stockings and bandages leads to better oedema reduction, up to approximately 40 mmHg. In terms of localized effects, bandages exhibited superior efficacy in diminishing calf circumference compared to compression stockings, however, the utilization of bandages at pressures exceeding 60 mmHg did not enhance the oedema reduction. However, compression stockings are often preferred over bandages due to higher patient compliance. For instance, Fabrizio Mariani et al. [89] conducted a comparative study investigating the use of elastic stockings and bandages following varicose vein surgery. The trial test revealed that patients using elastic stockings exhibited significantly better tolerance towards compression therapy compared to those using bandages. Additionally, elastic stockings demonstrated notable advantages over bandages in terms of walking and sliding. Although compression stockings may not provide as high pressure as bandages, the trial results indicated that the proportion of patients without oedema in the elastic stockings group (80%) was higher than in the bandages group (50%) in 7 days post-surgery.

2.5 Effect of lower limb muscle movement on oedema

2.5.1 Lower limb muscle distribution

Not only the elastic compression stockings and non-stretchable bandages, but the regular lower limb movements have been found to contribute to the reduction of oedema. Early research suggested that muscle movements of lower limb could have a positive effect on oedema reduction. The lower limb movements or specific exercise can activate the muscles and potentially compress the tissues, veins, and lymphatic vessels in the foot, therefore, lower limbs oedema can be reduced by facilitating contraction and relaxation of the muscles [90, 91]. In addition, the periodic calf flexion or extension movements can contribute to reduce lower limb oedema by pumping the excess fluid back toward the heart [7]. Therefore, these lower limb movements play a role in promoting smooth blood flow return from the lower limbs to the heart by activating the muscles surrounding the blood vessels.

Currently, kinesiology has become increasingly applied in the clinic. This section reviews the muscle distribution of the calf, muscle corresponding movements, and interaction between movement, muscles, and blood vessels on oedema.

Figure 2.5 illustrates the distribution of muscles in the calf, its posterior, cross-section, and anterior view of the calf, and the venous vasculature draining the lower limb with stimulated muscles. The anterior muscle, located at the front of calf near the tibia, include the tibialis anterior, extensor hallucis longus, and extensor digitorum longus. Lateral muscles are situated alongside the fibula and consist of the peroneus longus and peroneus brevis. The posterior muscles are gastrocnemius and inner soleus. In addition, the deep muscles such as tibialis posterior, flexor hallucis longus and flexor digitorum longus are positioned around the deep veins and arteries. Calf muscles are directly connected to the related lower limb movements, in other words, specified movements can activate the related muscles. There are definite movements that correspond to the calf muscles, they are mainly knee flexion, toe flexion or extension, foot plantarflexion or dorsiflexion, and foot eversion or inversion [92]. **Table 2.4** summarises the relationship between lower limb movements and corresponding calf muscles from the anterior to the lateral, posterior, and deep muscles.

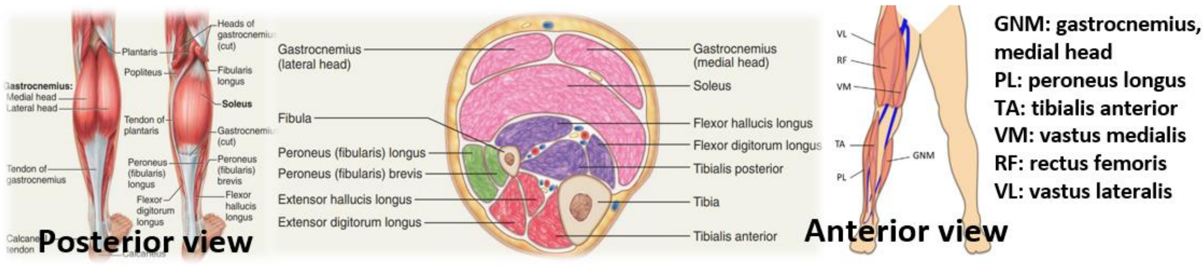

Figure 2. 5 The posterior, cross section, and the anterior view of the calf [93], and the venous vasculature draining lower limb with stimulated muscles [94].

Table 2. 4 The lower limb movements and corresponding calf muscles [92, 93].

Muscle type	Tibialis anterior	Extensor hallucis longus	Extensor digitorum longus	Peroneus longus and peroneus brevis	Gastrocnemius	Soleus	Tibialis anterior	Flexor hallucis longus and flexor digitorum longus
Activate movement	Foot inversion, Ankle dorsal flexion	Ankle dorsal flexion, Toe extension	Foot eversion, Ankle dorsal flexion, Toe extension	Plantar flexion, Everts the foot at the subtalar joint	Knee flexion, Plantar flexion	Plantar flexion	Foot inversion, Ankle dorsal flexion	Foot inversion, Plantar flexion, Toe flexion

2.5.2 Compression effect of lower limb skeletal muscles on blood vessels and tissues

The initial report of the venous pressure difference occurring during the operation of the calf muscle venous pump between popliteal veins and posterior tibial veins dates back nearly 70 years [95]. The calf pump system, encompassing the lower limbs' vein pump system, muscle pumps, distal calf pump, and foot pump, plays a crucial role in reducing lower limb oedema [33]. These components collectively compress the muscle tissues, exert pressure on the venous system, and promote lymph flow, which process contributes to a decrease in filtration pressure and aids in the oedema prevention [96-98]. In addition, the activities involving ankle mobilization have been found to significantly enhance venous return and lymph flow in the lower limbs [99, 100].

Earlier studies demonstrated a noticeable reduction (approximately 30 mmHg) in high hydrostatic pressure within the deep and superficial veins of the lower limb and foot when activating the calf muscle venous pump. Subsequently, the pressure gradually returns to its initial baseline following calf muscle contraction [101]. Therefore, exercises, movements, and changes in lower limb posture can influence venous blood pressure. In 1985, A. A. Pollack et al. [99] presented that the executing calf muscle contractions through toe-standing without walking led to a decrease in venous pressure at the ankle region. In 1988, L Walløe et al. [102] revealed that the rhythmic exercise had an influence on the blood flow. In later study in 2000, E. Stranden [33] described the effectiveness of the muscle venous pump during calf movements with different postures using variations in seat angle chairs to improve blood return in the lower limbs and prevent oedema. During the functioning of the calf muscle venous pump, an ambulatory pressure gradient of approximately 35 mmHg is observed between the femoral/popliteal vein and the deep lower limb veins [95]. In 2014, F. Frauziols et al. [57] demonstrated the effect of compression therapy on the percentage of contraction of the great and small saphenous veins in patients using the finite element model, in detail, under an elastic compression of 15~20 mmHg in an inactive muscle state, the percentage of contraction of the great saphenous veins and small saphenous veins were found to be 4.5% and 3.7%, respectively. Therefore, muscular compression can constrict the blood vessels within the lower limbs.

2.5.3 Lower limb skeletal muscles' effect on oedema

Movement, particularly walking, plays a crucial role in reducing the incidence of oedema. Even simple movements can reduce lower limb oedema in the early stages [7]. When individuals walk, the veins of the plantar and calf muscles are subjected to compression during flexion and stretching, leading to improved venous return [34]. Moreover, the compression pressure from the calf muscle when walking helps prevent lateral expansion and dilation of lower limb veins

[103], thus promoting fluid reabsorption and mitigating oedema. In the earlier time, a study conducted by J. Winkel [104] in 1981 found that a walk such as a 2 min walk every 15 min throughout the day resulted in an average reduction of 1.7% calf oedema increase. In 2002, M. R. Chester et al. [32] reported a study involving healthy subjects who sat with three different types (an office chair, a sit/stand chair, and standing) for 90 minutes. It was observed that sitting/standing resulted in a 2.9% circumference increase in lower limb, while standing alone led to a 1.7% circumference increase. Obviously, prolonged standing had more detrimental effects compared to sitting for long time [32, 105]. Leg elevation has been identified as one of the effective methods for oedema reduction in the clinic and it can be easily achieved in daily life. For example, resting the lower limbs at a 30° angle for three brief 20 ~ 30 minutes per day has proven effective in reducing oedema in elderly populations [106]. Additionally, a test presented by B.C.E. Quilici et al. [34] in 2009 compared the efficacy of resting in the Trendelenburg position versus performing muscle movements in reducing lower limb oedema. The results showed that the utilization of movements led to greater efficacy (mean volume reductions of the lower limbs of 92.9 mL) compared to resting in the Trendelenburg posture (mean volume reductions of the lower limbs of 135.4 mL). In 2009, an active foot pump system called StepIt was proposed [39], which involves plantarflexion or dorsiflexion movements and demonstrated the significant contribution of those calf muscle contractions in smaller increase of calf oedema. The researcher conducted the experiment involving long-term sitting healthy workers, using StepIt for at least 30-40 pumping movements per hour (6 hours one day) on one lower limb revealed that the average increase in calf volume was 3.1% compared to a 3.2% average increase in the unpumped leg. In research by Jose Maria Pereira de Godoy et al. [107] in 2010, healthy individuals during muscle movement (walking) observed a decrease in the mean interface pressure exerted by elastic stockings on the skin. However, these pressures can vary depending on the type of muscle movement and elastic stockings gradient, with higher

pressure elastic stockings producing larger pressure fluctuations during muscle activity. In 2012, Yen-Hui Lin et al. [42] investigated the effect of the lower limb movements on the oedema reduction in healthy individuals without musculoskeletal, cardiovascular, and diabetic problems. Participants performed movements involving wiggling their toes (ankle movement) or raising their legs (hip movement) for 4 minutes after standing for 30 minutes, repeated every 4 hours. The results indicated that the mean circumference increased by 1.13% during ankle movements, by 0.60% during hip movements, and by 1.26% while standing without movement, thereby muscle movement can reduce oedema after standing, and hip movements more effectively suppress oedema formation.

Furthermore, based on the studies on lower limb movements experiments for oedema reduction [32, 34, 39, 42, 104], several considerations should be noted. The subjects who attend in movement experiments should maintain proper posture during required exercises, avoid moist environments, such as baths or poorly ventilated areas, refrain from eating and drinking during testing.

2.6 Summary

After the literature review, there are the following challenge to overcome in oedema reduction research.

Regarding the assessment of the pressure required for prediction, the numerical models currently have the limitation that the most of them ignored the fluid exchange among blood vessel, tissues, and lymph under applying compression. Therefore, they cannot describe the fluid exchange phenomena during applying compression for the oedema reduction purpose. The numerical modelling about reducing lower limb oedema process should incorporate essential physiological parameters.

In terms of integrating compression and skeletal muscle movement for oedema reduction, there are sufficient separate studies of them. Medical compression stockings currently have favourable outcomes for both the prevention and initial treatment of lower limb oedema. Moreover, non-stretchable bandages can provide great pressure safely on the management of oedema. Besides, the lower limb movements through muscle contraction can effectively stimulate the vascular and lymphatic systems, leading to the reduction of lower limb oedema. The positive results of lower limb movements on oedema reduction highlight the significance of designing skeletal muscle movements that activate corresponding muscles and exert compression effects on blood vessels and interstitial fluid. However, there is currently a lack of sufficient numerical simulations, designed lower limb movements programme, and clinical trials investigating the efficacy of various compression methods combined with different lower limb movements on oedema reduction.

Reference

[1] G. A. Ryan, "THE PREVALENCE OF MUSCULOSKELETAL SYMPTOMS IN SUPERMARKET WORKERS," *Ergonomics,* vol. 32, no. 4, pp. 359-371, 1989, doi: 10.1080/00140138908966103.

[2] M. S. Redfern and R. Cham, "The Influence of Flooring on Standing Comfort and Fatigue," *AIHAJ - American Industrial Hygiene Association,* vol. 61, no. 5, pp. 700-708, 2000, doi: 10.1080/15298660008984580.

[3] P. M. King, "A comparison of the effects of floor mats and shoe in-soles on standing fatigue," *Applied ergonomics,* vol. 33, no. 5, pp. 477-484, 2002, doi: 10.1016/S0003-6870(02)00027-3.

[4] M. S. Redfern and D. B. Chaffin, "Influence of Flooring on Standing Fatigue," *Human factors,* vol. 37, no. 3, pp. 570-581, 1995, doi: 10.1518/001872095779049417.

[5] M. Tessari *et al.*, "Assessment of lower limbs edema in healthy workers who are exposed to long-term gravity," *Veins and lymphatics,* vol. 2, no. 2, pp. 19-e19, 2013, doi: 10.4081/vl.2013.e19.

[6] M. Tessari *et al.*, "Elastic stockings effect on leg volume variability in healthy workers under prolonged gravitational gradient exposure," *Veins and lymphatics,* vol. 4, no. 2, 2015, doi: 10.4081/vl.2015.5182.

[7] S. K. Tiwary, *Approach to Lower Limb Oedema,* 1st ed. 2022. ed. Singapore: Springer Singapore, 2022.

[8] R. Garza, R. Skoracki, K. Hock, and S. P. Povoski, "A comprehensive overview on the surgical management of secondary lymphedema of the upper and lower extremities related to prior oncologic therapies," *BMC cancer,* vol. 17, no. 1, pp. 468-468, 2017, doi: 10.1186/s12885-017-3444-9.

[9] C. E. Q. Belczak, J. M. P. De Godoy, R. N. Ramos, M. A. De Oliveira, S. Q. Belczak, and R. A. Caffaro, "Is the wearing of elastic stockings for half a day as effective as wearing them for the entire day?," *British journal of dermatology (1951),* vol. 162, no. 1, pp. 42-45, 2010, doi: 10.1111/j.1365-2133.2009.09396.x.

[10] Y. H. Won, M.-H. Ko, and D. H. Kim, "Intermittent pneumatic compression for prolonged standing workers with leg edema and pain," *Medicine (Baltimore),* vol. 100, no. 28, pp. e26639-e26639, 2021, doi: 10.1097/MD.0000000000026639.

[11] G. Cooper-Stanton, "Chronic oedema and lymphoedema: what is the difference?," *British journal of community nursing,* vol. 25, no. Sup4, pp. S31-S35, 2020, doi: 10.12968/bjcn.2020.25.Sup4.S31.

[12] A. Przysinda, W. Feng, and G. Li, "Diversity of Organism-Wide and Organ-Specific Endothelial Cells," *Current cardiology reports,* vol. 22, no. 4, pp. 19-19, 2020, doi: 10.1007/s11886-020-1275-9.

[13] E. Johnson, J. G. Betts, and P. DeSaix, *Anatomy and Physiology*. Open Textbook Library, 2013.

[14] M. Schünke, E. Schulte, and U. Schumacher, *Thieme atlas of anatomy : general anatomy and musculoskeletal system*, Plus version. ed. (Atlas of anatomy : general anatomy and musculoskeletal system.). Stuttgart ;: Thieme, 2010.

[15] J. P. Keener and J. Sneyd, *Mathematical physiology*, 2nd ed. ed. (Interdisciplinary applied mathematics ; 8.). New York: Springer, 2009.

[16] J. O'Brien, S. Chennubhotla, and R. Chennubhotla, "Treatment of edema," *American family physician,* vol. 71, pp. 2111-7, 07/01 2005.

[17] H.-Y. S. Huang and J. Lu, "Biaxial mechanical properties of bovine jugular venous valve leaflet tissues," *Biomechanics and modeling in mechanobiology,* vol. 16, no. 6, pp. 1911-1923, 2017, doi: 10.1007/s10237-017-0927-1.

[18] M. Barile, "Pulmonary Edema: A Pictorial Review of Imaging Manifestations and Current Understanding of Mechanisms of Disease," *European journal of radiology Open,* vol. 7, pp. 100274-100274, 2020, doi: 10.1016/j.ejro.2020.100274.

[19] K. P. M. D. Trayes, J. S. M. D. Studdiford, S. M. D. Pickle, and A. S. M. D. Tully, "Edema: Diagnosis and Management," *American family physician,* vol. 88, no. 2, pp. 102-110B, 2013.

[20] A. P. Gasparis, P. S. Kim, S. M. Dean, N. M. Khilnani, and N. Labropoulos, "Diagnostic approach to lower limb edema," *Phlebology,* vol. 35, no. 9, pp. 650-655, 2020, doi: 10.1177/0268355520938283.

[21] S. Cho and J. E. Atwood, "Peripheral edema," *The American journal of medicine,* vol. 113, no. 7, pp. 580-586, 2002, doi: 10.1016/s0002-9343(02)01322-0.

[22] S. H. Yale and J. J. Mazza, "Approach to diagnosing lower extremity edema," *Comprehensive Therapy,* vol. 27, no. 3, pp. 242-252, 2001/09/01 2001, doi: 10.1007/s12019-001-0021-5.

[23] A. Al Hajeri, "How to diagnose leg edema," *Bahrain Medical Bulletin*, vol. 30, pp. 123-5, 09/01 2008.

[24] F. Pomero *et al.*, "Approach to leg Edema," *Italian Journal of Medicine*, vol. 11, p. 267, 09/11 2017, doi: 10.4081/itjm.2017.771.

[25] W. H. Frishman, "Effects of nonsteroidal anti-inflammatory drug therapy on blood pressure and peripheral edema," *The American journal of cardiology*, vol. 89, no. 6, pp. 18-25, 2002, doi: 10.1016/S0002-9149(02)02233-6.

[26] J. P. O. T. R. L. C. H. T. M. Villeco, "Edema: A Silent but Important Factor," *Journal of hand therapy*, vol. 25, no. 2, pp. 153-162, 2012, doi: 10.1016/j.jht.2011.09.008.

[27] E. J. Topham and P. S. Mortimer, "Chronic lower limb oedema," *Clinical Medicine*, vol. 2, no. 1, p. 28, 2002.

[28] F. Lin, S. Zhang, Y. Sun, S. Ren, and P. Liu, "The management of varicose veins," *International surgery*, vol. 100, no. 1, pp. 185-189, 2015, doi: 10.9738/INTSURG-D-14-00084.1.

[29] G. Cooper-Stanton, "Chronic oedema and lymphoedema: what is the difference?," *British Journal of Community Nursing*, vol. 25, pp. S31-S35, 04/01 2020, doi: 10.12968/bjcn.2020.25.Sup4.S31.

[30] M. Todd, "Venous disease and chronic oedema: treatment and patient concordance," *Br J Nurs*, vol. 23, no. 9, pp. 466-470, 2014, doi: 10.12968/bjon.2014.23.9.466.

[31] M. Tessari, V. Tisato, E. Rimondi, P. Zamboni, and A. M. Malagoni, "Effects of intermittent pneumatic compression treatment on clinical outcomes and biochemical markers in patients at low mobility with lower limb edema," *Journal of vascular*

surgery. Venous and lymphatic disorders (New York, NY), vol. 6, no. 4, pp. 500-510, 2018, doi: 10.1016/j.jvsv.2018.01.019.

[32] M. R. Chester, M. J. Rys, and S. A. Konz, "Leg swelling, comfort and fatigue when sitting, standing, and sit/standing," *International journal of industrial ergonomics*, vol. 29, no. 5, pp. 289-296, 2002, doi: 10.1016/S0169-8141(01)00069-5.

[33] E. Stranden, "Dynamic leg volume changes when sitting in a locked and free floating tilt office chair," *Ergonomics*, vol. 43, no. 3, pp. 421-433, 2000, doi: 10.1080/001401300184503.

[34] B. C. E. Quilici, C. Gildo, J. M. P. De Godoy, B. S. Quilici, and C. R. Augusto, "Comparison of reduction of edema after rest and after muscle exercises in treatment of chronic venous insufficiency," *International archives of medicine*, vol. 2, no. 1, pp. 18-18, 2009, doi: 10.1186/1755-7682-2-18.

[35] I. Sugahara, M. Doi, R. Nakayama, and K. Sasaki, "Acute effect of wearing compression stockings on lower leg swelling and muscle stiffness in healthy young women," *Clinical physiology and functional imaging*, vol. 38, no. 6, pp. 1046-1053, 2018, doi: 10.1111/cpf.12527.

[36] G. Mosti, P. Picerni, and H. Partsch, "Compression stockings with moderate pressure are able to reduce chronic leg oedema," *Phlebology*, vol. 27, no. 6, pp. 289-296, 2012, doi: 10.1258/phleb.2011.011038.

[37] G. Mosti and H. Partsch, "Bandages or Double Stockings for the Initial Therapy of Venous Oedema? A Randomized, Controlled Pilot Study," *European journal of vascular and endovascular surgery*, vol. 46, no. 1, pp. 142-148, 2013, doi: 10.1016/j.ejvs.2013.04.015.

[38] Y.-L. Chen, P.-S. Huang, C.-W. Hsu, Y.-T. Chang, and H.-T. Nguyen, "Shank Circumference Reduction by Sleep Compression Stockings in University Students and Convenience Store Cashiers," *Healthcare (Basel),* vol. 10, no. 8, p. 1532, 2022, doi: 10.3390/healthcare10081532.

[39] D. Bergqvist, "Antiswelling effect of StepIt--an active foot pump system," *Journal of the American Podiatric Medical Association,* vol. 99, no. 1, pp. 20-22, 2009, doi: 10.7547/0980020.

[40] C. E. Q. Belczak, J. M. P. De Godoy, R. N. Ramos, M. A. De Oliveira, S. Q. Belczak, and R. A. Caffaro, "Influence of working shift on the formation of lower limb edema in normal individuals," *Jornal Vascular Brasileiro,* vol. 7, no. 3, pp. 225-230, 2008, doi: 10.1590/s1677-54492008000300007.

[41] "Findings from University of Copenhagen Provides New Data about Edema (The Effect of Compression Stocking On Leg Edema and Discomfort During a 3-hour Flight: a Randomized Controlled Trial)," p. 1275, 2019.

[42] Y.-H. Lin, C.-Y. Chen, and M.-H. Cho, "Effectiveness of leg movement in reducing leg swelling and discomfort in lower extremities," *Applied ergonomics,* vol. 43, no. 6, pp. 1033-1037, 2012, doi: 10.1016/j.apergo.2012.03.002.

[43] Y.-H. Lin, C.-Y. Chen, and M.-H. Cho, "Influence of shoe/floor conditions on lower leg circumference and subjective discomfort during prolonged standing," *Applied ergonomics,* vol. 43, no. 5, pp. 965-970, 2012, doi: 10.1016/j.apergo.2012.01.006.

[44] A. Banba *et al.*, "Measurement of Skin Thickness Using Ultrasonography to Test the Usefulness of Elastic Compression Stockings for Leg Edema in Pregnant Women," *Healthcare (Basel),* vol. 10, no. 9, p. 1754, 2022, doi: 10.3390/healthcare10091754.

[45] R. R. Seeley, *Anatomy & physiology*, 6th ed.. ed. (Anatomy and physiology). Boston: Boston : McGraw-Hill, 2003.

[46] M. Catanho, M. Sinha, and V. Vijayan, "Model of aortic blood flow using the Windkessel effect," *University of California of San Diago, San Diago,* 2012.

[47] T. M. Lassila, A. C. I. Malossi, M. Astorino, and S. Deparis, "Geometrical multiscale model of an idealized left ventricle with fluid-structure interaction effects coupled to a one-dimensional viscoelastic arterial network," in *Proceedings of the ECCOMAS Thematic International Conference on Simulation and Modeling of Biological Flows (SIMBIO 2011)*, 2011.

[48] A. L. Marsden and M. Esmaily-Moghadam, "Multiscale Modeling of Cardiovascular Flows for Clinical Decision Support," *Applied mechanics reviews,* vol. 67, no. 3, 2015, doi: 10.1115/1.4029909.

[49] C. A. Wiederhielm, "Dynamics of transcapillary fluid exchange," *The Journal of general physiology,* vol. 52, no. 1, p. 29, 1968, doi: 10.1085/jgp.52.1.29.

[50] L. Possenti *et al.*, "A computational model for microcirculation including Fahraeus-Lindqvist effect, plasma skimming and fluid exchange with the tissue interstitium," *International journal for numerical methods in biomedical engineering,* vol. 35, no. 3, pp. e3165-n/a, 2019, doi: 10.1002/cnm.3165.

[51] D. Notaro, L. Cattaneo, L. Formaggia, A. Scotti, and P. Zunino, "A mixed finite element method for modeling the fluid exchange between microcirculation and tissue interstitium," *Advances in discretization methods: discontinuities, virtual elements, fictitious domain methods,* pp. 3-25, 2016, doi: 10.1007/978-3-319-41246-7_1.

[52] A. Coccarelli, A. Prakash, and P. Nithiarasu, "A novel porous media-based approach to outflow boundary resistances of 1D arterial blood flow models," *Biomechanics and modeling in mechanobiology,* vol. 18, no. 4, pp. 939-951, 2019, doi: 10.1007/s10237-019-01122-8.

[53] E. Oner, G. Durur, and H. E. Cansunar, "A new technique to measure pressure in medical compression stockings," *TEXT RES J,* vol. 88, no. 22, pp. 2579-2589, 2017, doi: 10.1177/0040517517725121.

[54] H. Li, A. N. Priest, I. Patterson, M. J. Graves, and D. J. Lomas, "Subtractive non-contrast-enhanced MRI of lower limb veins using multiple flow-dependent preparation strategies," *MAGN RESON MED,* vol. 81, no. 3, pp. 1769-1783, 2019, doi: 10.1002/mrm.27530.

[55] M. De Maeseneer *et al.*, "Duplex Ultrasound Investigation of the Veins of the Lower Limbs after Treatment for Varicose Veins – UIP Consensus Document," *EUR J VASC ENDOVASC,* vol. 42, no. 1, pp. 89-102, 2011, doi: 10.1016/j.ejvs.2011.03.013.

[56] C. P. Y. Rohan, P. Badel, B. Lun, D. Rastel, and S. Avril, "Biomechanical response of varicose veins to elastic compression: A numerical study," *Journal of biomechanics,* vol. 46, no. 3, pp. 599-603, 2012, doi: 10.1016/j.jbiomech.2012.10.043.

[57] F. Frauziols *et al.*, "Prediction of the Biomechanical Effects of Compression Therapy by Finite Element Modeling and Ultrasound Elastography," *IEEE transactions on bio-medical engineering,* vol. 62, 12/04 2014, doi: 10.1109/TBME.2014.2378553.

[58] M. K. Jain and P. D. Wolf, "A Three-Dimensional Finite Element Model of Radiofrequency Ablation with Blood Flow and its Experimental Validation," *Annals of Biomedical Engineering,* vol. 28, no. 9, pp. 1075-1084, 2000, doi: 10.1114/1.1310219.

[59] M. K. Jain and P. D. Wolf, "In Vitro Temperature Map of Cardiac Ablation Demonstrates the Effect of Flow on Lesion Development," *Annals of Biomedical Engineering,* vol. 28, no. 9, pp. 1066-1074, 2000, doi: 10.1114/1.1310218.

[60] J. C. Vardakis *et al.*, "Investigating cerebral oedema using poroelasticity," *Med Eng Phys,* vol. 38, no. 1, pp. 48-57, Jan 2016, doi: 10.1016/j.medengphy.2015.09.006.

[61] Z. Hajati, F. S. Moghanlou, M. Vajdi, S. E. Razavi, and S. Matin, "Fluid-structure interaction of blood flow around a vein valve," *Bioimpacts,* vol. 10, no. 3, pp. 169-175, 2020, doi: 10.34172/bi.2020.21.

[62] J. Dong, K. K. L. Wong, and J. Tu, "Hemodynamics analysis of patient-specific carotid bifurcation: A CFD model of downstream peripheral vascular impedance," *International journal for numerical methods in biomedical engineering,* vol. 29, no. 4, pp. 476-491, 2013, doi: 10.1002/cnm.2529.

[63] G. Fortuny *et al.*, "Effect of anticoagulant treatment in deep vein thrombosis: A patient-specific computational fluid dynamics study," *J BIOMECH,* vol. 48, no. 10, pp. 2047-2053, 2015, doi: 10.1016/j.jbiomech.2015.03.026.

[64] S. M. Javid Mahmoudzadeh Akherat, K. Cassel, M. Boghosian, M. Hammes, and F. Coe, "A Predictive Framework to Elucidate Venous Stenosis: CFD & Shape Optimization," *Comput Methods Appl Mech Eng,* vol. 321, pp. 46-69, Jul 1 2017, doi: 10.1016/j.cma.2017.03.036.

[65] P. Assemat *et al.*, "Three-dimensional numerical simulation of blood flow in mouse aortic arch around atherosclerotic plaques," *Applied mathematical modelling,* vol. 38, no. 17-18, pp. 4175-4185, 2014, doi: 10.1016/j.apm.2014.01.004.

[66] Z. Xiong, D. Yuan, J. Wang, T. Zheng, and Y. Fan, "Influence of renal artery stenosis morphology on hemodynamics," *Computer methods in biomechanics and biomedical engineering,* vol. 24, no. 12, pp. 1294-1301, 2021, doi: 10.1080/10255842.2021.1883592.

[67] R. Liu, "Comfort and mechanical function of compression stockings," 2006.

[68] C. Ye and R. Liu, "Biomechanical prediction of veins and soft tissues beneath compression stockings using fluid-solid interaction model," *International Journal of Biomedical and Biological Engineering,* vol. 14, no. 10, pp. 285-290, 2020.

[69] C. Ye, R. Liu, X. Wu, F. Liang, M. T. C. Ying, and J. Lv, "New analytical model and 3D finite element simulation for improved pressure prediction of elastic compression stockings," *Materials & design,* vol. 217, p. 110634, 2022, doi: 10.1016/j.matdes.2022.110634.

[70] F. Collares and S. o. Faintuch, *Varicose veins*. New York: New York : Thieme, 2017.

[71] S. L. Keith *et al.*, "Do graduated compression stockings and pneumatic boots have an additive effect on the peak velocity of venous blood flow?," *Archives of Surgery,* vol. 127, no. 6, pp. 727-730, 1992, doi: 10.1001/archsurg.1992.01420060107016.

[72] T. Charles, D. Mackintosh, B. Healy, K. Perrin, M. Weatherall, and R. Beasley, "Merino wool graduated compression stocking increases lower limb venous blood flow:

A randomized controlled trial," *Adv Therapy*, vol. 28, no. 3, pp. 227-237, 2011, doi: 10.1007/s12325-010-0107-5.

[73] G. Marsden *et al.*, "A Cost-effectiveness Analysis of Surgery, Endothermal Ablation, Ultrasound-guided Foam Sclerotherapy and Compression Stockings for Symptomatic Varicose Veins," *EUR J VASC ENDOVASC*, vol. 50, no. 6, pp. 794-801, 2015, doi: 10.1016/j.ejvs.2015.07.034.

[74] R. Liu, T. T. Lao, Y. L. Kwok, Y. Li, and M. T.-C. Ying, "Effects of graduated compression stockings with different pressure profiles on lower-limb venous structures and haemodynamics," *Adv Therapy*, vol. 25, no. 5, pp. 465-478, 2008, doi: 10.1007/s12325-008-0058-2.

[75] V. Ibegbuna, K. T. Delis, A. N. Nicolaides, and O. Aina, "Effect of elastic compression stockings on venous hemodynamics during walking," *J Vasc Surg*, vol. 37, no. 2, pp. 420-425, 2003, doi: 10.1067/mva.2003.104.

[76] M. H. Meissner *et al.*, "Primary chronic venous disorders," *Journal of vascular surgery*, vol. 46, no. 6, pp. S54-S67, 2007, doi: https://doi.org/10.1016/j.jvs.2007.08.038.

[77] M. Hirai, H. Iwata, and N. Hayakawa, "Effect of elastic compression stockings in patients with varicose veins and healthy controls measured by strain gauge plethysmography," *SKIN RES TECHNOL*, vol. 8, no. 4, pp. 236-239, 2002, doi: 10.1034/j.1600-0846.2001.80401.x.

[78] H. Partsch, J. Winiger, and B. Lun, "Compression Stockings Reduce Occupational Leg Swelling," *Dermatologic surgery*, vol. 30, no. 5, pp. 737-743, 2004, doi: 10.1111/j.1524-4725.2004.30204.x.

[79] B.-B. Lee, J. Bergan, and S. Rockson, *Lymphedema: A Concise Compendium of Theory and Practice*. 2011, doi: 10.1007/978-0-85729-567-5.

[80] M. Zaleska, W. L. Olszewski, M. Cakala, J. Cwikla, and T. Budlewski, "Intermittent Pneumatic Compression Enhances Formation of Edema Tissue Fluid Channels in Lymphedema of Lower Limbs," *Lymphat Res Biol*, vol. 13, no. 2, pp. 146-53, Jun 2015, doi: 10.1089/lrb.2014.0010.

[81] P. M. Guedes, N. A. Saldanha, P. M. Matos, F. S. Carvalho, G. Veiga, and P. Norton, "Occupational leg edema-use of compression stockings," *Porto biomedical journal*, vol. 5, no. 6, pp. e093-e093, 2020, doi: 10.1097/j.pbj.0000000000000093.

[82] Y. Xiong, "Pressure management for medical compression stockings: prediction, computer integrated manufacturing and pressure monitoring by fabric sensors," 2022.

[83] W.-T. Yang *et al.*, "A randomized controlled trial of standard vs customized graduated elastic compression stockings in patients with chronic venous disease," *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, vol. 12, no. 2, p. 101678, 2024, doi: 10.1016/j.jvsv.2023.08.017.

[84] D. A. LAMPROU, R. J. Damstra, and H. Partsch, "Prospective, Randomized, Controlled Trial Comparing a New Two-Component Compression System with Inelastic Multicomponent Compression Bandages in the Treatment of Leg Lymphedema," *Dermatologic surgery*, vol. 37, no. 7, pp. 985-991, 2011, doi: 10.1111/j.1524-4725.2011.02002.x.

[85] T. M. Brock, A. P. Sprowson, S. Muller, and M. R. Reed, "Short-stretch inelastic compression bandage in knee swelling following total knee arthroplasty study

(STICKS): study protocol for a randomised controlled feasibility study," *Trials*, vol. 16, pp. 1-7, 2015, doi: 10.1186/s13063-015-0618-0.

[86] M. Karafa, A. Karafová, and A. Szuba, "A compression device versus compression stockings in long-term therapy of lower limb primary lymphoedema after liposuction," Journal of Wound Care, vol. 29, no. 1, pp. 28-35, 2020, doi: 10.12968/jowc.2020.29.1.28.

[87] A. de Sire, N. Fusco, E. Sajjadi, L. Lippi, C. Cisari, and M. Invernizzi, "Lymphedema rehabilitation using self-adaptive inelastic compression in breast cancer: A proof-of-principle study," *Applied Sciences*, vol. 11, no. 4, p. 1901, 2021, doi: 10.3390/app11041901.

[88] M. P. Goldman, J.-J. r. m. Guex, and R. A. Weiss, *Sclerotherapy : treatment of varicose and telangiectatic leg veins*, Sixth edition. ed. Edinburgh: Elsevier, 2017.

[89] F. M. D. Mariani *et al.*, "Multicenter randomized trial comparing compression with elastic stocking versus bandage after surgery for varicose veins," *Journal of vascular surgery*, vol. 53, no. 1, pp. 115-122, 2011, doi: 10.1016/j.jvs.2010.08.033.

[90] M. R. Fu *et al.*, "The Effects of Kinect-Enhanced Lymphatic Exercise Intervention on Lymphatic Pain, Swelling, and Lymph Fluid Level," *Integrative cancer therapies*, vol. 20, pp. 153473542110267-15347354211026757, 2021, doi: 10.1177/15347354211026757.

[91] L. Hansen, J. Winkel, and K. Jørgensen, "Significance of mat and shoe softness during prolonged work in upright position: based on measurements of low back muscle EMG, foot volume changes, discomfort and ground force reactions," *Applied ergonomics*, vol. 29, no. 3, pp. 217-224, 1998, doi: 10.1016/S0003-6870(97)00062-8.

[92] J. E. Muscolino, *Kinesiology : the skeletal system and muscle function*, 3rd edition. ed. St. Louis: Elsevier Inc., 2017.

[93] N. W. Dail, T. A. Agnew, and R. T. Floyd, *Kinesiology for manual therapies* (massage therapy series.). New York, N.Y: McGraw-Hill, 2011.

[94] D. R. S. Evans, K. J. Williams, P. H. Strutton, and A. H. Davies, "The comparative hemodynamic efficacy of lower limb muscles using transcutaneous electrical stimulation," *Journal of Vascular Surgery: Venous and Lymphatic Disorders,* vol. 4, no. 2, pp. 206-214, 2016, doi: 10.1016/j.jvsv.2015.10.009.

[95] C. Recek, "Conception of the Venous Hemodynamics in the Lower Extremity," *Angiology,* vol. 57, no. 5, pp. 556-563, 2006, doi: 10.1177/0003319706293117.

[96] J. A. O'Brien, H. E. Edwards, K. J. Finlayson, and G. Kerr, "Understanding the relationships between the calf muscle pump, ankle range of motion and healing for adults with venous leg ulcers: A review of the literature," *Wound practice & research,* vol. 20, no. 2, pp. 80-85, 2012.

[97] W. L. Olszewski, "Contractility Patterns of Human Leg Lymphatics in Various Stages of Obstructive Lymphedema," *ANN NY ACAD SCI,* vol. 1131, no. 1, pp. 110-118, 2008, doi: 10.1196/annals.1413.010.

[98] D. Yang, Y. K. Vandongen, and M. C. Stacey, "Variability and reliability of air plethysmographic measurements for the evaluation of chronic venous disease," *Journal of vascular surgery,* vol. 26, no. 4, pp. 638-642, 1997, doi: 10.1016/S0741-5214(97)70063-6.

[99] A. A. Pollack and E. H. Wood, "Venous Pressure in the Saphenous Vein at the Ankle in Man during Exercise and Changes in Posture," *Journal of applied physiology (1985),* vol. 1, no. 9, pp. 649-662, 1949, doi: 10.1152/jappl.1949.1.9.649.

[100] M. A. McNally, E. A. Cooke, and R. A. Mollan, "The effect of active movement of the foot on venous blood flow after total hip replacement," *JBJS,* vol. 79, no. 8, pp. 1198-1201, 1997, doi: 10.2106/00004623-199708000-00012.

[101] I. C. Hojensgard and H. Sturup, "Static and Dynamic Pressures in Superficial and Deep Veins of the Lower Extremity in Man," *Acta physiologica Scandinavica,* vol. 27, no. 1, pp. 49-67, 1953, doi: 10.1111/j.1748-1716.1953.tb00923.x.

[102] L. WallØE and J. Wesche, "Time course and magnitude of blood flow changes in the human quadriceps muscles during and following rhythmic exercise," *The Journal of physiology,* vol. 405, no. 1, pp. 257-273, 1988, doi: 10.1113/jphysiol.1988.sp017332.

[103] T. F. O'Donnell, Jr, D. A. Rosenthal, A. D. Callow, and B. L. Ledig, "Effect of Elastic Compression on Venous Hemodynamics in Postphlebitic Limbs," *JAMA,* vol. 242, no. 25, pp. 2766-2768, 1979, doi: 10.1001/jama.1979.03300250022022.

[104] J. Winkel, "SWELLING OF THE LOWER LEG IN SEDENTARY WORK-A PILOT STUDY," *Journal of Human Ergology,* vol. 10, no. 2, pp. 139-149, 1981, doi: 10.11183/jhe1972.10.139.

[105] T. Hasegawa, K. Inoue, O. Tsutsue, and M. Kumashiro, "Effects of a sit–stand schedule on a light repetitive task," *International journal of industrial ergonomics,* vol. 28, no. 3, pp. 219-224, 2001, doi: 10.1016/S0169-8141(01)00035-X.

[106] J. Guex and M. Perrin, "Edema and leg volume: methods of assessment," *Angiology*, vol. 51, no. 1, pp. 9-12, 2000, doi: 10.1177/000331970005100103.

[107] J. M. P. De Godoy, D. M. Braile, F. B. Perez, and M. De Fátima Guerreiro Godoy, "Effect of walking on pressure variations that occur at the interface between elastic stockings and the skin," *International wound journal*, vol. 7, no. 3, pp. 191-193, 2010, doi: 10.1111/j.1742-481X.2010.00673.x.

CHAPTER 3

MECHANISM OF THE FLUID EXCHANGE IN BLOOD VESSEL AND TISSUE

3.1 Introduction

The literature review in Chapter 2 reveals that current numerical models are limited in considering fluid exchange among blood vessels, tissues, and lymph while applying compression. Moreover, when utilizing the compression method to reduce oedema, it is crucial to comprehend the mechanism of fluid exchange in the blood and interstitial fluid, and apply appropriate compression based on this mechanism.

Therefore, this chapter first establishes a 2D simplified rigid numerical modelling that can achieve fluid exchange between blood and interstitial fluid and explain the mechanism in detail of how to achieve oedema reduction. Secondly, it considers physiological parameters assesses their impact on oedema reduction using the computational fluid dynamics (CFD) method and investigates the possibilities of pathological changes resulting from these physiological parameters. Finally, a physical experiment is conducted to verify the validity of the simplified numerical modelling.

3.2 Modelling fluid exchange in blood vessel and tissue

3.2.1 2D Simplified modelling

There are a lot of capillaries, arterioles, venules with large arteries and veins in the human body system, as shown in **Figure 3.1.** According to the anatomy size of the blood vessels, the range of the diameter and average wall thickness of blood vessel, the whole capillary bed is simplified as a 2D numerical model for convenient calculation (see **Figure 3.2**). The length of the whole model is 180 mm, the lengths of both artery and vein are 54 mm, and the length of capillary bed is 72 mm. The diameter of both artery and vein are 1mm. In addition, the vertical dimension of the capillary bed measures 25 mm. The interstitial fluid is symmetrically distributed around the central capillary bed, occupying 12.5 mm both above and below vertically.

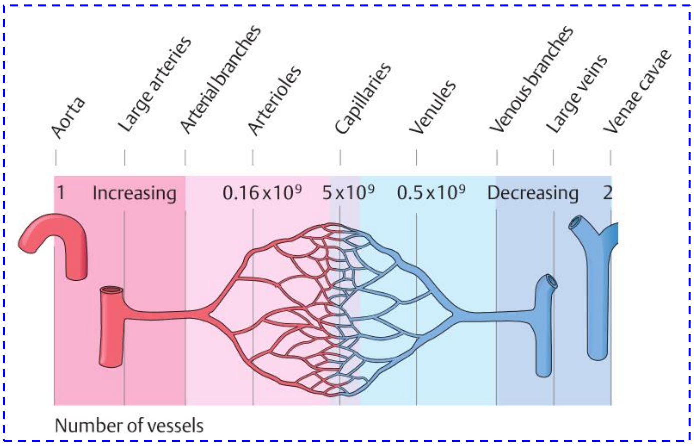

Figure 3. 1 Number of vessels [1].

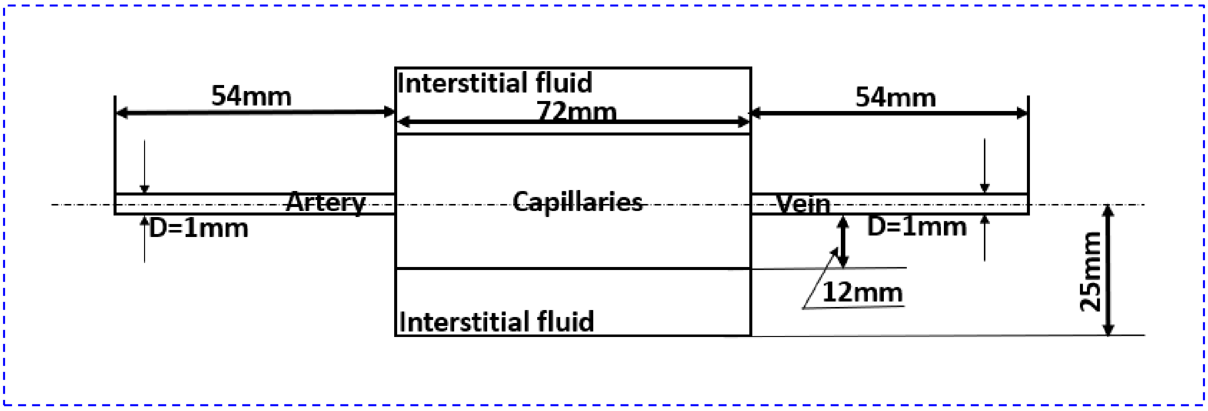

Figure 3. 2 The schematic diagram of the simplified numerical model size.

Figure 3.3 shows the distribution of the artery (red), capillary (purple), vein (blue), interstitial fluid (light yellow) and lymph (green) parts in the 2D simplified capillary bed model. The left vessel model represents an artery, the right vessel model represents a vein, and the middle arteriovenous connection area is the capillary bed. The upper and lower connecting area with capillary are the interstitial fluid area. The arterial end is the blood inlet from the heart. After the blood flowing into the capillary area from the artery, it undergoes fluid exchange with the interstitial fluid through the porous capillary wall. After that, the blood flows out from the venous end and returns to the heart. This fluid exchange includes the fluid filtration at the arterial end and fluid reabsorption at the venous end, and some of the interstitial fluid is reabsorbed through lymphatic vessels, the flow direction is shown as arrow direction in the **Figure 3.3**.

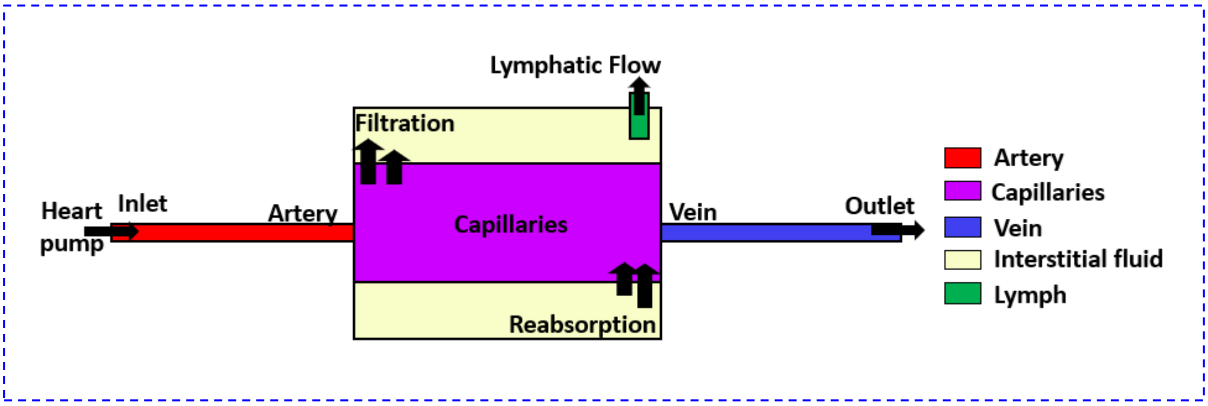

Figure 3. 3 The distribution of the artery (red), capillary (purple), vein (blue), interstitial fluid (light yellow) and lymph (green) part in the 2D simplified capillary bed model.

3.2.2 Assumptions and description equations

Before conducting numerical simulation, assumptions are drawn to ensure the numerical simulation be performed efficiently, which are listed as follows:

(1) The related fluid (blood and interstitial fluid) is incompressible, laminar, and homogenous for convenient calculation. (2) The fluid movement across the capillary membrane follows the Starling Hypothesis, which is mainly induced by two components: one is porous nature of the capillary wall, the other one is pressure difference of capillary and interstitial fluid. (3) The gravity is ignored.

In the numerical simulation, the fluid dynamics are governed by the continuity equation and incompressible Navier-Stokes equations. It should be noted that the blood is regarded as a homogeneous Newtonian fluid in the large diameter of blood vessels [2, 3].

In addition, the relationship between the fluid flux and pressure difference and the connection between pressure drop and kinetic and viscous energy losses are shown in equation (3-1) and

(3-2), respectively [4]. The pressure losses are attributed to concurrent kinetic and viscous energy losses, applicable to all flow types. In equation (3-2), the first term represents viscous losses, while the second term accounts for inertial or kinetic losses. These two equations correspond to both horizontal and vertical flow, as depicted in **Figure 3.3**.

$$Q=-\frac{\alpha\pi r^2}{\mu}\frac{\Delta P}{L} \tag{3-1}$$

$$\frac{|\Delta P|}{L}=150\frac{(1-\varepsilon)^2}{\varepsilon^3}\frac{\mu v_m}{d^2}+1.75\frac{1-\varepsilon}{\varepsilon^3}\frac{G v_m}{d} \tag{3-2}$$

In which, Q is the fluid flux, α is the permeability, $|\Delta P|$ is the pressure difference, L is the length of the model, ε is the porosity, v_m is the mean velocity, G is the shear module and d is the diameter of the model.

Therefore, the fluid flow Q is closely related to model parameters, such as radius r, length L, fluid velocity v_m, fluid viscosity μ, porosity ε, permeability α. Therefore, the influence of these physiological parameters on the oedema reduction will be studied in detail in section 3.3.

3.3 Numerical simulation of applying compression with different physiological parameters

3.3.1 Material parameters in simulation

To conform with the actual physiological parameters, the tissue parameters used in the numerical simulation are selected according to the literatures [1, 5-9], they are blood density, blood viscosity, pressure in vein, capillary porosity, tissue porosity, viscous resistance, inertial loss coefficient, interstitial fluid density, and inlet maximum velocity. And take these parameters as fixed parameters and analyse their influence on the reducing oedema separately.

Referenced physiological parameters value and unit using in the numerical simulation are listed in **Table 3.1**.

Table 3. 1 Referenced value of physiological parameters.

Parameters	Value (unit)		Reference
Blood density	1060 kg/m3		[5]
Blood viscosity	0.003 kg/(m·s)		[5]
Pressure in the vein	2000 Pa (=15 mmHg)		[1]
Capillary porosity	0.5		[9]
	Viscous resistance	Inertial loss coefficient	
	7.50E+09	7.00E+04	
Tissue porosity	0.2		[9]
	Viscous resistance	Inertial loss coefficient	
	1.88E+12	4.38E+06	
Interstitial fluid density	1000 kg/m3		[6]
Interstitial fluid viscosity	0.0035 kg/(m·s)		[7]
Inlet maximum velocity	9 cm/s		[8]

3.3.2 Discretization and boundary conditions

Firstly, the simplified numerical model, which is a rigid model including artery, vein, capillary bed, and tissue with the interstitial fluid, meshed with a total of 76000 cells, 153160 faces, 77161 nodes, and 14 partitions using quadrilateral mesh in the Ansys Fluent 16.0 software, as shown in **Figure 3.4. Table 3.2** presents the number and size of elements for the artery, vein, capillary bed, and tissue with the interstitial fluid. The capillary elements have variable density properties. The tissue and capillaries possess different porous element properties according to the different viscous resistance and inertial loss coefficients.

Table 3. 2 Element number and size in numerical model.

Component	Element number	Aspect ratio	Element size (mm^2)
Artery	6000	1.8	1.80E-08
Vein	6020	1.8	1.80E-08
Capillary bed	40000	1.934	6.26E-08
Tissue	24000	1.852	6.00E-08

Secondly, the boundary conditions of the numerical simulation are as follows. There is one inlet and three direction outlets in the simplified numerical model. The inlet of the artery is set to the blood inlet velocity, which is consistent with the actual blood velocity of the artery. After the blood flows into the capillary, the fluid exchange is performed. The capillary and interstitial fluid boundary condition is set as the porous media model. There are three direction outlets, one is the outlet of the vein, and the other two outlets of the interstitial fluid equivalent to the lymphatic flow. The reason for setting up this boundary condition is that the inlet and outlet rate are to be used as the indicator for analysing the degree of oedema reduction. As elaborated in Chapter 2, the 20 Liters of fluid leaves the capillaries each day, about 90% of them are reabsorbed, and approximately 10% are removed by lymphatic vessels [1, 10]. Therefore, the inlet flow and outlet flow should be controlled in these percentage range. Moreover, the uniformly distributed pressure is applied on the upper and lower ends of the interstitial fluid, which is equivalent to the external pressure exerted on the human tissue in the actual compression treatment. The schematic diagram of the boundary condition of the numerical model is shown in **Figure 3.5.** This CFD method's effectiveness in simulating fluid flow behaviour in the porous media model is verified using the physical experiment in section 3.4.

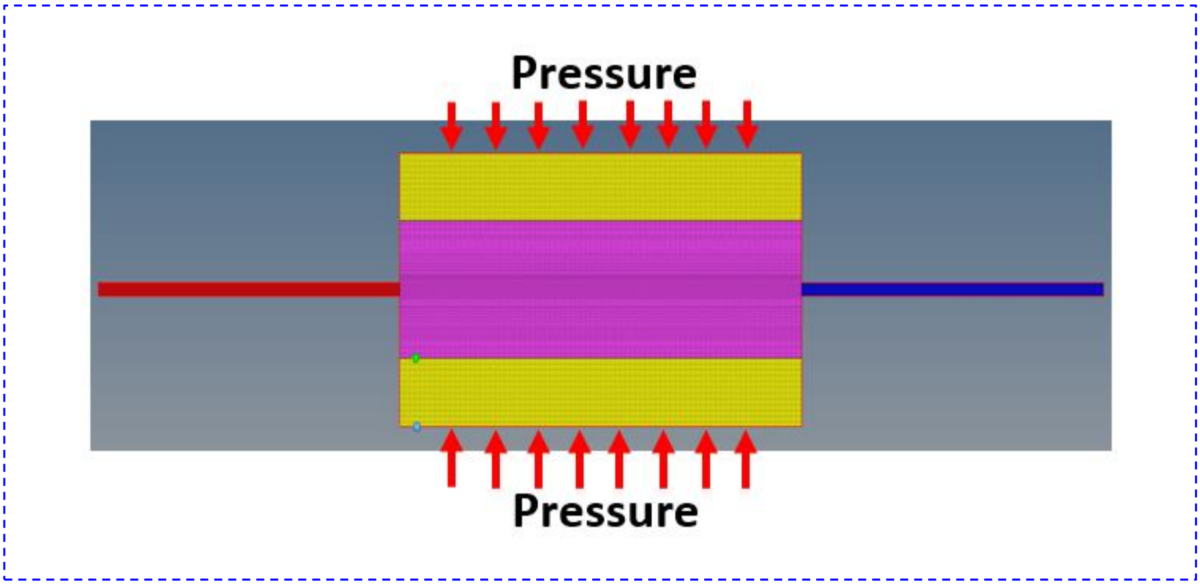

Figure 3. 4 Meshed simplified model with quadrilateral mesh.

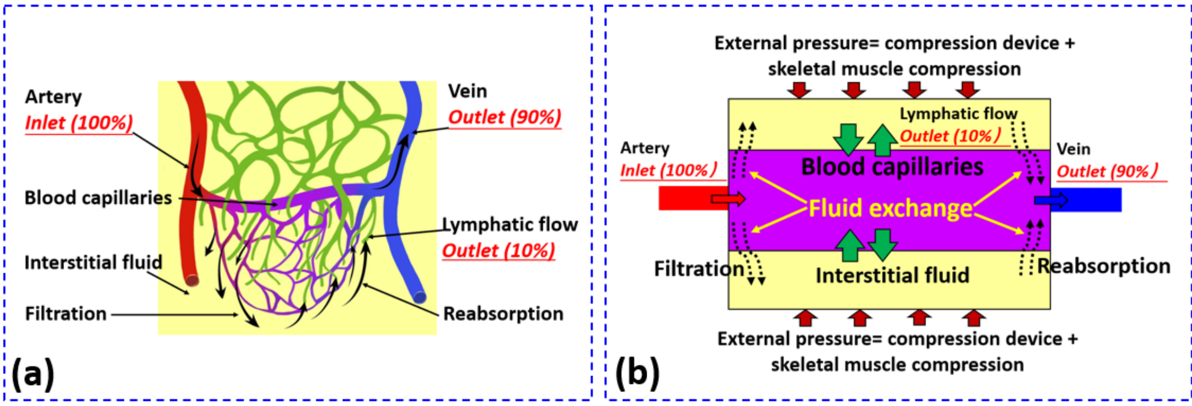

Figure 3. 5 (a) is the normal physiological structure of the blood capillary bed in the human body system, and (b) the schematic diagram of the boundary condition of the numerical model, the left red arrow shows the direction of blood inlet flow, the mutual opposite direction arrow in the capillaries area represents the direction of the fluid exchange, and the right blue arrow shows the direction of blood outlet flow.

Thirdly, the blood pulse velocity of the heart has pulse frequency, maximum and minimum velocity. In the literature [11], the actual cardiac input is achieved by Fourier Transform to obtain the first 10 modes of the actual cardiac blood flow velocity, as shown in **Figure 3.6,** which is the fitting graph of first 10 modes overlay when the blood flow is 3.57943 ml/s with time. In this research, the maximum velocity of the simplified model is set to 9 cm/s according to anatomy and physiology [8]. In addition, the inlet velocity data in **Figure 3.7** is obtained using the same first 10 modes in the literature [11] through MATLAB, showing the two periodic beats of the inlet velocity.

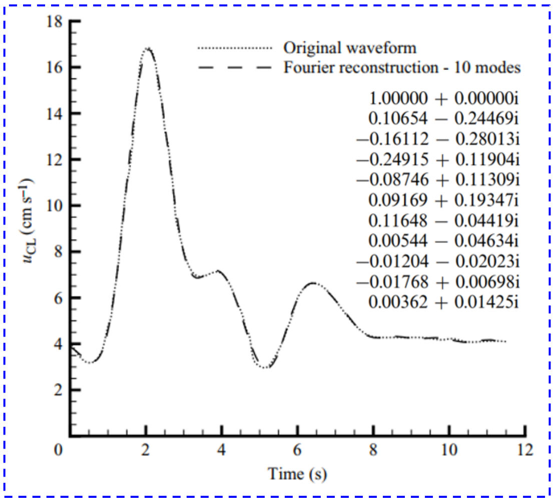

Figure 3. 6 The fitting graph of the first 10 modes overlay when the blood flow is 3.57943 ml/s, and the waveform data of one pulse cycle in the first ten orders [11].

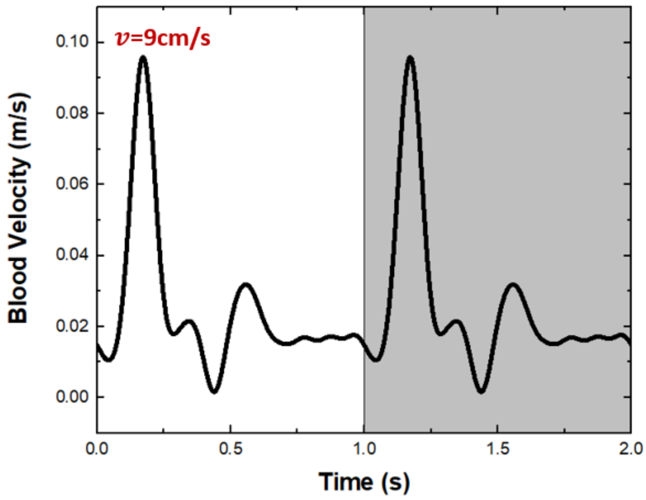

Figure 3. 7 The two periodic beats of the inlet velocity (with 9 cm/s maximum velocity) used in the numerical simulation.

3.3.3 Numerical simulation results

The influences of the actual physiological parameters are studied specifically and the contribution of different physiological parameters to reduce oedema is investigated under constant compression pressure through numerical simulation.

Because of the simplified numerical model, the parameters radius r and length L are fixed in the defined model. Therefore, following parameters will be analysed and discussed: tissue and capillary porosity ε, constant pressure P_c, blood viscosity μ, inlet velocity of blood v_i and heart rate f_i , and different type of pressure (constant compression pressure and harmonic compression pressure).

3.3.3.1 Meaning of mass rate

Firstly, the mass rate (unit: kg/s) is introduced because that the mass rate of blood flow in the inlet and outlet is important data to find the critical pressure of starting to reduce oedema. The critical pressure is the exerting pressure on the interstitial fluid, which makes the inlet flow to be reabsorbed through outlet flow in the vein by 90% and be reabsorbed through outlet in the lymph by 10%. In other words, the critical pressure is the point which starts to reduce oedema. Moreover, the percentage of every outlet is equal to the value of outlet/inlet separately in the vein or lymph outlet.

Under the fixed parameters in the **Table 3.1**, **Figure 3.8** shows the mass rate of the inlet in the artery (red line), the mass rate of the outlet in the vein (blue line), and the mass rate of the outlet in lymph (light green line) under 100 Pa and 4940 Pa compression pressure on the interstitial fluid, respectively. In the physiological normal case, the mass rate of the inlet in the artery should be equal to the mass rate of the outlet in the vein and lymph. The suitable pressure on the interstitial fluid can make the model increase the reabsorption in the vein. Therefore, the percentage of the outlet flow in the vein can be increased to achieve oedema reduction. In **Figure 3.8**, the positive direction (>0) shows the inlet flow, and the negative direction (<0) shows the outlet flow, it is remarked using the purple dot line.

Figure 3.8(a) shows the case of having oedema under 100 Pa compression pressure on the interstitial fluid, because the percentage of outlet in the vein is only 87.9%. **Figure 3.8(b)** shows the case of reduced oedema, because the percentage of outlet in the vein accounts for 109.9% under 4940 Pa compression pressure on the interstitial fluid. This percentage value under 4940 Pa pressure means that the outlet lymphatic flow becomes inlet, the interstitial fluid from tissue inlets to the blood vessel. The detailed data results of the **Figure 3.8** are revealed in the **Table 3.3** and **Table 3.4**. In **Table 3.4**, there is a negative value in the mean mass rate in lymph, which shows the interstitial fluid has entered the blood vessels because of the high compression pressure on the interstitial fluid, therefore, the percentage of outlet in the vein is more than 100%.

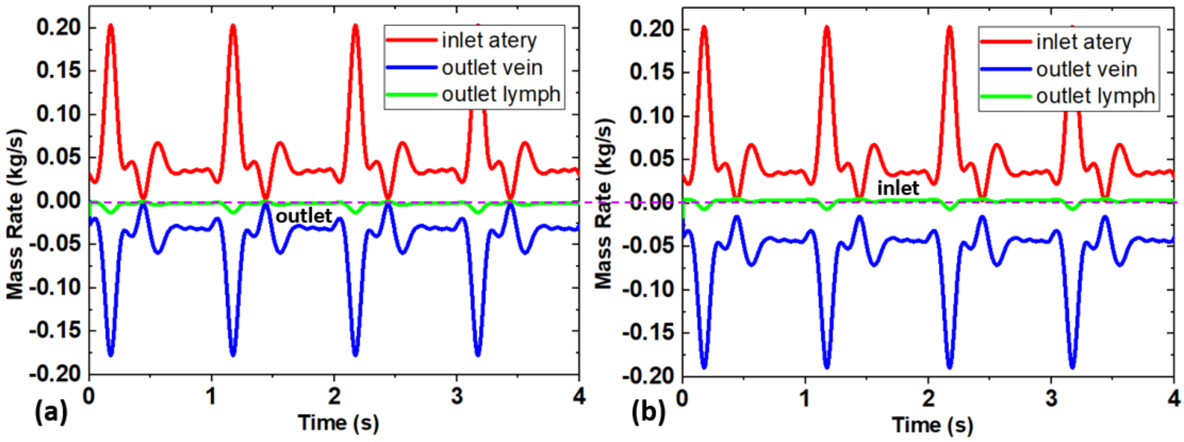

Figure 3. 8 Mass rate of the inlet in artery, outlet in vein, and outlet in lymph under (a) 100 Pa and (b) 4940 Pa compression pressure on the interstitial fluid.

Table 3. 3 Data result of the mean mass rate in **Figure 3.8(a).**

Pressure on the interstitial fluid	100 Pa
Mean mass rate in artery	0.0535 kg/s (100.0%)
Mean mass rate in the vein	0. 0470 kg/s (87.9%)
Mean mass rate in lymph	0.0065 kg/s (12.1%)

Table 3. 4 Data result of the mean mass rate in **Figure 3.8(b).**

Pressure on the interstitial fluid	4940 Pa
Mean mass rate in artery	0.0535 kg/s (100.0%)
Mean mass rate in the vein	0.0588 kg/s (109.9%)
Mean mass rate in lymph	-0.0050 kg/s inlet (-9.9%)

3.3.3.2 Influence of porosity ε

Secondly, the influence of porosity ε on the oedema reduction is studied. Porosity is the ratio between the void space and total volume of the media [9]. The fluid exchange is carried out through the capillary wall, and the capillary wall can be considered as the porous media structure. Therefore, porosity is an important parameter of oedema reduction in the porous media. Additionally, the porosity of different body tissues is different.

In the theoretical analysis, the equation (3-2) shows the relationship between pressure drop and kinetic and viscous energy losses. In the Ansys Fluent, kinetic and viscous energy losses are introduced to the moment equation (3-3) [4]:

$$M_i = -(\sum_{j=1}^{3} R_{ij}\mu v_j + \sum_{i=1}^{3} C_{ij}\frac{1}{2}\rho|v|v_j) \tag{3-3}$$

For the simple homogeneous media, equation (3-3) can be simplified that [4]:

$$M_i = -(\frac{\mu}{\alpha} v_i + C_2\frac{1}{2}\rho|v|v_i) \tag{3-4}$$

$$R_v = \frac{1}{\alpha} = 150\frac{(1-\varepsilon)^2}{d^2\varepsilon^3} \tag{3-5}$$

$$C_2 = \frac{3.5(1-\varepsilon)}{d\varepsilon^3} \tag{3-6}$$

In the porous media, the important factors in equation (3-4) are viscous resistance R_v and inertial losses C_2. The R_v and C_2 can be expressed using porosity ε , as shown in equation (3-5) and (3-6) [4]. Therefore, the porosity ε is one of the main input parameters in Ansys Fluent.

Under the fixed parameters in the **Table 3.1**, **Figure 3.9** reveals the critical pressure with the different tissue and capillary porosities. **Table 3.5** is different tissue porosities list with related viscous resistance and inertial losses coefficients, and **Table 3.6** is capillary porosities list with related viscous resistance and inertial losses coefficients [9]. Under the 0.5 of capillary porosity, **Figure 3.9(a)** shows that the increasing tissue porosity can cause nonlinearly increasing critical pressure. Specifically, when the tissue porosity increases, the blood flow from capillary to interstitial fluid increases because of the high artery pressure, therefore, the critical pressure will be required to increase. However, **Figure 3.9(b)** shows that the increasing capillary porosity can cause nonlinearly decreasing critical pressure. The reason is that increasing capillary porosity is equal to adding more porous media in the capillary bed of the simplified model to promote fluid exchange.

Table 3. 5 Tissue porosity parameters.

	Porosity	**Viscous resistance**	**Inertial loss coefficient**
Tissue	0.2	1.88E+12	4.38E+06
	0.22	1.34E+12	3.20E+06
	0.25	8.44E+11	2.10E+06
	0.27	6.35E+11	1.62E+06
	0.3	4.25E+11	1.13E+06
	0.35	2.31E+11	6.63E+05
Capillary	0.5	7.50E+09	7.00E+04

Table 3. 6 Capillary porosity parameters.

	Porosity	**Viscous resistance**	**Inertial loss coefficient**
Capillary	0.3	6.81E+10	4.54E+05
	0.35	3.70E+10	2.65E+05
	0.4	2.11E+10	1.64E+05
	0.45	1.24E+10	1.06E+05
	0.5	7.50E+09	7.00E+04
	0.55	4.56E+09	4.73E+04
	0.6	2.78E+09	3.24E+04
Tissue	0.25	8.44E+11	2.10E+06

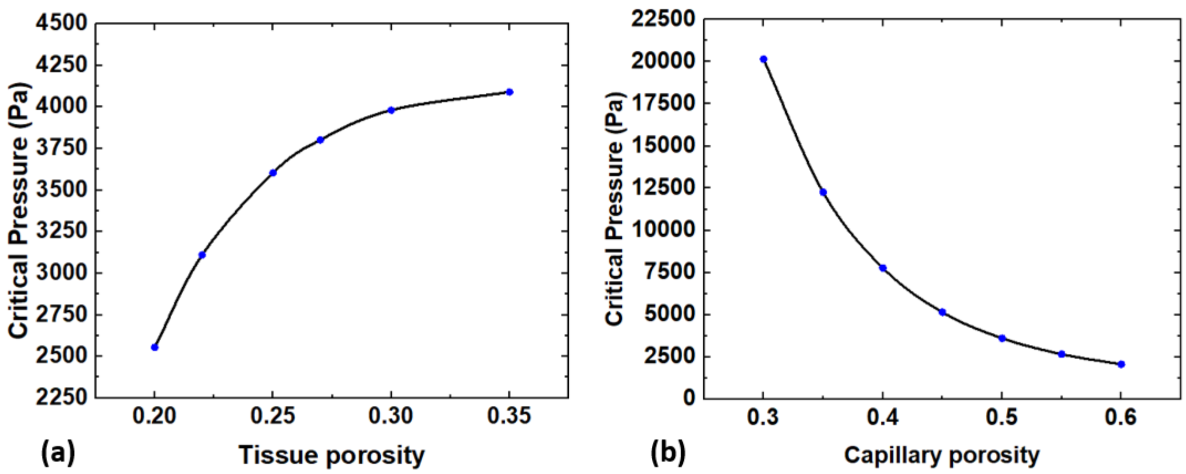

Figure 3. 9 The critical pressure with the different tissue and capillary porosities.

In addition, **Figure 3.10** presents the mass rate of the inlet and outlet with 0.25 and 0.35 of tissue porosity under 2000 Pa compression pressure, with fixed other parameters. It shows that increasing tissue porosity can cause the smaller outlet flow in the vein under applying the same compression pressure (0.25: vein output percentage is 93.6%; 0.35: vein output percentage is 88.0%), which makes generate oedema. Moreover, **Figure 3.10** reveals that the outlet flow of the vein has a pulse. This phenomenon is confirmed by the literature, flow is a time-dependent flow, especially in veins close to the heart because of the rhythmic activity of the right cardiac pump and breathing, as well as in the limb veins due to muscle contraction-assisted flow [12].

The porosity of the tissue or the capillary can be changed at different age levels, besides, it can be influenced by utilizing medicine. Therefore, according to the patient's age and differences in case status, applying reasonable compression is considered to reduce oedema.

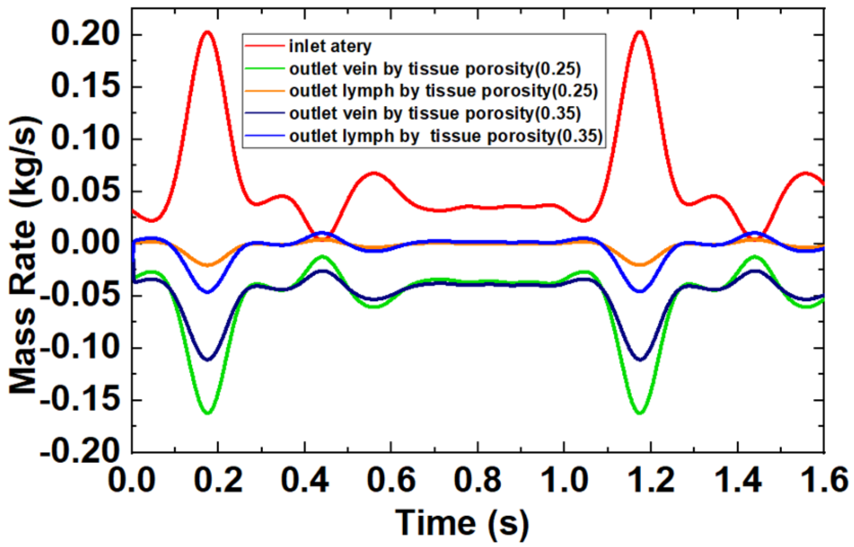

Figure 3. 10 Mass rate of the inlet and outlet with 0.25 and 0.35 of tissue porosity under 2000Pa compression pressure.

3.3.3.3 Influence of constant pressure Pc

Thirdly, the influence of constant pressure *Pc* on the oedema reduction is researched. The research object mainly focused on the influence of the compression treatment on the oedema reduction. Therefore, the constant pressure on the interstitial fluid is one of the important parameters. The constant pressure is exerted evenly distributed on the interstitial fluid boundary, which can be regarded as applied constant pressure on human skin or tissues.

Figure 3.11 presents the relationship between the percentage of vein output and constant pressure under the fixed parameters. Applied constant pressure range is from 0 Pa to 4940 Pa. When the interstitial fluid is compressed by more than 550 Pa, the defined simplified model starts to reduce oedema under the above setting parameters (the gray part in **Figure 3.11**). Additionally, it is found that the percentage of oedema reduction is proportional to the exerted constant pressure.

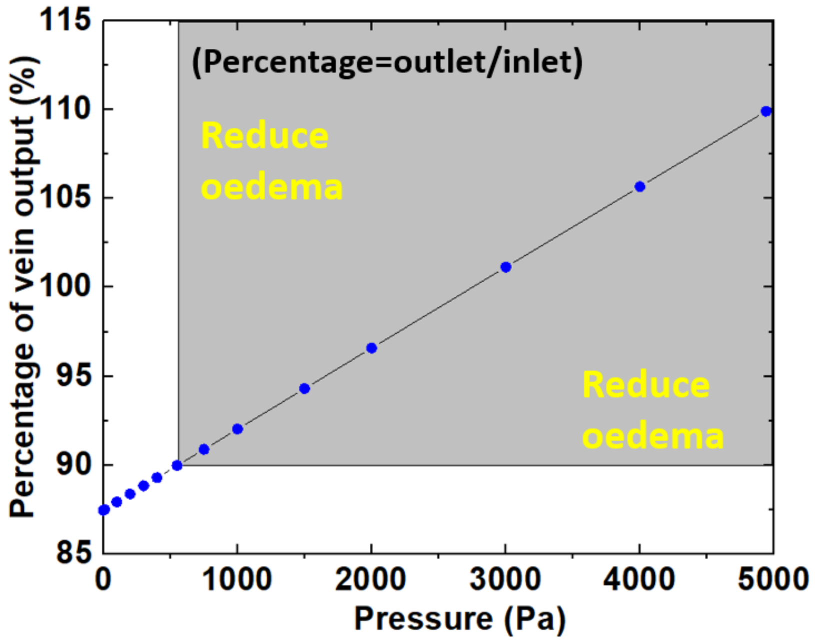

Figure 3. 11 The relationship between the percentage of vein output and constant pressure.

Then, **Figure 3.12** shows the mass rate of the inlet and outlet under the different constant pressures on the interstitial fluid. When the interstitial fluid is compressed by 4000 Pa, the percentage of outlet in the vein is achieved to 105.7%, as shown in **Figure 3.11.** According to the raising compression pressure, the interstitial fluid starts to enter the blood vessels, resulting to the percentage of outlet in the vein is more than 100%, as shown the pink line in **Figure 3.12(a)**. In this time, lymph flow performs inlet (mass rate >0, upper than purple dot line), referring to the yellow line in **Figure 3.12(b)**.

Increasing the constant pressure value on the interstitial fluid can contribute to oedema reduction under the fixed parameters. Therefore, high-level pressure compression stockings/devices can help effectively reduce oedema under the defined pressure range, however, further investigation is required to explore the potential issues that may arise from sustained increasing compression pressure.

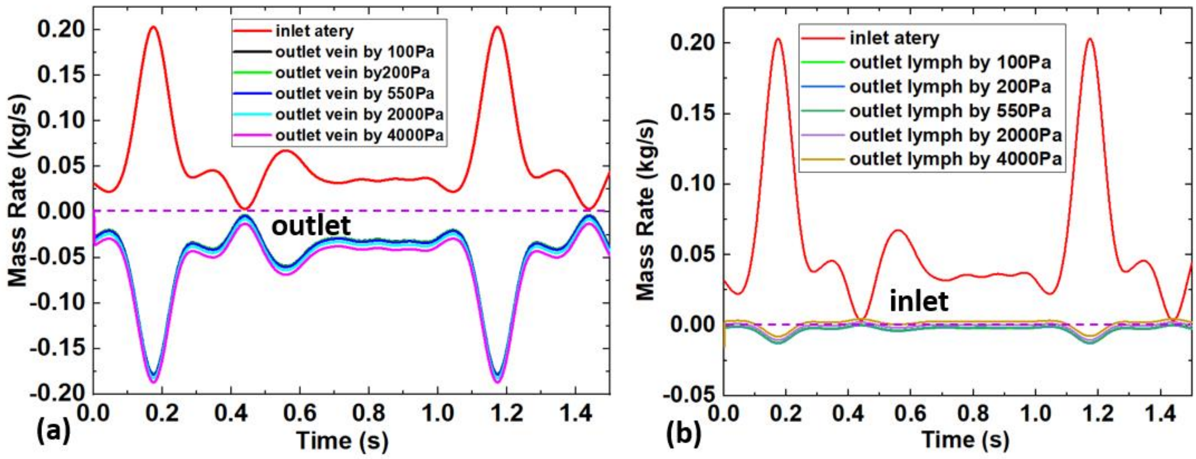

Figure 3. 12 Mass rate of the inlet and outlet under the different constant pressures, (a) shows mass rate of the inlet and outlet in the vein, and (b) shows mass rate of the inlet and outlet in the lymph.

3.3.3.4 Influence of blood viscosity μ

Fourthly, the influence of blood viscosity μ on the oedema reduction is studied. Blood viscosity is a critical physiological parameter of the human body because it can be changed with age or diseases. When the blood viscosity rises, the blood flow becomes slows, which causes blood vessel embolism or cardiovascular diseases. Besides, high value of the blood viscosity can damage and block capillaries, which also can cause oedema. Therefore, it is essential to study the influence of the blood viscosity.

According to the numerical simulation analysis, **Figure 3.13(a)** indicates the relationship between the percentage of vein output and blood viscosity under 750 Pa compression pressure with the fixed other parameters. It indicates that the increasing blood viscosity under the same pressure conditions can cause oedema because of the lower percentage of vein output with the increasing blood viscosity. Low blood viscosity can obtain the effect of the oedema reduction, as shown in the gray part in **Figure 3.13(a)**. This is consistent with the phenomenon that individuals with elevated blood viscosity are susceptible to developing oedema. Additionally, the percentage of outlet flow in the vein is nonlinear to the blood viscosity value. **Figure 3.13(b)** shows that a higher value of blood viscosity requires linearly increasing critical pressure of oedema reduction.

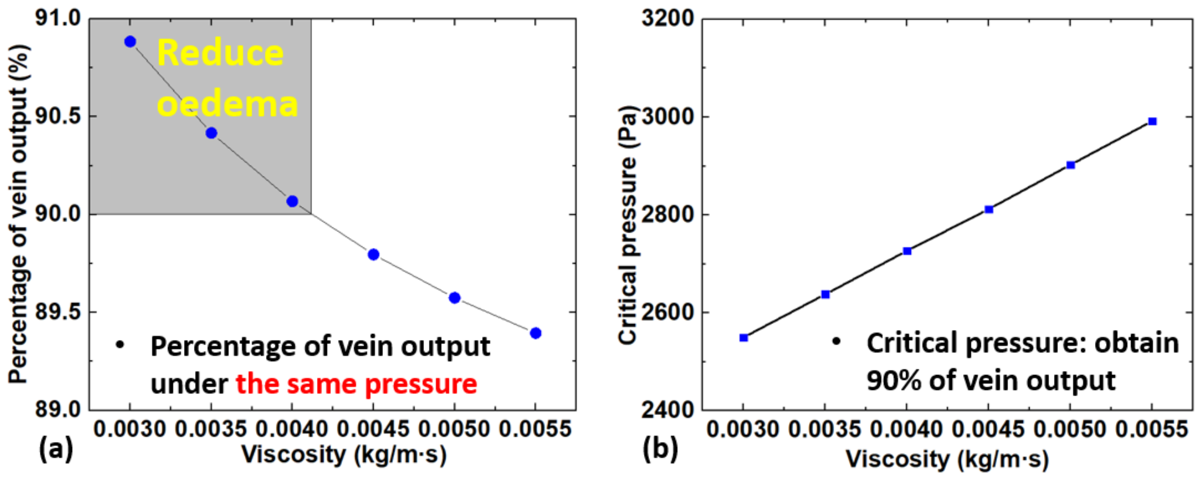

Figure 3. 13 (a) is the relationship between the percentage of vein output and different blood viscosities under 750 Pa compression pressure, (b) is the critical pressure values with the different blood viscosities.

Figure 3.14 and **Figure 3.15** perform the mass rate of the inlet and outlet with the different blood viscosities under the 750 Pa compression pressure. Due to the data lines being close together, **Figure 3.14** and **Figure 3.15** show the mass rate of the inlet and outlet in the vein and lymph, separately. Under the 750 Pa of compression pressure on the interstitial fluid, the increasing blood viscosity leads to decreasing outlet flow in the vein and increasing outlet flow in the lymph (see the enlarged view in **Figure 3.14(b)** and **Figure 3.15(b)**), which means increasing blood viscosity under the same compression pressure conditions can cause oedema. In addition, the blood viscosity change has a small influence on the outlet flow in the vein and lymph. Furthermore, the trend of mass rate change is conformed with physiology that increasing blood viscosity can induce to increase in resistance and decrease blood flow, because the blood viscosity is directly proportional to resistance and inversely proportional to flow [8].

However, elevated blood viscosity may contribute to the development of hyperlipidaemia. Therefore, when applying compression to reduce oedema, the influence of blood viscosity should be considered, even if it has a slight impact.

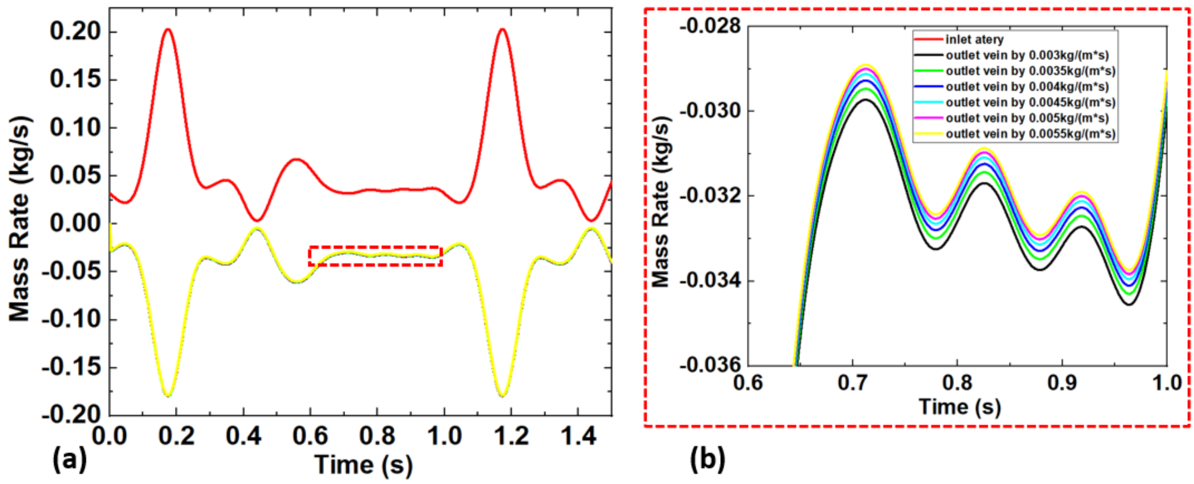

Figure 3. 14 (a) is the mass rate of the inlet and outlet in the vein under the different blood viscosities under 750 Pa compression pressure on the interstitial fluid, and (b) is the enlarged view of the red dashed box in (a).

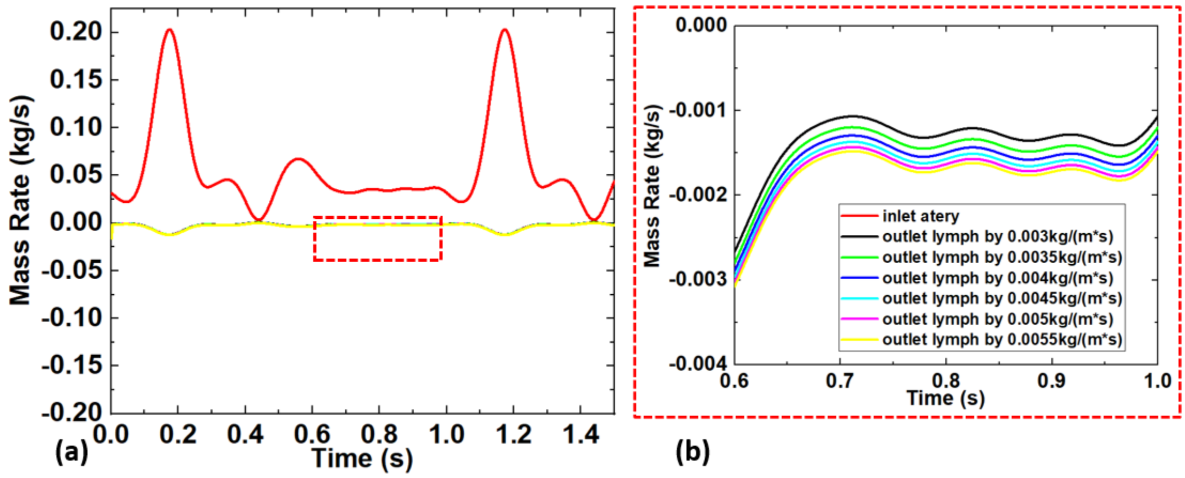

Figure 3. 15 (a) is the mass rate of the inlet and outlet in the lymph under the different blood viscosities under 750 Pa compression pressure on the interstitial fluid, and (b) is the enlarged view of the red dashed box in (a).

3.3.3.5 Influence of inlet blood velocity vi and heart rate fi

Fifthly, the influence of inlet blood velocity v_i and heart rate f_i on the oedema reduction are investigated. The inlet velocity has been introduced in section 3.3.2 and the inlet blood velocity is assumed as $v = \sin(2\pi f t) + At$, in which, f is the frequency (heart rate) and A is the amplitude of the blood velocity. Therefore, the flow in the one period beat can be written as equation (3-7):

$$Q_{\text{one period}} = \int_0^{1/f} [\sin(2\pi f t) + At]\, dt \quad (3\text{-}7)$$

Therefore,

$$Q_{\text{one period}} = A/f \quad (3\text{-}8)$$

For flow per second:

$$Q_{\text{one second}} = A \tag{3-9}$$

From the above deduced result, the mass rate is not influenced by the inlet velocity frequency. Therefore, the influence of the raising heart rate can be studied by increasing both inlet velocity and velocity frequency simultaneously.

Generally, the human heart rate is between 40 beats and 120 beats per minute, which is equivalent to 0.6 ~ 2 Hz [13]. And the blood velocity of between arterioles and artery is generally 7 cm/s ~ 21 cm/s [8], the distribution of the velocity of blood flow as shown in **Figure 3.16.**

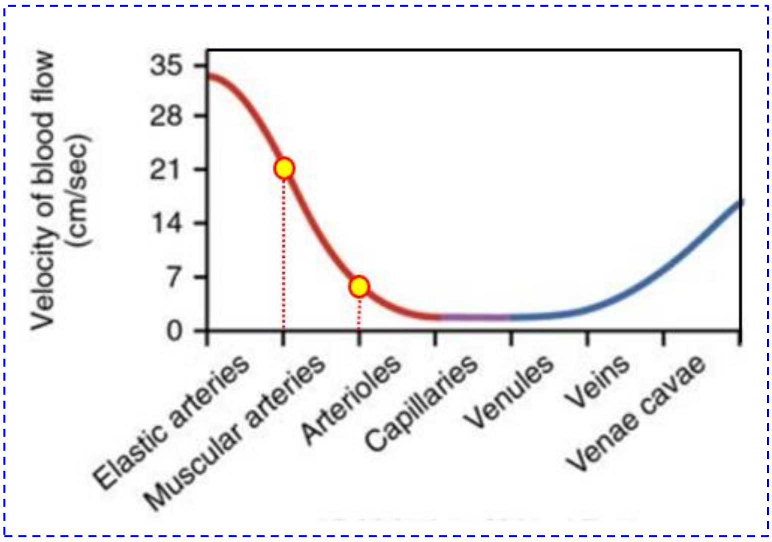

Figure 3. 16 The distribution of the velocity of blood flow [8].

Table 3.7 is the different inlet maximum velocities of blood and heart rates used in the numerical simulation. **Figure 3.17** expresses the relationship between the critical pressure with different inlet maximum velocities of blood and heart rates under the fixed other parameters. It shows that the critical pressure is proportionally increased with the raising inlet maximum velocity of blood and heart rate.

Table 3. 7 The data list of different inlet maximum velocities of blood and heart rates in the numerical simulation.

Inlet maximum velocity (cm/s)	Inlet frequency (beats/min)
6	40
9	60
12	80
15	100
18	120
22.5	150

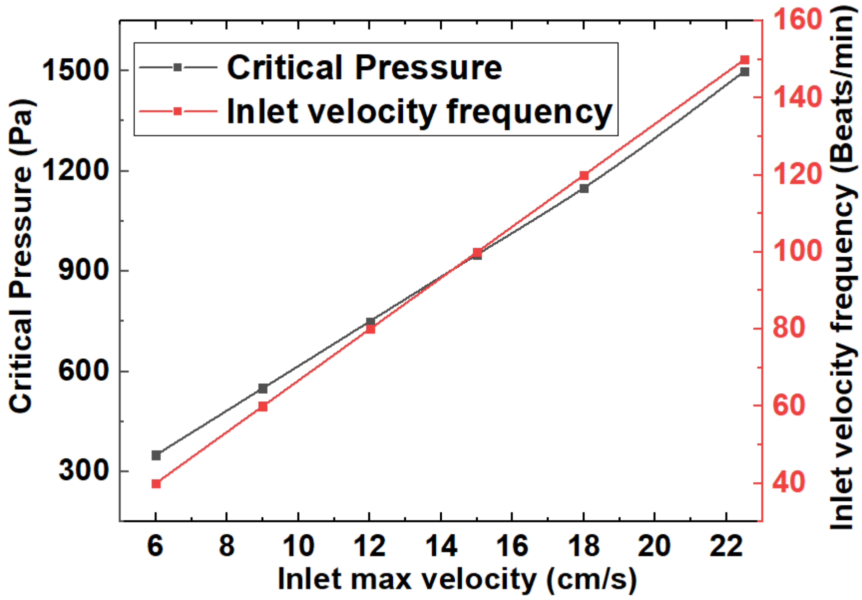

Figure 3. 17 The relationship between the critical pressure with different inlet maximum velocities of blood and heart rates.

Figure 3.18 expresses the mass rate of the inlet and outlet under the different inlet maximum velocities of blood and heart rates (40 ~ 150 beats/min) with the fixed other parameters. It shows that the inlet and outlet flow increase relatively by raising the two factors.

Heart rate can be influenced by age, diseases such as hypertension, physical activity, and so on. Therefore, it is important to consider varying age groups and specific medical histories when considering the application of compression therapy.

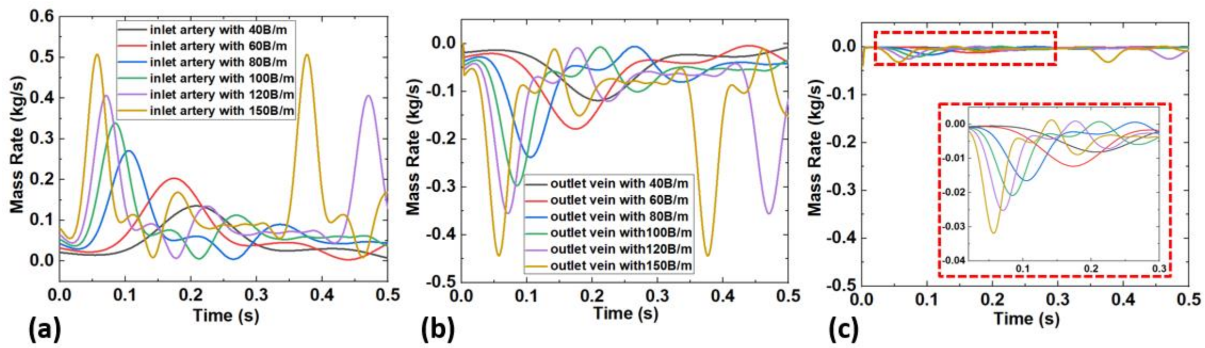

Figure 3. 18 The mass rate of the inlet and outlet under the different inlet maximum velocities of blood and heart rates. (a) is inlet mass rate, (b) is the mass rate of the vein outlet (c) is the mass rate of the lymph outlet, B/m: Beats/min.

3.3.3.6 Influence of different types of pressure

Sixthly, besides the constant pressure *Pc*, there are other types of pressure for compression treatment in oedema reduction, such as gradient or pulse pressure. In this section, the influence of harmonic compression pressure on the oedema reduction is researched. Regarding the harmonic pressure, the pressure amplitude and harmonic frequency as the main variables to analyse the effect on the oedema reduction. The harmonic compression pressure can be defined as the equation (3-10):

$$P(t) = A(1 - sin\frac{2\pi t}{T}) \quad (3\text{-}10)$$

Figure 3.19 is the relationship between the percentage of vein output and two types of pressure (constant, harmonic) under the same amplitude of pressure on the interstitial fluid with the fixed other parameters. Through comparing to the constant pressure *Pc* and harmonic compression pressure, **Figure 3.19** states that the harmonic pressure with the different amplitudes have the same results of different constant pressures on oedema reduction. It means that there is no obvious change between these two types of pressure.

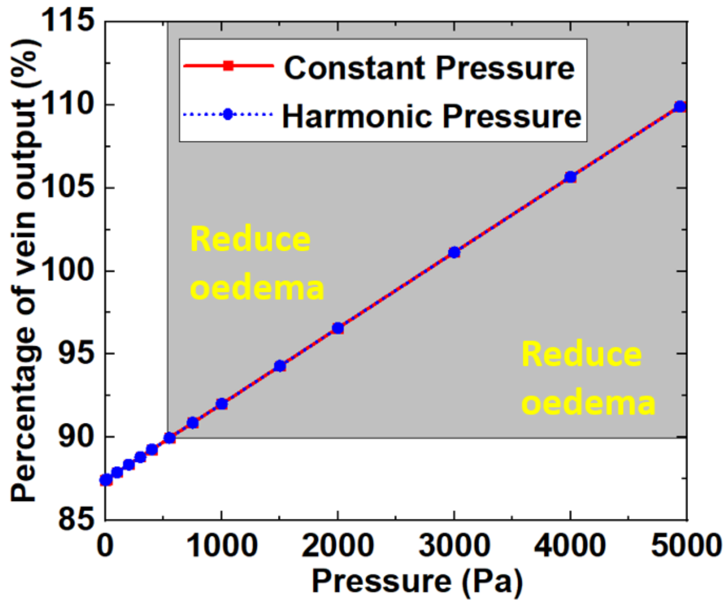

Figure 3. 19 The relationship between the percentage of vein output and two types of pressure with the same amplitude variation, the red line is the constant pressure, and the blue dot line is the harmonic pressure.

Besides, **Figure 3.20** shows the relationship between the percentage of vein output and different harmonic frequencies under 550 Pa pressure amplitude with the fixed other parameters. Considering the calculation time is transient, the range of the harmonic frequency is from 1 Hz to 100 Hz, listed in **Table 3.8**. According to the simulation results, the harmonic frequency has almost no effect on percentage of vein output under the same pressure amplitude.

Table 3. 8 The different harmonic frequencies.

Harmonic frequency (Hz)	Harmonic period Time (s)
1	1
2	0.5
5	0.2
10	0.1
20	0.05
100	0.01

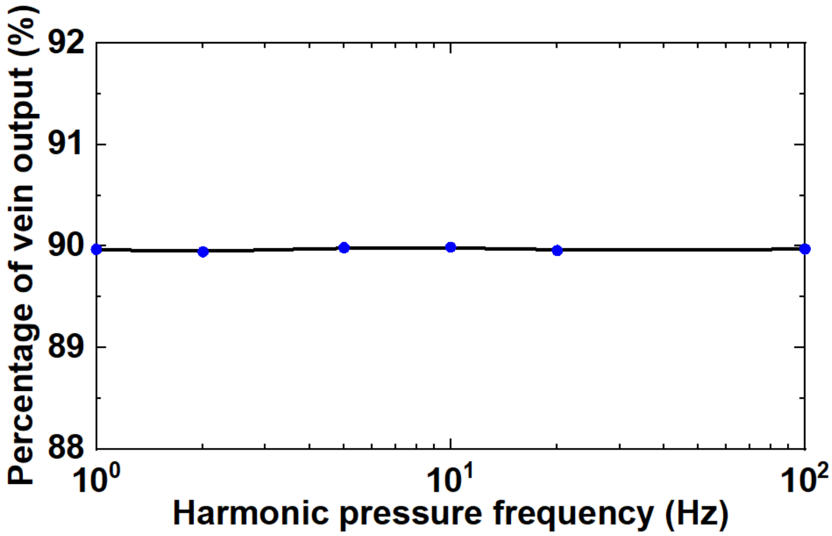

Figure 3. 20 The relationship between the percentage of vein output and different harmonic frequencies under 550 Pa pressure amplitude.

3.4 Physical experimental verification

3.4.1 Experimental setup

There are some assumptions of numerical modelling for convenient numerical calculations, they are listed in section 3.2.2. One of them is the movement across the capillary membrane follows the Starling Hypothesis. They are mainly induced by two components: one is porous nature of the capillary wall, the other one is pressure difference of capillary and interstitial fluid.

In which, the movement of the fluid exchange between blood and interstitial fluid across the capillary membrane follows the Starling Hypothesis. Therefore, the CFD method's effectiveness in simulating fluid flow behaviour in the porous media model should be verified using physical experiment.

In the physical experimental verification, the first step is to measure the pressure difference under different porosities of polyurethane filter which was porous media. The second step is to compare the pressure difference from numerical simulation and physical experimental results.

Figure 3.21 is the schematic diagram of the experimental setup. The fluid started to enter the soft tube from the water tank using pump. The soft tube (length: 19.50 cm, outer diameter:15.92 mm, thickness: 2 mm) was fixed in the fixed sink and enhanced with two fixed planes inside fixed sink. The fluid flowed back to the water tank finally. This was the closed circulation. Both the inlet and outlet sides of the soft tube had two fluid pressure sensors to measure the pressure of the inlet and outlet. In addition, one flow rate meter was fixed in the inlet side to control fluid flow for the same condition in each case. The data of both fluid pressure sensors and flow rate meter was collected by the data collector and obtained using MATLAB.

Figure 3.22 is the enlarged figure of the red dot box in **Figure 3.21,** it is the soft tube containing the porous media used in the physical experiment. The soft tube was elastic material, and the polyurethane filter was inserted inside tube. The polyurethane filter was utilized with two types, one PPI (pores per inch) was 15, the other PPI was 10. This porous media had different porosities and different volumes, as shown in **Table 3.9**.

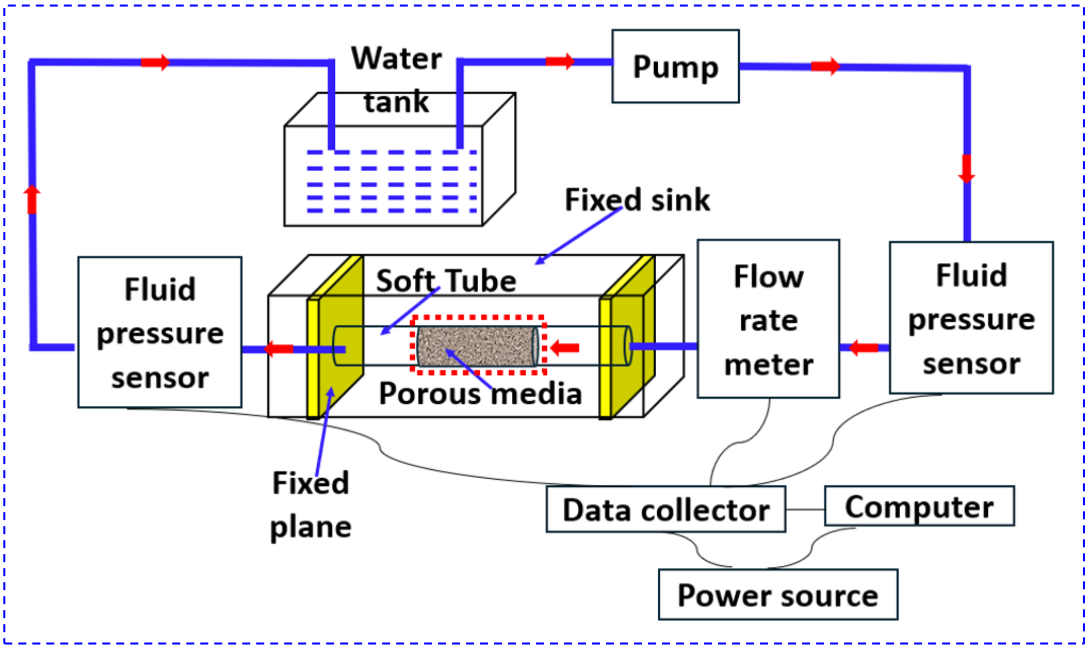

Figure 3. 21 The schematic diagram of the experimental setup.

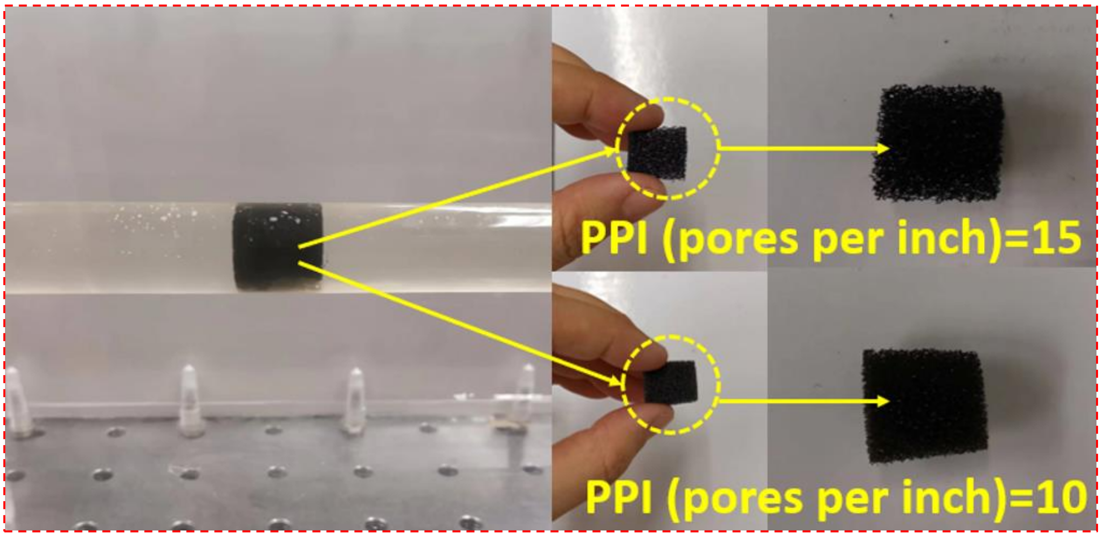

Figure 3. 22 The enlarged figure of the red dot box in the experimental setup is the soft tube containing the different porosities of porous media.

Table 3. 9 Different polyurethane filter parameters.

PPI (pores per inch)	10	15
Type1	Diameter: 13 mm, Length: 13 mm	

Type2	Diameter: 15 mm, Length: 13 mm

Using above experimental setup, the inlet flow and pressure difference between the inlet and outlet of soft tube were measured. The inlet flow was measured by the flow rate meter and its velocity demonstrated consistency under different pump revolutions within each case. Therefore, it can make sure the maintenance of consistent experimental conditions. The pressure difference was measured by the pressure sensors.

Figure 3.23(a) and **Figure 3.23(b)** are the relationship between pressure difference and number of revolutions under PPI with 10 and 15, respectively. As the number of revolutions increased, the flow rate concurrently increased, thereby inducing an elevation in the pressure difference of the tube. Comparing two different porosities of porous media revealed that the pressure difference of the soft tube was increased when the porosity was smaller. Additionally, a larger cross-sectional area (type 2) of porous media induced raising the pressure difference of the soft tube.

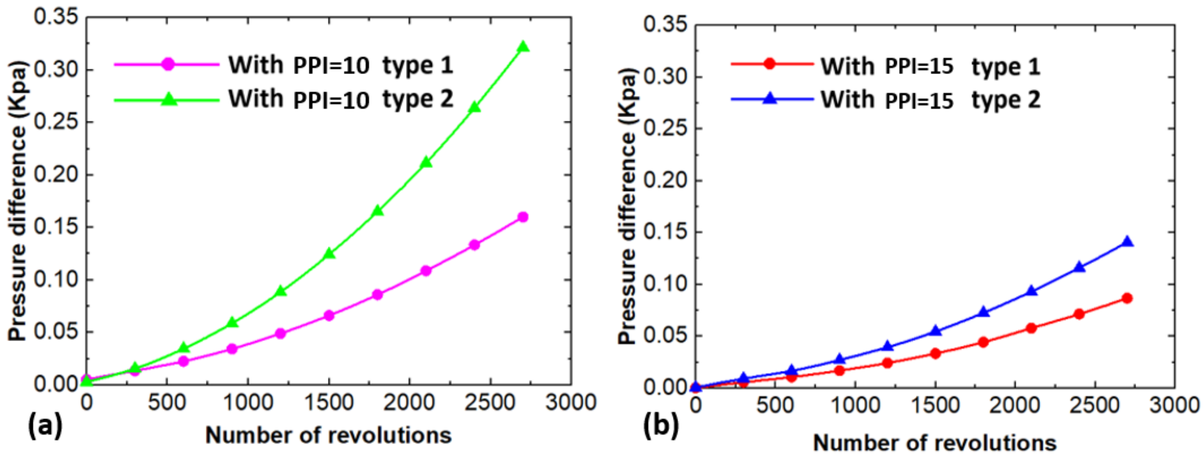

Figure 3. 23 The relationship between pressure difference and number of revolutions under different porosities, (a) is PPI=10 and (b) is PPI=15.

3.4.2 Comparation of numerical simulation and physical experiment results

The numerical simulation was carried out using the CFD method and compared to the physical experiment results to verify the CFD method's effectiveness in simulating fluid flow behaviour in the porous media model. In the numerical simulation, the numerical modelling of tube with 30 cm length was established, which was consistent with the distance between the two pressure sensors in the physical experiment setup. The diameter of the numerical modelling was 12 mm. The velocity was set the same as that of in the physical experiment in each boundary condition. The simplified model was meshed with 1037475 elements with Hexahedral mesh in the Ansys Fluent 16.0 software, as shown in **Figure 3.24(a)**. The pressure difference between input and output was calculated showing the static pressure distribution result in the numerical simulation, as shown in **Figure 3.24(b)** for one simulation case.

Compared with the results of numerical simulation and physical experiment, the pressure difference of porous media increases with the increase of inlet velocity (number of revolutions) and with decreased porosity of porous media in both results, as shown in **Figure 3.25**. It presents that the physical experiment and simulation results are basically consistent under the same model and parameters. Therefore, the CFD method effectively simulates fluid flow behaviour in the porous media model.

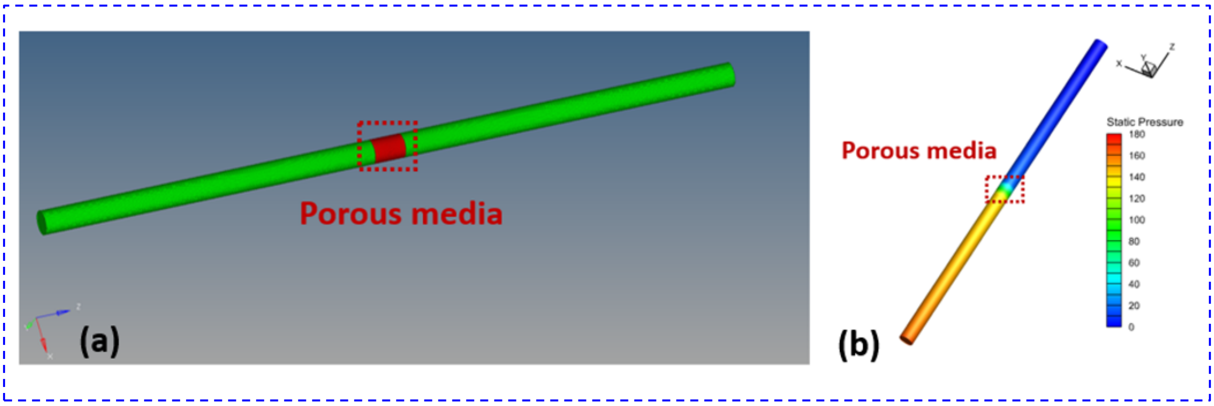

Figure 3. 24 (a) is the numerical model with mesh and (b) is the static pressure distribution in one simulation case.

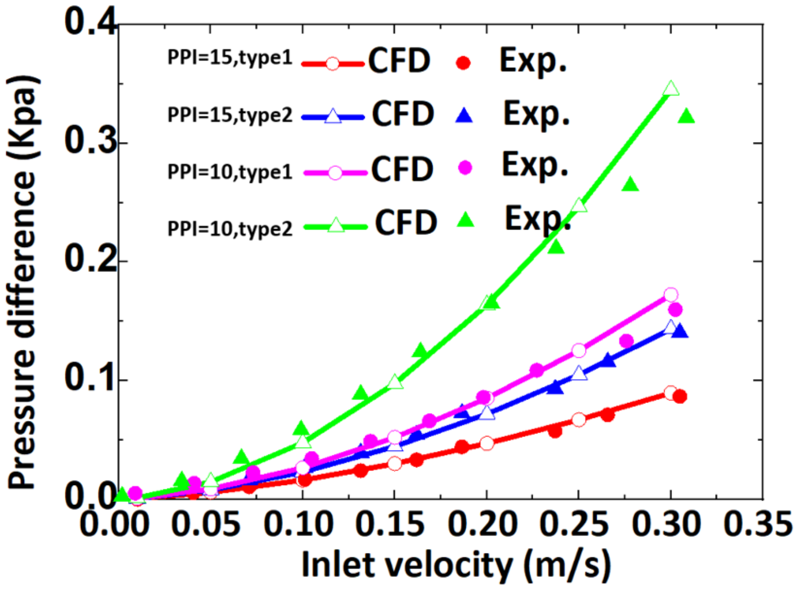

Figure 3. 25 Comparison of the results between numerical simulation using the CFD method and physical experiment. CFD is the numerical simulation, Exp.is the physical experiment.

3.5 Summary

In this chapter, the numerical 2D simplified capillary-blood-tissue model is developed to achieve fluid exchange between blood and interstitial fluid within porous media model. The simplified model comprises fluid and structural components, with the structural part encompassing the artery, vein, capillary bed, and tissue, and the fluid part encompassing blood and interstitial fluid. The mechanism of oedema reduction under compression pressure can be explained clearly using proposed 2D simplified numerical model.

Furthermore, the numerical simulation is carried on based on the control equations and assumptions. Through the computational fluid dynamics (CFD) method, the critical pressures on oedema reduction are calculated under the different physiological parameters, and the effects of these parameters on oedema reduction are investigated. The physiological parameters considered include porosity ε, blood viscosity μ, inlet velocity v_i and heart rate f_i, as well as constant pressure P_c and harmonic pressure. The results indicate that capillary and tissue porosity and inlet velocity significantly impact oedema reduction under constant compression pressure, while blood viscosity has a minor effect. Constant and harmonic pressures have similar effects on the percentage of vein output under the same compression pressure amplitude, and harmonic frequency has no sensitivity to the percentage of vein output. These physiological parameters can be influenced by age, disease, and exercise status.

Finally, the physical experiment is conducted to verify the CFD method's effectiveness in simulating fluid flow behaviour in porous media model.

The main contributions of this chapter are the development of the numerical model for capillary-blood-tissue, which can reflect the fluid exchange between the blood and interstitial fluid using the porous media model; clear elucidation for the mechanism of oedema reduction through numerical simulations; and the investigation of the critical pressures under various physiological parameters and effects of those parameters on oedema reduction using the proposed 2D simplified numerical model.

Reference

[1] M. Schünke, E. Schulte, and U. Schumacher, *Thieme atlas of anatomy: general anatomy and musculoskeletal system* (Atlas of anatomy: general anatomy and musculoskeletal system.). Stuttgart: Thieme, 2006.

[2] H. A. Baieth, "Physical parameters of blood as a non-Newtonian fluid," *International journal of biomedical science: IJBS,* vol. 4, no. 4, p. 323, 2008.

[3] D. Sankar and K. Hemalatha, "A non-Newtonian fluid flow model for blood flow through a catheterized artery—steady flow," *Applied mathematical modelling,* vol. 31, no. 9, pp. 1847-1864, 2007, doi: https://doi.org/10.1016/j.apm.2006.06.009.

[4] S. Ergun, "Fluid flow through packed columns," *Chemical Engineering Progress*, 48, 89-94, 1952.

[5] H. G. Bai, K. Naidu, and G. V. Kumar, "CFD analysis of aortic aneurysms on the basis of mathematical simulation," *Indian Journal of Science and Technology,* vol. 7, no. 12, p. 2020, 2014, doi: 10.17485/ijst/2014/v7i12/51676.

[6] W. Yao, Y. Li, and G. Ding, "Interstitial fluid flow: the mechanical environment of cells and foundation of meridians," *Evidence-Based Complementary and Alternative Medicine,* vol. 2012, no. 1, p. 853516, 2012, doi: 10.1155/2012/853516.

[7] C.-T. Chen, D. S. Malkus, and R. Vanderby Jr, "A fiber matrix model for interstitial fluid flow and permeability in ligaments and tendons," *Biorheology,* vol. 35, no. 2, pp. 103-118, 1998, doi: 10.1016/s0006-355x(99)80001-8.

[8] E. Johnson, J. G. Betts, and P. DeSaix, *Anatomy and Physiology*. Open Textbook Library, 2013.

[9] M. Zedelmair and A. Mukherjee, "Numerical Simulation of Insulin Depot Formation in Subcutaneous Tissue Modeled as a Homogeneous Anisotropic Porous Media," *Journal of Biomechanical Engineering*, vol. 143, no. 5, p. 051002, 2021, doi: 10.1115/1.4049811.

[10] A. Przysinda, W. Feng, and G. Li, "Diversity of Organism-Wide and Organ-Specific Endothelial Cells," *Current cardiology reports*, vol. 22, no. 4, pp. 19-19, 2020, doi: 10.1007/s11886-020-1275-9.

[11] S. D. Peterson and M. W. Plesniak, "The influence of inlet velocity profile and secondary flow on pulsatile flow in a model artery with stenosis," *Journal of fluid mechanics*, vol. 616, pp. 263-301, 2008, doi: 10.1017/S0022112008003625.

[12] M. Thiriet, "Venous Flow," in *PanVascular Medicine*, P. Lanzer Ed. Berlin, Heidelberg: Springer Berlin Heidelberg, pp. 1-25, 2013, doi: 10.1007/978-3-642-37393-0_27-1.

[13] H. Chang, J. Chen, and Y. Liu, "Micro-piezoelectric pulse diagnoser and frequency domain analysis of human pulse signals," *Journal of Traditional Chinese Medical Sciences*, vol. 5, no. 1, pp. 35-42, 2018, doi: 10.1016/j.jtcms.2018.02.002.

CHAPTER 4

EFFICACY EVALUATION OF LOWER LIMB OEDEMA REDUCTION

4.1 Introduction

This chapter is the practical experiment part for validating the numerical simulation results in Chapter 3. The trial test is conducted to determine whether applying compression and lower limb skeletal muscle movement can effectively reduce lower limb oedema.

In Chapter 4, there are two trial tests, the first trial is for young subjects and the second trial is for elderly subjects. The 1st trial test is the exploring phase for the efficacy of integrating three different compression methods with/without LLMs. The 2nd trial test is conducted according to the 1st trial test's most effective two integration methods.

Therefore, the lower limb movements (LLMs) are designed firstly. Then, every trial test design is introduced, encompassing participant selection, procedure, measurement methodologies, calibrations, and robustness analysis. Subsequently, the trial tests are conducted, and data analysis is executed using the paired sample t-test, one-way analysis of variance, and the independent t-test for analysing the significance of efficacy in volume change (VC) or circumference change (CC) under different wearing conditions, left or right legs and different gender with/without LLMs. Finally, the results and discussion are presented. In addition, the dynamic compression pressures during LLMs are measured to investigate the relationship between compression pressure change and the oedema reduction rate (volume/circumference reduction) at point C.

4.2 Method

4.2.1 Introduction of method

4.2.1.1 Patient consent

The study protocol was approved by PolyU and Helping Hand-Po Lam Jockey Club Housing for the Elderly in Hong Kong and conducted following the ethical principles for non-clinic research. Before the trial tests, consents were obtained from all the subjects.

4.2.1.2 Trial procedure

The 1st trial test was for young healthy subjects, the main purpose was to examine and explore the better suitable trial scheme for the 2nd trial test. The 2nd trial test was for elderly subjects suffering from mild lower limb oedema or who were prone to oedema through the selected combination approach from the former test. Ultimately, the optimal approach for reducing lower limb oedema was chosen to facilitate substantial practical trial, as the 3rd trial test outlined in Chapter 5. Detailed procedures of 1st and 2nd trial tests will be introduced in every trial test design section of the test.

4.2.2 Designed lower limb movements (LLMs)

Literature [1] illustrates the distribution of skeletal muscles in the calf, its cross-section, anterior and posterior view of the calf. The lower limb movements directly activate related calf muscles. From anterior to the lateral, posterior, and deep muscles, the relationship between lower limb movements and corresponding calf muscles are summarised in **Table 2.4** in the Chapter 2. The calf muscles are associated with specific movements, primarily including knee flexion, toe flexion or extension, foot plantarflexion or dorsiflexion, and foot eversion or inversion [2].

The contractions of skeletal muscles result in the compression of muscle tissues, application of pressure on the venous system, and facilitation of lymphatic flow. This contributes to a decrease in filtration pressure and prohibits oedema generation [3-5]. From the effect degree of skeletal muscles movements on reducing lower limb oedema [6-11], it can be revealed that gastrocnemius plays a greater role in reducing lower limb oedema according to effective skeletal muscles movements. Based on the above works of literature and skeletal muscles' corresponding movement analysis, a set of lower limb movements (LLMs) programme was designed, as shown in the **Figure 4.1.**

Specifically, step 1) Begin the warming-up process by kicking each lower limb 5 times and moving each ankle 5 times while seated. Step 2) Perform knee extension (stimulate gastrocnemius), let the ankle keep a right angle and straighten the leg out in front, then bend the knee to return to the floor, repeat 10 times for each lower limb, as shown in **Figure 4.1(a).** Step 3) Stand up and perform knee flexion upward (stimulate gastrocnemius), holding the chair if needed, repeat 30 times for each lower limb, as shown in **Figure 4.1(b).** Step 4) Take a rest for 1 min. Step 5) Stand up again and perform knee flexion backward (stimulate gastrocnemius), holding the chair if needed, repeat 30 times for each lower limb, as shown in **Figure 4.1(c)**. Step 6) Take a rest for 1 min. Step 7) Sit down and perform the ankle movements (stimulate gastrocnemius, soleus, tibialis posterior, tibialis anterior, flexor digitorum longus, flexor hallucis longus, extensor hallucis longus, extensor digitorum longus), do plantarflexion and dorsiflexion 10 times for each foot, and do eversion or inversion 10 times for each foot, as shown in **Figure 4.1(d).** Step 8) Stand up and perform ankle raises by making double heels rise while keeping toes on the floor, repeat 20 times, as shown in **Figure 4.1(e).** Step 9) Walking by swinging the calf backward and putting the foot lightly and slowly from the toe (stimulate gastrocnemius) for 2 mins, as shown in **Figure 4.1(f).** Step 10) Take a rest for 1 min.

During these LLMs, it is noticed that the number of every movement must be ensured and that every movement is completed as accurately as possible.

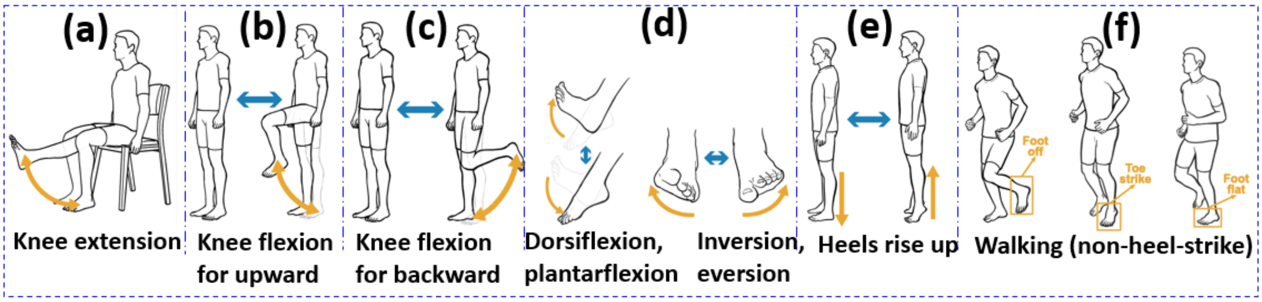

Figure 4. 1 Designed lower limb movements (LLMs),(Sketched by Manyui LEUNG in SFT, PolyU)

4.3 First trial test (young healthy subjects)

4.3.1 Participants

8 young healthy subjects were enrolled in the 1st trial test including 4 males and 4 females. The age range of the subjects was 24 to 33 years old, and the information on them is listed in **Table 4.1**. They did not have any diseases and had not undergone any surgery. We had 16 lower limbs in the 1st trial test.

Table 4. 1 Information of subjects.

Trial test	**The 1st trial test for young healthy subjects**		**The 2nd trial test for elderly subjects with mild oedema**	
No. of subjects	8		12	
Gender	Male	Female	Male	Female

No. of gender	4	4	6	6
Percentage of gender	50%	50%	50%	50%
Average age (years)	29.00 (27.00, 33.00)	27.75 (24.00, 33.00)	78.67 (69.00, 93.00)	85.33 (77.00,91.00)
Average BMI (kg/m^2)	21.80 (20.10, 24.20)	20.6 4 (18.70, 22.30)	29.10 (21.09, 35.43)	27.37 (25.30, 29.56)

4.3.2 The first trial test design

Firstly, it was conducted to complete consent, recording subjects' information such as height, weight, BMI, measuring the original volume and circumference of every lower limb. They were required to wear comfortable pants, and shoes that were easy to slip on and off. Secondly, subjects were asked to sit quietly on the high-chair with sit-stand position for 40 minutes for generating the lower limb oedema, with their feet completely touching the floor, as shown in **Figure 4.2(a).** This sitting position can compress the veins in thigh and hip areas, leading to poor circulation in lower limbs [12]. This generating oedema process was only carried out in the 1st trial test, for the elderly subjects was not applicable. After 40 minutes, average of increase change in volume is 54 cm^3 and average of increase change in circumference was 2% (at point C of the lower limb) in this proposed trial test, and those were 61cm^3 and 1.8%, respectively in literature [12]. In which, point B is the ankle region, the smallest circumference in the calf, and point C is the largest circumference in the calf. Thirdly, the volume and circumference of every lower limb were measured after oedema generation. Every measurement method is described in measurements section 4.3.3. Fourthly, subject started to reduce oedema with or without the application of non-stretchable WRAP and medical compression stocking (MCS) combined with or without lower limb movements (LLMs). Two sizes of MCS were available for subjects based on their lower limb measurements: size M (medium) corresponded to the circumference of 21~23 cm at point B and 34~40 cm at point C, while size L (large) corresponded to the circumference of 23~25 cm at point B and 36~42 cm at point C. They wore the WRAP/MCS/No-wearing for every lower limb for individual test. This means that each subject required 3 separate days to test different WRAP/MCS/No-wearing test conditions. Fifthly, the interface pressure of points B and C was measured after wearing the WRAP or MCS to ensure that they were at Class I level (18~21 mmHg at point B). Sixthly, the subjects were divided into experimental (4 subjects) and control group (4 subjects). In the experimental group, each subject completed the one set of designed LLMs with wearing gradient MCS **(Figure 4.2(b)) /** gradient WRAP **(Figure 4.2(c)) /** No-wearing conditions. During designed LLMs, the compression pressure change at point C was recorded. The point C is located gastrocnemius position, where the most obvious skeletal muscles changes occur when the muscle contractions and lengthens. However, in the control group, each subject maintained sitting position during the same time nearly 15 minutes without LLMs, but they also wore WRAP/MCS/No-wearing conditions. Seventhly, the interface pressure of points B and C was measured again to observe whether the interface pressure changed after LLMs/sitting. Finally, subject wore off WRAP or MCS and the volume and circumference of every lower limb were measured. The flow chart of the 1st trial test is shown in **Figure 4.3.**

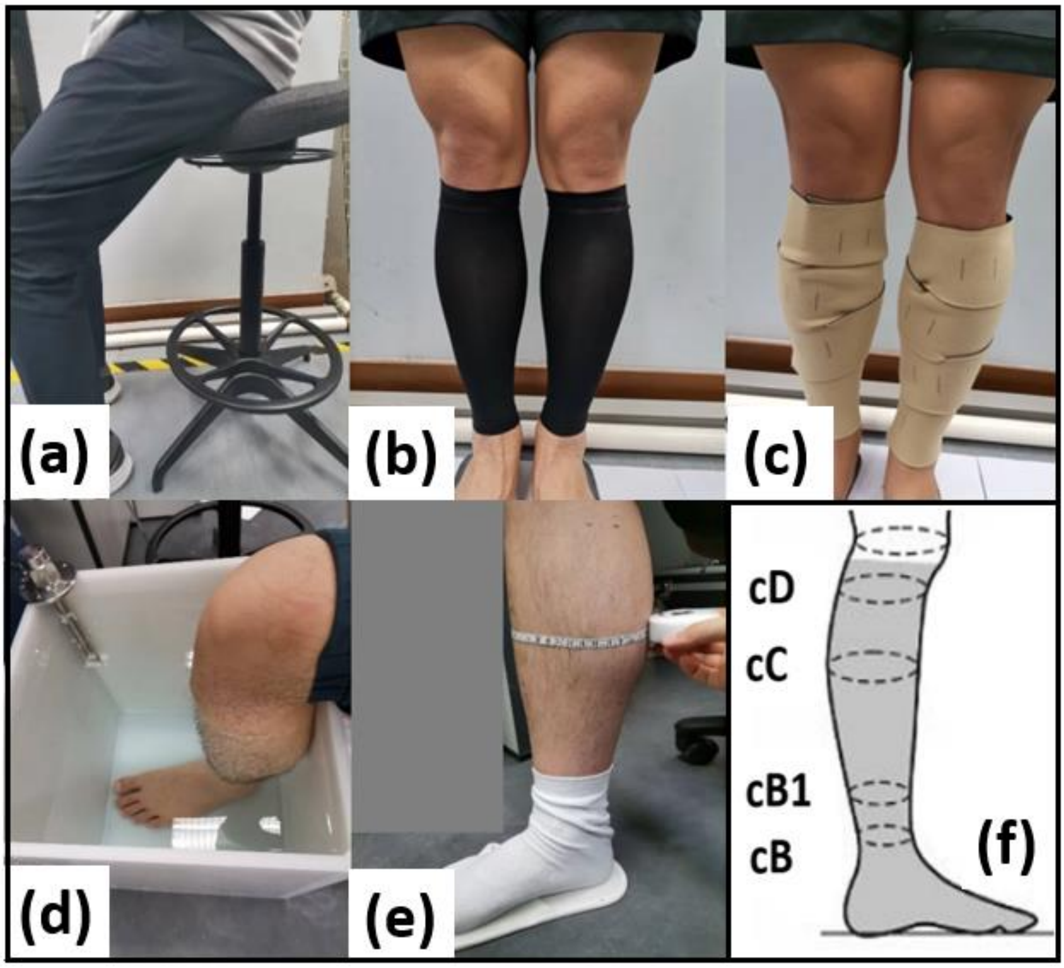

Figure 4. 2 (a) Sit on the high-chair with sit-stand position. (b) Wearing gradient medical compression stocking (MCS) condition. (c) Non-stretchable gradient WRAP condition. (d) Measurement of lower limb volume using water displacement volumetry. (e) Measurement of lower limb circumference using soft tape measure. (f) Every point position of the lower limb in standard RAL- GZ 387/1 [13].

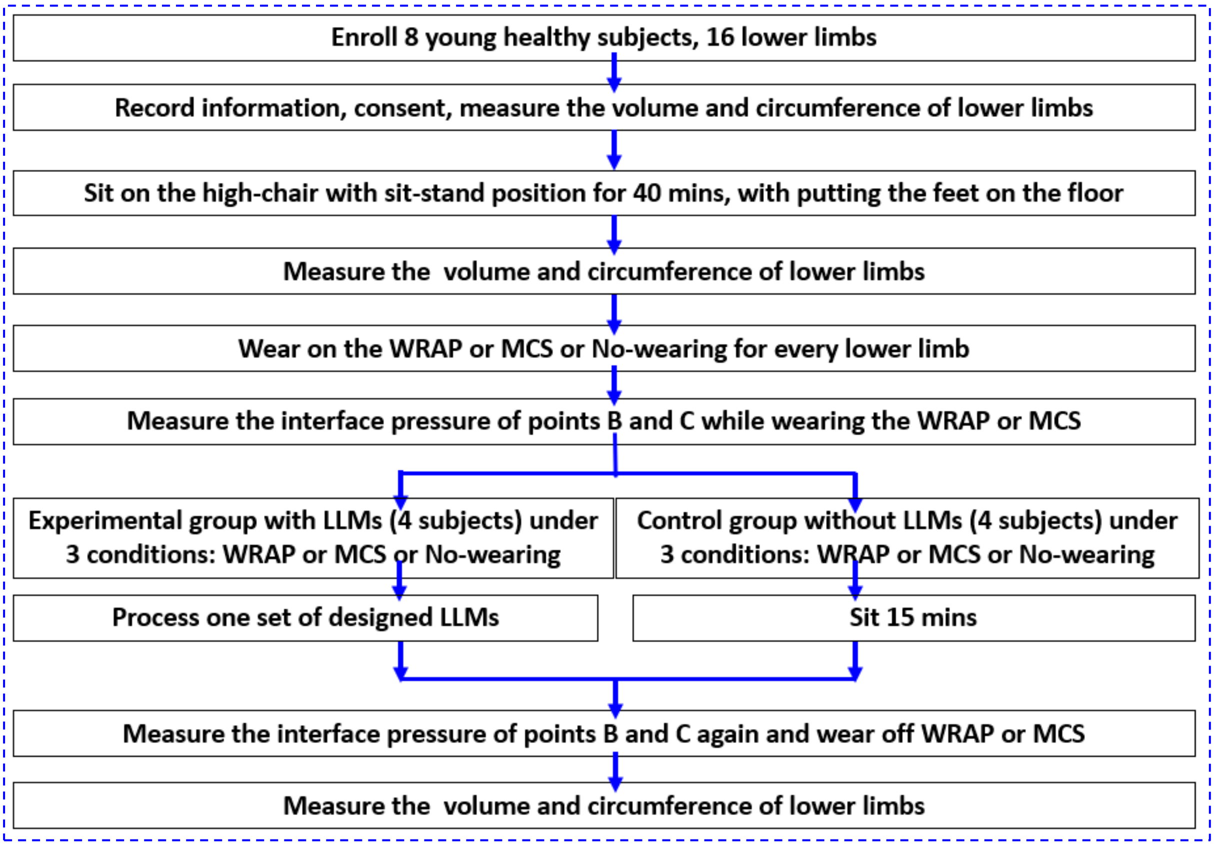

Figure 4. 3 The flow chart of the 1st trial test.

4.3.3 Measurement

The lower limb (calf) volume and circumference were measured 3 times for each condition test, original, after 40 minutes of sitting and after wearing WRAP/MCS/No-wearing, respectively. And each measurement was repeated three times. 1) The lower limb volume was measured using water displacement volumetry method, as shown in **Figure 4.2(d).** 2) The lower limb circumference was measured using soft tape measure, as shown in **Figure 4.2(e).** The lower limb circumferences were measured at points B, B1, C, and D in standard RAL- GZ 387/1, see in **Figure 4.2(f)**. To ensure accuracy when measuring the circumference, three points were selected at equal intervals around the circumference of the circle on the same plane.

4.3.4 Calibration and volume and circumference robustness analysis

To ensure measurement repeatability, the volume and circumference robustness were analysed. Firstly, the level gauge was used to measure the lower limb volume. The minimum measurement unit of level gauge was 0.1mm. According to the calibration with ruler (minimum measurement unit was 1mm), the error of height change was 3.1%, therefore, level gauge was available.

Secondly, to guarantee the repeatability of the volume measurement, 3 volunteers were tested continually on their left and right lower limb volume using water displacement volumetry, the water temperature was nearly normal body temperature. They repeated 10 times. From the **Figure 4.4(a),** it showed that volume measurement had good repeatability. **Figure 4.4(b)** was the mean volume and standard deviation of 3 volunteers' left and right lower limbs, showing good robustness. The detailed recording data are shown in **Table 4.2**.

Thirdly, to guarantee the repeatability of the circumference measurement, 4 volunteers were tested continually for 3 days on their one lower limb circumference using soft tape. They repeated 10 times per day. **Figure 4.4(c)** showed that circumference measurement had good repeatability for 3 days and had good robustness, the mean circumference and standard deviation of 4 volunteers were in **Figure 4.4(d)**, and the detailed data are shown in **Table 4.3**.

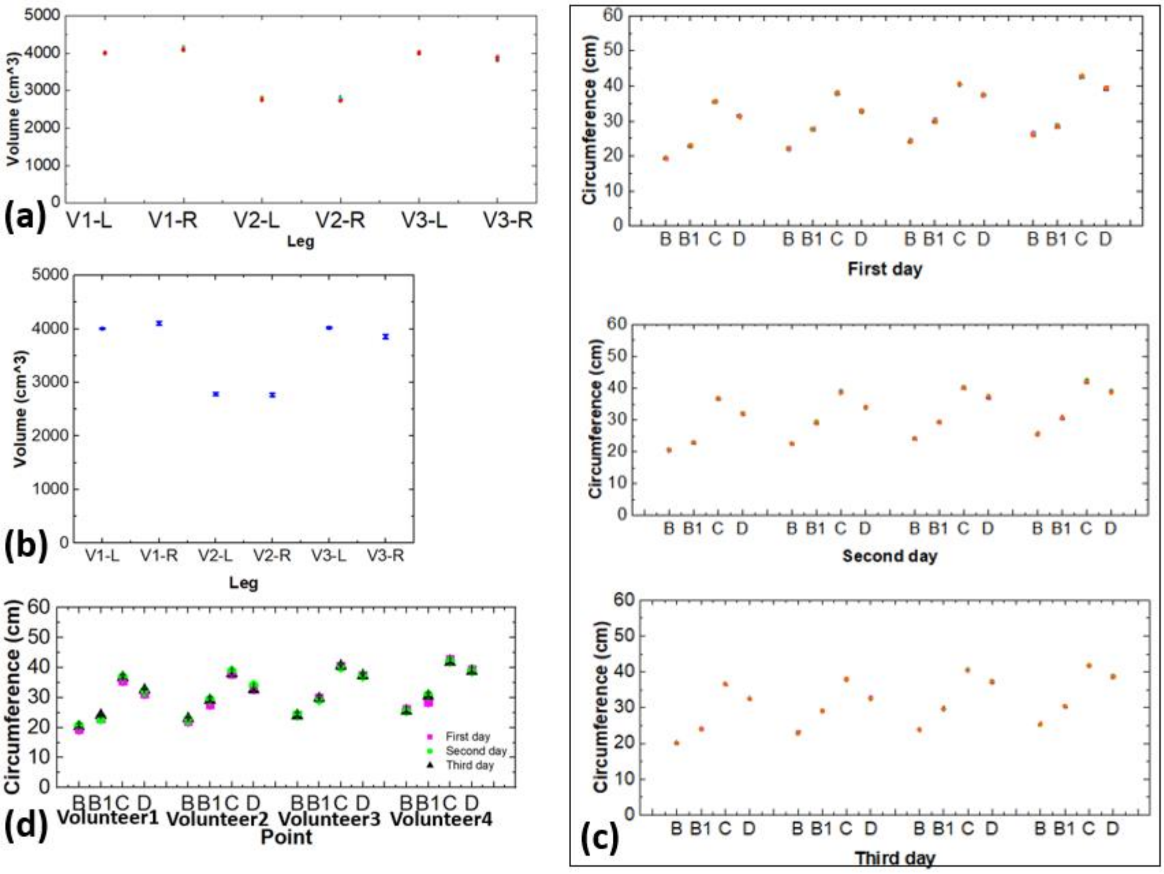

Figure 4. 4 Volume robustness analysis: (a)10 times repeat measurement of 3 volunteers' left and right lower limbs, (b) mean volume and standard deviation of 3 volunteers' left and right lower limbs, V: volunteer, L: left, R: right. Circumference robustness analysis: (c)10 times repeat measurement of 4 volunteers' lower limbs continuing 3 days (points B, B1, C, and D), (d) mean circumference and standard deviation of 4 volunteers' lower limbs continuing 3 days (points B, B1, C, and D).

Table 4. 2 The data of mean volume and standard deviation of volume measurement.

	Volunteer 1		Volunteer 2		Volunteer 3	
Lower limb	Left	Right	Left	Right	Left	Right
Volume (Unit: cm^3)	4002.9±13.3	4106.4±36.0	2783.1±28.0	2765.7±30.0	4021.1±13.5	3858.5±39.6

Table 4. 3 The data of mean circumference and standard deviation circumference measurement.

	Volunteer 1			Volunteer 2			Volunteer 3			Volunteer 4		
Measurement Point (Unit: cm)	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
B	19.3 ±0.1	20.6 ±0.0	20.2 ±0.1	22.0 ±0.1	22.5 ±0.1	23.0 ±0.2	24.2 ±0.1	24.2 ±0.1	23.9 ±0.1	26.1 ±0.2	25.6 ±0.2	25.4 ±0.1
B1	22.9 ±0.1	22.9 ±0.0	24.1 ±0.1	27.7 ±0.1	29.2 ±0.2	29.1 ±0.1	29.9 ±0.2	29.4 ±0.1	29.7 ±0.1	28.4 ±0.1	30.8 ±0.1	30.4 ±0.1
C	35.5 ±0.2	36.8 ±0.1	36.6 ±0.1	37.9 ±0.1	38.7 ±0.1	38.0 ±0.1	40.5 ±0.1	40.1 ±0.1	40.5 ±0.1	42.7 ±0.1	42.2 ±0.2	41.8 ±0.1
D	31.3 ±0.1	32.0 ±0.1	32.5 ±0.1	32.8 ±0.1	34.0 ±0.1	32.7 ±0.1	37.4 ±0.1	37.2 ±0.2	37.3 ±0.2	39.3 ±0.2	39.0 ±0.2	38.7 ±0.1

4.3.5 Interface pressure (IP)

Before and after trial tests, the interface pressure (IP) of points B and C was measured by the airbag sensor to ensure that the initial compression pressures of the WRAP or MCS were in the Class I level and investigate IP change while using WRAP or MCS. Comparing IP change at points B and C between experimental and control groups, it showed that IP of MCS with LLMs was more stable, see in **Figure 4.5(c)**. There was no obvious change in IP values between the experimental and control groups in **Figure 4.5**. The average and standard deviation of IP at points B and C before and after LLMs/sitting is shown in **Table 4.4.**

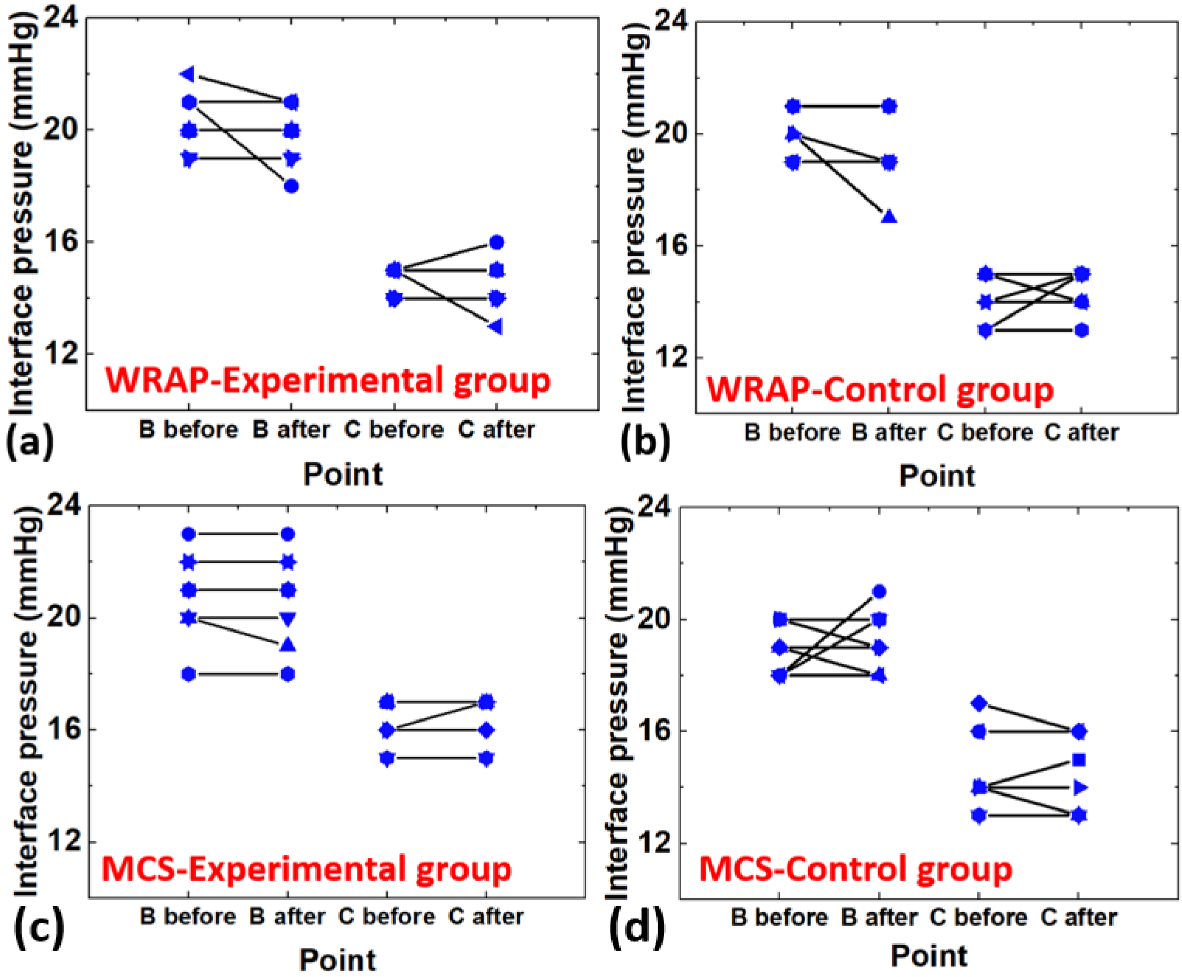

Figure 4. 5 The interface pressure (IP) change of WRAP/ MCS before and after LLMs/sitting at points B and C. (a) is WRAP in experimental (b) is WRAP in control, (c) is MCS in experimental, and (d) is MCS in control groups.

Table 4. 4 The average and standard deviation of IP at points B and C before and after LLMs/sitting when wearing WRAP/MCS.

Unit: mmHg		WRAP-experimental	WRAP - control	MCS-experimental	MCS-control
Point B	Before LLMs/sitting	20±1	20±1	21±1	19±1
	After LLMs/sitting	20±1	19±1	21±2	19±1

Point C	Before LLMs/sitting	15±0	14±1	16±1	15±1
	After LLMs/sitting	15±1	14±1	16±1	15±1

4.4 The first trial test analysis (young healthy subjects)

4.4.1Volume change (VC) of lower limb

Statistical significance analysis was performed using IBM SPSS Statistics. T-test was analysed and p-value <0.001 was considered extremely significant (***), 0.001< p-value <0.01 was considered very significant (**), 0.01< p-value <0.05 was significant (*), and p-value >0.05 was not significant (ns).

Before each section data analysis, data selection was conducted that singular values were deleted within the measurement error range and deleted absolute changes greater than 5%. Every condition had 24 samples (n=24) in the experimental group and 24 samples (n=24) in the control group, too. They were consistent with normal distribution.

This analysis hypothesized a significant difference in lower limb volume before and after wearing WRAP/MCS/No-wearing conditions in the experimental and control groups.

Firstly, in the experimental group, VC before and after LLMs under WRAP/MCS/No-wearing conditions were analysed using the paired sample t-test. According to Figure **4.6,** the paired sample t-test revealed the extremely significant difference all in VC before and after LLMs under WRAP/MCS/No-wearing conditions (p <0.001). With the same method, VC after sitting 15 minutes under WRAP/MCS/No-wearing conditions in control group were also shown extremely significant difference (p <0.001), see in **Figure 4.7.** Both experimental and control groups had extremely significant changes, but the mean reduction value with LLMs in the experimental group was greater than control group. The calf volume data results including baseline, after applying a combination of the compression and LLMs, and after only applying compression under different wearing conditions are listed in **Table 4.5**.

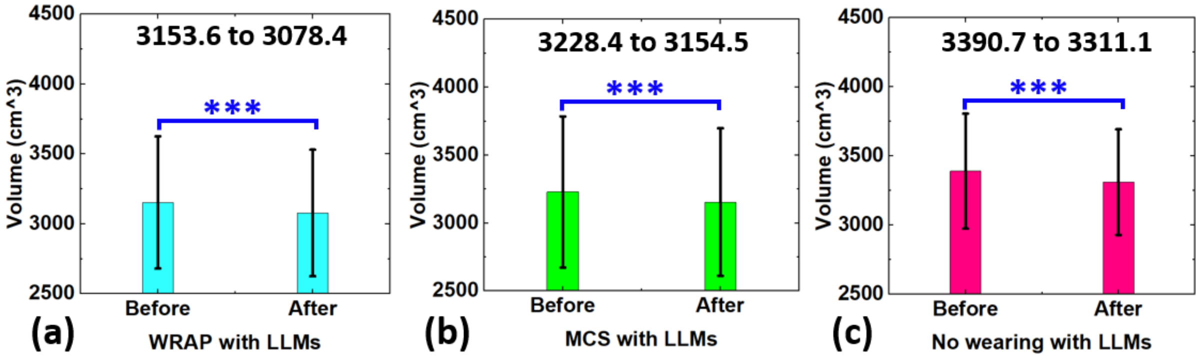

Figure 4. 6 The lower limb (calf) volume change before and after LLMs in the experimental group under WRAP/MCS/No-wearing conditions and p-value, (a) is WRAP, (b) is MCS, (c) is No-wearing condition.

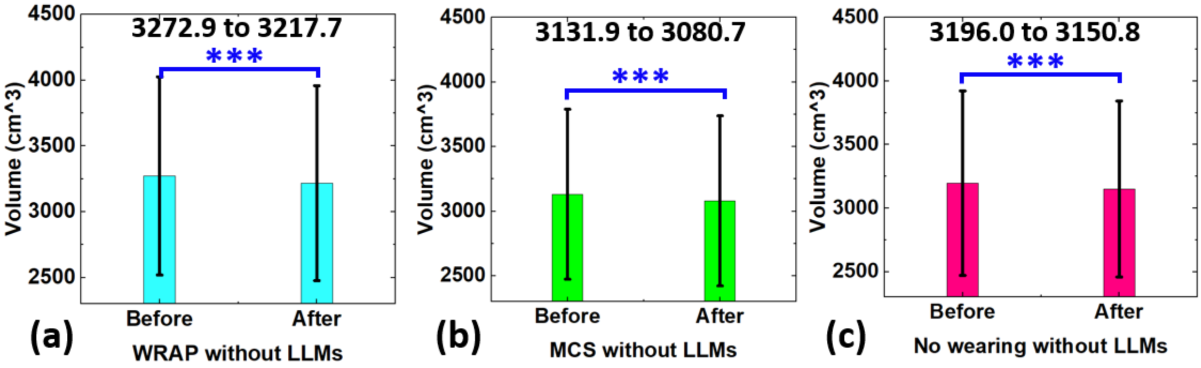

Figure 4. 7 The lower limb (calf) volume change before and after sitting 15 minutes in the control group under WRAP/MCS/No-wearing conditions and p-value, (a) is WRAP, (b) is MCS, (c) is No-wearing condition.

Table 4. 5 Detailed data of lower limb (calf) volume baseline, results after LLMs and after 15 minutes sitting under WRAP/MCS/No-wearing conditions and p-value.

Calf volume (unit: cm^3)	Experimental group		Control group	
Different conditions	Base line	After LLMs	Base line	After 15 mins sitting
WRAP	3153.6±472.6	3078.3±452.7 ***	3272.9±753.4	3217.7±740.7 ***
MCS	3228.4±556.2	3154. 5±542.7 ***	3131.9±658.1	3080.7±658.1 ***
No-wearing	3390.7±415.8	3311.1±381.4 ***	3196.0±726.2	3150.8±692.4 ***

4.4.2 Statistical significance analysis of volume reduction under WRAP/MCS/No-wearing conditions

Secondly, the statistical significance analysis of the volume reduction under WRAP/MCS/No-wearing conditions was carried out between experimental and control groups. Data of absolute changes greater than 5% were deleted, and they were consistent with normal distribution.

It was hypothesized that there was a significant difference in the absolute volume reduction value and volume reduction rate in at least two of the three different wearing conditions in the experimental and control groups.

One-way analysis of variance was conducted to compare whether the absolute volume reduction value and volume reduction rate among the WRAP/MCS/No-wearing conditions were significantly different in the experimental and control groups. According to **Figure 4.8** and **Figure 4.9,** it showed that there was no significant change of each other among WRAP/MCS/No-wearing conditions in both groups. With LLMs in experimental group, WRAP induced more volume reduction change (Mean=-66.3, SD=51.0) and rate (Mean=-2.1, SD=1.5) than MCS and No-wearing, see in **Figure 4.8(a)** and **Figure 4.9(a)**. Without LLMs, MCS revealed more volume reduction change (Mean=-51.2, SD=46.8) and rate (Mean=-1.7, SD=1.5) than WRAP and bare leg, but there was more standard deviation when No-wearing in the control group, see in **Figure 4.8(b)** and **Figure 4.9(b)**. Therefore, no significant change in the volume reduction value and volume reduction rate were presented among three different conditions, however, from mean reduction value and rate listed in **Table 4.6**, cases with LLMs induced more volume reduction than without LLMs.

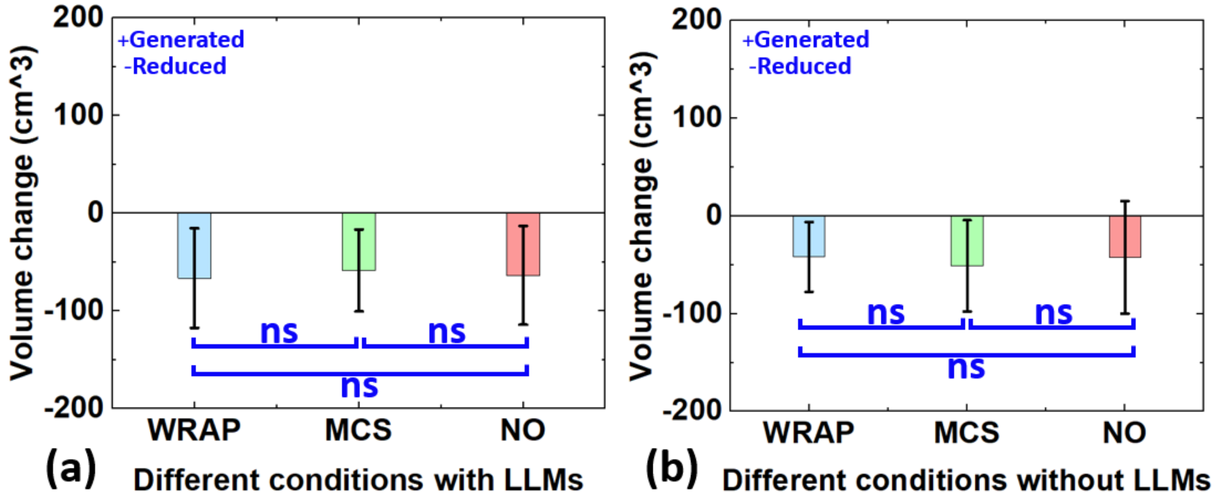

Figure 4. 8 Influence of WRAP/MCS/No-wearing conditions on the lower limb (calf) in absolute volume reduction value, (a) is with LLMs in the experimental group and (b) is without LLMs in the control group.

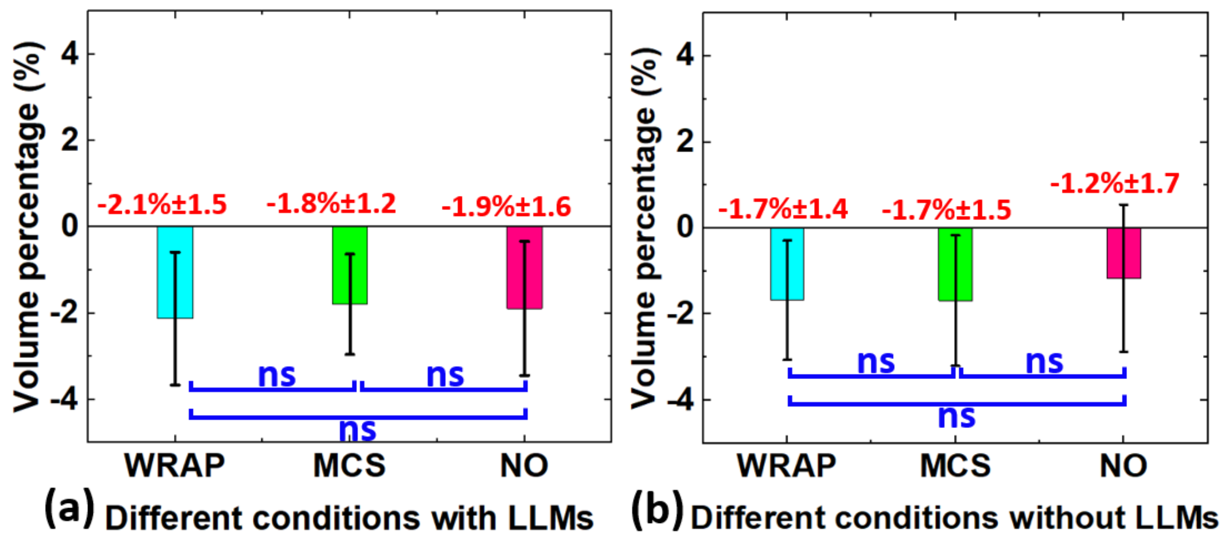

Figure 4. 9 Influence of WRAP/MCS/No-wearing conditions on the lower limb (calf) in volume reduction rate (volume percentage), (a) is with LLMs in the experimental group and (b) is without LLMs in the control group.

Table 4. 6 The lower limb (calf) volume reduction value and reduction rate under different conditions with/without LLMs.

Calf volume	Experimental group, "-" = reduce		Control group, "-" = reduce	
Different conditions	Absolute value of change (cm^3)	Change rate (%)	Absolute value of change (cm^3)	Change rate (%)
WRAP	-66.3±51.0	-2.1±1.5	-41.9±35.6	-1.7±1.4
MCS	-58.5±42.0	-1.8±1.2	-51.2±46.8	-1.7±1.5
No-wearing	-63.5±50.5	-1.9±1.6	-42.4±57.6	-1.2±1.7

Thirdly, the independent t-test was conducted to hypothesize that the left and right leg volume reduction rate significantly differed under three conditions in the experimental and control groups.

Figure 4.10(a) presented that there was a significant change between left leg (Mean=-2.5, SD=1.1) and right leg (Mean=-1.2, SD=0.9) when wearing MCS in the experiment group. And a significant change was shown between left leg (Mean=-2.3, SD=1.4) and right leg (Mean=-1.1, SD=1.2) when wearing WRAP in the control group, see in **Figure 4.10(b)**. Applying compression with LLMs had more mean reduction rate than the control group and the left leg showed more volume reduction both with LLMs and without LLMs, as shown in **Table 4.7**.

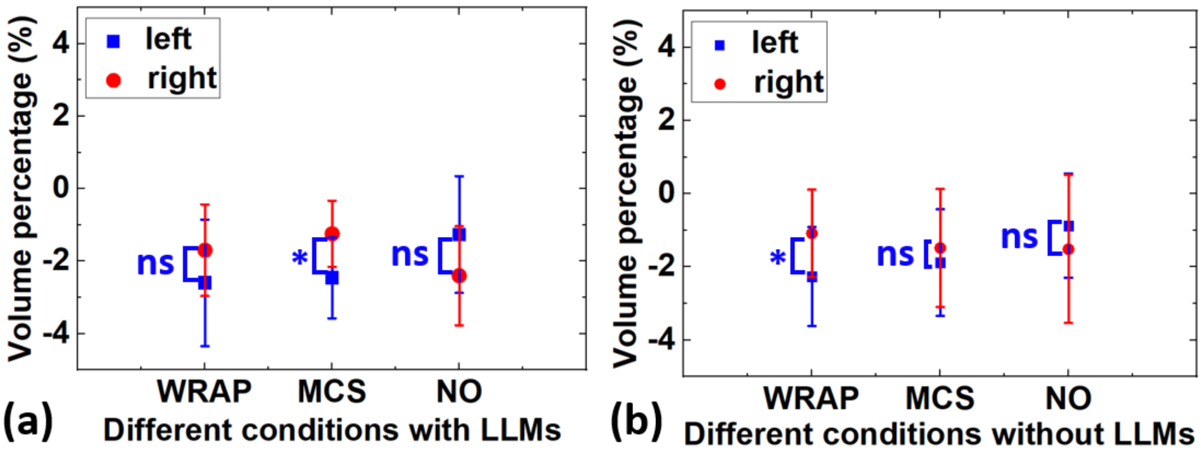

Figure 4. 10 Influence of WRAP/MCS/No-wearing conditions on the left and right lower limb (calf) volume reduction rate (volume percentage), (a) is with LLMs in the experimental group and (b) is without LLMs in the control group.

Table 4. 7 Detailed data of different conditions on the left and right lower limb (calf) volume reduction rate with/without LLMs and p-value.

Calf volume change rate (%)	Experimental group		Control group	
Different conditions	Left lower limb	Right lower limb	Left lower limb	Right lower limb
WRAP	-2.6±1.7	-1.7±1.3	-2.3±1.4*	-1.1±1.2
MCS	-2.5±1.1*	-1.2±0.9	-1.9±1.5	-1.5±1.6
No-wearing	-1.3±1.6	-2.4±1.4	-0.9±1.4	-1.5±2.0

Fourthly, the independent t-test was conducted to hypothesize that volume reduction rate of different gender significantly differed under three conditions in the experimental and control groups.

Figure 4.11(a) and **Table 4.8** revealed that males (Mean=-2.6, SD=0.9) had an extremely significant change than females (Mean=-0.8, SD=1.1) with bare leg in the experiment group. And a significant change was shown between males (Mean=-2.2, SD=1.5) and females (Mean=-0.1, SD=0.9) with bare leg in the control group, as shown in **Figure 4.11(b)**. In each group, significant effects were observed among male participants with bare lower limbs.

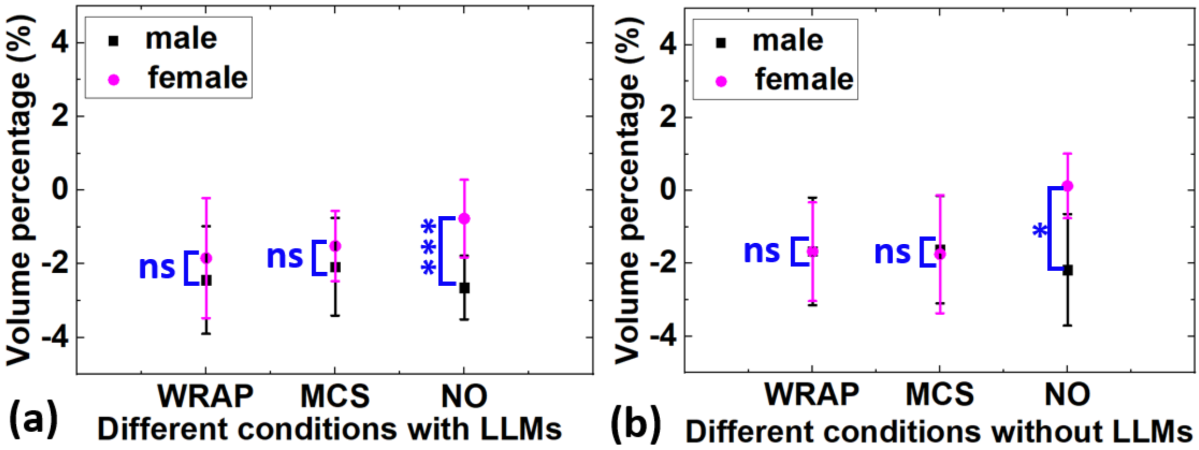

Figure 4. 11 Influence of WRAP/MCS/No-wearing conditions on the males and females' lower limb (calf) volume reduction rate (volume percentage), (a) is with LLMs in the experimental group and (b) is without LLMs in the control group.

Table 4. 8 Detailed data of different conditions on the males and females' lower limb (calf) volume reduction rate with/without LLMs and p-value.

Calf volume change rate (%)	Experimental group		Control group	
Different conditions	Male	Female	Male	Female
WRAP	-2.4±1.5	-1.8±1.6	-1.7±1.5	-1.7±1.4
MCS	-2.1±1.3	-1.5±1.0	-1.6±1.5	-1.7±1.6
No-wearing	-2.6±0.9***	-0.8±1.1	-2.2±1.5*	0.1±0.9

4.4.3 Circumference change (CC) of lower limb

In research of lower limb circumference change, data selection was also conducted that singular values were deleted within the measurement error range and deleted absolute changes greater than 5% before every data analysis. Both the experimental and control groups had 24 samples (n=24) in every condition, and they were consistent with normal distribution.

It was hypothesized that there was a significant difference in lower limb circumference before and after wearing WRAP/MCS/No-wearing conditions in the experimental and control groups.

Firstly, applying compression and LLMs in the experimental group, CC before and after LLMs under WRAP/MCS/No-wearing conditions were analysed through the paired sample t-test. The paired sample t-test showed the extremely significant difference all in CC before and after LLMs under WRAP/MCS/No-wearing conditions ($p < 0.001$), as shown in **Figure 4.12.** With the same method, CC after sitting 15 minutes under WRAP/MCS/No-wearing conditions in control group were also shown extremely/very significant difference ($p < 0.001$) except at point D in WRAP ($p > 0.05$) and at the same point in No-wearing ($p > 0.05$), as shown in **Figure 4.13.** Compared to experimental and control groups, at points B and B1 had extremely significant changes in both groups ($p < 0.001$). The reduction values at point D were bigger in the experimental group than in the control group. The calf circumference data results including baseline, after applying a combination of the compression and LLMs, and after only applying compression under different wearing conditions are listed in **Table 4.9** and **Table 4.10**.

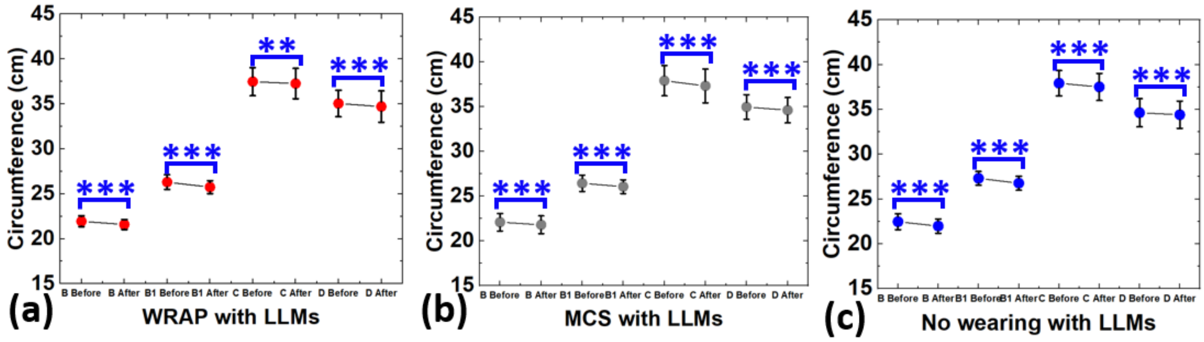

Figure 4. 12 The lower limb (calf) circumference (B, B1, C, D) change before and after LLMs in the experimental group under different wearing conditions and p-value, (a) is WRAP, (b) is MCS, (c) is No-wearing condition.

Table 4. 9 Detailed data of lower limb (calf) circumference baseline, results after LLMs under WRAP/MCS/No-wearing conditions, and p-value.

Calf circumference, unit: cm								
Point	B		B1		C		D	
Different conditions	Base line	After LLMs	Base line	After LLMs	Base line	After LLMs	Base line	After LLMs
WRAP	21.9±0.6	21.6±0.6***	26.3±0.8	25.7±0.7***	37.5±1.6	37.3±1.7**	35.0±1.5	34.7±1.7***
MCS	22.1±1.0	21.8±1.0***	26.4±0.9	26.1±0.8***	37.9±1.7	37.3±1.9***	35.0±1.4	34.6±1.4***
No-wearing	22.5±0.9	22.0±0.8***	27.3±0.8	26.8±0.8***	37.9±1.4	37.5±1.5***	34.6±1.6	34.4±1.5***

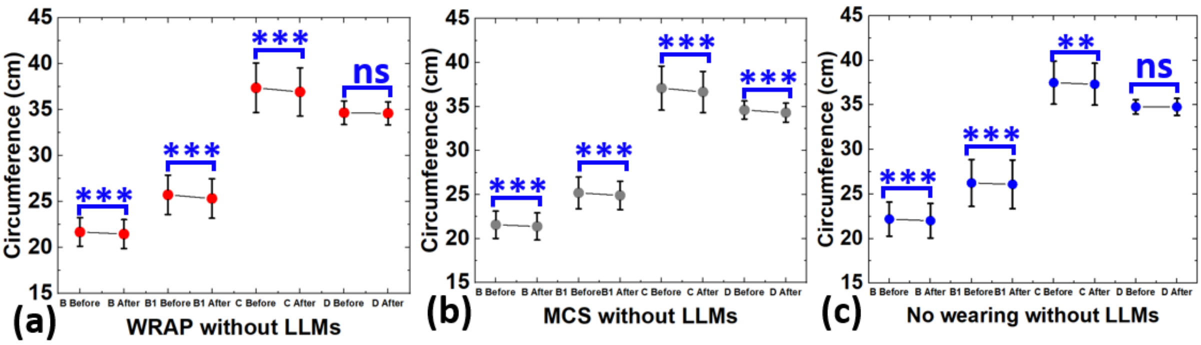

Figure 4. 13 The lower limb (calf) circumference (B, B1, C, D) change before and after sitting 15 minutes in the control group under different wearing conditions and p-value, (a) is WRAP, (b) is MCS, (c) is No-wearing condition.

Table 4. 10 Detailed data of lower limb (calf) circumference baseline, results after 15 minutes of sitting under WRAP/MCS/No-wearing conditions, and p-value.

Calf circumference, unit: cm								
Point	B		B1		C		D	
Different conditions	Base line	After 15mins sitting	Base line	After 15mins sitting	Base line	After 15mins sitting	Base line	After 15mins sitting
WRAP	21.7±1.6	21.5±1.6***	25.7±2.1	25.3±2.1***	37.4±2.7	36.9±2.6***	34.7±1.3	34.6±1.3ns
MCS	21.6±1.6	21.4±1.5***	25.2±1.8	24.9±1.6***	37.1±2.5	36.7±2.3***	34.6±1.0	34.3±1.1***
No-wearing	22.2±1.9	22.0±1.9***	26.2±2.6	26.1±2.7***	37.5±2.4	37.3±2.3**	34.8±0.8	34.8±0.9ns

4.4.4 Statistical significance analysis of circumference reduction under WRAP/MCS/No-wearing conditions

Secondly, the statistical significance analysis of the circumference reduction under WRAP/MCS/No-wearing conditions was conducted between experimental and control groups. Data of absolute changes greater than 5% were deleted, and they were consistent with normal distribution.

It was hypothesized that a significant difference in the absolute circumference reduction value and circumference reduction rate existed in at least two of the three different wearing conditions in the experimental and control groups.

One-way analysis of variance was applied to compare whether the absolute circumference reduction value and circumference reduction rate among WRAP/MCS/No-wearing conditions were significantly different in the experimental and control group. It was obtained that there was no significant reduction rate change of each other among WRAP/MCS/No-wearing conditions in the experimental group, see in **Figure 4.14(a).** However, regards to the absolute value of CC with LLMs in the experimental group, wearing MCS significantly reduced circumference than WRAP at point C ($p < 0.05$), wearing WRAP significantly reduced circumference than bare leg ($p < 0.05$) at point D, see in **Figure 4.15(a).** Only sitting in the control group, with regards to the absolute CC value and circumference reduction rate in **Figure 4.14(b)** and **Figure 4.15(b),** wearing WRAP could significantly reduce circumference compared to the bare leg at point B1 ($p < 0.05$), and wearing WRAP and MCS significantly had circumference reduction than the bare leg at point C ($p < 0.05$). At point D without LLMs, wearing MCS extremely significantly reduced circumference than wearing WRAP ($p < 0.001$) and bare leg ($p < 0.05$). Therefore, applying compression was more effective than the bare leg at point C, MCS could effectively reduce the circumference at point D without LLMs. In both groups, the biggest circumference percentage changes were observed at point B1 among 4 points, WRAP (-1.7%), MCS (-1.9%), No-wearing (-1.8%) with LLMs, WRAP (-1.5%), MCS (-1.1%), No-wearing (-0.6%) without LLMs**.** Overall, from the detailed data in **Table 4.11** and **Table 4.12,** there were more circumference reductions when carrying out LLMs than when carrying out compression only.

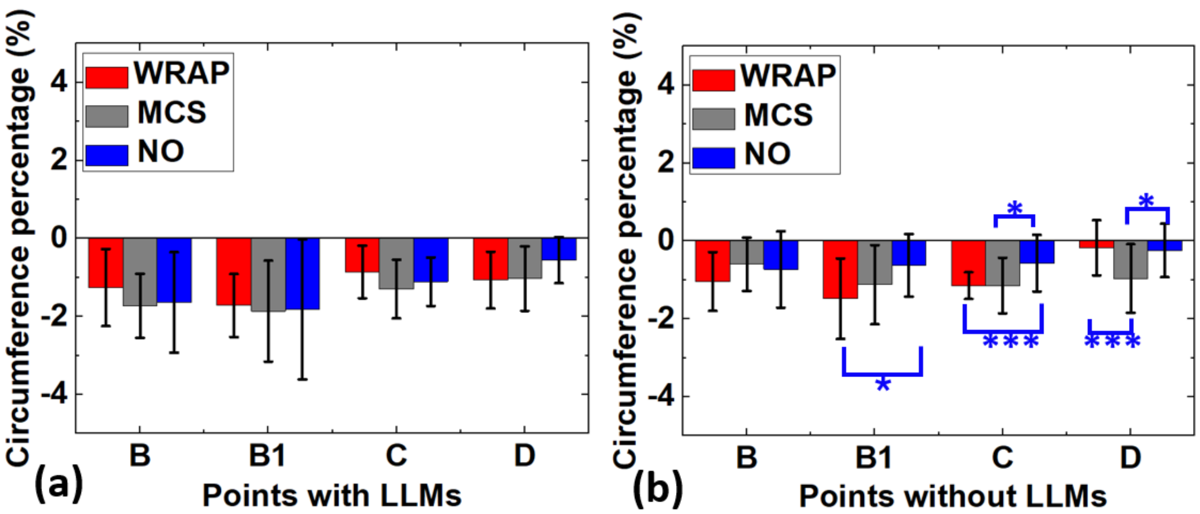

Figure 4. 14 Influence of WRAP/MCS/No-wearing conditions on the lower limb (calf) circumference reduction rate (circumference percentage), (a) is the experimental group with LLMs and, (b) is the control group without LLMs.

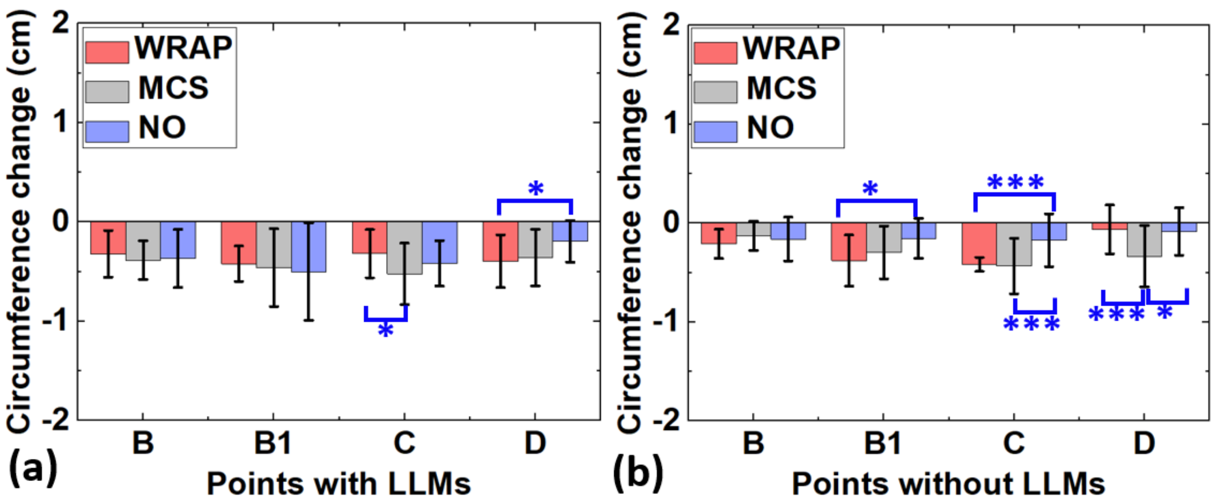

Figure 4. 15 Influence of WRAP/MCS/No-wearing conditions on the lower limb (calf) circumference reduction value, (a) is the experimental group with LLMs and, (b) is the control group without LLMs.

Table 4. 11 The lower limb (calf) circumference reduction value and reduction rate under different wearing conditions with LLMs.

Experimental group, "-" = reduce								
Point	B		B1		C		D	
Different conditions	Absolute value of change (cm)	Change rate (%)	Absolute value of change (cm)	Change rate (%)	Absolute value of change (cm)	Change rate (%)	Absolute value of change (cm)	Change rate (%)
WRAP	-0.3±0.2	-1.3±1.0	-0.4±0.2	-1.7±0.8	-0.3±0.2	-0.9±0.7	-0.4±0.3	-1.1±0.7
MCS	-0.4±0.2	-1.7±0.8	-0.5±0.4	-1.9±1.3	-0.5±0.3	-1.3±0.8	-0.4±0.3	-1.0±0.8
No-wearing	-0.4±0.3	-1.6±1.3	-0.5±0.5	-1.8±1.8	-0.4±0.2	-1.1±0.6	-0.2±0.2	-0.6±0.6

Table 4. 12 The lower limb (calf) circumference reduction value and reduction rate under different wearing conditions without LLMs.

Control group, "-" = reduce								
Point	B		B1		C		D	
Different conditions	Absolute value of change (cm)	Change rate (%)	Absolute value of change (cm)	Change rate (%)	Absolute value of change (cm)	Change rate (%)	Absolute value of change (cm)	Change rate (%)
WRAP	-0.2±0.1	-1.0±0.8	-0.4±0.3	-1.5±1.0	-0.4±0.1	-1.1±0.3	-0.1±0.2	-0.2±0.7
MCS	-0.1±0.1	-0.6±0.7	-0.3±0.3	-1.1±1.0	-0.4±0.3	-1.1±0.7	-0.3±0.3	-1.0±0.9
No-wearing	-0.2±0.2	-0.7±1.0	-0.2±0.2	-0.6±0.8	-0.2±0.3	-0.6±0.7	-0.1±0.2	-0.2±0.7

Thirdly, the independent t-test was conducted to hypothesize that the left and right leg circumference reduction rate significantly differed in experimental and control groups.

Figure 4.16(a) showed that there was an extremely significant ($p < 0.005$) change between left leg (Mean=-1.8, SD=0.5) and right leg (Mean=-0.6, SD=0.4) when wearing WRAP at point D in the experiment group. And a significant change ($p < 0.05$) was also obtained between right leg (Mean=-1.6, SD=0.8) and left leg (Mean=-0.6, SD=0.6) when wearing MCS at point D in the same group, as shown in **Figure 4.16(b)**. The detailed data is listed in **Table 4.13**.

Applying compression without LLMs in control group, a significant change ($p < 0.05$) was obtained between right leg (Mean=-2.2, SD=0.9) and left leg (Mean=-1.3, SD=0.7) when wearing WRAP at point B1, but left leg had more significant change ($0.001 < p < 0.01$) than right leg at point D with WRAP, as shown in **Figure 4.17(a)**. In addition, the right leg had a significant change ($p < 0.05$) than left leg at point C in bare leg, see in **Figure 4.17(c)**. The detailed data is listed in **Table 4-14**. In both groups, there was an obvious circumference reduction rate in the left leg than the right one at point D when wearing WRAP.

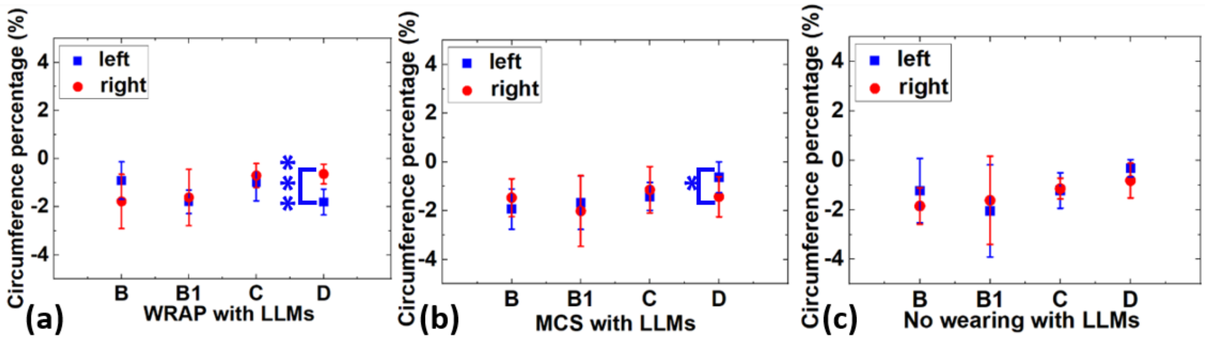

Figure 4. 16 Influence of different wearing conditions on the left and right lower limb (calf) circumference reduction rate (circumference percentage) with LLMs in the experimental group, (a) is WRAP, (b) is MCS, (c) is No-wearing condition.

Table 4. 13 Detailed data of different wearing conditions on the left and right lower limb (calf) circumference reduction rate with LLMs and p-value.

Experimental group, circumferences change rate, unit: %, "-" = reduce				
Point	B	B1	C	D

Different conditions	Left lower limb	Right lower limb	Left lower limb	Right lower limb	Left lower limb	Right lower limb	Left lower limb	Right lower limb
WRAP	-0.9±0.8	-1.8±1.1	-1.8±0.5	-1.6±1.2	-1.0±0.8	-0.7±0.5	-1.8±0.5 ***	-0.6±0.4
MCS	-1.9±0.8	-1.5±0.8	-1.7±1.1	-2.0±1.5	-1.4±0.6	-1.1±1.0	-0.6±0.6	-1.4±0.8 *
No-wearing	-1.2±1.3	-1.8±0.7	-2.0±1.9	-1.6±1.8	-1.2±0.7	-1.1±0.4	-0.3±0.3	-0.8±0.7

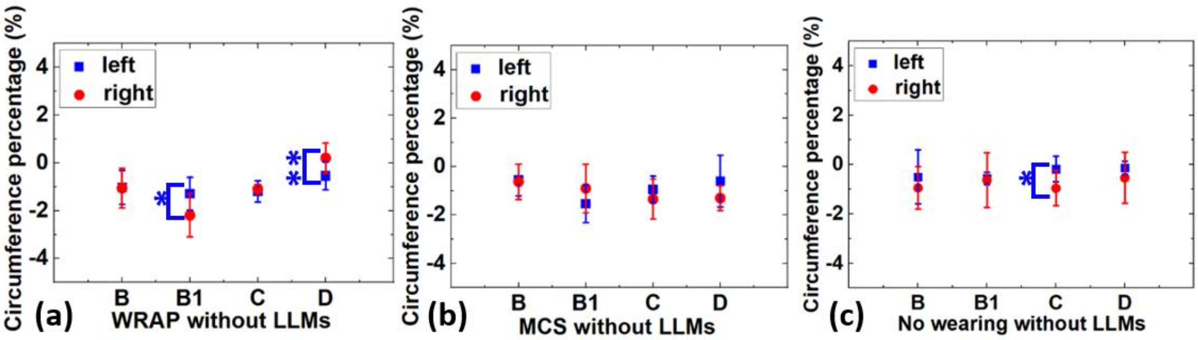

Figure 4. 17 Influence of different wearing conditions on the left and right lower limb (calf) circumference reduction rate (circumference percentage) without LLMs in the control group, (a) is WRAP, (b) is MCS, (c) is No-wearing condition.

Table 4. 14 Detailed data of different wearing conditions on the left and right lower limb (calf) circumference reduction rate without LLMs and p-value.

Control group, circumferences change rate, unit: %, "-" = reduce								
Point	B		B1		C		D	
Different conditions	Left lower limb	Right lower limb	Left lower limb	Right lower limb	Left lower limb	Right lower limb	Left lower limb	Right lower limb
WRAP	-1.0±0.7	-1.1±0.8	-1.3±0.7	-2.2±0.9 *	-1.2±0.4	-1.1±0.2	-0.5±0.6 **	0.2±0.6
MCS	-0.5±0.7	-0.6±0.7	-1.5±0.8	-0.9±1.0	-0.9±0.5	-1.3±0.8	-0.6±1.1	-1.3±0.5
No-wearing	-0.5±1.1	-0.9±0.9	-0.6±0.3	-0.6±1.1	-0.2±0.5	-1.0±0.7 *	-0.1±0.3	-0.5±1.0

Fourthly, the independent t-test was conducted to hypothesize that circumference reduction rate of males and females significantly differed under three conditions in the experimental and control groups.

It obtained that there was a very significant (0.001< p <0.01) change between males (Mean=-2.3, SD=0.7) and females (Mean=-1.3, SD=0.7) when wearing WRAP at point B1 in the experiment group, see in **Figure 4.18(a)**. And an extremely significant change (p <0.005) was obtained between males (Mean=-1.7, SD=0.4) and females (Mean=-0.7, SD=0.7) when wearing MCS at point C in the same group, as shown in **Figure 4.18(b)**. With the bare leg in **Figure 4.18(c)**, a significant change was in females at point B1 (p <0.05).

In the control group only applying compression without LLMs in **Figure 4.19(a)** and **Figure 4.19(b)**, a significant change (p <0.05) was achieved between females (Mean=-1.3, SD=0.3) and males (Mean=-0.7, SD=0.6) when wearing WRAP at point B, but males had more significant reduction change (p <0.005) than females at points B1 and C with MCS. In addition, females had more significant change than males at points B1(p <0.005) and D (p <0.05) in bare leg, see in **Figure 4.19(c)**.

Compared to the two groups in **Table 4.15** and **Table 4.16**, with bare legs of both groups, females showed obvious circumference reduction rate than males at B1 point. In addition, when wearing the MCS of both groups, males had an extremely significant circumference reduction at point C compared to females.

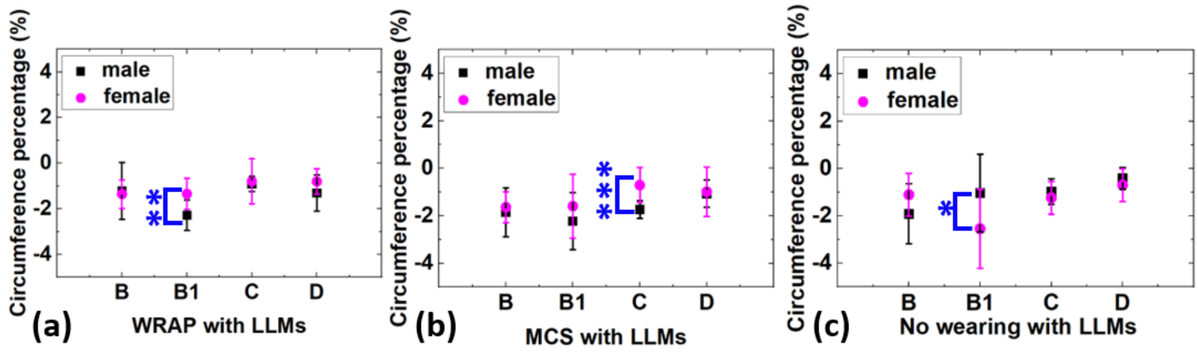

Figure 4. 18 Influence of different wearing conditions on the males and females' lower limb (calf) circumference reduction rate (circumference percentage) with LLMs in the experimental group, (a) is WRAP, (b) is MCS, (c) is No-wearing condition.

Table 4. 15 Detailed data of different wearing conditions on the males and females' lower limb (calf) circumference reduction rate with LLMs and p-value.

Experimental group, circumferences change rate, unit: %, "-" = reduce								
Point	B		B1		C		D	
Different conditions	Male	Female	Male	Female	Male	Female	Male	Female
WRAP	-1.2±1.2	-1.4±0.6	-2.3±0.7 **	-1.3±0.7	-0.9±0.3	-0.8±1.0	-1.3±0.8	-0.8±0.6
MCS	-1.9±1.0	-1.6±0.7	-2.2±1.2	-1.6±1.3	-1.7±0.4 ***	-0.7±0.7	-1.1±0.6	-1.0±1.0
No-wearing	-1.9±1.3	-1.1±0.9	-1.0±1.6	-2.5±1.7 *	-1.0±0.5	-1.2±0.7	-0.4±0.5	-0.7±0.7

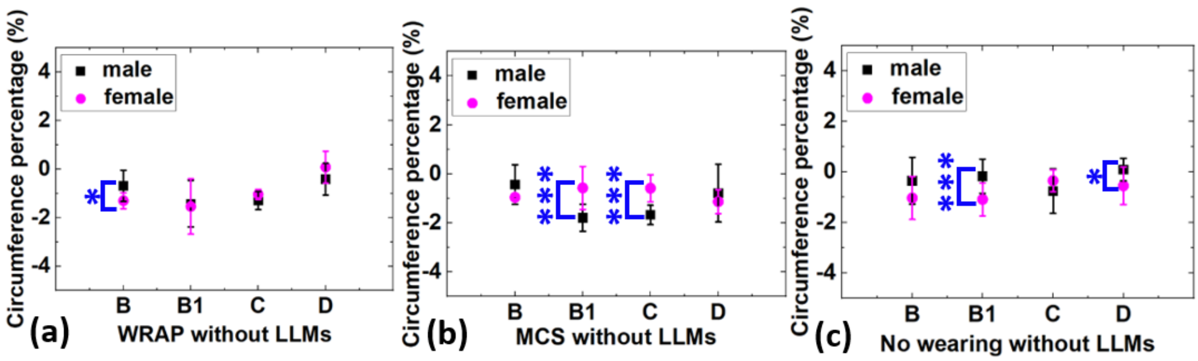

Figure 4. 19 Influence of different wearing conditions on the males and females' lower limb (calf) circumference reduction rate (circumference percentage) without LLMs in the control group, (a) is WRAP, (b) is MCS, (c) is No-wearing condition.

Table 4. 16 Detailed data of different wearing conditions on the males and females' lower limb (calf) circumference reduction rate without LLMs and p-value.

Control group, circumferences change rate, unit: %, "-" = reduce								
Point	B		B1		C		D	
Different conditions	Male	Female	Male	Female	Male	Female	Male	Female
WRAP	-0.7±0.6	-1.3±0.3 *	-1.4±1.0	-1.5±1.1	-1.3±0.4	-1.0±0.2	-0.4±0.7	0.1±0.7
MCS	-0.4±0.8	-1.0±0.0	-1.8±0.6 ***	-0.6±0.9	-1.7±0.4 ***	-0.6±0.5	-0.8±1.2	-1.1±0.5
No-wearing	-0.3±0.9	-1.0±0.8	-0.2±0.7	-1.1±0.7 ***	-0.8±0.9	-0.3±0.4	0.1±0.4	-0.6±0.7 *

4.4.5 Compliance

It was inquired as to which compression stockings (MCS/WRAP) were preferred among young healthy subjects, MCS was preferred by 25%, while WRAP was preferred by 75% due to the convenience of wearing WRAP.

4.5 Transition trial test

The integration of applying compression and LLMs had an obvious effect on reducing circumference of the lower limb than bare leg from the 1st trial test. The purpose of this transition trial test was to investigate the efficacy of the proposed combination of LLMs and WRAP or MCS for the elderly subjects. The reason is that elderly individuals have different physiological parameters and skeletal muscle activity than young individuals. It was carried out with the same conditions and procedures of the 1st trial test for recruited one elderly volunteer (70 years old, female, with mild lower limb oedema, see in **Figure 4.20**). Only the circumference was measured to evaluate the oedema reduction and there was no long time sitting for oedema generation step.

The elderly volunteer completed two sets of LLMs sequentially, and the CC was measured twice after each completed LLMs, to compare and investigate how many sets of LLMs could be available for elderly individuals. Because 30 minutes of exercise is usually suitable for elderly individuals, the maximum number of LLMs was 2 sets for each case in the transition trial test. The transition trial test cases were divided into the combination of MCS and LLMs (**Figure 4.20(a)**), the combination of WRAP and LLMs (**Figure 4.20(b)**), bare leg with LLMs (**Figure 4.20(c)**), and application of MCS or WRAP without LLMs (**Figure 4.20(d)**), separately on 4 different days.

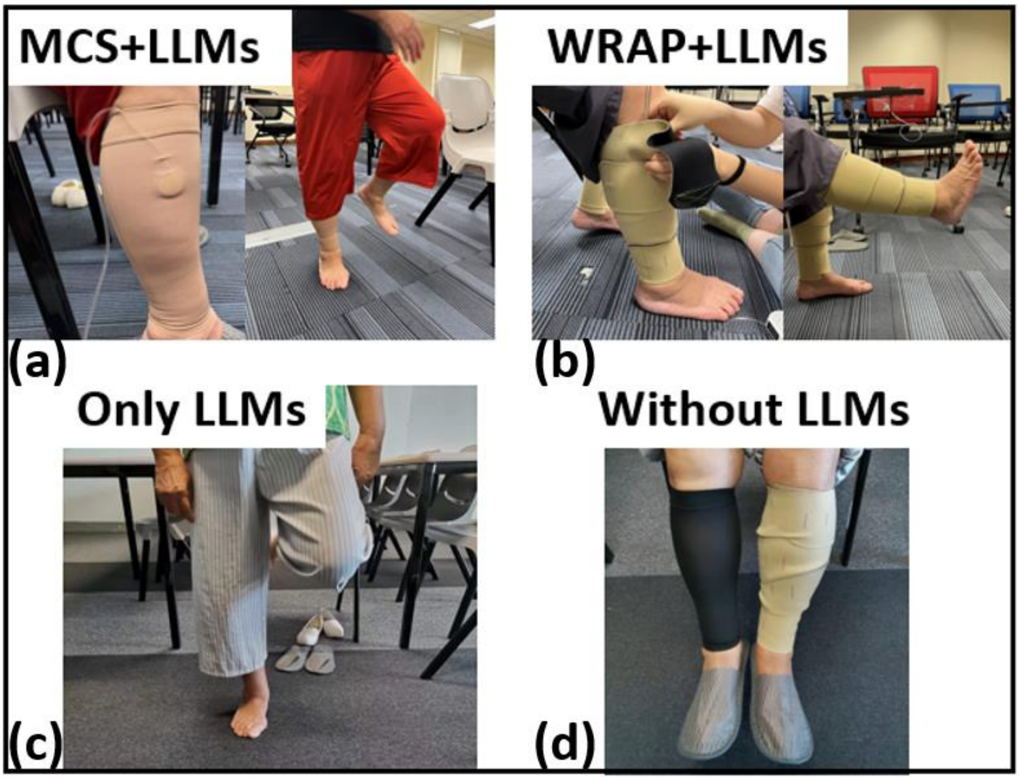

Figure 4. 20 Different wearing conditions were tested separately on 4 different days for an elderly mild oedema volunteer.

From this transition trial test, it was also achieved that integrating of applying compression and LLMs had an obvious effect on reducing the lower limb circumference than the bare leg. In addition, completing 2 sets of LLMs had more circumference reduction than 1 set. When completing 1 and 2 sets of LLMs in **Figure 4.21** and **Figure 4.22,** the conditions with only LLMs, only with WRAP or MCS showed the smallest circumference reduction rate, except points B1 and C of the right leg (**Figure 4.21(b)**). The detailed data of circumference reduction rate are listed in **Table 4.17 and Table 4.18**. Therefore, in the 2nd trial test, the case involving bare leg was omitted, and the WRAP and MCS were continuously chosen to apply compression pressure to evaluate their efficacy on oedema reduction with/without LLMs.

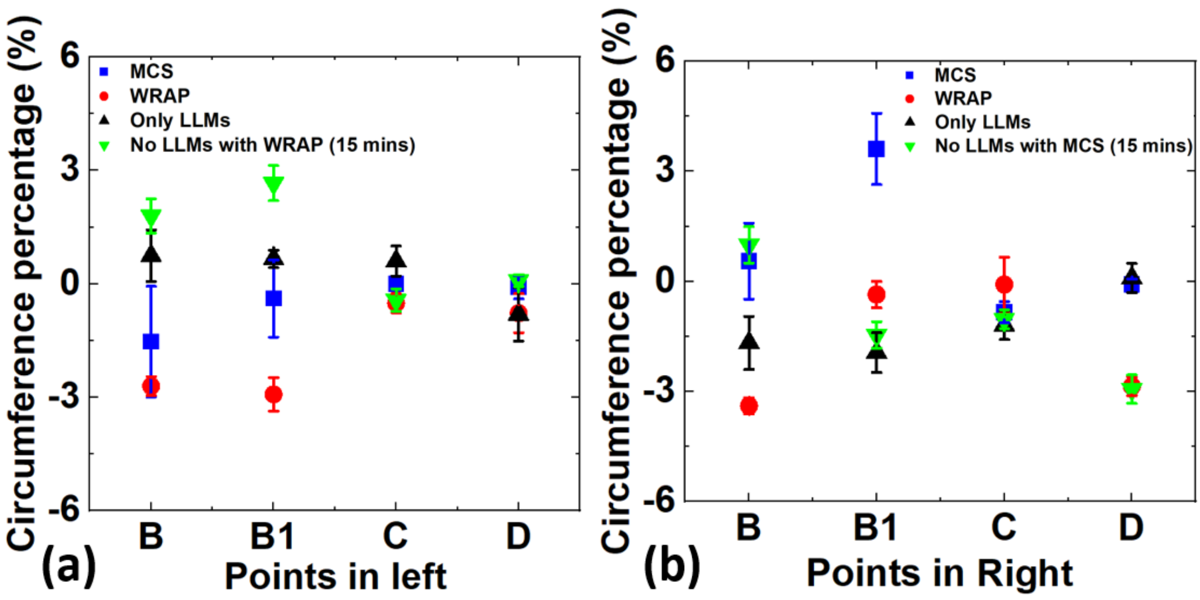

Figure 4. 21 Influence of WRAP/MCS/No-wearing conditions on the lower limb (calf) circumference reduction rate (circumference percentage) after completing one set LLMs or after 15 minutes sitting, (a) is left lower limb, and (b) is right lower limb.

Table 4. 17 Detailed data of Figure 4.21, circumferences reduction rate (%) of after completing one set LLMs or after 15 minutes sitting.

"-" = reduce, "+" = generate oedema	Left lower limb, *no LLMs with WRAP*				Right lower limb, *no LLMs with MCS*			
Point	B	B1	C	D	B	B1	C	D
WRAP	-2.7±0.2	-2.9±0.4	-0.5±0.3	-0.8±0.5	-3.4±0.2	-0.4±0.4	-0.1±0.7	-2.9±0.3
MCS	-1.5±1.5	-0.4±1.0	0.0±0.0	-0.1±0.3	0.6±1.0	3.6±1.0	-0.8±0.3	-0.1±0.2
Only LLMs	0.7±0.7	0.7±0.2	0.6±0.4	-0.8±0.7	-1.7±0.7	-1.9±0.5	-1.2±0.4	0.1±0.4
No LLMs (15 mins)	1.8±0.5	2.7±0.5	-0.4±0.3	0.1±0.2	1.0±0.5	-1.5±0.4	-1.0±0.3	-2.9±0.4

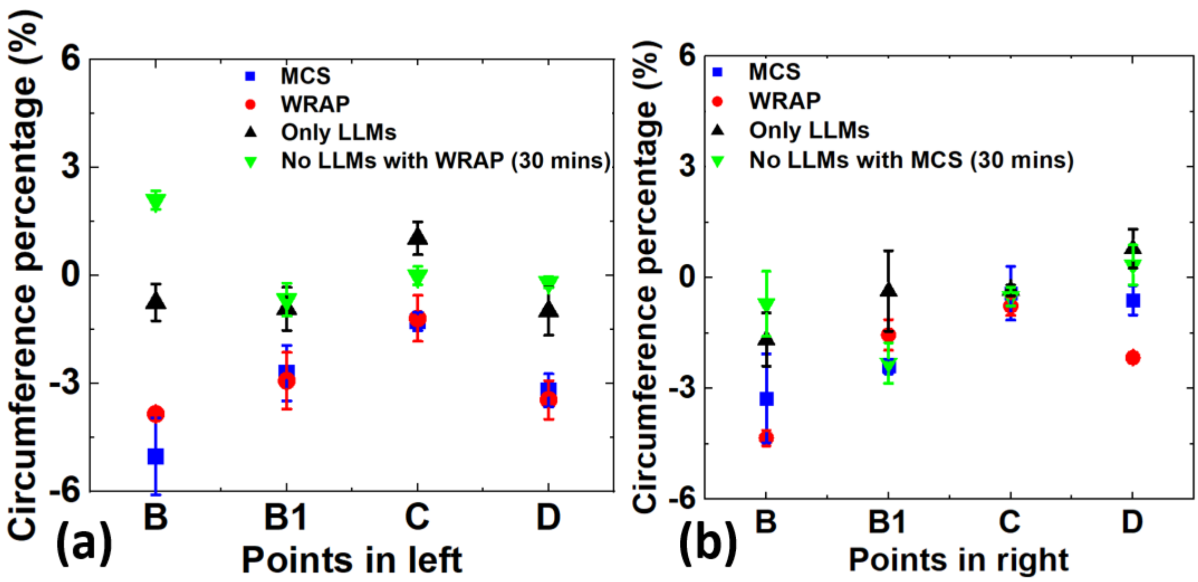

Figure 4. 22 Influence of WRAP/MCS/No-wearing conditions on the lower limb (calf) circumference reduction rate (circumference percentage) after completing two sets LLMs or after 30 minutes sitting, (a) is left lower limb and (b) is right lower limb.

Table 4. 18 Detailed data of Figure 4.22, circumferences change rate (%) of after completing two sets LLMs or after 30 minutes sitting.

"-" = reduce, "+" = generate oedema	Left lower limb, *no LLMs with WRAP*				Right lower limb, *no LLMs with MCS*			
Point	B	B1	C	D	B	B1	C	D
WRAP	-3.8±0.0	-2.9±0.8	-1.2±0.6	-3.5±0.5	-4.3±0.2	-1.6±0.4	-0.8±0.3	-2.2±0.1
MCS	-5.0±1.1	-2.7±0.8	-1.3±0.3	-3.2±0.5	-3.3±1.2	-2.4±0.2	-0.4±0.7	-0.6±0.4
Only LLMs	-0.7±0.5	-0.9±0.6	1.0±0.5	-1.0±0.7	-1.7±0.7	-0.4±1.1	-0.3±0.1	0.8±0.5
No LLMs (30 mins)	2.1±0.3	-0.7±0.5	0.0±0.3	-0.2±0.2	-0.7±0.9	-2.3±0.5	-0.5±0.3	0.3±0.5

4.6 The second trial test (elderly mild oedema subjects)

4.6.1 Participants

In the 2nd trial test, 12 elderly subjects with mild lower limb oedema or who were prone to lower limb oedema in daily life participated, including 6 males and 6 females. The detailed information on them is listed in **Table 4.1** in section 4.3.1. The elderly subjects in the 2nd trial test were between the ages of 65 and 93. They were able to move independently without assistance and had no history of musculoskeletal, cardiovascular, or diabetic problems. Therefore, we had 24 lower limbs in the 2nd trial test.

4.6.2 The second trial test design

The 2nd trial test was carried out at a temperature of 25.6°C with a humidity of 54%. By turning on the air conditioner, the temperature was effectively controlled to approximately 24°C. The 2nd trial test was conducted in the afternoon, and the entire test was completed within the same day.

Firstly, subjects completed consent before the trial, recording information such as height, weight, and BMI, and measuring the original circumference of every subject's lower limb. Secondly, subject started to reduce oedema with or without the application of non-stretchable

WRAP or medical compression stocking (MCS) combined with or without LLMs. Two sizes of MCS were available for subjects, determined by their lower limb measurements. The subjects were divided into experimental (8 subjects: 4 pairs WRAP and 4 pairs MCS) and control group (4 subjects: 2 pairs WRAP and 2 pairs MCS). Thirdly, the interface pressure of points B and C was measured after wearing the WRAP or MCS to ensure initial interface pressure at Class I level (18~21 mmHg at point B). Fourthly, 4 subjects in the experimental group completed one set of designed lower limb movements (LLMs) with wearing WRAP and another 4 subjects completed one set of designed LLMs with wearing MCS. During these LLMs, dynamic compression pressure at point C was recorded. In the control group, every 2 subjects maintained a sitting position for 15 minutes without LLMs while wearing WRAP and MCS, respectively. Fifthly, subjects wore off WRAP or MCS and the circumference of the lower limb was measured after LLMs or 15 minutes sitting. In the 2nd trial test, elderly subjects conducted 2 sets of LLMs in sequence based on the transition trial effect. LLMs process was the same as that in the 1st trial test. Therefore, sixthly, subjects wore on the WRAP or MCS again, and the interface pressure of points B and C was measured again. Seventhly, subjects repeated the second time of LLMs in the experimental group and repeated 15 minutes sitting in the control group. Finally, subjects wore off WRAP or MCS, and the circumference of every lower limb was measured, and subjects completed questionnaires. The flow chart of the 2nd trial test is shown in **Figure 4.23.**

It was imperative to guarantee that all personnel conducting measurements exhibited professionalism, accuracy, and efficiency while minimizing measurement errors.

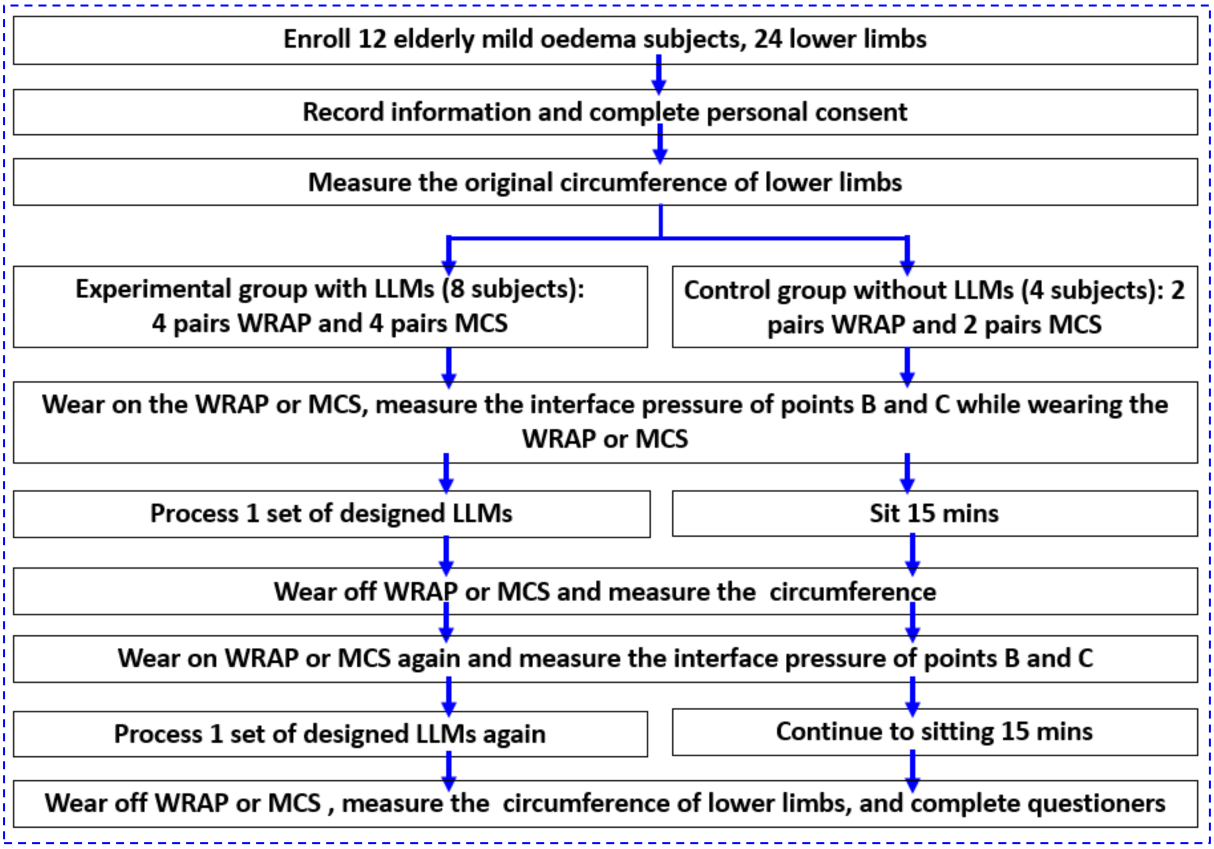

Figure 4. 23 The flow chart of the 2nd trial test.

4.6.3 Measurement

For elderly subjects, we performed solely lower limb circumference measurements. This decision was made in consideration of the potential inconvenience for elderly individuals from the water displacement volumetry method. They were original circumference, those after completing every set of LLMs (2 sets in the experimental group) and after every sitting 15 minutes (twice in the control group), respectively.

Each measurement was repeated three times. It was also measured using the soft tape measure at B, B1, C, and D points in standard RAL-GZ 387/1. To ensure precision in measuring the circumference, three equidistant points were chosen along the leg circumference, all on the same plane.

4.6.4 Interface pressure (IP)

The IP of points B and C when subjects after wearing WRAP or MCS were measured by the airbag sensor to guarantee that the initial compression pressures of the WRAP or MCS were at Class I level. **Figure 4.24** was the IP at point B and point C when wearing WRAP or MCS before the first LLMs or sitting, and **Figure 4.25** was the IP at point B and point C when wearing WRAP or MCS before the second LLMs or sitting. They showed most of the pressures at point B were guaranteed between 18~21 mmHg.

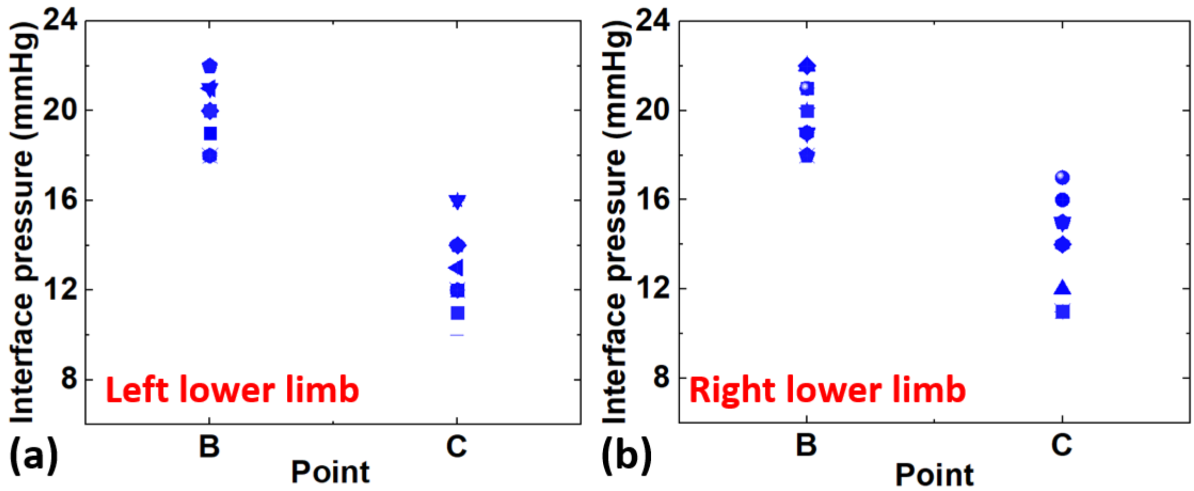

Figure 4. 24 Interface pressure (IP) at point B and point C after wearing for the first time to WRAP or MCS, (a) is the left lower limb, and (b) is the right lower limb.

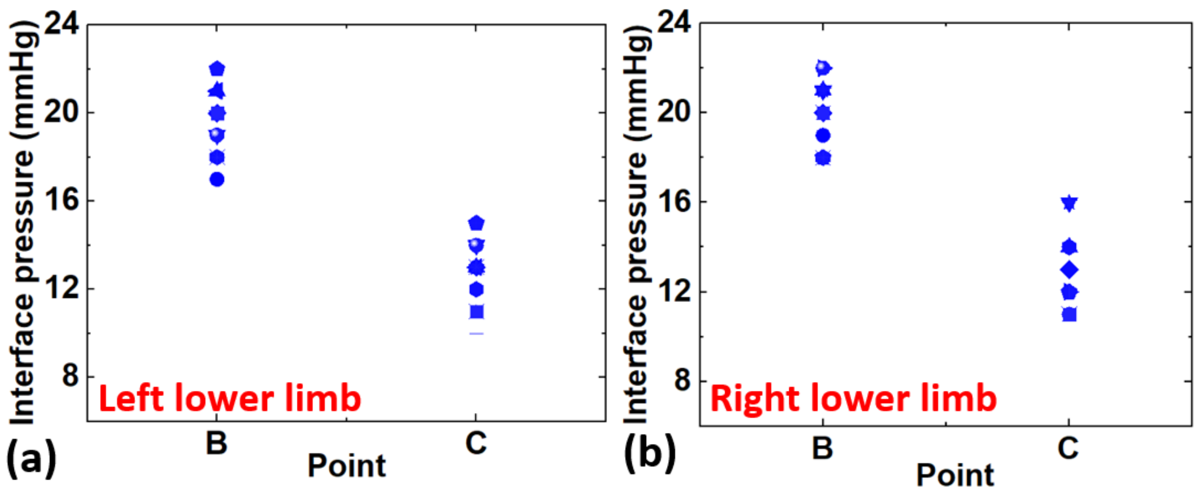

Figure 4. 25 Interface pressure (IP) at point B and point C after wearing for the second time to WRAP or MCS, (a) is the left lower limb, and (b) is the right lower limb.

4.7 The second trial test analysis (elderly mild oedema subjects)

4.7.1 Circumference change (CC) of lower limb

In the analysis of the 2nd trial test results, data selection was conducted that singular values were deleted within the measurement error range and deleted absolute changes greater than 5% before each section data analysis. WRAP and MCS conditions in the experimental group each had 24 samples (n=24). In the control group, the WRAP condition had 6 samples (n=6), and the MCS condition had 12 samples (n=12). All samples were consistent with a normal distribution.

It was hypothesized that a significant difference in lower limb circumference existed before and after wearing WRAP or MCS in the experimental and control groups.

Firstly, utilizing WRAP or MCS with LLMs in the experimental group, CC before and after LLMs when wearing WRAP or MCS conditions were analysed through the paired sample t-test. The paired sample t-test presented an extremely significant difference in CC after completing 2 sets of LLMs when wearing MCS at points B ($p_{2nd} <0.001$), B1 ($p_{2nd} <0.001$), and D ($p_{2nd} <0.001$), as shown in **Figure 4.26(b).** In addition, it was evident that no obvious difference change was observed after completing 1 set LLMs except point B1(MCS) when wearing two conditions, see **Figure 4.26(a)** and **(b)**. Compare the WRAP and MCS in the experimental group, the smaller standard deviation showed when wearing MCS than WRAP in the experimental group. The calf circumference data results including baseline, after using a combination of the compression and 1/2 sets LLMs under WRAP or MCS conditions are listed in **Table 4.19**.

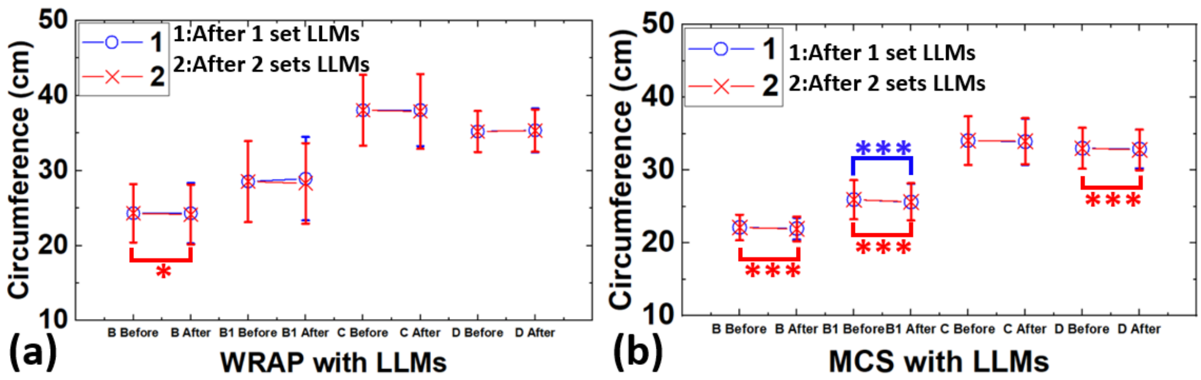

Figure 4. 26 The lower limb (calf) circumference (B, B1, C, D) change before and after completing 1/2 sets LLMs in the experimental group under WRAP/MCS conditions and p-value, (a) is WRAP and (b) is MCS.

Table 4. 19 Detailed data of lower limb (calf) circumference baseline, results after completing 1/2 sets LLMs under WRAP/MCS conditions, and p-value.

Experimental group, calf circumference, unit: cm, "-" = reduce, After LLMs1: After 1 set LLMs, After LLMs2: After 2 sets LLMs												
Point	B			B1			C			D		
Different conditions	Baseline	After LLMs1	After LLMs2	Baseline	After LLMs1	After LLMs2	Baseline	After LLMs1	After LLMs2	Baseline	After LLMs1	After LLMs2
WRAP	24.3 ±3.9	24.3 ±4.0	24.2±4.0*	28.5 ±5.4	28.9±5.6	28.3±5.4	38.0 ±4.7	38.1 ±4.8	37.9 ±5.0	35.2 ±2.7	35.4 ±2.9	35.3±2.8
MCS	22.1 ±1.8	22.0 ±1.5	21.9±1.7***	25.9 ±2.7	25.6±2.5***	25.6±2.5***	34.1 ±3.3	33.9 ±3.2	34.0 ±3.2	33.0 ±2.8	32.9 ±2.7	32.8±2.8***

With the same method, **Figure 4.27** revealed that CC after sitting 15 minutes and 30 minutes while wearing WRAP or MCS conditions in control group were shown extremely significant difference in a lot of points. The diminishment in the after 30 minutes data quantity was due to the early departure of one subject utilizing WRAP, therefore the baseline data was different in **Figure 4.27(a)**. Regarding only applying compression, MCS in **Figure 4.27(b)** could reduce the circumference effectively at points B (p_{1st} <0.001, p_{2nd} <0.001) and B1(p_{1st} <0.001, p_{2nd} <0.001) both after sitting for 15 minutes and 30 minutes cases. However, only sitting without movement, the oedema reappeared after 30 minutes (increase of circumference), especially at point B1 when both wearing WRAP and MCS.

Compared to experimental and control groups, the reduction values at point D were more obvious when wearing MCS in the experimental group. The circumference data results including baseline, after 15 or 30 minutes of sitting while wearing WRAP/MCS conditions are listed in **Table 4.20**.

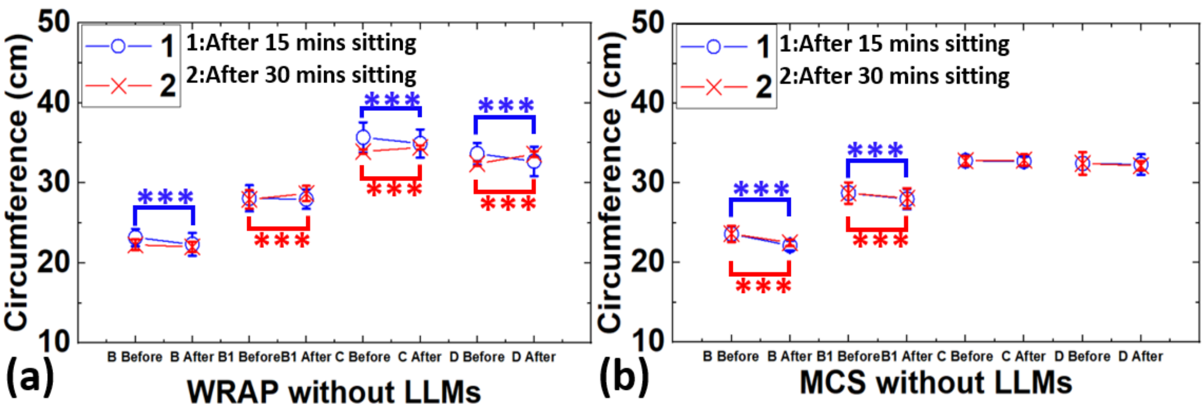

Figure 4. 27 The lower limb (calf) circumference (B, B1, C, D) change before and after 15/30 minutes sitting in the control group under WRAP/MCS conditions and p-value, (a) is WRAP and (b) is MCS.

Table 4. 20 Detailed data of lower limb (calf) circumference baseline, results after 15/30 minutes of sitting under WRAP/MCS conditions, and p-value.

Control group, calf circumference, unit: cm, “-” = reduce																
Point	B				B1				C				D			
Different conditions	Baseline	After 15 mins	Base line	After 30 mins	Base line	After 15 mins	Base line	After 30 mins	Base line	After 15 mins	Base line	After 30 mins	Base line	After 15 mins	Base line	After 30 mins
WRAP	23.2 ±1.1	22.3 ±1.4 ***	22.3 ±0.7	22.0 ±0.7	28.1 ±1.6	28.0 ±1.2	27.9 ±1.2	28.7 ±0.9 ***	35.7 ±1.9	34.9 ±1.8 ***	33.9 ±0.3	34.4 ±0.3 ***	33.7 ±1.4	32.7 ±1.8 ***	32.4 ±0.3	33.6 ±0.4 ***
MCS	23.6 ±1.0	22.2 ±0.6 ***	23.6 ±1.0	22.5 ±0.4 ***	28.7 ±1.3	28.0 ±1.3 ***	28.7 ±1.3	28.1 ±1.3 ***	32.8 ±0.6	32.7 ±0.6	32.8 ±0.6	32.9 ±0.7	32.5 ±1.4	32.3 ±1.3	32.5 ±1.4	32.2 ±0.6

4.7.2 Statistical significance analysis of circumference reduction under WRAP and MCS conditions

Secondly, the experimental and control groups conducted statistical significance analysis of the circumference reduction under WRAP or MCS.

The independent t-test was conducted to hypothesize that the circumference reduction value and circumference reduction rate were significantly different between utilizing WRAP and MCS in the experimental and control groups.

Figure 4.28(a) presented that at points B1 and C, MCS (B1: $Mean_{1st}$=-0.3, SD_{1st}=0.5, p_{1st} <0.05; C: $Mean_{1st}$=-0.1, SD_{1st} =0.4, p_{1st} <0.05) had a significant decrease in the absolute CC value than WRAP (B1: $Mean_{1st}$=0.0, SD_{1st}=0.6; C: $Mean_{1st}$=0.1, SD_{1st}=0.3) after completing 1 set of LLMs compared to the baseline data. The absolute CC value after completing 2 sets of LLMs had a very small drop compared to the completed 1 set of LLMs in the experimental group. Conversely, the control group in **Figure 4.28(b)** exhibited an extremely obvious gap between WRAP and MCS at several points. Nonetheless, upon remaining sedentary for 30 minutes, absolute CC value without LLMs increased significantly.

Regarding the reduction rate of circumference, at point B1, MCS ($Mean_{1st}$=-1.1, SD_{1st}=2.2, p_{1st} <0.05) demonstrated a statistically significant decrease compared to WRAP ($Mean_{1st}$=0.1,

SD_{1st}=2.1) after completing 1 set of LLMs. At point B, both WRAP and MCS experienced more circumference reduction rate after completing 2 sets of LLMs than observed in completing 1set of LLMs, as shown in **Figure 4.29(a)**. Notably, the reduction rate when wearing MCS ($Mean_{1st}$=-0.4, SD_{1st}=2.1; $Mean_{2nd}$=-0.8, SD_{2nd}=1.7) at point B surpassed that of WRAP ($Mean_{1st}$=-0.1, SD_{1st}=1.3; $Mean_{2nd}$=-0.5, SD_{2nd}=1.4), see the detailed data in **Table 4.21.** There were substantial extremely significant differences between WRAP and MCS within the control group at several points in **Figure 4.29(b)**. However, relative to the oedema reduction trend observed in the experimental group, the data from the control group revealed a significant increase in the circumference reduction rate of both WRAP and MCS after 30 minutes of sedentary behaviour, particularly in the case of WRAP, as shown in **Figure 4.29(b)** and **Table 4.22**.

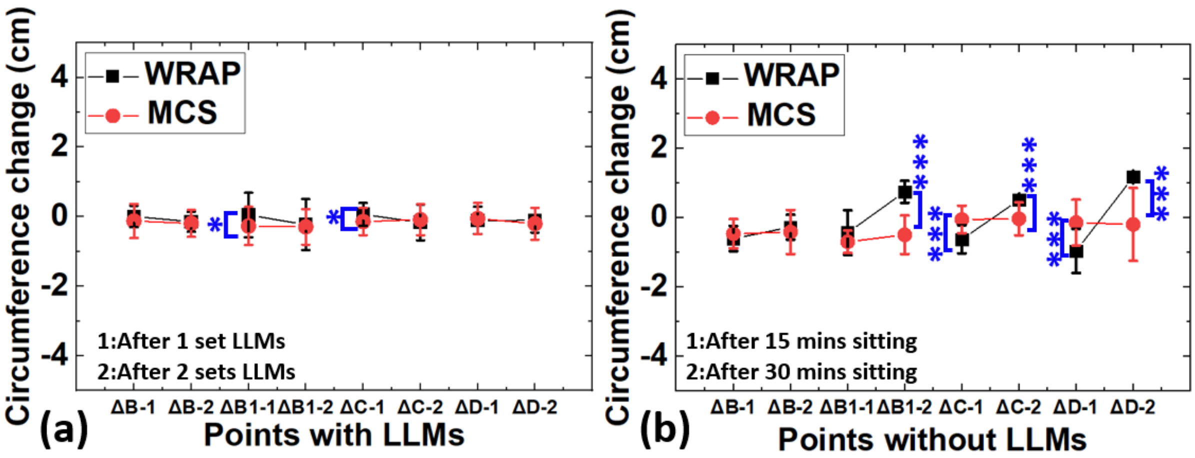

Figure 4. 28 Influence of WRAP and MCS conditions on the lower limb (calf) circumference change value, (a) is after completing 1/2 sets LLMs in the experimental and (b) is after 15/30 minutes sitting in the control group.

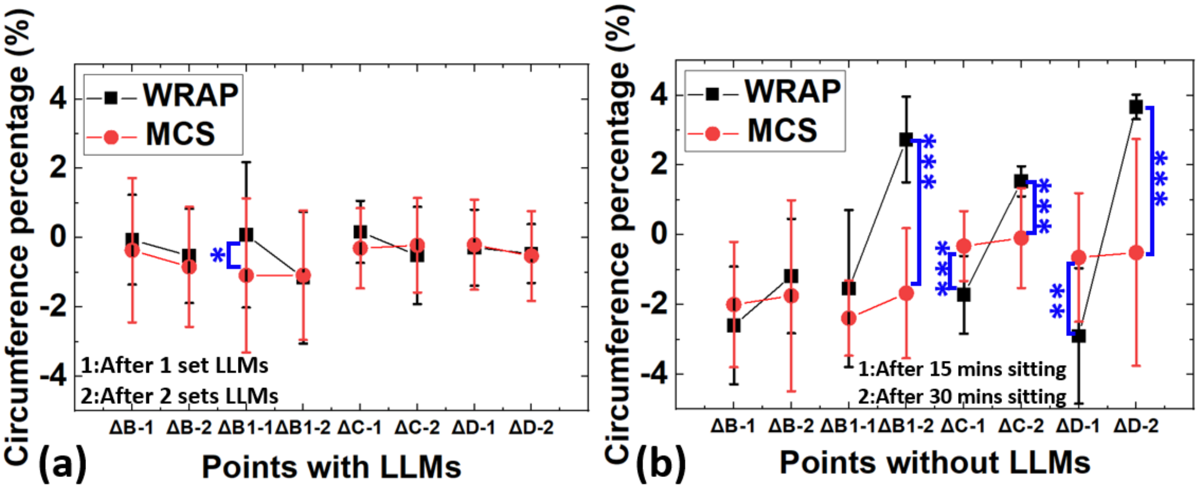

Figure 4. 29 Influence of WRAP and MCS conditions on the lower limb (calf) circumference reduction rate (circumference percentage), (a) is after completing 1/2 sets LLMs in the experimental and (b) is after 15/30 minutes sitting in the control group.

Table 4. 21 The lower limb (calf) circumference change value and reduction rate under WRAP and MCS conditions after completing 1/2 sets LLMs and p-value.

Experimental group, Change value: absolute value of change (cm), rate: change rate (%), "-" = reduce, 1: After 1 set LLMs, 2: After 2 sets LLMs																
Point	B				B1				C				D			
Different conditions	change value 1	change value 2	rate 1	rate 2	change value 1	change value 2	rate 1	rate 2	change value 1	change value 2	rate 1	rate 2	change value 1	change value 2	rate 1	rate 2
WRAP	0.0±0.3	-0.1±0.3	-0.1±1.3	-0.5±1.4	0.0±0.6	-0.2±0.7	0.1±2.1	-1.2±1.9	0.1±0.3	-0.2±0.5	0.2±0.9	-0.5±1.4	-0.1±0.4	-0.1±0.4	-0.3±1.1	-0.5±0.8
MCS	-0.1±0.5	-0.2±0.4	-0.4±2.1	-0.8±1.7	-0.3±0.5*	-0.3±0.5	-1.1±2.2*	-1.1±1.9	-0.1±0.4*	-0.1±0.4	-0.3±1.2	-0.2±1.4	-0.1±0.5	-0.2±0.5	-0.2±1.3	-0.5±1.3

Table 4. 22 The lower limb (calf) circumference change value and reduction rate under WRAP and MCS conditions after 15/30 mins sitting and p-value.

Control group, Change value: absolute value of change (cm), rate: change rate (%),

"-" = reduce, 1: after 15 minutes sitting, 2: after 30 minutes sitting																
Point	B				B1				C				D			
Different conditions	change value 1	change value 2	rate 1	rate 2	change value 1	change value 2	rate 1	rate 2	change value 1	change value 2	rate 1	rate 2	change value 1	change value 2	rate 1	rate 2
WRAP	-0.6±0.4	-0.3±0.4	-2.6±1.7	-1.2±1.6	-0.4±0.6	0.8±0.3	-1.5±2.2	2.7±1.2	-0.6±0.4 ***	0.5±0.1	-1.7±1.1 ***	1.5±0.4	-1.0±0.6 ***	1.2±0.1	-2.9±1.9 ***	3.7±0.4
MCS	-0.5±0.4	-0.4±0.6	-2.0±1.8	-1.8±2.7	-0.7±0.3	-0.5±0.6 ***	-2.4±1.1	-1.7±1.9 ***	0.0±0.4	0.0±0.5 ***	-0.3±1.0	-0.1±1.4 ***	-0.1±0.7	-0.2±1.1 ***	-0.7±1.8	-0.5±3.3 ***

Thirdly, the independent t-test was conducted to hypothesize that circumference reduction rate of the left and right legs significantly differed between using WRAP and MCS in the experimental and control groups.

Figure 4.30(a) demonstrated that there was no significant change between left leg and right leg when wearing WRAP in the experiment group. When wearing MCS with LLMs, the right leg ($Mean_{1st}$=-1.3, SD_{1st}=2.1) had more circumference reduction rate than wearing WRAP ($Mean_{1st}$=-0.1, SD_{1st}=0.6) at point B after completing 1 set of LLMs, as shown in **Table 4.23**. In addition, at point C ($0.001< p_{1st} <0.01$) and point D ($0.001< p_{2nd} <0.01$), the left leg had significant circumference reduction rate than the right leg in **Figure 4.30(b)**. The detailed data is in **Table 4.23**.

Applying compression without LLMs in the control group, there was obvious generation of circumference in WRAP after 30 minutes sitting, as shown in **Figure 4.31(a).** When wearing MCS without LLMs in **Figure 4.31(b)**, the left leg ($Mean_{2nd}$=-2.8, SD_{2nd}=1.6, $p_{2nd} <0.05$) had more circumference reduction rate than right one ($Mean_{2nd}$=2.0, SD_{2nd}=1.3) at point B1 after sitting 30 minutes. And there was the same trend at point D after sitting 30 minutes (left leg: $Mean_{2nd}$=-3.0, SD_{2nd}=1.4, $p_{2nd} <0.001$, right leg: $Mean_{2nd}$=3.8, SD_{2nd}=0.3). The detailed data of the control group is listed in **Table 4.24**.

After completing 2 sets of LLMs/30 minutes sitting in two groups, the left leg wearing MCS had obvious circumference reduction rate compared to the right one at point D. Relatively, the experimental group that completed LLMs tended to reduce circumference, however, the control group only applied compression making the circumference recovery (from reduction circumference to generation circumference) easier.

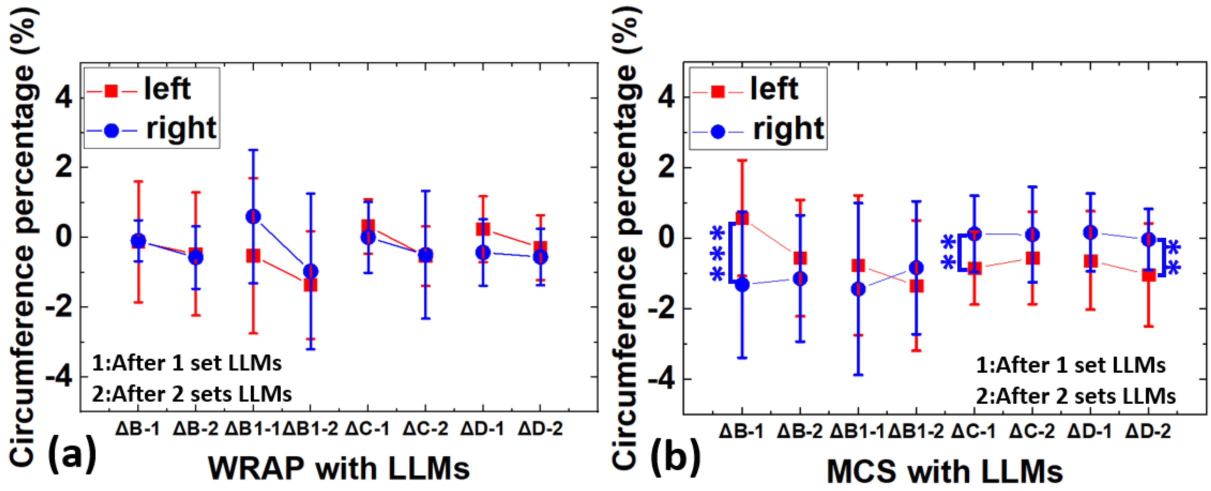

Figure 4. 30 Influence of WRAP and MCS conditions on the left and right lower limb (calf) circumference reduction rate (circumference percentage) after completing 1/2 sets LLMs in the experimental group, (a) is WRAP, (b) is MCS.

Table 4. 23 Detailed data of different wearing conditions on the left (L) and right (R) lower limb (calf) circumference reduction rate after completing 1/2 sets LLMs and p-value.

Experimental group, circumferences change rate, unit: %, "-" = reduce, 1: After 1 set LLMs, 2: After 2 sets LLMs																
Point	B				B1				C				D			
Different conditions	L1	L2	R1	R2	L1	L2	R1	R2	L1	L2	R1	R2	L1	L2	R1	R2
WRAP	-0.1±1.7	-0.5±1.8	-0.1±0.6	-0.6±0.9	-0.5±2.2	-1.4±1.5	0.6±1.9	-1.0±2.2	0.3±0.8	-0.5±0.9	0.0±1.0	-0.5±1.8	0.2±0.9	-0.3±0.9	-0.4±1.0	-0.6±0.8

MCS	0.6±1.6	-0.6±1.7	-1.3±2.1***	-1.1±1.8	-0.8±2.0	-1.3±1.9	-1.4±2.4	-0.8±1.9	-0.8±1.0**	-0.6±1.3	0.1±1.1	0.1±1.4	-0.6±1.4	-1.0±1.5**	0.2±1.1	0.0±0.9

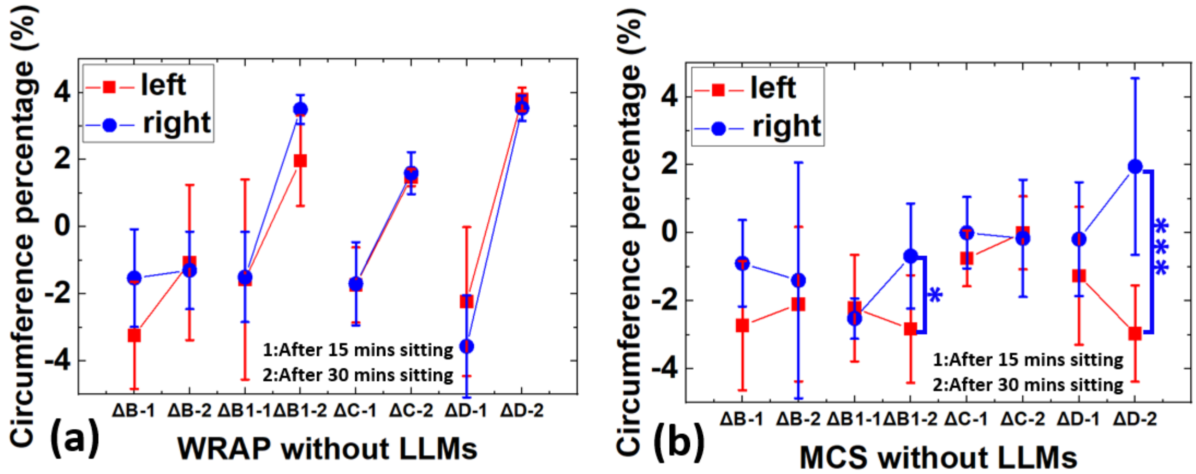

Figure 4. 31 Influence of WRAP and MCS conditions on the left and right lower limb (calf) circumference reduction rate (circumference percentage) after 15/30 minutes sitting in the control group, (a) is WRAP, (b) is MCS.

Table 4. 24 Detailed data of different wearing conditions on the left (L) and right (R) lower limb (calf) circumference reduction rate after 15/30 minutes sitting and p-value.

Control group, circumferences change rate, unit: %, "-" = reduce, 1: after 15 minutes sitting, 2: after 30 minutes sitting																
Point	B				B1				C				D			
Different conditions	L1	L2	R1	R2	L1	L2	R1	R2	L1	L2	R1	R2	L1	L2	R1	R2
WRAP	-3.2±1.6	-1.1±2.3	-1.5±1.5	-1.3±1.2	-1.6±3.0	2.0±1.3	-1.5±1.3	3.5±0.4	-1.7±1.1	1.5±0.3	-1.7±1.2	1.6±0.6	-2.2±2.2	3.8±0.3	-3.6±1.5	3.5±0.4
MCS	-2.7±1.9	-2.1±2.3	-0.9±1.3	-1.4±3.5	-2.2±1.6	-2.8±1.6*	-2.5±0.6	-0.7±1.5	-0.8±0.8	0.0±1.1	0.0±1.1	-0.2±1.7	-1.3±2.0	-3.0±1.4***	-0.2±1.7	2.0±2.6

Fourthly, it was hypothesized that circumference reduction rate of different gender was significantly different between using WRAP and MCS in the experimental group.

The independent t-test revealed that the females had more effect on circumference reduction rate when applying combination of WRAP and 2 sets of LLMs, as shown in **Figure 4.32(a).** And there was significant circumference reduction rate in female group when wearing MCS at point B ($p_{1st} < 0.05$, $p_{2nd} < 0.05$) and B1($p_{1st} < 0.05$, $p_{2nd} < 0.001$) in **Figure 4.32(b)**. Both WRAP and MCS could influence on the reduction oedema at B point in females. Males without LLMs data was not enough to analyse. Therefore, the control group had not been analysed. Detailed data of the experimental group is listed in **Table 4.25**.

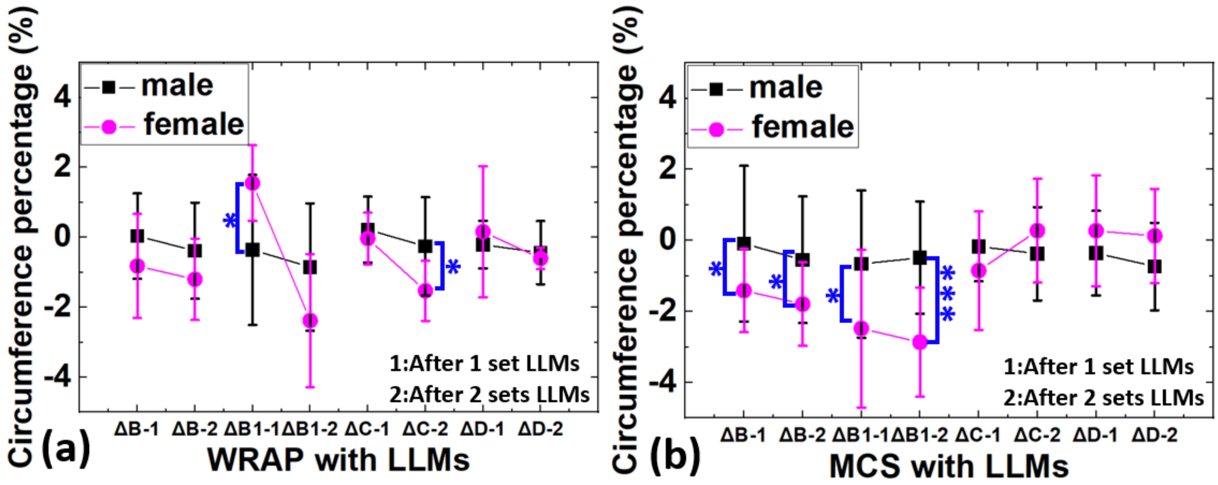

Figure 4. 32 Influence of WRAP and MCS conditions on the males and females' lower limb (calf) circumference reduction rate (circumference percentage) after completing 1/2 sets LLMs in the experimental group, (a) is WRAP, (b) is MCS.

Table 4. 25 Detailed data of different wearing conditions on the males and females' lower limb (calf) circumference reduction rate after completing 1/2 sets LLMs and p-value.

Experimental group, circumferences change rate, unit: %, "-" = reduce, 1: After 1 set LLMs, 2: After 2 sets LLMs																
Point	B				B1				C				D			
Different conditions	M1	M2	F1	F 2	M1	M2	F1	F 2	M1	M2	F1	F 2	M1	M2	F1	F 2

WRAP	0.0±1.2	-0.4±1.4	-0.8±1.5	-1.2±1.2	-0.4±2.1*	-0.9±1.8	1.6±1.1	-2.4±1.9	0.2±0.9	-0.3±1.4	0.0±0.7	-1.5±0.9*	-0.2±0.7	-0.4±0.9	0.2±1.9	-0.6±0.3
MCS	-0.1±2.2	-0.5±1.8	-1.4±1.2*	-1.8±1.2*	-0.7±2.1	-0.5±1.6	-2.5±2.2*	-2.9±1.5***	-0.2±1.0	-0.4±1.3	-0.9±1.7	0.3±1.5	-0.4±1.2	-0.7±1.2	0.3±1.6	0.1±1.3

4.8 Result

4.8.1 Data analysis of young healthy subjects

In this chapter, the following analyses were conducted: 1) Comparative analysis examining alterations in lower limb volume and circumference change rate after the application of WRAP/MCS/bare leg conditions. 2) Statistical significance analysis of various compression stockings with the integration of lower limb movements (LLMs). 3) Evaluation of the impact of different gender and left/right legs on the oedema mitigation. According to these analyses, their results and discussions are summarized.

Measurement: Volume measurement using the water displacement volumetry method is simple but needs sufficient space, water resources, and disinfection in time. In addition, it should be considered how to decrease the foot volume. Circumference measurement can be a good method of assessment for evaluating oedema situation. It can reflect the change at B, B1, C and D points in detail.

Analysis on volume measurement: Significant volume reduction was observed when LLMs were conducted in the experimental group. 1) The VC before and after LLMs/sitting under WRAP/MCS/No-wearing conditions were analysed between the experimental and control groups, and results revealed an extremely significant difference ($p < 0.001$) in VC for both groups. However, the experimental group exhibited greater mean reduction values than the control group. 2) The statistical significance analysis of the lower limb volume reduction value and rate under WRAP/MCS/No-wearing conditions indicated no significant differences among conditions within each group. However, WRAP (Mean: -66.3 cm^3 SD: 51.0 cm^3) induced more volume reduction than MCS (Mean: -58.5 cm^3 SD: 42.0 cm^3) and bare leg (Mean: -63.5 cm^3 SD: 50.5 cm^3) in the group within LLMs, while MCS (Mean: -51.2 cm^3 SD: 46.8 cm^3) showed more reduction than the other two conditions (WRAP: Mean: -41.9 cm^3 SD: 35.6cm^3, bare leg: Mean: -42.4 cm^3 SD: 57.6 cm^3) in the group without LLMs. 3) Significant differences were observed between the left and right legs when wearing WRAP or MCS, left legs generally exhibited more volume reduction than right legs. This phenomenon might be attributed to the subject's sample, as all participants were right-handed, potentially resulting in greater development of the muscles in the right leg. Consequently, it was reasonable that the right leg muscles exhibit a greater expansion after completing LLMs. Furthermore, the males had significant lower limb volume reduction rate compared to females with bare lower limbs regardless of whether they conducted the LLMs ($p < 0.05$).

Analysis on circumference measurement: It indicated significant circumference reduction when carrying out LLMs in the experimental group, and applying compression was better than bare leg for oedema reduction. 1) CC before and after LLMs/sitting under WRAP/MCS/No-wearing conditions were statistically analysed between the experimental and control groups, and results showed an extremely significant difference ($p < 0.001$) in CC before and after LLMs/sitting for both groups. 2) The statistical significance analysis of the lower limb circumference reduction value and rate under WRAP/MCS/No-wearing conditions presented that wearing MCS with LLMs (Mean: -1.3% SD: 0.8%) showed greater circumference reduction compared to wearing WRAP with LLMs (Mean: -0.9% SD: 0.7%) at point C, and wearing WRAP with LLMs (Mean: -1.1% SD: 0.7%) was more effective in oedema reduction than bare leg with LLMs (Mean: -0.6% SD: 0.6%) at point D. 3) In both groups, there was a very significant circumference reduction rate in the left leg than the right one at point D when wearing WRAP ($0.001 < p < 0.01$). When wearing the MCS of both groups, males had an extremely significant circumference reduction at point C compared to females ($p < 0.001$). Besides, with bare legs of both groups, females showed significant circumference reduction rate than males at B1 point ($p < 0.05$). 4) Regarding the preference between wearing MCS and WRAP, more than half of young healthy subjects preferred WRAP due to its convenience of wearing on.

4.8.2 Data analysis of elderly subjects with oedema

Analysis on circumference measurement: It demonstrated the integration of MCS and LLMs in the experimental group showed a consistent oedema reduction, while the control group exhibited temporary efficacy without sustained reduction. 1) Application of MCS with 2 sets of LLMs significantly reduced the circumference at various points B, B1, and D. MCS ($Mean_{1st}$=-1.1%, SD_{1st}=2.2%) showed a significant circumference reduction compared to WRAP ($Mean_{1st}$=0.1%, SD_{1st}=2.1%) at point B1 after completing 1 set of LLMs ($p_{1st} < 0.05$). WRAP and MCS showed a significant circumference reduction in the control group but without sustained efficacy over time. Significant circumference increases were observed after 30 minutes of sedentary behaviour, especially when wearing WRAP. 2) At point D, the left leg wearing MCS had very significant circumference reduction rate compared to the right one both after completing 2 sets of LLMs and after 30 minutes of sitting ($0.001 < p_{2nd} < 0.01$). Gender differences suggested potentially greater efficacy in females, particularly with wearing MCS combined with LLMs.3) Completing 2 sets of LLMs had better efficacy than 1 set on oedema reduction.

4.8.3 Relationship between fluctuation pressure and lower limb circumference reduction rate

The dynamic pressures of point C were measured when subjects carried on the lower limb movements (LLMs) in the experimental groups. Through analysis of the relationship of compression pressure values and circumference reduction rate at point C, the LLMs could produce pressure fluctuations, which can help to reduce oedema. During the skeletal muscles movement, a reduction in the average pressure applied by the stockings on the skin is observed, which is no longer constant but variable [10]. Obviously, the mean values of measured dynamic pressure at point C decreased compared to the initial IP values at the same point before starting LLMs in both trial tests.

However, this fluctuating pressure effectively reduced the circumference. From **Figure 4.33** to **Figure 4.44** shows the dynamic mean pressure values at point C during LLMs when wearing WRAP and MCS in the 1st/2nd test, and every corresponding reduction rate of circumference at point C. **Figure 4.33~Figure 4.36** are for the 4 young healthy subjects and **Figure 4.37~Figure 4.44** are for the elderly subjects. Corresponding data records are listed in the related **Table 4.26**~**Table 4.37**.

Based on the data, the young subjects produced higher pressure on the skin through the integration of the compression stockings with LLMs. The dynamic mean pressures were measured at 13.3 mmHg in WRAP and 10.5 mmHg in MCS at point C. This increased compression pressure is attributed to the more activating skeletal muscles in young healthy subjects. However, WRAP's non-stretchable elasticity makes it susceptible to loosening during LLMs. Despite the high mean dynamic pressure, it can slightly reduce pressure on the skin with movement, leading to a low circumference reduction rate.

The elderly group were pressured to a smaller compression combined with LLMs than the young group due to the little skeletal muscle contraction changes. The elderly subjects resulted in dynamic mean pressures of 5.1 mmHg (=679.9 Pa) in WRAP and 6.5 mmHg (=866.6 Pa) in MCS at point C. These dynamic mean pressure values containing compression stockings and muscles' contraction were higher than the critical pressure value (550 Pa) which can start oedema reduction in normal physiological parameters in the numerical simulation in Chapter 3 (see in **Figure 3.11**).

Therefore, the results indicate that muscle movement effectively applies compression pressure on the tissues, and the approach of low-pressure compression with skeletal muscle movement can effectively achieve oedema reduction.

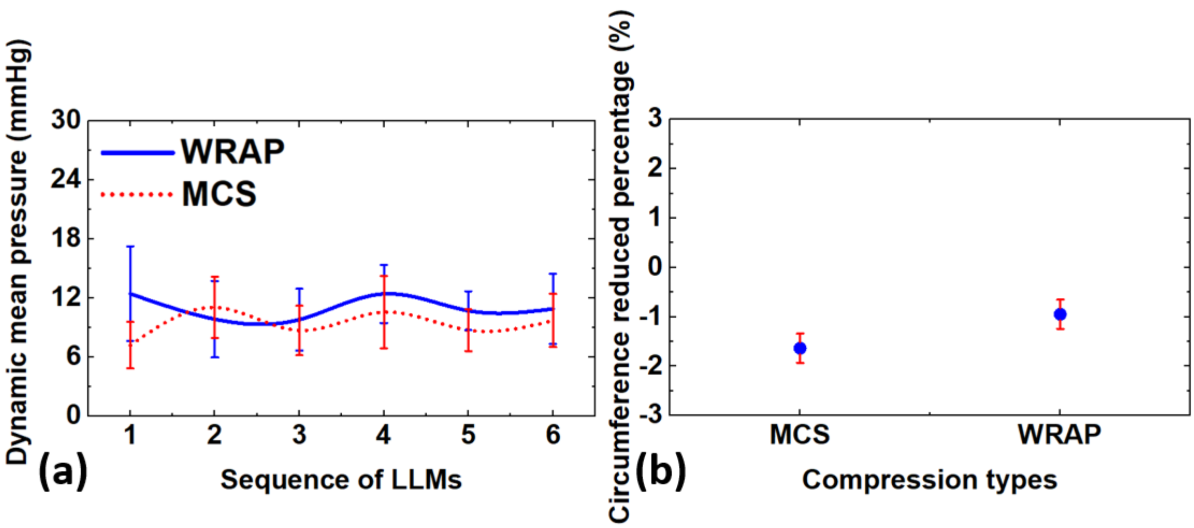

Figure 4. 33 (a) is the dynamic mean pressure change at point C during LLMs when wearing WRAP and MCS in the 1st test, and (b) is the corresponding circumference reduction rate at point C (subject 1).

Table 4. 26 Data record of **Figure 4.33.**

	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
WRAP	11.2 (9.8, 12.5)	-0.9±0.3

MCS	9.2 (7.2, 11.1)	-1.6±0.3

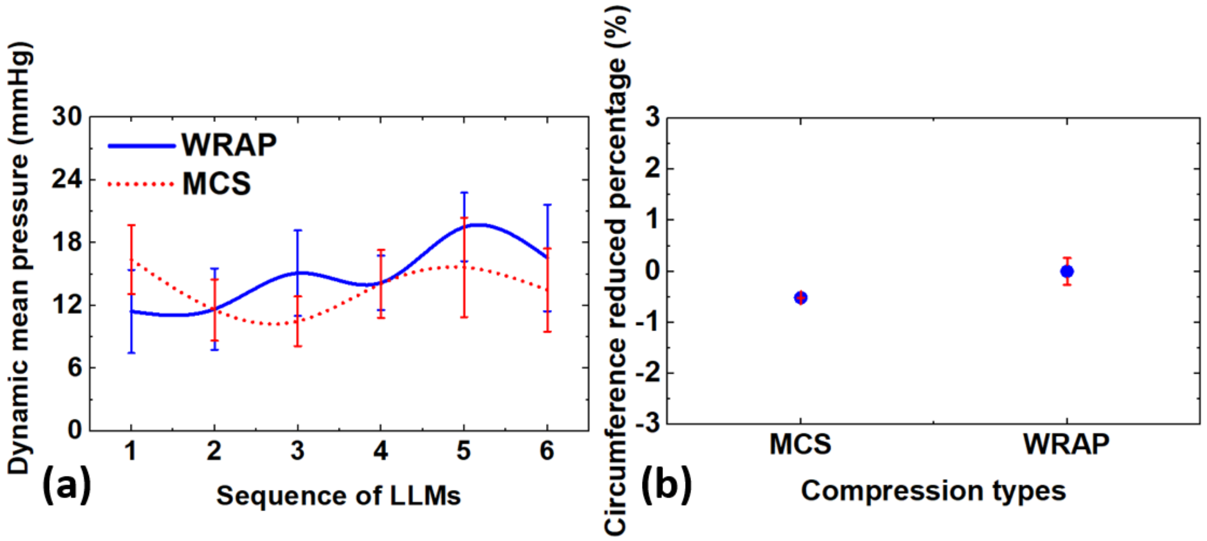

Figure 4. 34 (a) is the dynamic mean pressure change at point C during LLMs when wearing WRAP and MCS in the 1st test, and (b) is the corresponding circumference reduction rate at point C (subject 2).

Table 4. 27 Data record of **Figure 4.34.**

	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
WRAP	15.5 (11.4, 19.5)	0.0±0.3
MCS	13.5 (10.5, 16.4)	-0.5±0.0

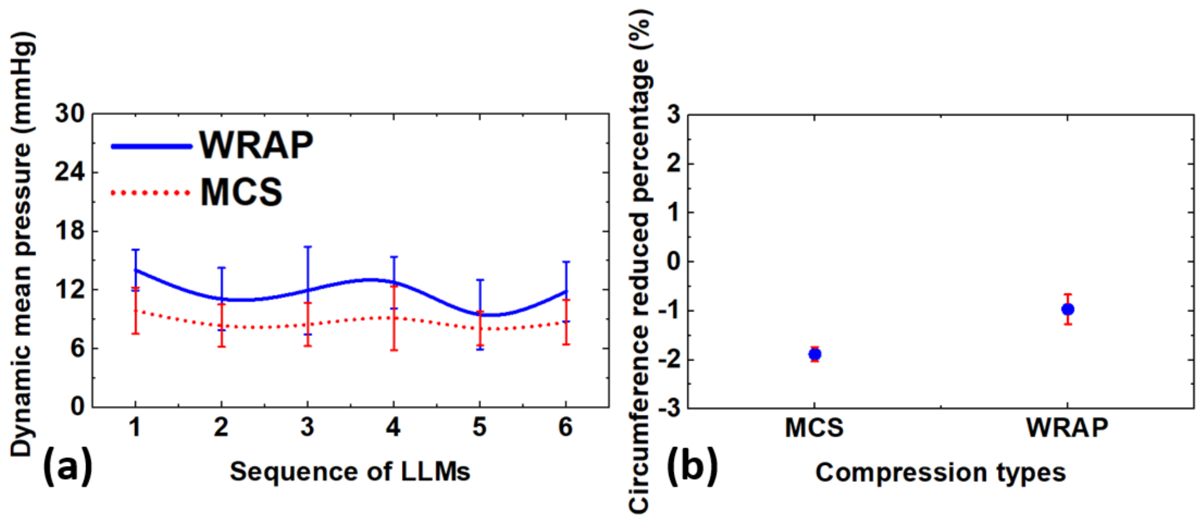

Figure 4. 35 (a) is the dynamic mean pressure change at point C during LLMs when wearing WRAP and MCS in the 1st test, and (b) is the corresponding circumference reduction rate at point C (subject 3).

Table 4. 28 Data record of **Figure 4.35.**

	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
WRAP	11.8 (9.5, 14.1)	-1.0±0.3
MCS	9.0 (8.1, 9.9)	-1.9±0.1

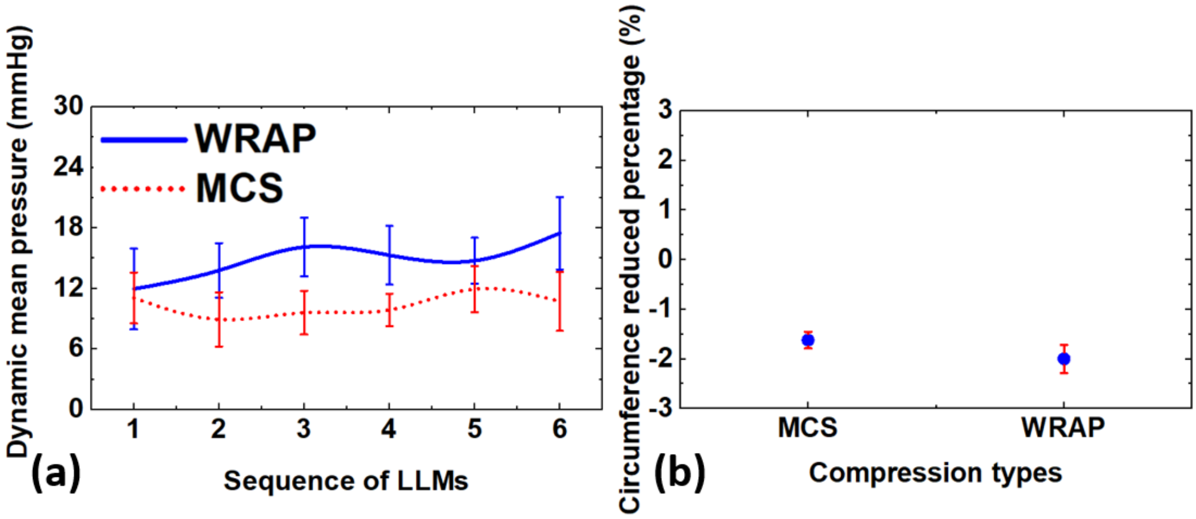

Figure 4. 36 (a) is the dynamic mean pressure change at point C during LLMs when wearing WRAP and MCS in the 1st test, and (b) is the corresponding circumference reduction rate at point C (subject 4).

Table 4. 29 Data record of **Figure 4.36.**

	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
WRAP	14.8 (12, 17.5)	-2.0±0.3
MCS	10.4 (8.9, 11.9)	-1.6±0.2

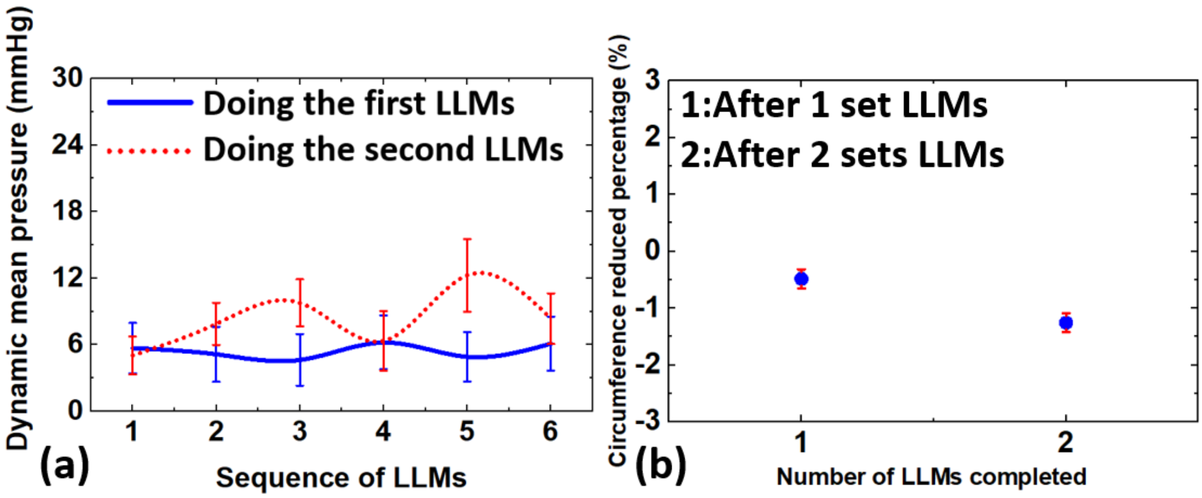

Figure 4. 37 (a) is the dynamic mean pressure change at point C during 1/2 sets LLMs when wearing MCS in the 2nd test, and (b) is the corresponding circumference reduction rate at point C (subject 5).

Table 4. 30 Data record of **Figure 4.37.**

MCS	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
After 1 set LLMs	5.4 (4.6, 6.2)	-0.5±0.2
After 2 sets LLMs	8.7 (5.0, 12.3)	-1.3±0.2

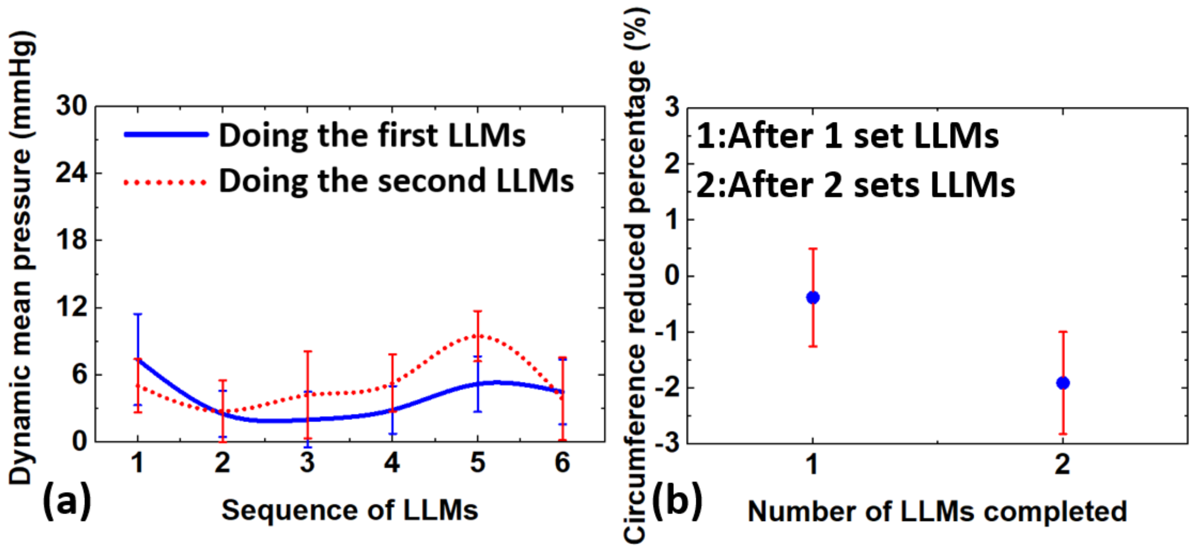

Figure 4. 38 (a) is the dynamic mean pressure change at point C during 1/2 sets LLMs when wearing WRAP in the 2nd test, and (b) is the corresponding circumference reduction rate at point C (subject 6).

Table 4. 31 Data record of **Figure 4.38.**

WRAP	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
After 1 set LLMs	4.7 (2.0, 7.4)	-0.4±0.9
After 2 sets LLMs	6.2 (2.8, 9.5)	-1.9±0.9

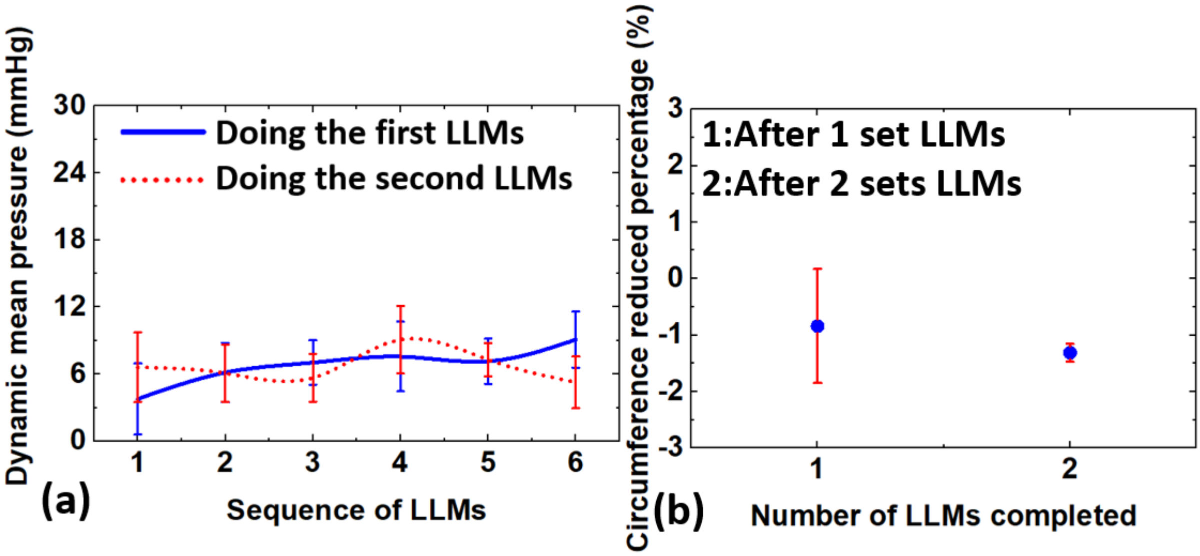

Figure 4. 39 (a) is the dynamic mean pressure change at point C during 1/2 sets LLMs when wearing MCS in the 2nd test, and (b) is the corresponding circumference reduction rate at point C (subject 7).

Table 4. 32 Data record of **Figure 4.39.**

MCS	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
After 1 set LLMs	6.5 (3.8, 9.1)	-0.8±1.0
After 2 sets LLMs	7.2 (5.3, 9.1)	-1.3±0.2

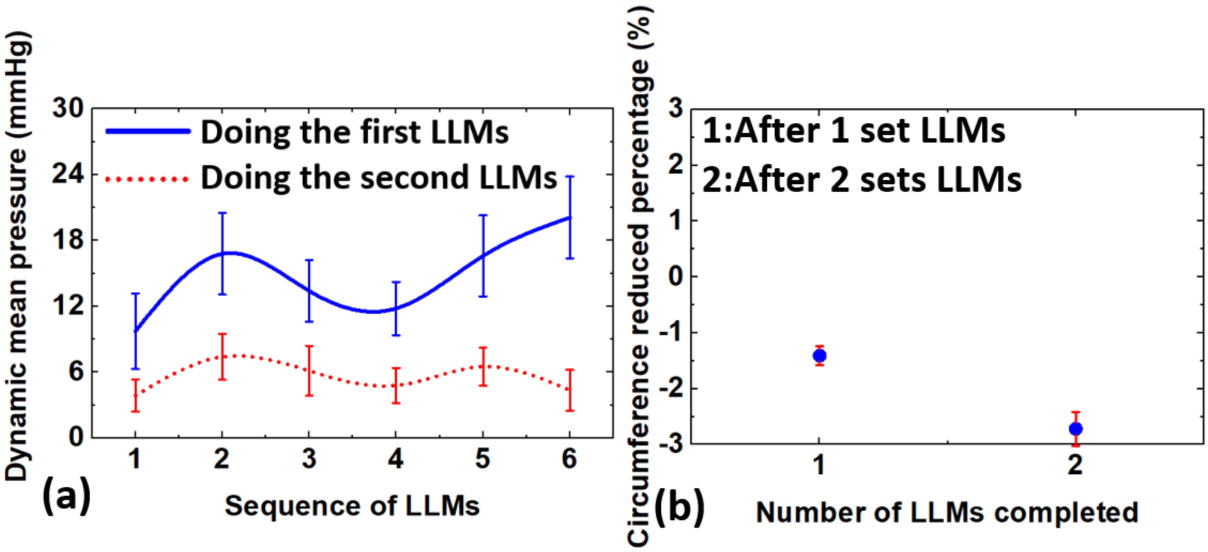

Figure 4. 40 (a) is the dynamic mean pressure change at point C during 1/2 sets LLMs when wearing WRAP in the 2nd test, and (b) is the corresponding circumference reduction rate at point C (subject 8).

Table 4. 33 Data record of **Figure 4.40.**

WRAP	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
After 1 set LLMs	14.9 (9.7, 20.1)	-1.4±0.2
After 2 sets LLMs	5.7 (3.9, 7.4)	-2.7±0.3

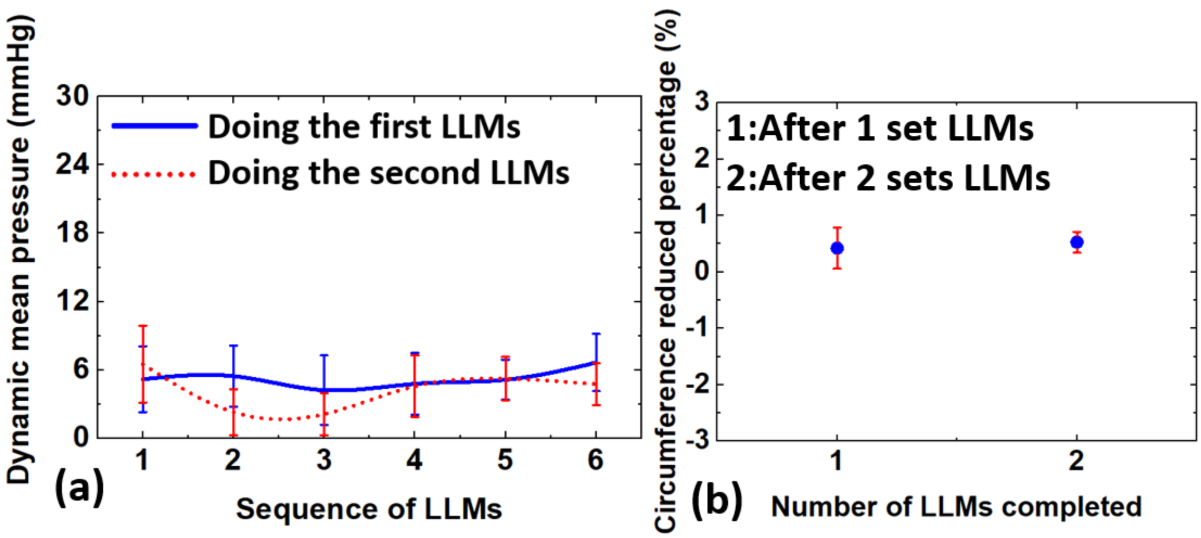

Figure 4. 41 (a) is the dynamic mean pressure change at point C during 1/2 sets LLMs when wearing MCS in the 2nd test, and (b) is the corresponding circumference reduction rate at **point C (subject 9).**

Table 4. 34 Data record of **Figure 4.41.**

MCS	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
After 1 set LLMs	5.5 (4.2, 6.7)	0.4±0.4
After 2 sets LLMs	4.3 (2.1, 6.5)	0.5±0.2

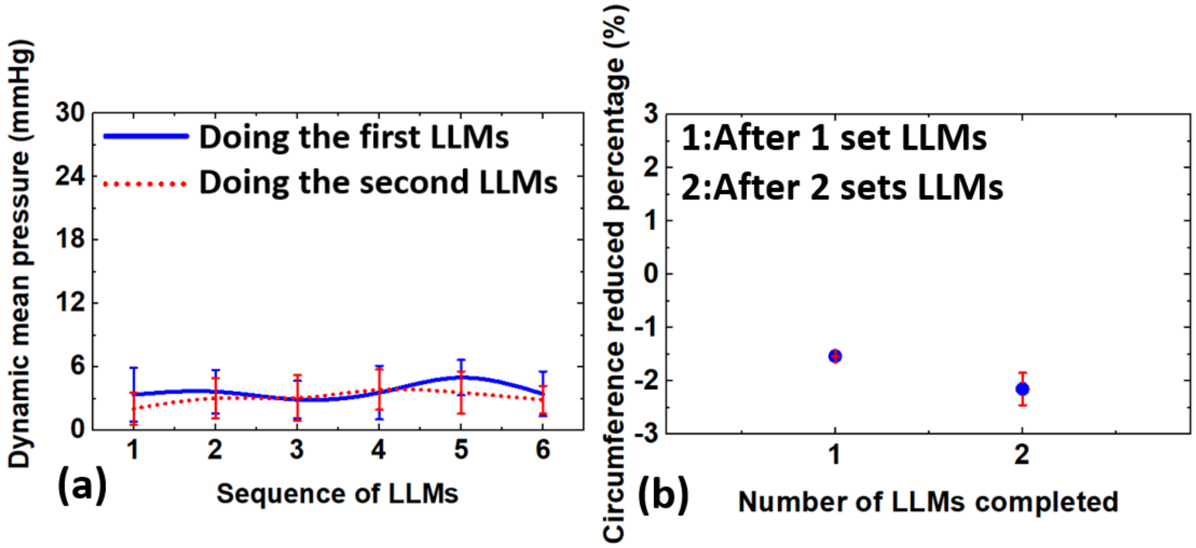

Figure 4. 42 (a) is the dynamic mean pressure change at point C during 1/2 sets LLMs when wearing MCS in the 2nd test, and (b) is the corresponding circumference reduction rate at point C (subject 10).

Table 4. 35 Data record of **Figure 4.42.**

MCS	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
After 1 set LLMs	4.0 (2.9, 5.0)	-1.5±0.0
After 2 sets LLMs	2.9 (2.0, 3.8)	-2.2±0.3

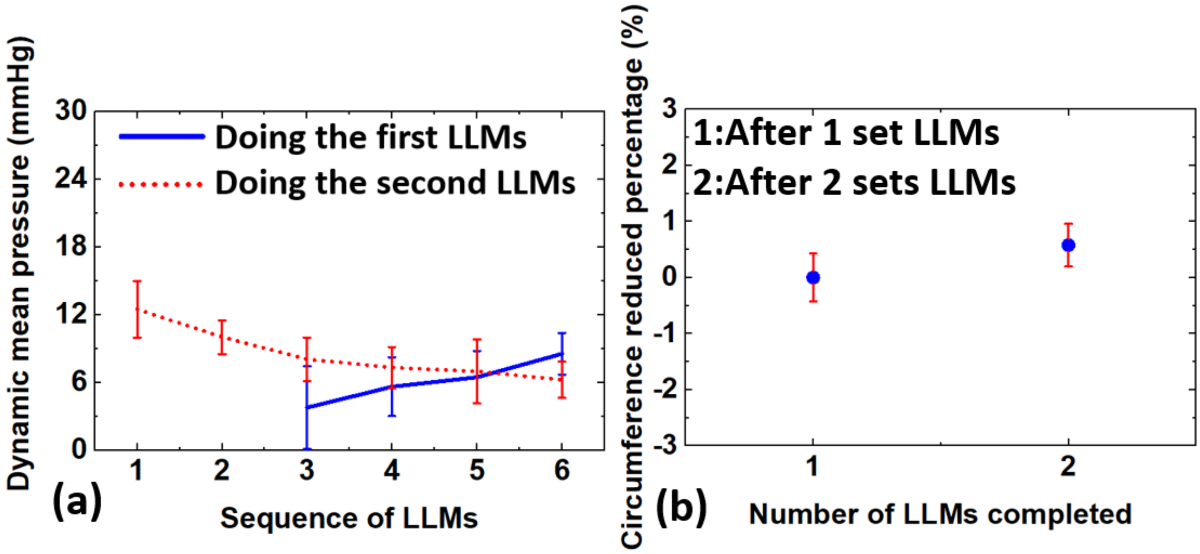

Figure 4. 43 (a) is the dynamic mean pressure change at point C during 1/2 sets LLMs when wearing MCS in the 2nd test, and (b) is the corresponding circumference reduction rate at point C (subject 11).

Table 4. 36 Data record of **Figure 4.43.**

MCS	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
After 1 set LLMs	6.2 (3.8, 8.6)	0.0±0.4
After 2 sets LLMs	9.4 (6.3, 12.5)	0.6±0.4

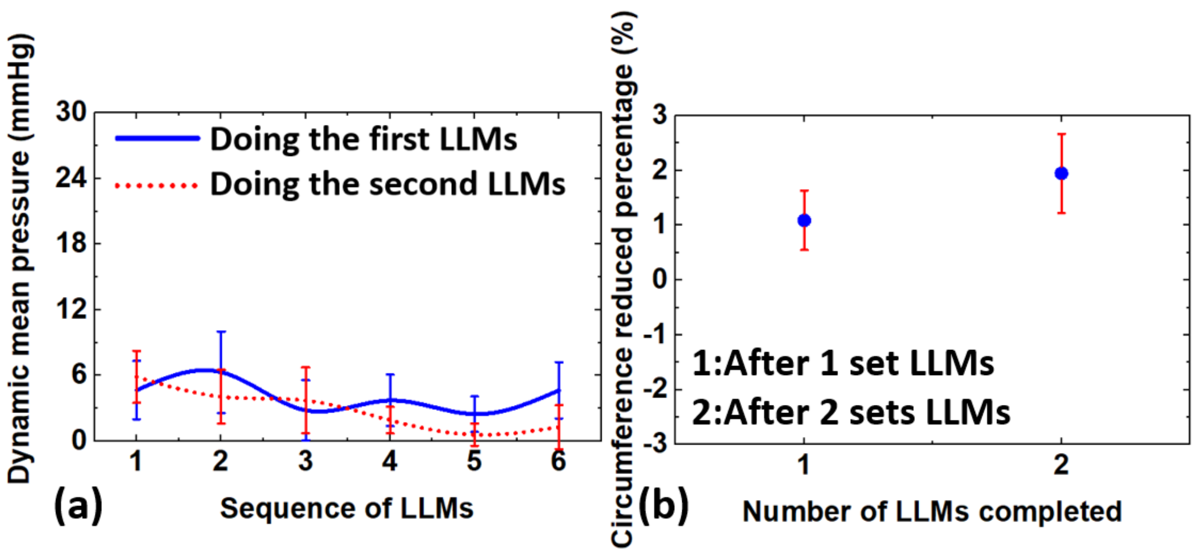

Figure 4. 44 (a) is the dynamic mean pressure change at point C during 1/2 sets LLMs when wearing WRAP in the 2nd test, and (b) is the corresponding circumference reduction rate at point C (subject 12).

Table 4. 37 Data record of **Figure 4.44.**

WRAP	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
After 1 set LLMs	4.4 (2.5, 6.3)	1.1±0.5
After 2 sets LLMs	3.3 (0.6, 5.9)	1.9±0.7

4.8.4 Compare of gradient pressure and uniform pressure

The compression pressure value of WRAP could be manually adjusted, it presented the gradient pressure in the whole trial test for consistency to the MCS. In this part, the WRAP was adjusted to uniform pressure on the calf from point B to point D for comparison to the gradient pressure distribution on the circumference reduction. Because of only comparing the two subjects, the results were not able to be analysed statistically, however, during the lower limb movements (LLMs), the interface pressure on the lower limb at point C performed that the uniform pressure applied by the WRAP obviously was higher than the gradient pressure. The circumference reduction rate was greater correspondently. **Table 4.38** and **Table 4.39** are the dynamic mean pressure with different movements and corresponding circumference reduction rate when applying uniform and gradient pressure. **Figure 4.45(a)** and **(b)** are the two legs' calf circumference (B, B1, C, D) change value under gradient pressure and uniform pressure with WRAP condition for subject 1, and **Figure 4.45(d)** and **(e)** are their circumference reduction rate. **Figure 4.45(c)** and **(f)** are the dynamic mean pressure at point C during LLMs when applying gradient and uniform pressure, and the corresponding circumference reduction rate at point C for subject 1, respectively. In which, **Figure 4.45(f)** is the red dash rectangular data of point C in **Figure 4.45(d). Figure 4.45(g)** to **Figure 4.45(l)** are the same relative data of subject 4. **Figure 4.45(l)** is the red dash rectangular data of point C in **Figure 4.45(j).**

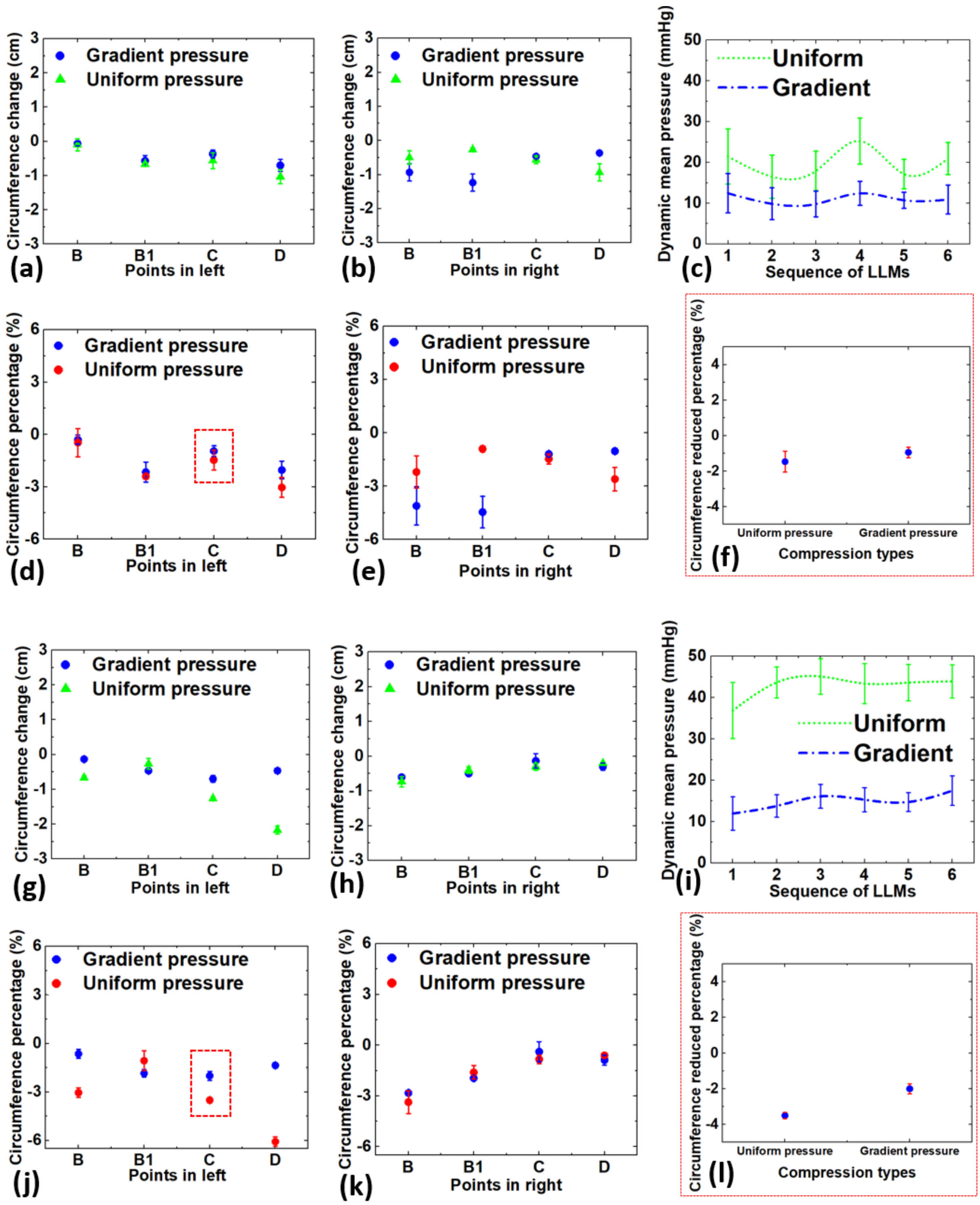

Figure 4. 45 The circumference change value, (a) and (b) for subject 1, (g) and (h) for subject 4), and circumference reduction rate (circumference percentage), (d) and (e) for subject 1, (j) and (k) for subject 4. The dynamic mean pressure during LLMs with circumference reduction rate, (c) and (f) for subject 1, (i) and (l) for subject 4.

Table 4. 38 Data record of **Figure 4.45(c)** and **Figure 4.45(f).**

WRAP	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
Uniform pressure	20.9 (16.5, 25.3)	-1.5±0.6
Gradient pressure	11.2 (9.8, 12.5)	-0.9±0.3

Table 4. 39 Data record of **Figure 4.45(i)** and **Figure 4.45(l).**

WRAP	Dynamic mean pressure with different movements (mmHg)	Circumference change rate (%)
Uniform pressure	41.0 (36.9, 45.1)	-3.5±0.2
Gradient pressure	14.8 (12, 17.5)	-2.0±0.3

4.9 Discussion

This chapter evaluated whether the critical pressure value of starting oedema was suitable in Chapter 3. It was conducted designing and executing trial tests for young healthy and elderly mild oedema subjects. Then, comparative assessments of lower limb volume and circumference measurement methods under 3 different conditions (WRAP/MCS/No-wearing), statistical significance analysis in different compression stockings with or without the integration of lower limb movements (LLMs) on oedema mitigation, and an evaluation of the left/right legs and different gender’s impact on oedema reduction were analysed.

1)Volume measurement using the water displacement volumetry method was discussed, highlighting its simplicity but the requirement for enough space, water resources, and timely disinfection. Circumference measurement was considered a viable assessment method, particularly for detailed changes at different points of lower limb.

2)It was combined numerical simulation to provide a substantial volume of trial test data and conducted a thorough statistical analysis. The results revealed that circumference measurement analysis further supported the efficacy of the integration of the compression stockings and LLMs, showing the sustained reduction in lower limb oedema. The number of LLMs, different gender and left/right leg were also statistically analysed as factors influencing efficacy on oedema reduction.

3)The dynamic pressure was measured and analysed the corresponding circumference reduction rate for every subject in the experimental group. The dynamic mean pressure values declined and fluctuated during LLMs. The dynamic mean pressure values containing compression stockings and muscles' contraction were higher than the critical pressure of 550 Pa in the simulation in Chapter 3. These results show that the integration of the low-pressure compression with skeletal muscle movement can reduce oedema effectively. In addition, the trial results validate the critical pressure required to reduce oedema effectively.

4)The results can provide compelling evidence supporting the efficacy of combining low-pressure compression therapy with skeletal muscle movement in oedema reduction. It holds promises for preventing or reducing lower limb oedema and offers valuable references for doctors and researchers investigating compression therapy.

4.10 Summary

In this chapter, the lower limb movements (LLMs) and two trial tests were designed and conducted. The different trial test designs for young healthy and elderly mild oedema subjects, the steps of specific LLMs, and applied measurements were elaborated systemically. Then, their efficacy in reducing lower limb oedema was statistically analysed utilizing volume and circumference measurements.

Data analysis revealed that: Firstly, young male subjects showed significant reduction rate in lower limb volume compared to females when bare leg, regardless of whether they conducted LLMs. Secondly, in young subjects when wearing MCS with LLMs, there was significant reduction rate in circumference at point C compared to wearing WRAP with LLMs; and wearing WRAP with LLMs showed significant reduction rate in circumference at point D compared to bare leg with LLMs in the 1st trial test. However, more than half of young subjects preferred WRAP due to its convenience in wearing. Thirdly, during the LLMs, the interface pressure on the lower limb at point C demonstrated that the uniform pressure by the WRAP was higher than the gradient pressure, resulting in correspondingly larger reduction rate of the circumference. Fourthly, integrating low-pressure (Class I) compression with conducting 2 sets of LLMs significantly reduced circumference at points B, B1, and D, particularly when wearing MCS in the 2nd test involving elderly subjects. In addition, oedema recurrence was observed after 30 minutes for the elderly subjects in the absence of LLMs, and completing 2 sets of LLMs was more effective than 1 set in oedema reduction. Fifthly, for both young healthy subjects wearing WRAP and elderly subjects wearing MCS, their left leg had very significant circumference reduction rate at point D compared to the right one, regardless of whether LLMs were conducted. Finally, the dynamic mean pressures at point C were measured at 13.3 mmHg (WRAP) and 10.5 mmHg (MCS) in the young group. The elderly group resulted in dynamic mean pressures of 5.1 mmHg (=679.9 Pa) in WRAP and 6.5 mmHg (=866.6 Pa) in MCS at point C.

This chapter has validated the efficacy of the critical pressure threshold of 550 Pa in simulation with normal physiology parameters, as previously discussed in Chapter 3. It has been demonstrated that muscle movement effectively exerts compression pressure on the tissues. Furthermore, the integration of low-pressure compression with skeletal muscle movement has proven to be effective in oedema reduction through practical trials.

Reference

[1] N. W. Dail, T. A. Agnew, and R. T. Floyd, *Kinesiology for manual therapies* (massage therapy series.). New York, N.Y: McGraw-Hill, 2011.

[2] J. E. Muscolino, *Kinesiology : the skeletal system and muscle function*, 3rd edition. ed. St. Louis: Elsevier Inc., 2017.

[3] J. A. O'Brien, H. E. Edwards, K. J. Finlayson, and G. Kerr, "Understanding the relationships between the calf muscle pump, ankle range of motion and healing for adults with venous leg ulcers: A review of the literature," *Wound practice & research,* vol. 20, no. 2, pp. 80-85, 2012.

[4] W. L. Olszewski, "Contractility Patterns of Human Leg Lymphatics in Various Stages of Obstructive Lymphedema," *ANN NY ACAD SCI,* vol. 1131, no. 1, pp. 110-118, 2008, doi: 10.1196/annals.1413.010.

[5] D. Yang, Y. K. Vandongen, and M. C. Stacey, "Variability and reliability of air plethysmographic measurements for the evaluation of chronic venous disease," *Journal of vascular surgery,* vol. 26, no. 4, pp. 638-642, 1997, doi: 10.1016/S0741-5214(97)70063-6.

[6] B. C. E. Quilici, C. Gildo, J. M. P. De Godoy, B. S. Quilici, and C. R. Augusto, "Comparison of reduction of edema after rest and after muscle exercises in treatment of chronic venous insufficiency," *International archives of medicine,* vol. 2, no. 1, pp. 18-18, 2009, doi: 10.1186/1755-7682-2-18.

[7] T. F. O'Donnell, Jr, D. A. Rosenthal, A. D. Callow, and B. L. Ledig, "Effect of Elastic Compression on Venous Hemodynamics in Postphlebitic Limbs," *JAMA,* vol. 242, no. 25, pp. 2766-2768, 1979, doi: 10.1001/jama.1979.03300250022022.

[8] J. Winkel, "SWELLING OF THE LOWER LEG IN SEDENTARY WORK-A PILOT STUDY," *Journal of Human Ergology,* vol. 10, no. 2, pp. 139-149, 1981, doi: 10.11183/jhe1972.10.139.

[9] D. Bergqvist, "Antiswelling effect of StepIt--an active foot pump system," *Journal of the American Podiatric Medical Association,* vol. 99, no. 1, pp. 20-22, 2009, doi: 10.7547/0980020.

[10] J. M. P. De Godoy, D. M. Braile, F. B. Perez, and M. De Fátima Guerreiro Godoy, "Effect of walking on pressure variations that occur at the interface between elastic stockings and the skin," *International wound journal,* vol. 7, no. 3, pp. 191-193, 2010, doi: 10.1111/j.1742-481X.2010.00673.x.

[11] Y.-H. Lin, C.-Y. Chen, and M.-H. Cho, "Effectiveness of leg movement in reducing leg swelling and discomfort in lower extremities," *Applied ergonomics,* vol. 43, no. 6, pp. 1033-1037, 2012, doi: 10.1016/j.apergo.2012.03.002.

[12] M. R. Chester, M. J. Rys, and S. A. Konz, "Leg swelling, comfort and fatigue when sitting, standing, and sit/standing," *International journal of industrial ergonomics,* vol. 29, no. 5, pp. 289-296, 2002, doi: 10.1016/S0169-8141(01)00069-5.

[13] E. Akçagün, H. Siddique, and A. Yılmaz, "Development of seamed compression socks and comparison with class i socks using existing mathematical models," *Uludağ Üniversitesi Mühendislik Fakültesi Dergisi,* vol. 28, no. 3, pp. 741-760, 2023, doi: 10.17482/uumfd.1268849.

CHAPTER 5

EFFICACY AND COMPLIANCE EVALUATION OF LOW-PRESSURE GRADIENT COMPRESSION STOCKINGS WITH LOWER LIMB MOVEMENTS ON SUBSTANTIAL GROUPS

5.1 Introduction

In Chapter 4, it was observed that the application of Class I MCS with LLMs led to a significant reduction in calf circumference at various points among elderly subjects. Therefore, the low-pressure gradient compression stocking (Class I MCS) was chosen for the 3rd trial test on substantial groups in this chapter. The primary objective of this chapter is to evaluate the efficacy and compliance of low-pressure MCS when integrated with lower limb movements (LLMs) in a large group.

The study of this chapter focused on a lot of the elderly population to conduct a comprehensive analysis of the reduction in lower limb oedema resulting from the integration of low-pressure MCS and LLMs. This analysis included not only measurements of lower limb circumference change, factors impact based on the comparisons of left and right legs, gender, and BMI (Body mass index) but also a thorough assessment of the quality of life (QoL) of the participants, as well as the preference and tolerance of the intensity of the designed LLMs. Carrying on the

QoL of the participants wearing low-pressure MCS is to gauge compliance and conducting the PRETIE-Q is to assess the acceptance of the designed LLMs.

5.2 Method

5.2.1 Patient consent

This 3rd trial test protocol was also approved by Helping Hand-Po Lam Jockey Club Housing for the Elderly in Hong Kong and conducted following the ethical principles for non-clinic research. Consent was obtained from all subjects before conducting the 3rd trial test.

5.2.2 Trial procedure

The 3rd trial test involved a sizable cohort of elderly subjects afflicted with mild lower limb oedema or prone to oedema regularly. The subjects were divided into two groups the experimental group conducted designed LLMs in conjunction with wearing low-pressure MCS, while the control group solely utilized low-pressure MCS to reduce oedema. A comprehensive description of the 3rd trial test design and measurement are provided in sections 5.3.2 and 5.3.3, respectively.

5.3 Efficacy and compliance evaluation

5.3.1 Participants

In the 3rd trial test, 18 elderly subjects with mild lower limb edema or who were prone to lower limb edema in daily life were recruited, including 4 males and 14 females. 36 lower limbs were studied from individuals aged 65 to 93 years old who were able to move independently without assistance and had no history of musculoskeletal, cardiovascular, or diabetic problems. Detailed subjects' information is listed in **Table 5.1**.

Table 5. 1 Information of subjects.

The 3rd trial test		
No. of subjects	18	
Gender	Male	Female
No. of gender	4	14
Percentage of gender	22%	78%
Average age (years)	82.50 (71.00, 93.00)	80.36 (66.00, 92.00)
Average BMI (kg/m2)	24.94 (18.78, 28.39)	25.95 (18.98, 31.81)

5.3.2 The third trial test design

The 3rd trial test was conducted at 24.4°C with a humidity of 47%. The air conditioner was turned on to control the temperature to nearly 24°C. The 3rd trial test took place in the afternoon and its design was similar to the 2nd trial test in Chapter 4.

Firstly, it was conducted to complete consent, recording subjects' information including height, weight, BMI. Secondly, the original circumference of the subjects' lower limb was measured using soft tape. Thirdly, subjects were divided into experimental and control group, they were all with wearing low-pressure MCS (MCS), however, 7 subjects in the experimental group were integrated with lower limb movements (LLMs), 11 subjects were without conducting LLMs in the control group. MCS was available in two sizes, determined by the subjects' lower limb measurements. Fourthly, the interface pressure of points B and C was measured after wearing the MCS to ensure they were at Class I level (18~21 mmHg at point B) for both groups. Fifthly, 7 subjects in the experimental group completed the one set of designed LLMs with wearing MCS, while 11 subjects in the control group maintained sitting position 15 minutes without LLMs but wearing MCS. Sixthly, subjects required to wear off MCS and the circumference of the lower limb was measured after LLMs or 15 minutes sitting. Seventhly, subjects wore MCS again and the interface pressure of points B and C was measured again. Eighthly, subjects repeated the second time of LLMs in the experimental group and repeated 15 minutes sitting in the control group. Ninthly, subjects wore off MCS and the circumference of every lower limb were measured again. Finally, subjects completed Quality of life (QoL) questionnaires [1] and the subjects in experimental group completed the questionnaires of inventory of exercise habits [2]. The flow chart of the 3rd trial test is shown in **Figure 5.1.**

It was also critical to guarantee that all personnel conducting measurements presented professionalism, accuracy, and efficiency while minimizing measurement errors.

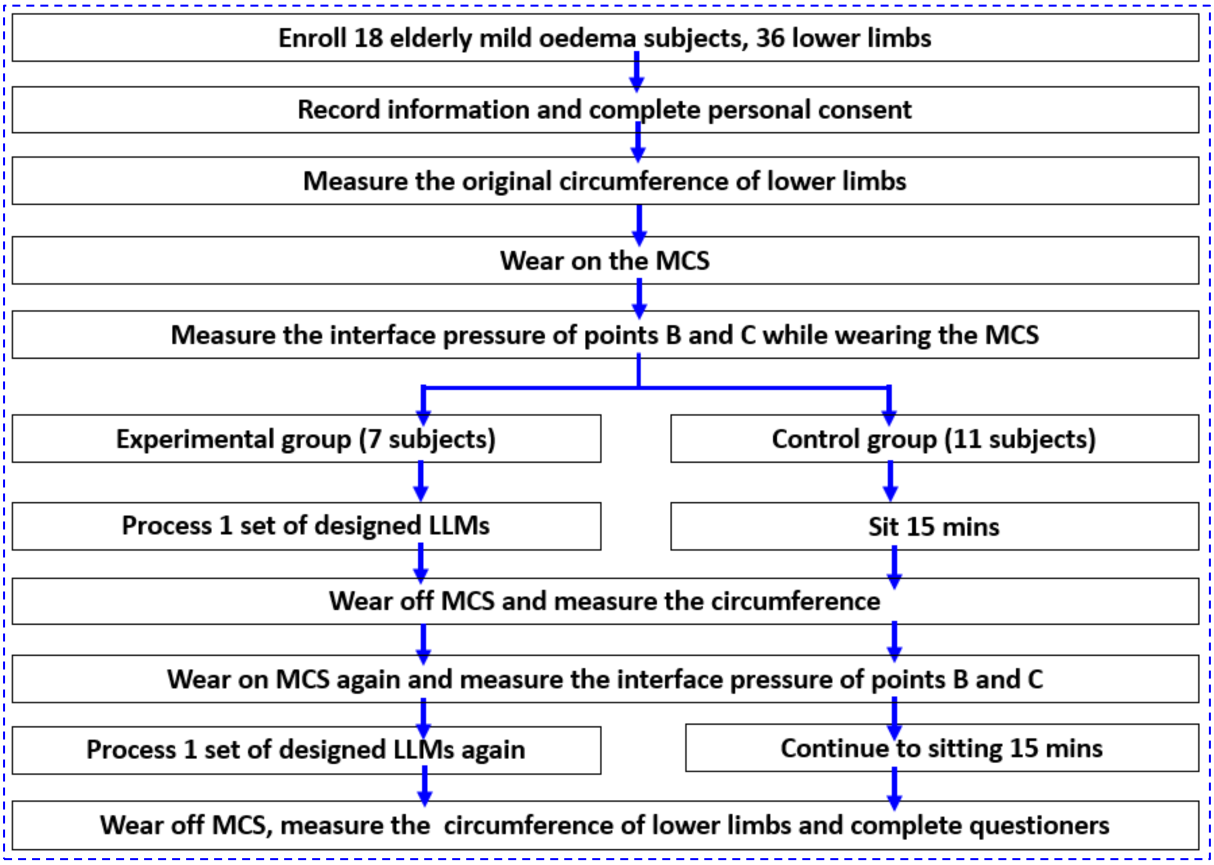

Figure 5. 1 The flow chart of the 3rd trial test in Chapter 5.

5.3.3 Measurement

The circumference of the lower limb was measured three times for each test, including the original circumference and subsequent measurements taken after every 15 minutes of sitting (twice in the control group) or after completing each set of designed LLMs (two sets in the experimental group). Each measurement was repeated three times. The lower limb circumference was also measured at B, B1, C, and D points (standard RAL-GZ 387/1) using the soft tape. To ensure measurement accuracy, three equidistant points could be selected on the same circumference within the same plane.

5.3.4 Interface pressure (IP)

Then, every subject's IP of points B and C in both groups after wearing MCS was measured by the airbag sensor to ensure that the initial compression pressures were in the Class I level. **Figure 5.2** and **Figure 5.3** are the IP at point B and point C after wearing MCS for the first and the second time. They showed pressures at point B were mostly guaranteed between nearly 18~21 mmHg.

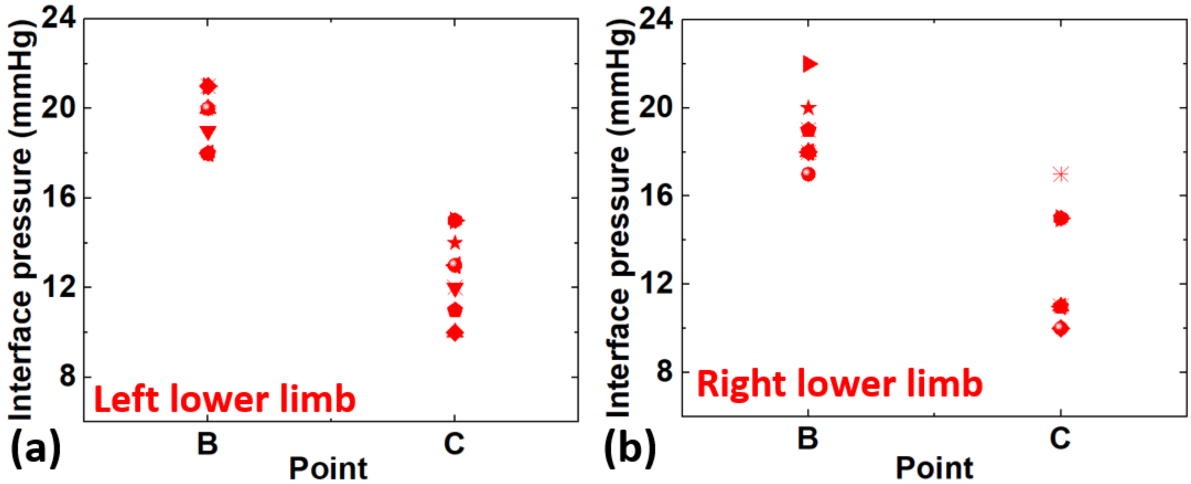

Figure 5. 2 Interface pressure (IP) at point B and point C after wearing MCS for the first time, (a) is the left lower limb, and (b) is the right lower limb.

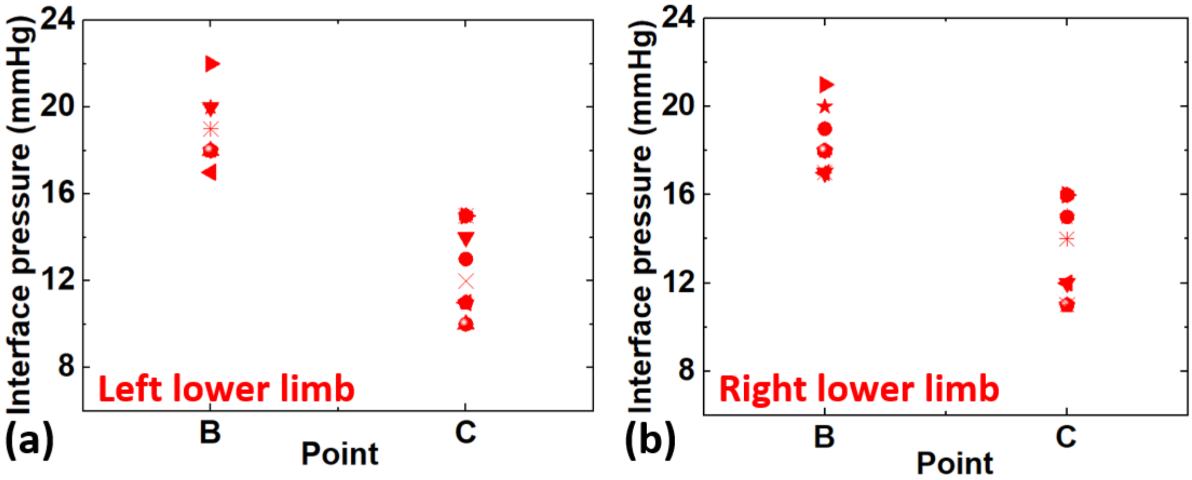

Figure 5. 3 Interface pressure (IP) at point B and point C after wearing MCS for the second time, (a) is the left lower limb, and (b) is the right lower limb.

5.3.5 Circumference change (CC)

In the analysis of CC, the singular values were deleted within the measurement error range and deleted changes greater than 5% before data analysis in following section. It had 30 samples (n=30) in the experimental group and 66 samples (n=66) in the control group. They were consistent with normal distribution.

It was hypothesized that a significant CC showed before and after wearing low-pressure MCS in experimental and control groups.

Same as in Chapter 4, the p-value <0.001 was considered extremely significant (***), 0.001 < p-value <0.01 was considered very significant (**), 0.01 < p-value <0.05 was significant (*), and p-value >0.05 was not significant (ns), the unmarked values in the Table were part of the not significant (ns) group.

Firstly, CC before and after LLMs/sitting integrating with wearing low-pressure MCS were analysed using the paired sample t-test in the experimental and control groups. The paired sample t-test exhibited that CC after completing 2 sets of LLMs were bigger than that of after completing 1 set LLMs in the experimental group. This was confirmed to the result of completing 2 sets of LLMs having better efficacy than 1 set of LLMs on oedema reduction in Chapter 4. Especially, point B had a significant circumference decrease (p_{2nd} <0.05), and point D had an extremely significant circumference reduction (p_{2nd} <0.001) in **Figure 5.4(a)**.

In the control group, only utilizing the low-pressure MCS for 15 minutes and 30 minutes were no obvious CC at points B1 and C, as shown in **Figure 5.4(b)**. However, there was significant CC after sitting 30 minutes at points B (p_{2nd} <0.05), and point D revealed a significant change after 15 minutes (p_{1st} <0.05) and 30 minutes (p_{2nd} <0.001) of sitting while wearing low-pressure MCS.

Compared to two groups, both groups had significant differences before and after LLMs/sitting wearing low-pressure MCS at points B and D. It could explain that the low-pressure (Class I level) MCS effectively reduced lower limb circumference at points B and D in the elderly population, and conducting 2 sets of LLMs integrated with the compression method could help reduce circumference at more points including points B, B1, C, and D, referring to the data in **Table 5.2.** The circumference reduction rate of the two groups were revealed in the next section 5.3.6 in detail, and the standard deviation of the measured circumference in the experimental group was significantly smaller than the control group, as shown in **Figure 5.4(a)** and **Figure 5.4(b)**. The measured data listed in **Table 5.2** are original calf circumference (baseline), calf circumference of the first measurement (after completing 1 set LLMs/after 15 minutes sitting), and calf circumference of the second measurement (after completing 2 sets LLMs/after 30 minutes sitting).

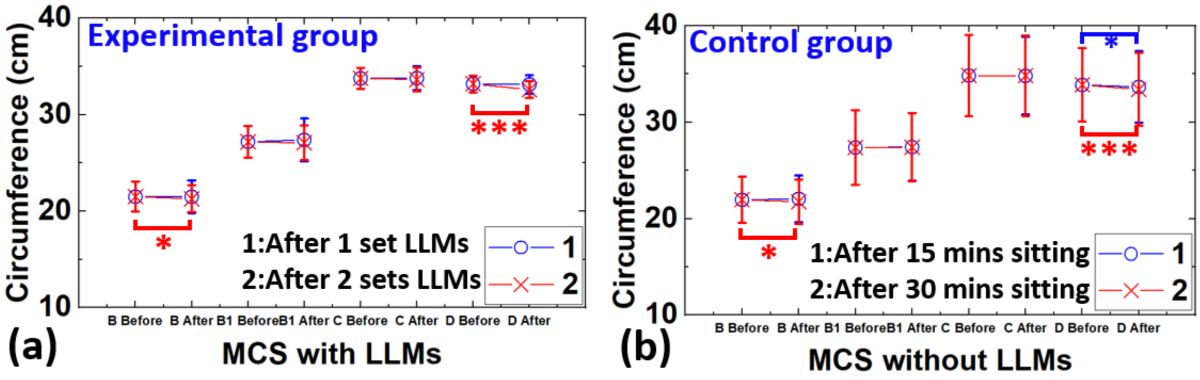

Figure 5. 4 The lower limb (calf) circumference (B, B1, C, D) change with wearing MCS and p-value, (a) is before and after completing 1/2 sets LLMs in the experimental and (b) is before and after 15/30 minutes sitting in the control group.

Table 5. 2 Detailed data of lower limb (calf) circumference baseline, results after completing LLMs (1/2 sets LLMs) and no LLMs (15/30 minutes sitting), and p-value.

Calf circumference, unit: cm, First measure: after 1 set LLMs/after 15 minutes sitting, Second measure: after 2 sets LLMs/after 30 minutes sitting												
Point	B			B1			C			D		
Different conditions	Base line	First measure	Second measure	Base line	First measure	Second measure	Base line	First measure	Second measure	Base line	First measure	Second measure
LLMs	21.5±1.6	21.5±1.7	21.3±1.4 *	27.2±1.6	27.4±2.2	27.1±1.8	33.8±1.1	33.8±1.2	33.6±1.2	33.2±0.9	33.1±0.9	32.6±0.9 ***
No LLMs	21.9±2.4	22.1±2.4	21.8±2.3 *	27.4±3.9	27.4±3.5	27.4±3.5	34.8±4.2	34.8±4.0	34.8±4.2	33.9±3.8	33.7±3.7 *	33.4±3.8 ***

5.3.6 Statistical significance analysis of circumference reduction under different factors

Secondly, the statistical significance analysis of the oedema reduction efficacy under different factors when wearing low-pressure MCS was conducted using the independent t-test. Data of changes bigger than 5% were deleted, and they were consistent with normal distribution. The experimental group consisted of subjects who wore low-pressure MCS while carrying out LLMs, while the control group consisted of subjects who only wore low-pressure MCS without LLMs.

It was hypothesized that the circumference reduction rate of the experimental group was significantly higher than the control group.

The result revealed that the circumference reduction rate at point D, the experimental group ($Mean_{2nd}$=-2.3, SD_{2nd}=2.0, p_{2nd} <0.05) was significantly bigger than the control group ($Mean_{2nd}$=-1.2, SD_{2nd}=2.1), as shown in **Figure 5.5**. It showed that the subjects completing 2 sets of LLMs had greater circumference reduction rate than those who sat 30 minutes at point D. In addition, the experimental group had more efficacy in circumference reduction than the control group after completing 2 sets of LLMs at points B1, C, and D, see in **Table 5.3**. It means that the approach of the LLMs integrated with low-pressure MCS was a better choice than only utilizing the low-pressure MCS to reduce lower limb oedema. In specific, at point B1, the individuals who engaged in LLMs once and twice showed more circumference reduction rate compared to those who did not conduct LLMs.

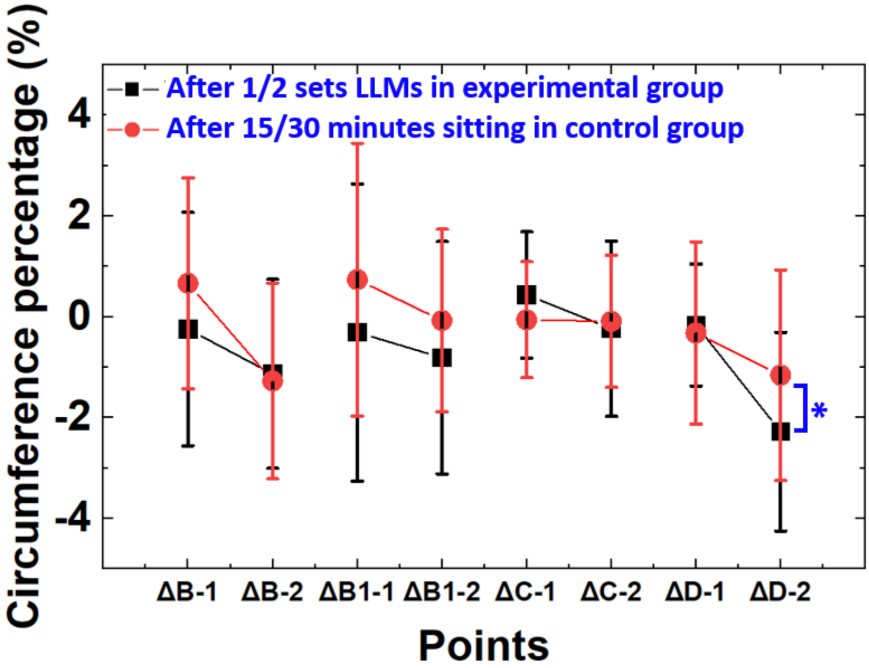

Figure 5. 5 The lower limb (calf) circumference reduction rate (circumference percentage) when wearing MCS in both groups, the black square line is after completing 1/2 sets LLMs in the experimental and the red circle line is after 15/30 minutes sitting in the control group.

Table 5. 3 Detailed data of the lower limb (calf) circumference reduction rate with/without LLMs and p-value.

Change rate: circumference change rate, unit: %, "-" = reduce, LLMs: 1: After 1 set LLMs, 2: After 2 sets LLMs, No LLMs: 1: after 15 minutes sitting, 2: after 30 minutes sitting								
Point	B		B1		C		D	
Different conditions	Change rate 1	Change rate 2	Change rate 1	Change rate 2	Change rate 1	Change rate 2	Change rate 1	Change rate 2
LLMs	-0.2±2.3	-1.1±1.9	-0.3±2.9	-0.8±2.3	0.4±1.2	-0.2±1.7	-0.2±1.2	-2.3±2.0 *
No LLMs	0.7±2.1	-1.3±1.9	0.7±2.7	-0.1±1.8	-0.1±1.2	-0.1±1.3	-0.3±1.8	-1.2±2.1

Thirdly, the independent t-test was conducted to hypothesize that the circumference reduction rate of the left and right leg significantly differed in the experimental and control groups.

There were significant changes between the left leg and right leg when completing LLMs once and twice at points B and B1 in the experimental group. The right leg had more circumference reduction at point B (p_{1st} <0.001, p_{2nd} <0.001), while left leg had more circumference reduction at point B1 (0.001< p_{1st} <0.01, p_{2nd} <0.001), as shown in **Figure 5.6(a)**. At all points except the right leg at point C, both legs showed the efficacy of circumference reduction after completing 2 sets of LLMs, which could reflect that the approach of the LLMs integrated with low-pressure MCS was a good choice for elderly oedema subjects.

Applying low-pressure MCS without LLMs in the control group, the right leg ($Mean_{2nd}$=-1.2, SD_{2nd}=1.2, p_{2nd} <0.001) had more circumference reduction rate than the left one ($Mean_{2nd}$=0.7, SD_{2nd}=1.6) at point B1 after 30 minutes of sitting. In addition, the left leg ($Mean_{1st}$=-1.0, SD_{1st}=1.9, p_{1st} <0.001; $Mean_{2nd}$=-2.1, SD_{2nd}=2.1, p_{2nd} <0.001) had more circumference reduction rate than the right one ($Mean_{1st}$=0.5, SD_{1st}=1.5; $Mean_{2nd}$=-0.2, SD_{2nd}=1.4) at point D after sitting for 30 minutes, as shown in **Figure 5.6(b)**.

Compared to the two groups in **Table 5.4**, there was no significant change in circumference reduction rate at point C, the region of point C was the largest circumference of the calf and the most highly developed area of the gastrocnemius muscle.

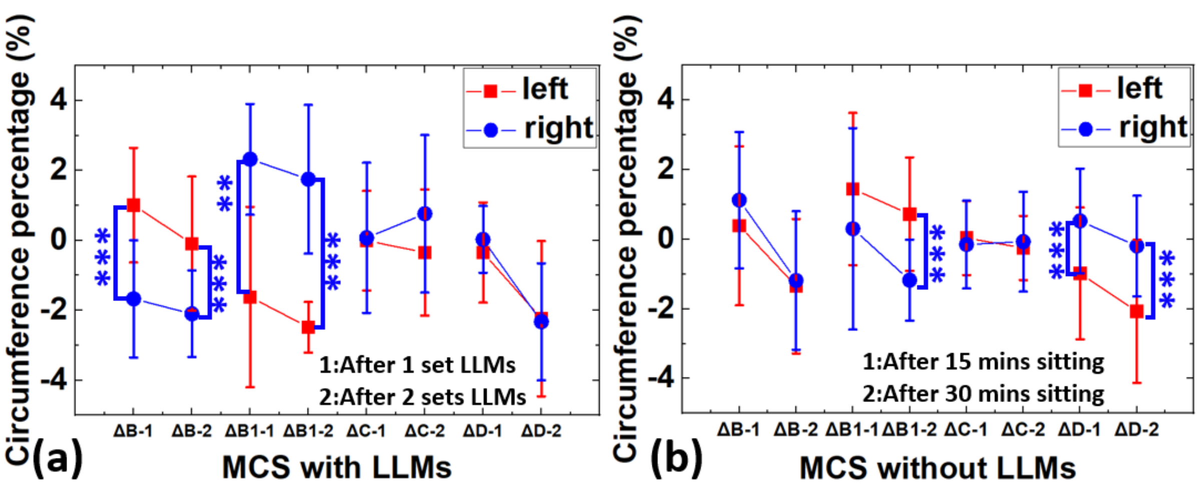

Figure 5. 6 Influence of MCS with/without LLMs on the left and right lower limb (calf) circumference reduction rate (circumference percentage), (a) is the experimental group after completing 1/2 sets LLMs, and (b) is the control group after 15/30 minutes sitting.

Table 5. 4 Detailed data of the left (L) and right (R) lower limb (calf) circumference reduction rate with/without LLMs and p-value.

Circumference change rate, unit: %, "-" = reduce, LLMs: 1: After 1 set LLMs, 2: After 2 sets LLMs, No LLMs: 1: after 15 minutes sitting, 2: after 30 minutes sitting																
Point	B				B1				C				D			
Different conditions	L1	L2	R1	R2	L1	L2	R1	R2	L1	L2	R1	R2	L1	L2	R1	R2
LLMs	1.0±1.6	-0.1±1.9	-1.7±1.7 ***	-2.1±1.2 ***	-1.6±2.6 **	-2.5±0.7 ***	2.3±1.6	1.8±2.1	0.0±1.4	-0.3±1.8	0.1±2.1	0.8±2.3	-0.3±1.4	-2.2±2.2	0.0±1.0	-2.3±1.7
No LLMs	0.4±2.3	-1.4±1.9	1.1±2.0	-1.2±2.0	1.4±2.2	0.7±1.6	0.3±2.9	-1.2±1.2 ***	0.0±1.1	-0.3±0.9	-0.2±1.3	-0.1±1.4	-1.0±1.9 ***	-2.1±2.1 ***	0.5±1.5	-0.2±1.4

Fourthly, due to the limited sample size of participants engaging in LLMs resulting in insufficient data in the experimental group, the analysis of gender impact only focused on the control group.

The independent t-test was processed to hypothesize that circumference reduction rate of different gender significantly differed in the control group.

For maintaining sedentary wearing low-pressure MCS, the circumference reduction rate of the males was larger than females at points B, C, and D, as shown in **Figure 5.7.** Moreover, there were extremely significant circumference reduction rate in the males ($Mean_{1st}$=-0.6, SD_{1st}=0.6, p_{1st} <0.001; $Mean_{2nd}$=-0.7, SD_{2nd}=1.1, p_{2nd} <0.001) than females ($Mean_{1st}$=0.3, SD_{1st}=1.3;

Mean$_{2nd}$=0.1, SD$_{2nd}$=1.1) at point C, as shown in **Table 5.5**. It revealed that applying low-pressure MCS without LLMs could be more effective for males than females.

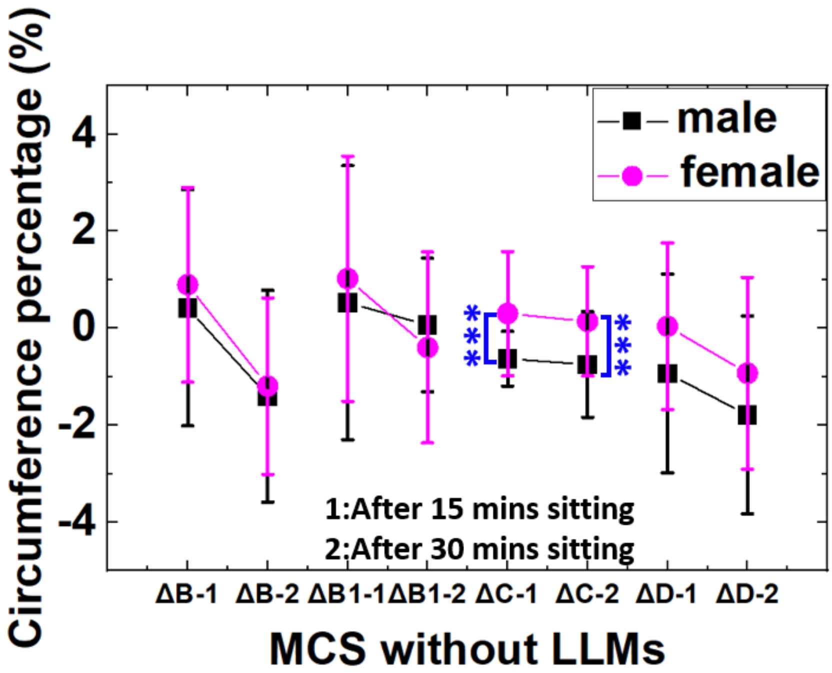

Figure 5. 7 Influence of MCS without LLMs on the males and females' lower limb (calf) circumference reduction rate (circumference percentage) after 15/30 minutes of sitting in the control group.

Table 5. 5 Detailed data of the males and females' lower limb (calf) circumference reduction rate without LLMs and p-value.

Circumference change rate, unit: %, "-" = reduce, No LLMs: 1: after 15 minutes sitting, 2: after 30 minutes sitting																
Point	B				B1				C				D			
Different conditions	M1	M2	F1	F2	M1	M2	F1	F2	M1	M2	F1	F2	M1	M2	F1	F2
No LLMs	0.4±2.4	-1.4±2.2	0.9±2.0	-1.2±1.8	0.5±2.8	0.1±1.4	1.0±2.5	-0.4±2.0	-0.6±0.6 ***	-0.7±1.1 ***	0.3±1.3	0.1±1.1	-0.9±2.1	-1.8±2.0	0.0±1.7	-0.9±2.0

Fifthly, not only the different legs result from more developed muscles or the different gender but also normal weight or overweight can affect the oedema reduction efficacy, therefore, the body mass index (BMI) is one of the research factors in oedema reduction.

BMI is defined as body weight divided by height squared (unit is kg/m^2), and it is currently utilized in clinical settings to diagnose excess obesity and underweight conditions in patients [3, 4]. It can be considered as ideal or healthy body weight status when the BMI range of 18.5~24.9. According to the different BMI values, they can be classified as overweight status (BMI: 25.0~29.9), class 1 obesity (BMI: 30~34.9), class 2 obesity (BMI: 35.0~39.9), and class 3 obesity (BMI: ≥ 40.0), which are employed to assess the risk of obesity-related comorbidities, such as class 1 obesity belongs to the low risk, class 2 one is moderate risk, and high risk is shown in class 3 obesity [5, 6].

Individuals with obesity are susceptible to lower limb oedema. Therefore, this section investigated the impact of different BMI levels (BMI ≤ 24.9 and BMI >24.9) on the oedema reduction in the experimental and control groups. Before commencing the trial test, personal information, height, and weight with participants' consent forms were already collected, thus obtaining the BMI data of the subjects.

The independent t-test was processed to hypothesize that circumference reduction rate of different BMI was significantly different in the experimental and control groups.

Figure 5.8(a) revealed that the group of BMI ≤ 24.9 when completing 2 sets of LLMs integrated with low-pressure MCS had more circumference reduction rate than completing 1 set of LLMs in the experimental group. In addition, there was insufficient data at point B1 in the experimental group after data processing. The subjects with BMI >24.9 had almost no circumference change result between completing 1 and 2 sets of LLMs at point B ($Mean_{1st}$=-1.0, SD_{1st}=2.0; $Mean_{2nd}$=-1.0, SD_{2nd}=2.4), while there was increased circumference trend at point C, see in **Table 5.6**. At point D, BMI ≤ 24.9 subjects ($Mean_{2nd}$=-3.7, SD_{2nd}=1.1, p_{2nd} <0.001) had extremely significant circumference reduction rate than BMI >24.9 ($Mean_{2nd}$=-1.3, SD_{2nd}=1.9) when completing 2 sets of LLMs.

In the control group, the circumference reduction rate of subject with normal BMI (point B: $Mean_{2nd}$=-2.1, SD_{2nd}=2.0, p_{2nd} <0.05; point B1: $Mean_{2nd}$=-1.3, SD_{2nd}=0.5, p_{2nd} <0.001) had significantly greater than those of BMI >24.9 (point B: $Mean_{2nd}$=-1.0, SD_{2nd}=1.9; point B1: $Mean_{2nd}$=0.2, SD_{2nd}=1.8) at points B and B1 after 30 minutes of sitting, as shown in **Figure 5.8(b)**.

It is noteworthy that the comparison between the two groups showed a similar CC trend in BMI at point C not only with BMI ≤ 24.9 but also with BMI >24.9. Normal BMI subjects presented an initial circumference increase followed by a decreasing trend, whereas overweight subjects revealed a subsequent circumference increase after an initial decrease. Among the two groups, subjects with BMI ≤ 24.9 (normal range) had more significant circumference reduction rate at certain points than those with BMI >24.9.

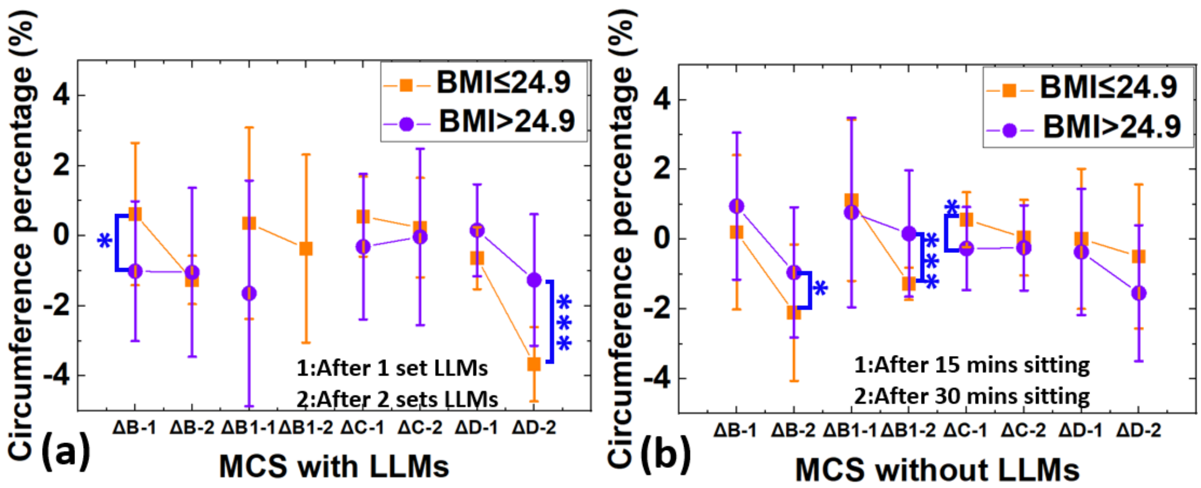

Figure 5. 8 Influence of MCS with/without LLMs on the BMI ≤ 24.9 and BMI >24.9 lower limb (calf) circumference reduction rate (circumference percentage), (a) is the experimental

group after completing 1/2 sets LLMs, and (b) is the control group after 15/30 minutes sitting.

Table 5. 6 Detailed data of the BMI ≤ 24.9 and BMI >24.9 lower limb (calf) circumference reduction rate with/without LLMs and p-value.

Circumference change rate, unit: %, "-" = reduce, LLMs: 1: After 1 set LLMs, 2: After 2 sets LLMs, No LLMs: 1: after 15 minutes sitting, 2: after 30 minutes sitting #: BMI ≤ 24.9, ##: BMI >24.9																
Point	B				B1				C				D			
Different conditions	#1	#2	##1	##2	#1	#2	##1	##2	#1	#2	##1	##2	#1	#2	##1	##2
LLMs	0.6±2.0	-1.3±0.7	-1.0±2.0 *	-1.0±2.4	0.4±2.7	-0.4±2.7	-1.6±3.2	—	0.6±1.1	0.2±1.4	-0.3±2.1	0.0±2.5	-0.6±0.9	-3.7±1.1 ***	0.2±1.3	-1.3±1.9
No LLMs	0.2±2.2	-2.1±2.0 *	1.0±2.1	-1.0±1.9	1.1±2.3	-1.3±0.5 ***	0.8±2.7	0.2±1.8	0.6±0.8	0.0±1.1	-0.3±1.2 *	-0.2±1.2	0.0±2.0	-0.5±2.1	-0.4±1.8	-1.5±1.9

5.3.7 Compliance

Disease-specific quality of life (QoL) measures may provide greater sensitivity in detecting and quantifying significant changes, which are helpful and critical for doctors, medical staff, or patients [7]. The VEINES-QOL/Sym questionnaire is a disease-specific quality of life assessment instrument for chronic venous disorders of the leg (CVDL) [1, 7-9], high values are indicative of better results [1, 7, 9]. This questionnaire demonstrated robust psychometric properties not only in individuals with deep vein thrombosis [1], but also with venous leg diseases [9]. The oedema is one of the conditions in CVDL [9]. Therefore, the VEINES-QOL/Sym questionnaire was used for subjects in this research. This questionnaire not only includes inquiries regarding leg conditions in general now, but also mostly focuses on lower limb problems within the past four weeks. However, owing to the constrained duration of our trial tests, elderly subjects were allocated approximately 30 minutes to apply compression integrated with LLMs in the experimental group and 30 minutes to apply compression stocking only in the control group. Consequently, subjects were prompted to respond to their lower limb feelings focusing on the experiences after the trial tests for the questionnaire assessment. The elderly subjects may face difficulties in reading the questionnaire, therefore, they were orally supported by research if needed, while refraining from offering responses either directly or implicitly.

Figure 5.9 shows the mean QoL score analysis when wearing WRAP and MCS in the 2nd trial and wearing MCS in the 3rd trial tests. They were obtained from the elderly mild oedema subjects from the Helping Hand party that participated in the 2nd trial test in Chapter 4 (**Figure 5.9 (a)**), as well as from the large-scale trial conducted with elderly mild oedema subjects from the same party in the 3rd trial test in Chapter 5 (**Figure 5.9 (b)**).

The study utilized the independent t-test to assess the significant satisfaction with different gradient compression stockings (WRAP and MCS) in the 2nd trial and low-pressure MCS with/without LLMs in the 3rd trial tests. **Figure 5.9 (a)** indicated that when utilizing WRAP/MCS with LLMs in the experimental group, the QoL score was higher for those utilizing WRAP (Mean:96.80, SD:9.83) compared to MCS (Mean:91.75, SD:7.85). While in the control group without LLMs, MCS (Mean:91.25, SD:12.29) led to a greater increase in QoL score compared to WRAP (Mean:88.50, SD:6.36), referring to **Table 5.7.** However, there was no statistically significant difference between the two types of compression stockings within each group.

When comparing the two groups in the 2nd trial test, it was shown that MCS maintained an almost consistent QoL score in both groups, see in **Table 5.7**. The application of WRAP integrated with LLMs resulted in greater scores than applying WRAP compression alone. This may have resulted from the application of WRAP manually adjusting its gradient compression pressure levels, leading to minor variations in the tightness experienced by individual participants during wearing or lower limb movements, despite the compression pressure complying with required specifications before trial testing. Therefore, the application of MCS in both groups revealed similar satisfaction scores among the subjects.

According to the efficacy of oedema reduction result from the 2nd trial test, the low- pressure MCS was chosen for the large-scale trial. **Figure 5.9 (b)** showed the QoL score when wearing low- pressure MCS with LLMs or without LLMs in the 3rd trial test. It found that there was no significant QoL difference between both groups. However, subjects wearing low-pressure MCS with LLMs in the experimental group expressed a little higher score (Mean:92.40, SD:6.50) than those wearing MCS without LLMs in the control group (Mean:91.50, SD:12.12), referring to **Table 5.7.** The result indicated that subjects experienced higher satisfaction when utilizing low-pressure MCS with LLMs. Furthermore, the QoL score in the presence of LLMs was observed to be more stable with a smaller standard deviation compared to the absence of LLMs.

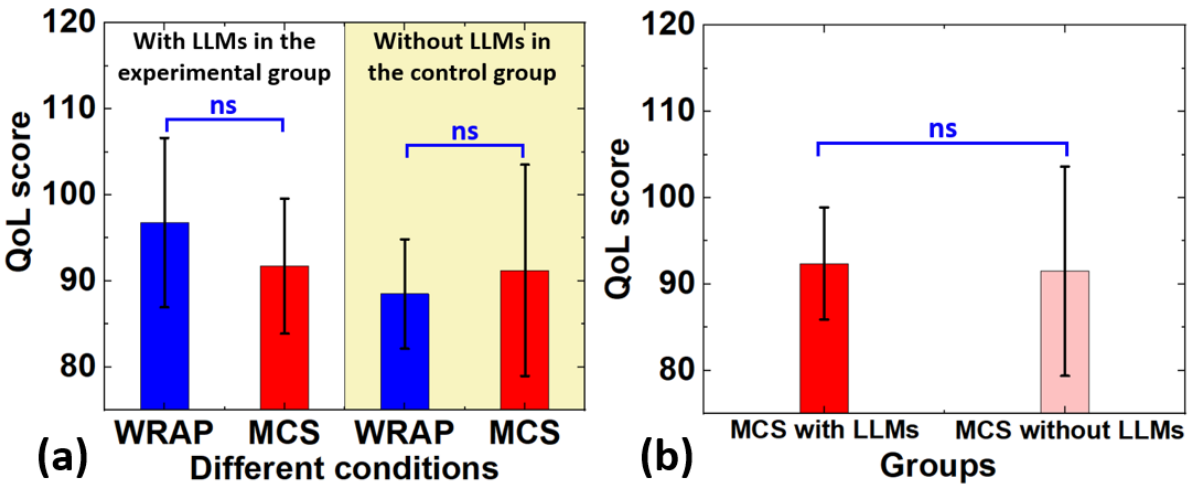

Figure 5. 9 QoL score comparison, (a) is the mean QoL score analysis when applying WRAP and MCS in the experimental group with LLMs (white background) and in the control groups

without LLMs (light yellow background) in the 2nd trial test, and (b) is the mean QoL score analysis when applying low-pressure MCS in the experimental group with LLMs and the control group without LLMs in the 3rd trial test.

Table 5. 7 Detailed data on the mean score of QoL in the 2nd trial and 3rd trial tests.

Groups	Conditions	Mean QoL score in the 2nd trial test	Mean QoL score in the 3rd trial test
Experimental group with LLMs	WRAP	96.80±9.83	——
	MCS	91.75±7.85	92.40±6.50
Control group without LLMs	WRAP	88.50±6.36	——
	MCS	91.25±12.29	91.50±12.12

Concerning the designed lower limb movements (LLMs), existing literature has documented the efficacy of each skeletal muscle movement in reducing lower limb edema. However, the acceptance and popularity of the proposed set of LLMs among elderly individuals remains uncertain. Because there is variability among individuals in terms of their preferred exercise intensity and their tolerance for such intensity [10]. Therefore, a survey is required to be conducted to assess the preference and tolerance of exercise intensity to further confirm whether designed LLMs are acceptable among them.

There are several questionnaires to survey exercise intensity, such as the International Physical Activity Questionnaire-7 (IPAQ-7) [11], which can evaluate the duration of physical activity at specific intensities over the past seven days; the Connor-Davidson Resilience Scale (CD-

RISC) [12] which can be utilized to measure resilience levels; and Preference for and Tolerance of the Intensity of Exercise Questionnaire (PRETIE-Q) and so on.

The PRETIE-Q was developed and introduced by Ekkekakis et al. [2], it was utilized in this chapter. PRETIE-Q comprises 16 items, with two 8-item scales dedicated to preference and tolerance, respectively, and each item is accompanied by a 5-point response scale [10, 13-15]. The higher aggregate score indicates an increased perceived preference and tolerance for exercise intensity [15]. The PRETIE-Q demonstrates internal consistency and structural validity, suggesting its potential for diverse applications within the field of exercise science [10]. This questionnaire can contribute to enhance exercise adherence and intend to the overall improvement of population health [15].

The PRETIE-Q scores were obtained from those who had conducted LLMs in experimental groups from the Helping Hand party in the 2nd trial and the 3rd trial tests. The independent t-test was conducted to assess the significant difference between wearing different gradient compression stockings (WRAP and MCS) on the tolerance and preference of designed LLMs in the 2nd trial test and wearing low-pressure MCS on those in the 3rd trial tests.

The analysis results from **Figure 5.10** showed that there was no statistically significant difference between wearing the two types of compression stockings in the tolerance and preference for exercise intensity in the 2nd trial test. For the preference for exercise intensity, MCS (Mean:23.00, SD:3.46) performed higher scores than WRAP (Mean:22.60, SD:3.21) even if the difference is not obvious, as shown in **Table 5.8**. In the 3rd trial test, MCS (Mean:25.80, SD:1.79) also performed higher preference score than that in the 2nd trial test. These results indicated that the approach of LLMs integrated with low-pressure MCS was widely favoured among the elderly population. Nevertheless, the tolerance score yielded opposite results. One potential explanation is that the WRAP has non-stretchable elasticity, which makes it prone to loosening during LLMs, leading to a slight reduction in pressure on the skin.

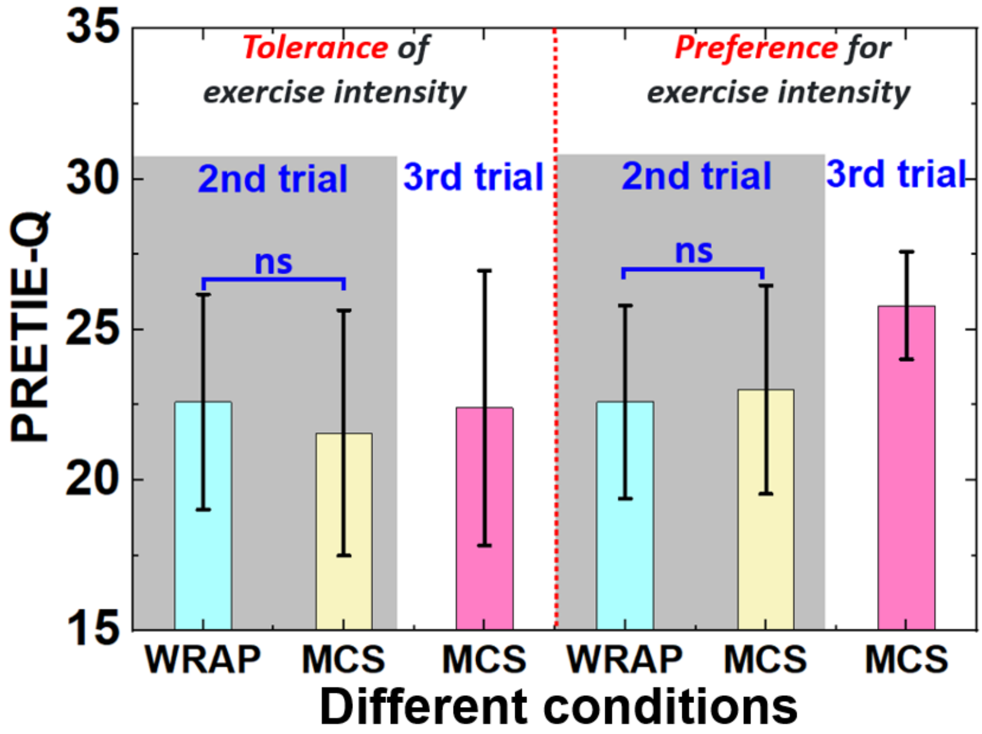

Figure 5. 10 The mean score of tolerance of exercise intensity and preference for exercise intensity in PRETIE-Q analysis when wearing WRAP and MCS in the 2nd trial (grey background) and MCS in the 3rd trial (white background) tests.

Table 5. 8 Detailed data of mean score of tolerance of exercise intensity and preference for exercise intensity in PRETIE-Q analysis in the 2nd trial and 3rd trial tests.

Intensity of Exercise	Conditions	Mean QoL score in the 2nd trial test	Mean QoL score in the 3rd trial test
Tolerance of exercise intensity	WRAP	22.60±3.58	——
	MCS	21.57±4.08	22.40±4.56

Preference for exercise intensity	WRAP	22.60±3.21	——
	MCS	23.00±3.46	25.80±1.79

5.4 Result

As a result, firstly, the paired sample t-test analysis showed that completing 2 sets of lower limb movements (LLMs) integrated with low-pressure MCS resulted in a larger circumference reduction compared to completing 1 set at points B (1 set LLMs: -0.2±2.3%; 2 sets LLMs: -1.1±1.9%, $p < 0.05$) and D (1 set LLMs:-0.2±1.2%; 2 sets LLMs: -2.3±2.0%, $p < 0.001$). This was consistent with the 2nd trial test results and suggests that the approach of LLMs integrated with low-pressure MCS effectively reduced lower limb circumference in the elderly population.

Secondly, the independent t-test analysis indicated that at point D, the experimental group which wore low-pressure MCS while carrying out LLMs ($Mean_{2nd}$: -2.3%, SD_{2nd}: 2.0%, $p_{2nd} < 0.05$) had significantly higher circumference reduction rate than the control group ($Mean_{2nd}$: -1.2%, SD_{2nd}: 2.1%). This shows that the approach of LLMs integrated with low-pressure MCS was a better choice than only applying low-pressure MCS to reduce lower limb oedema. Besides, in the 2nd trial test, the findings of the application of MCS without LLMs resulted in the reappearance of oedema, which was not observed in the 3rd trial test.

Thirdly, through statistics analysis, it was found that significant differences in circumference reduction rate between the left and right legs, gender, and BMI categories. It was observed that males applying low-pressure MCS without LLMs were more effective than females and had extremely significant circumference reduction rate compared to females at point C ($p_{1st} < 0.001$,

p_{2nd} <0.001). Furthermore, among the experimental and control groups, subjects with BMI ≤ 24.9 (normal range) had more significant circumference reduction rate at certain points than those with BMI >24.9 (p <0.05).

Finally, the quality of life (QoL) scores and the tolerance/preference for exercise intensity utilizing different gradient compression stockings (WRAP and MCS) in the 2nd trial and low-pressure MCS in the 3rd trial tests were analysed. The results indicated that the QoL score when wearing MCS combined with LLMs was more stable than without LLMs. Furthermore, the approach of LLMs integrated with low-pressure MCS was widely favoured among the elderly population.

5.5 Summary

In this chapter, the third trial test was conducted to evaluate the efficacy and compliance of low-pressure gradient compression stocking (MCS) combined with lower limb movements (LLMs) on reducing lower limb oedema in elderly populations, and statistical significance analysis was performed. The study demonstrated that the integration of 2 sets of LLMs with low-pressure MCS had a significant effect in reducing lower limb oedema at point D than only applying the low-pressure MCS in the elderly population, and 2 sets of LLMs were confirmed again more effectively than the conducted 1 set, especially points B and D. Males had significantly more reduction in circumference at point C when using low-pressure MCS without LLMs compared to females. Additionally, subjects with BMI ≤ 24.9 had a more significant reduction in lower limb circumference at certain points compared to those with BMI >24.9 among the experimental and control groups. Furthermore, the approach of the LLMs integrated with low-pressure MCS showed a more stable score of quality of life (QoL) than without LLMs and it was more well-received in terms of exercise intensity preference among the elderly population.

Reference

[1] S. R. Kahn *et al.*, "VEINES-QOL/Sym questionnaire was a reliable and valid disease-specific quality of life measure for deep venous thrombosis," *Journal of clinical epidemiology,* vol. 59, no. 10, pp. 1056.e1-1056.e4, 2006, doi: 10.1016/j.jclinepi.2005.10.016.

[2] P. Ekkekakis, E. E. Hall, and S. J. Petruzzello, "Some like it vigorous: Measuring individual differences in the preference for and tolerance of exercise intensity," *Journal of Sport and Exercise Psychology,* vol. 27, no. 3, pp. 350-374, 2005.

[3] L. Yang and G. A. Colditz, "Prevalence of Overweight and Obesity in the United States, 2007-2012," *JAMA Internal Medicine,* vol. 175, no. 8, pp. 1412-1413, 2015, doi: 10.1001/jamainternmed.2015.2405.

[4] S. Ikramuddin *et al.*, "Effect of Reversible Intermittent Intra-abdominal Vagal Nerve Blockade on Morbid Obesity: The ReCharge Randomized Clinical Trial," *JAMA*, vol. 312, no. 9, pp. 915-922, 2014, doi: 10.1001/jama.2014.10540.

[5] C. M. Peterson, D. M. Thomas, G. L. Blackburn, and S. B. Heymsfield, "Universal equation for estimating ideal body weight and body weight at any BMI," *The American journal of clinical nutrition*, vol. 103, no. 5, pp. 1197-1203, 2016, doi: 10.3945/ajcn.115.121178

[6] A. Must, J. Spadano, E. H. Coakley, A. E. Field, G. Colditz, and W. H. Dietz, "The Disease Burden Associated With Overweight and Obesity," *JAMA : the journal of the American Medical Association*, vol. 282, no. 16, pp. 1523-1529, 1999, doi: 10.1001/jama.282.16.1523.

[7] J. M. Bland *et al.*, "Validation of the VEINES-QOL quality of life instrument in venous leg ulcers: repeatability and validity study embedded in a randomised clinical trial," *BMC cardiovascular disorders,* vol. 15, pp. 1-12, 2015, doi: 10.1186/s12872-015-0080-7.

[8] G. A. Ribeiro-Samora, M. L. V. Carvalho, R. M. F. de Moura, and D. A. G. Pereira, "Limitations of VEINES QOL/SYM for discriminating chronic venous insufficiency severity," *Jornal vascular brasileiro,* vol. 19, pp. e20180096-e20180096, 2019, doi: 10.1590/1677-5449.180096.

[9] D. L. Lamping, S. Schroter, X. Kurz, S. R. Kahn, and L. Abenhaim, "Evaluation of outcomes in chronic venous disorders of the leg: Development of a scientifically rigorous, patient-reported measure of symptoms and quality of life," *Journal of vascular surgery,* vol. 37, no. 2, pp. 410-419, 2003, doi: 10.1067/mva.2003.152.

[10] P. Ekkekakis, J. Thome, S. J. Petruzzello, and E. E. Hall, "The Preference for and Tolerance of the Intensity of Exercise Questionnaire: A psychometric evaluation among college women," *Journal of sports sciences,* vol. 26, no. 5, pp. 499-510, 2008, doi: 10.1080/02640410701624523.

[11] C. L. Craig *et al.*, "International physical activity questionnaire: 12-country reliability and validity," *Medicine & science in sports & exercise,* vol. 35, no. 8, pp. 1381-1395, 2003, doi: 10.1249/01.MSS.0000078924.61453.FB.

[12] K. M. Connor and J. R. T. Davidson, "Development of a new resilience scale: The Connor-Davidson Resilience Scale (CD-RISC)," *Depression and anxiety,* vol. 18, no. 2, pp. 76-82, 2003, doi: 10.1002/da.10113.

[13] D. S. Teixeira *et al.*, "Preference for and tolerance of the intensity of exercise questionnaire (PRETIE-Q): validity, reliability and gender invariance in Portuguese health club exercisers," *Current psychology (New Brunswick, N.J.),* vol. 42, no. 5, pp. 4119-4132, 2023, doi: 10.1007/s12144-021-01718-3.

[14] B. P. C. Smirmaul, P. Ekkekakis, I. P. Teixeira, P. M. Nakamura, and E. Kokubun, "Preference for and Tolerance of the Intensity of Exercise questionnaire: Brazilian Portuguese version," *Revista brasileira de cineantropometria & desempenho humano,* vol. 17, no. 5, pp. 550-564, 2015, doi: 10.5007/1980-0037.2015v17n5p550.

[15] T. Wang *et al.*, "Validity and Reliability of the Preference for and Tolerance of the Intensity of Exercise Questionnaire among Chinese College Students," *International Journal of Mental Health Promotion,* vol. 25, no. 1, pp. 127--138, 2023, doi: 10.32604/ijmhp.2022.022504.

CHAPTER 6

CONCLUSIONS AND FUTURE WORK

6.1 Conclusions

This thesis aimed to investigate the reduction of lower limb oedema through the integration of gradient compression stockings with dedicated designed physical movements, encompassing modelling, mechanism, and efficacy evaluation. Initially, a 2D simplified numerical modelling was developed to simulate fluid exchange in blood vessels and tissues using the porous media model. Subsequently, the critical pressures for oedema reduction were calculated under varying physiological parameters. The method of the trial tests, design, measurement method, and lower limb movements were then designed to evaluate the efficacy of lower limb oedema reduction. The trial tests consisted of three-phases. The first trial test involved young healthy subjects and investigated the integration of Class I level (standard RAL-GZ 387/1) gradient medical compression stockings (MCS), non-stretchable WRAP, and bare leg with/without lower limb movements, using volume and circumference measurements to evaluate oedema reduction. The most two effective integration approaches were then selected for the second trial test, which involved elderly subjects with mild oedema. This second trial test evaluated the efficacy of oedema reduction through the integration of Class I level gradient WRAP, MCS, with/without lower limb movements, using circumference measurements. Additionally, it was investigated in the first two trial tests that included the statistical significance analysis of different wearing conditions on oedema reduction, the effect of adding lower limb movements, impact factors of oedema relief, as well as the relationship between dynamic compression pressure during lower limb movements and reduction in lower limb circumference. Finally, the third trial test statistically evaluated the efficacy and compliance of low-pressure gradient MCS with/without lower limb movements in reducing lower limb oedema in substantial groups and assessed the acceptance of the designed lower limb movements among elderly subjects.

The conclusions are as follows:

1) The numerical 2D simplified capillary-blood-tissue model was developed to achieve fluid exchange between blood and interstitial fluid within the porous media model. The developed model can explain the mechanism of oedema reduction under compression pressure. The validity of the numerical model using the porous media model was verified through physical experiment.

2) Filtration, equivalent to 90% reabsorption and 10% lymphatic flow, serves as an indicator for calculating the critical pressure in numerical simulation to initiate oedema reduction. The developed model initiates oedema reduction when a constant compression pressure threshold of over 550 Pa is applied to the interstitial fluid under defined normal physiological parameters. Additionally, the percentage of oedema reduction is proportional to the exerted constant compression pressure.

3) Critical pressures for oedema reduction are calculated under different physiological parameters, and their effects are investigated using the computational fluid dynamics (CFD) method. The study found that capillary and tissue porosity, as well as inlet velocity, significantly impact oedema reduction under constant compression pressure, while blood viscosity has a minor effect. Constant and harmonic pressures have similar effects on the percentage of vein output under the same pressure amplitude, and harmonic frequency presents no sensitivity to the percentage of vein output.

4) In the case of young healthy subjects, WRAP (Mean: -66.3 cm^3 SD: 51.0 cm^3) demonstrated greater reduction in lower limb volume compared to MCS (Mean: -58.5 cm^3 SD: 42.0 cm^3) and bare leg (Mean: -63.5 cm^3 SD: 50.5 cm^3) within the group conducting lower limb movements, while MCS (Mean: -51.2 cm^3 SD: 46.8 cm^3) presented more volume reduction than WRAP (Mean: -41.9 cm^3 SD: 35.6cm^3) and bare leg (Mean: -42.4 cm^3 SD: 57.6 cm^3) in the group without lower limb movements, as evaluated through water displacement volumetry. However, no significant statistical differences were observed among wearing conditions within each group. Additionally, males showed significantly lower limb volume reduction percentage compared to females with bare lower limbs, regardless of whether they conducted lower limb movements ($p <0.05$).

5) Significant circumference reductions were observed in young healthy subjects who conducted lower limb movements, and applying compression was more effective than bare leg for oedema reduction. At point C, MCS with lower limb movements (Mean: -1.3% SD: 0.8%) showed greater circumference reduction compared to WRAP with lower limb movements (Mean: -0.9% SD: 0.7%), while at point D, WRAP with lower limb movements (Mean: -1.1% SD: 0.7%) was more effective than bare leg with lower limb movements (Mean: -0.6% SD: 0.6%). Concerning the manually adjustable WRAP, it was found that during lower limb movements, the interface pressure on the lower limb at point C showing the uniform pressure exerted by the WRAP exceeded the gradient pressure, resulting in correspondingly larger circumference reduction rate. Furthermore, at point C, males showed an extremely significant circumference reduction compared to females when applying MCS, either with or without conducting lower limb movements ($p <0.001$).

6) In the case of elderly subjects with mild oedema, MCS was better than WRAP in oedema reduction when subjects were without conducting lower limb movements in the second trial test. In addition, the integration of MCS and lower limb movements consistently achieved oedema reduction compared to using MCS alone. MCS with 1 set of lower limb movements ($Mean_{1st}$=-1.1%, SD_{1st}=2.2%) showed significant circumference reduction compared to WRAP ($Mean_{1st}$=0.1%, SD_{1st}=2.1%) at point B1 (p_{1st} <0.05). MCS with 2 sets of lower limb movements significantly reduced the circumference at more points B, B1, and D. The third trial test with the substantial group also confirmed this finding. The third trial test further revealed that subjects with a BMI ≤ 24.9 performed more significant circumference reduction rate at certain points than those with a BMI >24.9, regardless of whether lower limb movements were conducted (p <0.05).

7) The dynamic mean pressure at point C declined and fluctuated during lower limb movements. The young healthy group performed dynamic mean pressures of 13.3 mmHg in WRAP and 10.5 mmHg in MCS at point C. The elderly group showed dynamic mean pressures of 5.1 mmHg (=679.9 Pa) in WRAP and 6.5 mmHg (=866.6 Pa) in MCS at point C. These dynamic mean pressure values containing compression stockings and muscles' contraction were higher than the critical pressure of 550 Pa with normal physiological parameters in the numerical simulation.

8) A comparison between different age groups revealed that: i) at point D, both young healthy subjects wearing WRAP (0.001 < p <0.01) and elderly subjects (0.001 < p_{2nd} <0.01) wearing MCS showed very significant circumference reduction rate in their left legs compared to the right one, regardless of whether lower limb movements were conducted. ii) Circumference measurement was deemed a superior assessment method

due to its ability to reflect detailed changes at different points. iii) Additionally, more than half of young subjects preferred WRAP due to its convenience in wearing. However, integrating the lower limb movements with low-pressure MCS demonstrated a more stable quality of life (QoL) score than without lower limb movements and it was better received in terms of exercise intensity preference among the elderly population. iv) Ultimately, the integration of low-pressure compression with physical movements was evaluated for its effective efficacy in oedema reduction through practical trials.

6.2 Limitations

The critical pressure thresholds of various conditions were calculated through numerical simulation, and the efficacy of integrating low-pressure compression with skeletal muscle movement in oedema reduction was evaluated across different age groups in practical trials. These findings can serve as valuable references for clinical staff. However, there are still limitations that need to be addressed.

1) The anatomical structure of the human lower limbs is highly intricate, and the exchange of fluid between muscle tissue and blood vessels involves numerous complex factors. Therefore, the model may require further development under clinical technology support to consider the more complex factors of the lower limb system.

2) In terms of practical trials, the current research focuses on the short-term combination of compression pressure and lower limb movements. This programme could be extended to a longer duration, such as six months, one year, or two years, to comprehensively assess long-term efficacy, as well as the physical changes and potential side effects associated with prolonged use and maintenance of lower limb movements.

6.3 Future work

1) The fluid-structure interaction (FSI) can be considered in the numerical model to consider the effect of the flexible change in muscle tissue under compression treatment on oedema resorption.

2) The efficacy of each lower limb movement on oedema reduction of the lower limb can be statistically analysed separately to provide a more comprehensive understanding of their impact. Several strategies can be employed to minimize the coefficients of variation in data analysis: (1) augmenting and optimizing the trial sample size and data collection, (2) enhancing measurement precision and reducing measurement errors to reduce the standard deviation, and (3) increasing trial test efficiency by improving the trial process and measurement methods to increase the mean value of the outcome.

3) For many elderly individuals, engaging in active lower limb movements may require the supervision and support of a caregiver for their safety and proactive. The auxiliary lower limb devices that promote active health can be further developed, incorporating features such as reminders, adjustable movement circulation, and the application of external pressure to integrate low-pressure compression with skeletal muscle movement. Additionally, the development of such devices with real-time measurement capabilities for interface pressure change, lower limb circumference change, muscle status, heart rate, and other physiological parameters will be a good prospect for the integration of wearable systems and active health.