# EFFECTS OF LOW INTENSITY BLOOD FLOW RESTRICTION AND HIGH INTENSITY RESISTANCE TRAINING ON MUSCLE STIFFNESS

by

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# EFFECTS OF LOW INTENSITY BLOOD FLOW RESTRICTION AND HIGH INTENSITY RESISTANCE TRAINING ON MUSCLE STIFFNESS

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# ACADEMIC ETHICS AND INTEGRITY STATEMENT

I, Ömer Batın Gözübüyük, hereby certify that I am aware of the Academic Ethics and Integrity Policy issued by the Council of Higher Education (YÖK) and I fully acknowledge all the consequences due to its violation by plagiarism or any other way.

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# ABSTRACT

# EFFECTS OF LOW INTENSITY BLOOD FLOW RESTRICTION AND HIGH INTENSITY RESISTANCE TRAINING ON MUSCLE STIFFNESS

Blood flow restriction training (BFR) has become a popular training method recently. Both athletic and non-athletic populations prefer BFR over high intensity training (HI) due to the use of much lower loads. Although the mechanical tension of BFR is considered lower than that of HI, the metabolic stress is much higher. It has been shown that imposing high loads to a muscle during training affects stiffness of the muscles acutely. However the long-term effects of HI training on the subjected muscle's stiffness is not studied extensively. Moreover, it is not known how the BFR training affects this property. We compared the effects of 6 weeks of BFR and HI -elbow flexion- training on stiffness of biceps brachii muscle. Seventeen healthy participants volunteered for the study, randomly divided into BFR (n=8) and HI (n=9) groups. BFR group trained with 30-40% of their 1 repetition maximum (1-RM) and HI group trained with 75-85% of 1-RM. Prior to and at the end of the study, passive stiffness of the biceps brachii was measured with shear-wave elastography (SWE) and Myoton-Pro device. Hypertrophy effects (B-mode ultrasound) and strength gains (1-RM test) were also measured. Training did not induce a significant change of SWE in HI group (13.83±2.49 kPa pretraining, 14.72± 3.01 kPa post training) or in BFR group (14.26±3.64 kPa pretraining, 14.69±4.87 kPa posttraining) ($p>0.05$). Stiffness measured by Myoton device did not change in HI group (202.52±16.42 N/m pretraining, 205.12±18.6 N/m posttraining) or in BFR group (208.92±19.62 N/m pretraining, 206.15±15.52 N/m posttraining)($p>0.05$). Both groups improved in terms of hypertrophy ($p<0.001$) and strength gains ($p<0.0001$). Our study showed that BFR training did not alter passive mechanical properties of the subjected muscle in the long term, thus providing information regarding the efficacy and safety of BFR training.

**Keywords:** Occlusive training, elastic modulus, ultrasound, myoton, shear-wave, elastography

# ÖZET

## DÜŞÜK YOĞUNLUKLU DOLAŞIM KISITLAYICI VE YÜKSEK YOĞUNLUKLU KUVVET ANTRENMANLARININ KAS SERTLİĞİNE ETKİLERİNİN KARŞILAŞTIRILMASI

Dolaşım kısıtlayıcı antrenman (DKA), son dönemlerde popüler hale gelen bir kuvvet antrenmanı yöntemidir. Gerek sporcular, gerekse sporcu olmayan bireyler düşük ağırlıklar ile çalışılabildiğinden bu yöntemi yüksek yoğunluklu antrenmana (YYA) tercih etmektedirler. DKA sırasında kasa uygulanan mekanik gerim etkisi YYA'dan düşük olsa da, metabolik stres etkisi daha yüksektir.Kasların yüksek ağırlıklarla antrene edilmesinin, kaslarda akut olarak sertlik artışına yol açtığını bilinmektedir. Ancak kronik dönemde YYA'ların kas sertliği üzerine etkisi konusundaki bilgi sınırlıdır. DKA'nın kas sertliğini uzun dönemde nasıl etkilediği ise bilinmemektedir. Çalışmamızın amacı, 6 haftalık YYA ve DKA yöntemleri ile yapılan dirsek fleksiyonu egzersizinin biceps brachii kası sertliğine etkisini araştırmaktı. 17 sağlıklı gönüllü DKA (n=8) ve YYA (n=9) gruplarına ayrıldı. DKA grubu 1 defada kaldırılan maksimum ağırlıkların (1-RM) %30-40'ı ile, YYA grubu ise 75-85%'i ile kuvvet antrenmanı yaptı. Çalışmanın başında ve sonunda, kas pasif sertlikleri shear-wave elastografi (SWE) ve Myoton-Pro cihazları ile ölçüldü. Hipertrofi etkileri B-mod ultrason ile, kuvvet kazanımları ise 1-RM testi ile ölçüldü. SWE değerleri YYA grubunda (13.83±2.49 kPa öncesi, 14.72±3.01 kPa sonrası) ve DKA grubunda (14.26±3.64 kPa öncesi, 14.69±4.87 kPa sonrası) anlamlı bir değişim göstermedi ($p>0.05$). Myoton ölçümleri de sertlik değerlerinde de anlamlı bir değişim göstermedi (YYA grubu 202.52±16.42 N/m öncesi, 205.12±18.6 N/m sonrası; ve DKA grubu 208.92±19.62 N/m öncesi, 206.15±15.52 N/m sonrası)($p>0.05$). İki grupta da hipertrofi ($p<0.001$) ve kuvvet kazanımları ($p<0.0001$) görüldü. Çalışmamız, DKA'nın kasın pasif mekanik özelliklerini uzun dönemde etkilemediğini göstermiş ve bu metodun etkili ve güvenli bir alternatif olabileceği bilgisine katkı sunmuştur.

**Anahtar Sözcükler:** Okluzif antrenman, shear-wave elastografi, ultrason, myoton, pasif sertlik

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# LIST OF SYMBOLS

| | |
|---|---|
| $\triangle$ | Delta |
| $\alpha$ | Alpha |
| a | Acceleration |
| c | Shear wave velocity |
| E | Young’s Modulus |
| l | Length |
| m | Mass/Meter |
| N | Newton |
| s | Second |
| p | Density |

# LIST OF ABBREVIATIONS

| | |
|---|---|
| B-mode | Brightness Mode |
| BFR | Blood-flow Restriction |
| CI | Confidence Interval |
| df | Degrees of freedom |
| HI | High Instensity |
| Hz | Hertz |
| ICC | Intraclass Correlation Coefficient |
| IQR | Interquartile Range |
| cm | Centimeter |
| kg | Kilogram |
| kPa | Kilopascal |
| ms | Milisecond |
| RM | Repetition Maximum |
| ROM | Range of Movement |
| RPE | Rate of percieved exertion |
| SD | Standard Deviation |
| SE | Standard Error |
| SWE | Shear Wave Elastography |

# 1. INTRODUCTION

## 1.1 Locomotion and Muscle Strength

Locomotion, the broad term for movement, describes the living organism to change its place by using dedicated systems. At the cellular level, locomotion is achieved by simple flagella, or other cytoskeleton components. As the organism becomes more complex and organized, locomotion needs a series of actions of organs act upon each other such as a limb swing supported by the spine and counter-balanced by the head of a mammal. The higher organisms that use the musculoskeletal system for locomotion learn how to move as early as in utero, and develop new skills, as they grow older. The most complex of all, humans, have the finest musculoskeletal skills such as playing a violin, dancing a ballet, or using an aeroplane or hitting the bull's eye in archery. Although most of these higher skills are organized intensely by central and peripheral nervous system; the finest movements still depend on muscles that are pliable enough to move, but firm enough to function.

In order to function more efficiently and for longer durations, humans developed strength training. Lack of enough muscle strength or recent strength imbalance between the extremities is one of main risk factors of sustaining an injury [1]. The strength training involves the extremities, the core and/or neck of the body, being pulled towards or pushed against a resistance, which is a stable, elastic or a handheld weight. By doing so, the ability to generate force improves in time. The trainable characteristics of musculoskeletal fitness are muscular strength, power, hypertrophy and local muscular endurance. Other performance outcomes such as speed, balance, jumping ability are also positively affected by this type of training [2]. Compared to other forms of exercises such as aerobic activities or flexibility training, strength training is the most effective method for developing musculoskeletal strength. Fitness programs include at least one type of strength training, which are prescribed by many major health organizations to improve health and fitness for all age groups of the population [2].

## 1.2 Adaptive Stress of Strength Training

Resistance training brings an increase in muscle strength and mass. Although it is commonly agreed that there is a close relationship between muscle size and the force generation capacity, strength gains do not linearly correlate with muscle mass change with training [3, 4]. In addition to this, strength training poses an adaptive stress on the skeletal muscle. With this stress, the muscle remodels its internal architecture, potentially reconfiguring external orientation and hence its shape. It is widely experienced that, trained muscles increase their tone and become stiffer. Many athletes stop strength training 1-to-3 days prior to the competition due to fear of sustaining an injury. This fear is based on the general principles of a tired muscle, i.e. glycogen-depleted or increased metabolic byproducts inside the muscle tissue, which then detoriates the subsequent functioning of the muscle tissue. A neuro-muscular tiredness is another component of a tired muscle. This is characterized by delayed neuro-muscular conduction velocity (central component) or excitability at the end-plate (peripheral component) [5]. However, the biomechanical properties of the 'injury-candidate' muscle are still unclear. Specifically, if a stiffer muscle gets more susceptible to injury or not, is not known. Similarly, the characteristics of the 'ideal' muscle tone for sports participation are also not known. Certainly, sports-related overuse or overtraining alters muscle stiffness leading to an increase [6]. Moreover, some coaches believe higher-toned muscles are needed prior to competition thus apply strength training more often in their team, whereas others believe the opposite, and very often avoid performing strength training in the competitive season.

## 1.3 Muscle Stiffness

Muscle tone or stiffness, defines the physical characteristics of the muscle as a sum of contractile and viscoelastic properties [7]. The contractile properties are activated by central nervous system, whereas the viscoelastic properties define the muscle's passive or resting tension [8].

In the clinical setting, resting muscle tone is often assessed by its quality on palpation by the examiner, judging the muscle's pliability, hardness or firmness. The outcome of such measurement is therefore subjective and not reliable. However, the stiffness of the muscle, basically 'its resistance to length change', can be measured by several objective methods including; tensiomyography, myotonometer or Myoton® device. Magnetic resonance elastography and ultrasound elastography are two other advanced methods that can detect soft tissue elasticity of both superficial and deep tissues.

## 1.4 Measuring Muscle Stiffness

### 1.4.1 Myoton®

Myoton® is a non-invasive device that can quantify stiffness, tension and elasticity of the superficial myofascial structures [9]. The device applies a slight pressure on the underlying soft tissues by a test probe. An electromagnet produces a force impulse transferred to the probe. This impulse causes a certain deformation of the tissue under the probe for a short, pre-determined period of time. The probe end releases following the cease of the current to the electromagnet, while the soft tissue performs damped natural oscillations that are sensed by the test probe. An acceleration-transducer placed at the probe end enables recording of the soft tissue deformation-time characteristics. At the maximum compression point of the soft tissue being investigated, the corresponding acceleration amax determined and is used to characterize the resistance force of the soft tissue (force = $\mathrm{m}_{probe}$ x $\mathrm{a}_{max}$, where mprobe is the mass of the testing probe end). For the corresponding deformation depth $\triangle$l, the viscoelastic stiffness of the soft tissue is determined (stiffness = force/deformation i.e., ($\mathrm{m}_{probe}$ x $\mathrm{a}_{max}$)/ $\triangle$l) [9].

For a proper measurement, a method needs to be both valid and reliable. Validity ensures that the measurement actually evaluates the intended measure, and reliability is the extent of a consistent measurement outside of measurement error [10]. Validity of the Myoton device has been studied in healthy individuals [9, 11] which indicates that the stiffness measurements of muscle show a near-linear increase with increasing electromyographic measurements of muscle activation and force during a voluntary isometric contraction. This relationship suggests that the myotonometer output is a valid recording of the muscle stiffness rather than that of the subcutaneous tissue [9]. The reliability of myotonometric methods with the previous versions [12,13] and the latest version [14] of the Myoton device on healthy subjects revealed moderate to very high reliability in previous studies. However, this technique cannot evaluate deeper muscles and the measurement can be affected by skinfold thickness and the stiffness of the skin [13].

### 1.4.2 Shear Wave Elastography

Shear wave elastography is an imaging technique, which quantifies tissue stiffness by measuring the speed of shear waves in tissue. Using ultrasound shear-wave elastography (SWE), the examiner may evaluate deeper structures both in resting state and during contraction using an echography probe. Shear Waves are a type of mechanical wave, which can only propagate in a solid (Figure 1.1). These techniques use dynamic excitation to generate Shear Waves in the body. The waves are then monitored as they travel through tissue by a real-time imaging modality.

Under simplifying assumptions, the Shear Wave speed ($c_t$) in a medium is related to the Young's modulus (E), which is a measure of stiffness:

$$E = 3pc_t^2 \tag{1.1}$$

where p is density. Therefore, by estimating the Shear Wave speed, the underlying tissue stiffness can be quantified. A low speed corresponds to a soft, and a high speed to a stiff medium. In the area in which shear velocity is higher (i.e., the area that is determined to be stiffer) is displayed in red on the screen, whereas if the shear

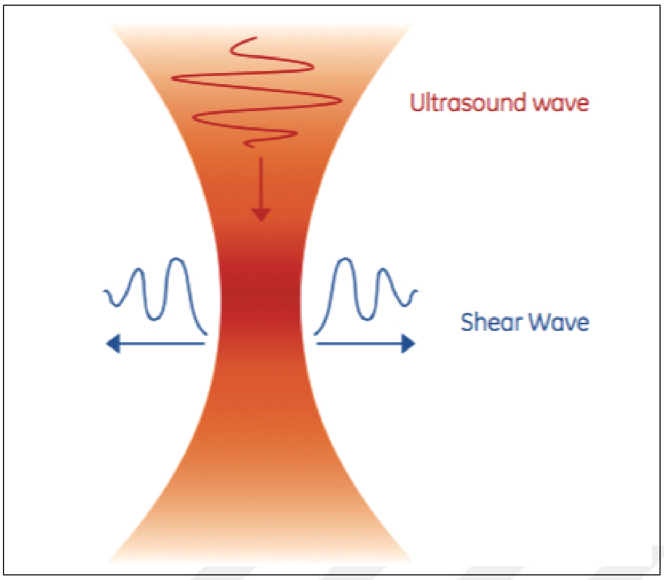

**Figure 1.1** Ultrasound wave and direction of a shear wave.

velocity is lower (the area is determined to be softer) it is displayed in blue on the screen. The shear wave speed can be directly used as a proxy for stiffness or converted to Young's Modulus. In muscle elastography studies, the linear material hypothesis is accepted because amplitude of the shear wave is very small and nonlinear effects can be neglected [15]. Additionally, the equation considers purely elastic material and implicitly neglects viscous effects. The influence of viscosity on shear wave velocity measurements has been previously studied and showed that, the velocity is almost independent from the frequency of the mechanical shock when measured longitudinally, indicating no significant viscous effects [15].

One of the major features of some commercially available SWE systems (e.g., Toshiba Applio Series) is that images can be viewed using three different display modes after freezing: Speed mode (shear velocity [m/s]), Elasticity mode (kPa), and Propagation (arrival time contour) mode (Figure 1.2).

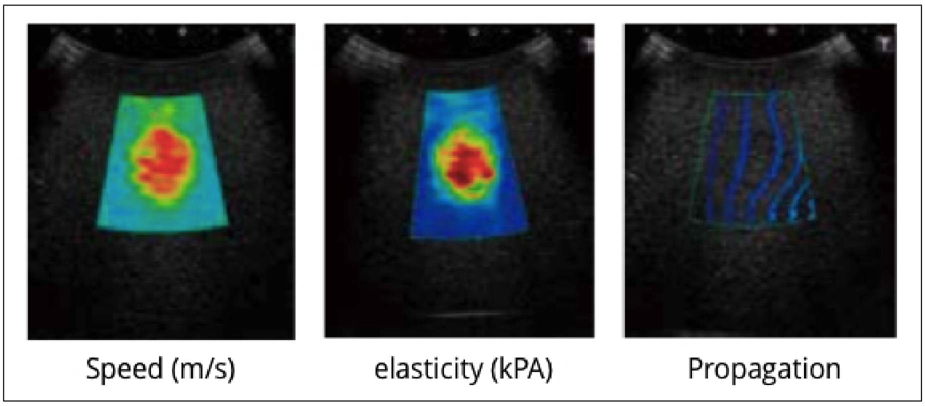

**Figure 1.2** Three different display modes of Toshiba Applio 500 ultrasound system.

With the propagation mode display, it is possible to observe whether the shear waves propagate properly through the tissue in a single still image displayed in propagation mode.

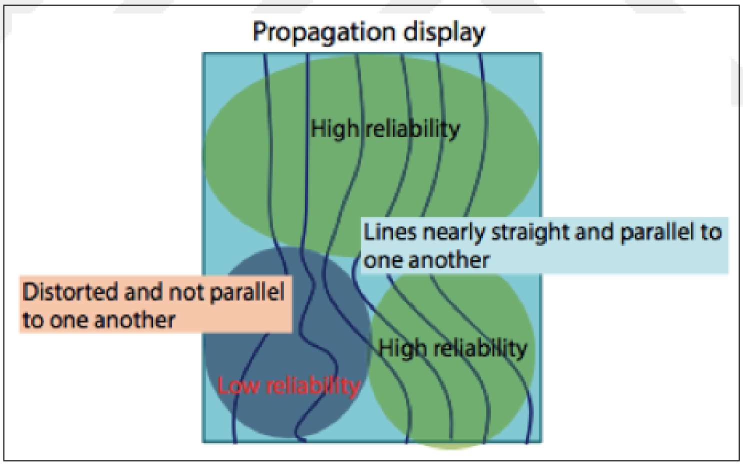

**Figure 1.3** Sample propagation waves and the high and low reliability areas.

The intervals between the displayed contour lines are wider in stiff tissues and narrower in soft tissues. In areas where the contour lines are parallel, the shear waves propagate properly and the reliability of the obtained data is high (Figure 1.3).

## 1.5 Determination of Maximum Strength

In order to commence a strength training program wisely, the maximum strength of an individual is to be determined utilizing several methods. Most commonly used methods are; one-repetition maximum method, cable tensiometry, dynamometry or computer-assisted, electromechanical and isokinetic methods [16].

### 1.5.1 One-Repetition Maximum (1-RM) Method

One-repetition maximum (1-RM) method is widely utilized to assess muscle strength of an individual, especially in physical education faculties, sporting clubs and in individual or team sports settings. In this method, the tester (an athletic trainer, physiotherapist or so) makes a reasonable guess at an initial weight close to, but below, the person's maximum lifting capacity. After performing a general warm-up of 3-5 minutes of light activities involving the muscle to be tested, light static stretching is performed. The initial guessed weight is around 50% of the estimated 1-RM of the individual to be lifted 8 times. This is followed by another set of 3 repetitions at 70% of the estimated 1-RM. Subsequent lifts are single repetitions and progressively heavier until the subject can not perform the motion properly. Weight is added (usually between 1 and 5 kg) to the exercise device progressively on subsequent attempts (1 to 5 minutes of rest in between) until the person reaches his/her maximum lifting capacity. The maximum amount of weight that could be lifted and lowered by the subjects in a proper form with full range of motion is considered as 1-RM [17].

### 1.5.2 Isokinetic Dynamometer Method

Isokinetic dynamometer, an electromechanical accommodating resistance instrument, has a speed controlling mechanism, which accelerates to a preset constant velocity with force application. After this speed is attained, the mechanism adjusts automatically to provide a counterforce to variations in force generated by muscle as movement continues throughout the strength curve. Therefore, maximum force or any percentage of maximum effort generates throughout the full range of movement (ROM) at a pre-established velocity of the limb movement. This provides training and measurement under a continuum from high-velocity (lower-force) to low-velocity (higher-force) conditions. A microprocessor inside the dynamometer continuously monitors the immediate level of applied force. Although isokinetic systems seems more precise and standart, a variety of factors must be controlled or accounted for in order to generate reliable and valid data. Some examples of these factors are; choice of variable measured (peak torque, work, power, etc.), proper positioning and stabilizing body parts prior to and during testing and data reduction procedures [17].

After determination of the muscle strength, one may train the muscles near their current maximum force. The important factor is the overload intensity that governs strength improvements. The most popular type of resistance training involves raising and lowering an external weight against gravity. The proper arrangement of training volume, intensity and frequency ensures strengthening of specific muscles in a progressive manner. Physical therapists first used a three-sets regimen in the late 1940s in order to improve the strength of previously injured limbs of soldiers returning from World War II [16]. The procedure involved three sets of exercises, each consisting of 10 repetitions done consecutively, similar to the regimen used today [2].

## 1.6 Strength Training Methods – High Intensity versus Low Intensity

The American College of Sports Medicine recommends resistance training using a level of intensity of at least %70 of a 1-repetition maximum (1RM), which is defined earlier as the maximum amount of weight a person can lift for no more than once with a proper form [2]. Generally, strength trainings that utilize loads which are at or above 75-85% of 1-RM is considered high intensity (HI), those use between 60-75% of 1-RM is moderate intensity and $<$60% is low intensity (LI) [2].

In order to increase muscular strength, historical guidelines advocate exercise loads of approximately 70% of 1RM to be used, and trainings should consist of 1 to 3 sets of exercises for each muscle group for optimum strength improvement for novice individuals. Progression of training regime to intermediate and advanced levels necessitates multiple-set programs [2]. This is undoubtedly physically tiring, burdensome and may have a potential for increased risk of injury and overreaching [18]. Some individuals prefer lower intensities than higher ones for such reasons, additionally, when only high-intensity training is encouraged in order to gain more strength, some people may get discouraged by this and refrain from doing any type of strength training.

Recent research has demonstrated that LI training can stimulate muscle hypertrophy comparable in magnitude to that observed with HI training [19]. However, cross-sectional comparisons suggest that hypertrophy and strength gains observed with low-intensity training might not be as substantial as those achieved with the high-intensity training [20]. Therefore, practicioners of musculoskeletal medicine were in search of a method, which could provide substantial gains comparable to that of HI, but not as burdensome.

## 1.7 Blood Flow Restriction Training (BFR)

A relatively new method, augmentation of low-intensity resistance training with ‘blood flow restriction’ (BFR) on the other hand, has been shown to enhance hypertrophy and strength gains of the training, using loads as low as 20-30% of 1RM [21, 22]. The training load of 20% 1RM is considered equivalent to the physical activities of daily life [23]. The occlusion/blood flow restriction training involves decreasing blood flow to a muscle, by application of a wrapping device, such as a blood pressure cuff or elastic wraps [24]. It is considered that an ischeamic and hypoxic muscular environment generated during BFR causes high levels of metabolic stress and mechanical tension, which have been described as primary hypertrophy factors [25]. Although the level of mechanical tension associated with BFR resistance training is low, both mechanical and metabolic stress are primary factors of muscle hypertrophy [25]. The metabolic mileau occuring during BFR training theoretically activates other mechanisms such as elevated systemic hormone production, cell swelling, production of reactive oxygen species, intramuscular anabolic/anticatabolic signalling and increased fast-twitch fibre recruitment; which are responsible for muscle growth [19]. The findings from studies, which investigated the effects of BFR in the clinical setting, have important implications for individuals who cannot tolerate the mechanical burden of heavy-load exercise. However, the long-term effects of BFR resistance training on muscle tissue stiffness are not studied widely. The mechanical tension, the flow restriction itself or the altered hormonal environment that BFR training imposes on the muscle tissue may in turn change the passive mechanical properties of the tissue.

## 1.8 Research Questions

It has been shown using elastography that, after moderate intensity strength training, there is a substantial increase in muscle stiffness which returns to its initial values within an hour [26]. A maximal-eccentric type exercise regime resulting a delayed onset of muscle soreness, in comparison, increased shear modulus acutely by 46%; this time decreasing back to its normal values within 48 hours of the exercise [27]. Chronic effects of strength training, in contrast, not studied extensively. In one study, the shear modulus of triceps brachii muscle was evaluated after 6 weeks of moderate-to-high intensity training program, showing no change in this measure [28]. However, to our knowledge, there is no study measuring muscle stiffness in long-term after a BFR training program. Knowing how restricting an extremity's blood flow to a certain extent during lifting a weight affects the elastic properties of the working muscle can provide useful information and comparing the outcomes with a classical high intensity hypertrophy training regime could be valuable regarding the tissue effects of both methods. This information additionally can help musculoskeletal clinicians and sports scientists with regard to prescribing muscle strength training regimens in different settings (low load vs. high load), at different time periods (out season or in season training planning for athletes), for different age groups and people with different prior physical capacities (novice athlete or professional athlete). Additionally, if BFR training results in stiffening of the muscle, which is used during the training, then this may have negative effects on long-term muscular performance. Theoretically the stiffened muscle becomes more prone to athletic injury, thus BFR training may not be a safe alternative to high intensity training for certain settings, i.e. in-season planning of strength training for professional athletes.

Briefly, answering this question could be of help: Is BFR training different than HI training in terms of local tissue effects? To answer this, an objective method – or methods, as in our case in order to increase validity – of measuring muscle stiffness shall be combined with standart training regimens adapted for a muscle, which is responsible from a simple, isolated movement of a limb segment. Biceps brachii is one of those muscles among that are studied widely in hypertrophy settings. Moreover, compared to the upper-limb, providing an effective occlusion to lower limb is technically challenging. Other advantages of studying biceps brachii are, almost everyone already knows or easily learns how to train this muscle, and finally imaging biceps brachii on ultrasound is relatively easy.

## 1.9 Aim of the Study

Therefore, the aim of this study is to assess and compare passive elastic properties of the biceps brachii muscle using Myoton and SWE before and after 6 weeks of two types of strength trainings: high intensity and low intensity performed using a blood flow restriction.

# 2. METHODS

## 2.1 Ethical Approval

Experimental procedures were in strict agreement with the guidelines and regulations concerning human welfare and experimentation set by Turkish law and approved by a Committee on Ethics of Human Experimentation at Istanbul University, Istanbul; with a document number 300-04, 29-02-2016.

## 2.2 Participants

Seventeen healthy participants (9 males and 8 females, age 24.1±3.7yr, body mass 65.8±13.7kg, and height 170±7.5cm) volunteered for the study. The study group consisted of college students who did not perform regularly any moderate or vigorous physical activity. Participants who have any systemic disease, local or systemic infection, who use any medication or who performed any type of strength training in last 72 hours or sustained an injury severe enough to require treatment or prevent activity more than one week in the previous year were excluded from the study. Following a detailed explanation of the purpose and methodology of the experiments, the subjects gave their written informed consent. Participants were then divided into two groups randomly; high intensity (HI group, n=9; 5 males and 4 females, training load 75-85% of their 1-RM) and low intensity with blood flow restriction (BFR group, n=8; 4 males and 4 females, training load 30-40% of their 1-RM with blood flow restriction) group.

## 2.3 General Outline of the Study

After the group allocations, ultrasound (muscle thickness and SWE) and Myoton mearuements were performed. Following this, participants' elbow flexion (biceps brachii) muscle strength is measured, revealing each participants' 1-RM strength. Determination of the free weights to be worked with for both groups was based on this 1-RM testing. Both groups started to perform one-on-one guided relevant strength training for 6 weeks, followed by the aforementioned measurements taking place with the same order once again. The study protocol is outlined in the Figure 2.1.

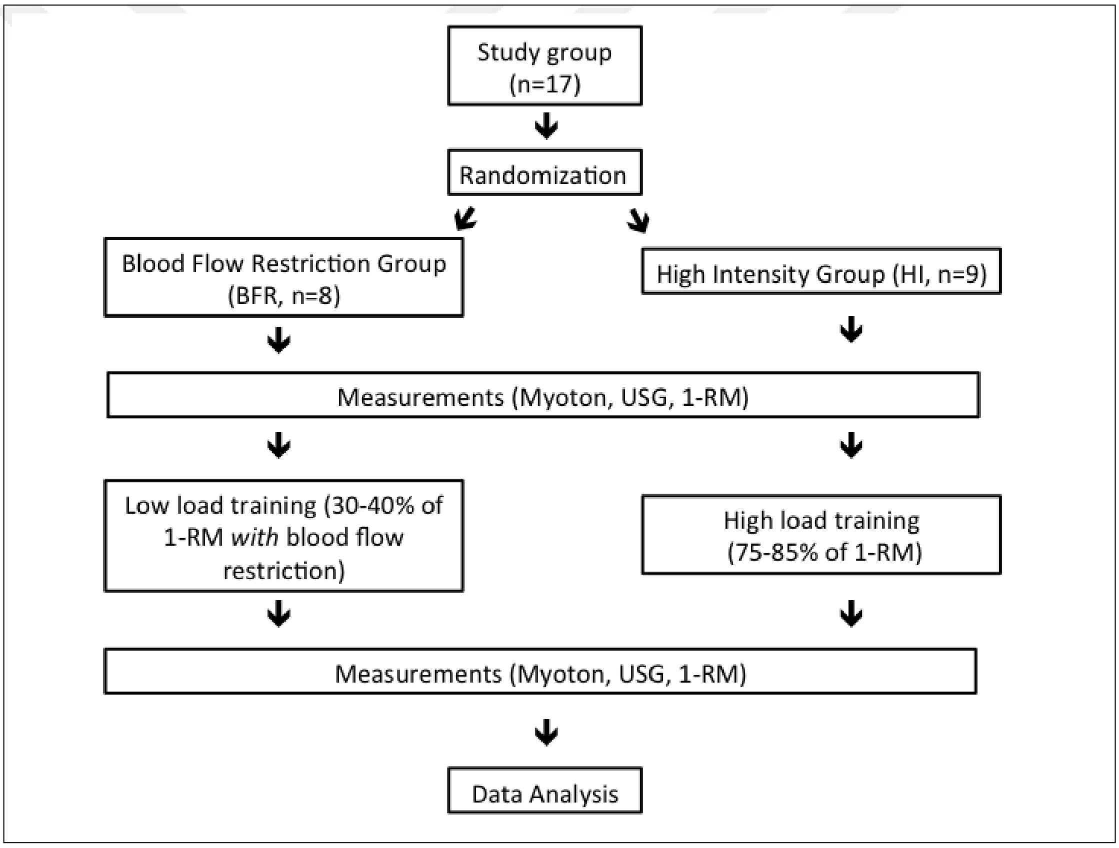

**Figure 2.1** Outline of the study.

## 2.4 Measurements

The first session of measurements consisted of Myoton and ultrasonography, and the other session consisted of 1-RM testing, which took part in separate days, but during the same time period of the day (10 AM - 13 PM). The order of testing was the same for all participants. One clinician, experienced and trained in ultrasonography and the use of Myoton device, performed the first set of measurements, and was blinded to the groups throughout study. Experienced athletic trainers performed the 1-RM test.

### 2.4.1 Myoton®

At the day of measurements, the participants were asked to rest for 10 minutes sitting on a chair before the Myoton® testing. The reference point of measurement was the %66 distal point of the line drawn between the anterior acromion and elbow crest in a 90 degrees flexed elbow, determined as the subjects were sitting as outlined in the literature before [29]. After marking this point with a skin marker, additional points were marked, each 1-cm apart from the reference point, forming a 3x3 square matrix in order to increase reliability (Figure 2.2).

Subjects were then tested in supine position, lying with the shoulder externally rotated and elbows extended and wrist supinated. A standard rigid roller surrounded with a towel placed under the wrist to flex the elbow approximately 15 degrees from the horizontal to take the stretch off the muscle and to enable relaxation (Figure 2.3) [30].

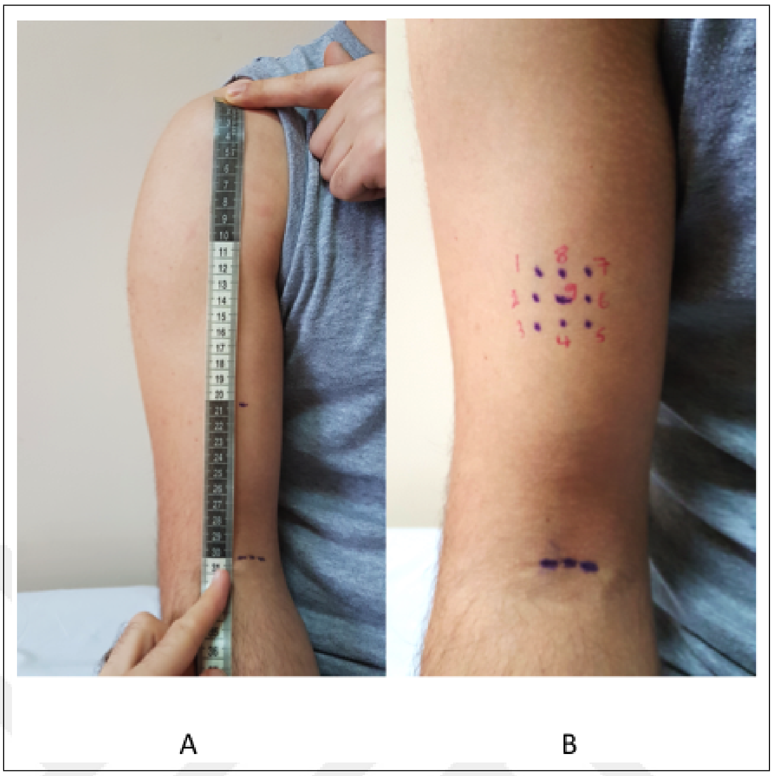

**Figure 2.2** Marking the skin on biceps brachii muscle of the participants, A) Measuring the reference point, B) Marked points on the arm, from 1 to 9.

**Figure 2.3** Position of the participants during Myoton measurements.

Each measurement session started from the same point and ended at the same point. Measurements were performed on the non-dominant arm by placing the probe of the device (3mm diameter) perpendicular on the skin over the biceps brachii muscle with constant preload (0.18 Newton) to pre-compress subcutaneus tissues (Figure 2.4). The device then delivered a short (15ms), low force (0.4 Newton) mechanical impulse, inducing damped natural oscillations of the underlying soft tissues.

**Figure 2.4** MyotonPro® device and assesment technique.

### 2.4.2 Ultrasonography Measurement

The thickness and stiffness of the biceps brachii muscle were then measured using a real-time ultrasound scanner (Toshiba, Applio 500, Japan). A multifrequency broadband linear transducer (14L5) with 60mm footprint was used to take B-mode transverse images of the biceps brachii muscle, as participants were sitting upwards, their arm externally rotated at 45 degrees, elbow flexed at 90 degrees and hands supinated. The forearms of the participants were supported at all times in order to provide passive state. The thickness between the brachialis fascia and subcutaneus fat tissue (Figure 2.5) was measured at the same site as the Myoton measurements.

Three transverse images for thickness measurements were obtained from the same reference point; and then the probe was oriented longitidunally (in the plane of the muscle fascicles) in order to perform shear-wave elastography measurement.

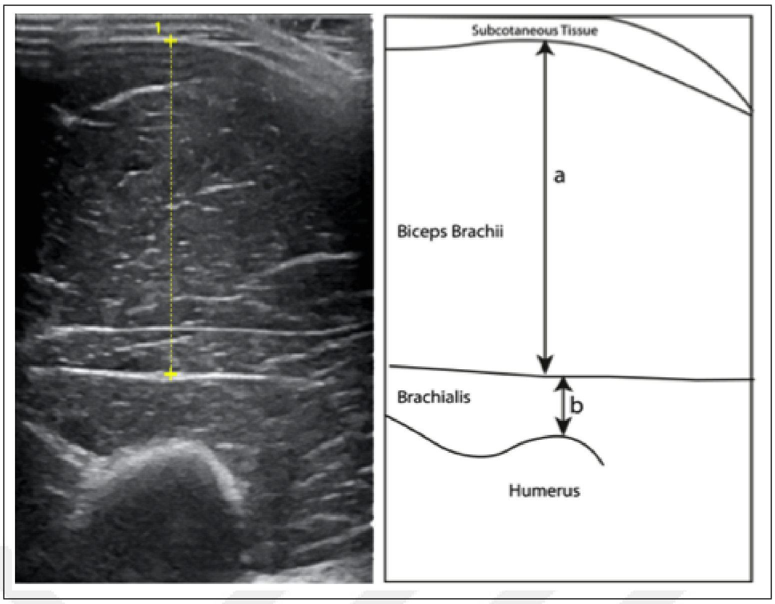

**Figure 2.5** An example of the axial image obtained with the ultrasound system and scheme represents different layers.

During the procedures, a resting platform was set under the forearm in order to place the muscle in a position as slack as possible [15]. Subjects were asked to stay as relaxed as possible. Since a slight contraction could be observed in real time on the shear map, the acquisition was performed only when a stable shear modulus value was obtained.

The shear-wave propagation mapping of the device re-assured if the obtained map was reliable, i.e. propagation waves were parallel to each other, and thus a 1-cm diameter ROI circle was placed at the site where the propagation lines were most parallel inside the map for calculation of the numeric stiffness value (Figure 2.6).

All the procedure of shear-mapping and calculating the stiffness using a ROI circle were repeated three times and the values were averaged for a session.

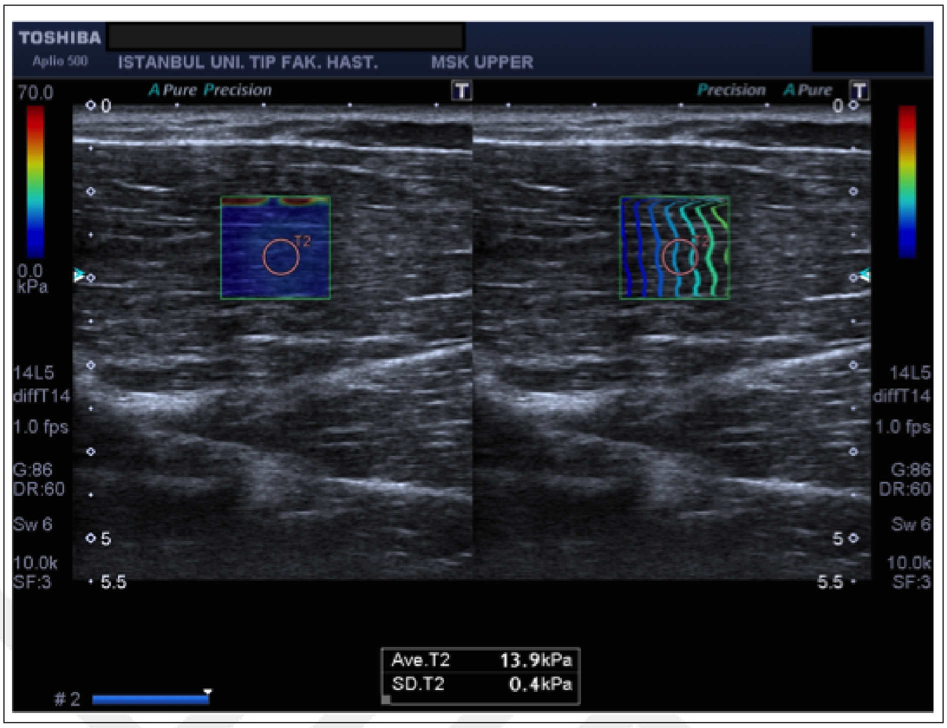

**Figure 2.6** An example of the longitidunal image obtained with the ultrasound system and obtained shear wave with color map on the left and the propagation map on the right.

### 2.4.3 One Repetition Maximum (1-RM) Measurements

Two to three days apart, 1-RM testing was conducted. The concentric 1-RM test for the biceps curl began with a warm-up at a light resistance 50% 1-RM (5–10 repetitions). After 8 repetitions of a warm-up weight, a heavier weight of approximately 70% of 1-RM was attempted for 3 repetitions following a 2-minute recovery period. The subsequent loads were attempted once and increased in 0.5 - to 1kg increments until only 1 successful repetition could be completed. Each participant's 1-RM was determined in approximately 5 attempts because all 1-RMs were found within these attempts [31].

## 2.5 Blood Flow Restriction Method

Blood flow restriction was obtained by using an elastic wrap 76mm in width. The wrap was applied proximally to the subjects' upper arm near the inferior border of the deltoid muscle by the same athletic trainer who accompanied all training sessions. To provide optimal squeeze pressure, a 10-point pressure scale was used. The participants were introduced to the scale as, '10 out of 10' represents the intense pressure felt with pain, '7 out of 10' represents moderate pressure without eliciting any pain and '0 out of 10' represents no pressure at all. The participants were asked whether they understood the pressure scale and if they did not, the points system was repeated until comprehension. The desired pressure was set between 7-8 as outlined previously in the literature [32]. The wrap stayed on the extremity during 3 sets of a movement and was released in between movements.

## 2.6 Trainings

Subjects performed three different elbow flexion movements (preacher Z-bar curl, standing barbel curl and dumbell curl) with different amount of free weights in each group, for 3 sets (Figure 2.7). The BFR group trained with 30-40% of their 1-RM and the HI group trained with 75-85%, without the elastic wrap. The training loads and repetitions used across sets in our study are outlined in Table 2.1.

After a standardized warm up of 15 minutes stationary bicylce, the groups trained 3 sets of each 3 different movements for biceps brachii. There was 30 seconds of rest between each set and 3 minutes between each set of movement. Every training session was accompanied by one of the athletic trainers and subjects were asked to rate the exertion level of each work-out session via 15-grade scale for ratings of percieved exertion, the RPE scale [33].

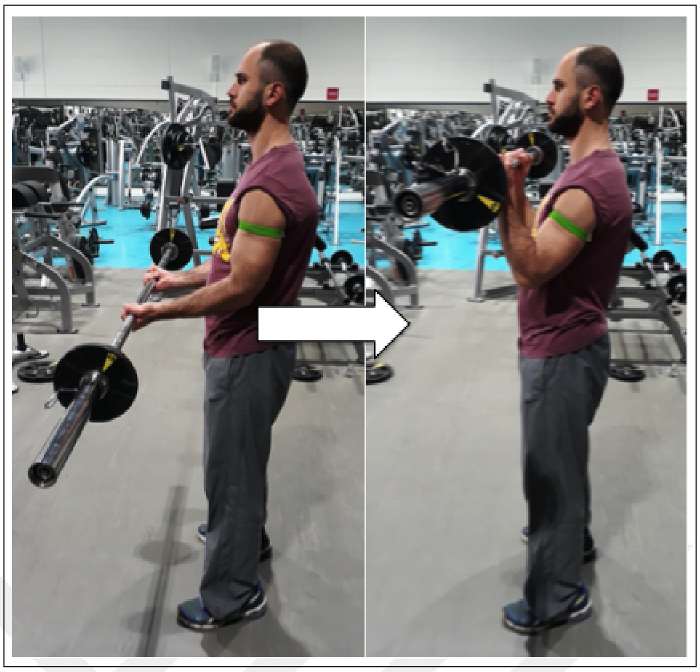

**Figure 2.7** Participant training with a barbell and blood flow restriction.

**Table 2.1**
Training protocol used in our study. HI: High intensity group, BFR: Blood-flow-restriction training group. Entries are given as % of 1-RM, number of repetitions.

| **Movements** | **1$^{st}$ Set** | **s$^{nd}$ Set** | **3$^{rd}$ Set** |
|---|---|---|---|
| **HI group** | | | |
| Z-barbel curl | 75%, 10 reps | 80%, 8 reps | 85%, 6 reps |
| Preacher Curl | 75%, 10 reps | 80%, 8 reps | 85%, 6 reps |
| Dumbell Curl | 75%, 10 reps | 80%, 8 reps | 85%, 6 reps |
| **BFR group** | | | |
| Z-barbel curl | 30%, 30 reps | 30%, 30 reps | 30%, 30 reps |
| Preacher Curl | 30%, 30 reps | 30%, 30 reps | 40%, 15 reps |
| Dumbell Curl | 30%, 30 reps | 30%, 30 reps | 40%, 15 reps |

After the training period of 6 weeks; Myoton, ultrasound elastography and 1-RM testings were repeated with the same order and protocols outlined above. There were no adverse events or injury throughout the study. One of the participans has left the study due to lack of presence.

## 2.7 Data Processing and Statistical Analyses

The data was analyzed with SPSS v.21. Variables are summarized as mean and standard deviation. Normal distribution was checked using Kolmogorov-Smirnof and Shapiro-Wilk tests. In order to detect any significant changes before and after the protocol, Wilcoxon rank test was performed. Mann Whitney U test was used to evaluate differences between groups, and factorial ANOVA was used to evaluate the intervention effects. $p<0.05$ was set as the lowest significance level.

# 3. RESULTS

## 3.1 Demographic Data

There was no statistically significant difference for age, height and body mass between the participants in the high intensity and blood flow restriction groups (Table 3.1).

**Table 3.1**
Demographic data of both groups (mean±SD).

| Demographic data of the HI and BFR groups | | | |
|---|---|---|---|
| | HI (n=9) | BFR (n=8) | p |
| Age, years | 23.89±3.52 | 24.25±4.06 | 0.815 |
| Height, cm | 169.55±7.60 | 170.25±7.89 | 0.888 |
| Body mass, kg | 67.44±13.73 | 64.00±14.34 | 0.541 |

## 3.2 Muscle Thickness

Our reliability of measuring biceps muscle thickness and stiffness was studied in a prior study (please see APPENDIX A for details). At both baseline and post intervention, there were no statistically significant difference between groups for thickness values. As evident from Figure 3.1., there was a significant main effect of intervention on muscle thickness F (1,15) = 42.977, p<0,001, but no significant main effect of group F (1, 15) =0.011, p=0.917 and no significant interaction F (1, 15) =0.145, p=0.709 (Table 3.2).

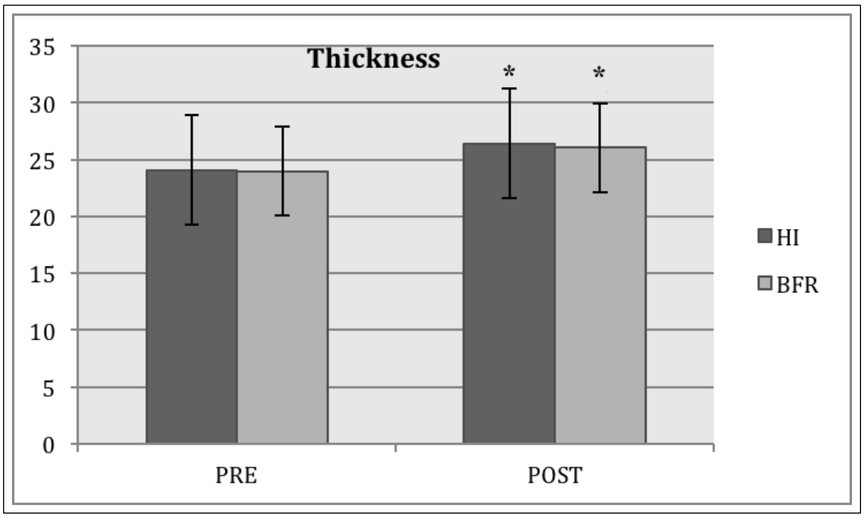

**Figure 3.1** Bar graphs for thickness measures before and after training of both groups. Error bars represent standard deviation (SD). (* $p<0.05$).

**Table 3.2**
Thickness measures before and after training of both groups.

| Group | Pre mean±SD | Postmean±SD | % change | p |
|---|---|---|---|---|
| HI | 24.09±4.63 | 26.42±5.29 | 8.8 | 0.011 |
| BFR | 23.98±4.06 | 26.06±3.79 | 8.6 | 0.012 |
| p | 1.000 | 0.888 | N/A | N/A |

## 3.3 Muscle Strength (1-RM)

At both baseline and post intervention, there were no statistically significant difference between groups for 1-RM strength. The elbow flexion strength of the participants increased significantly in both groups after 6 weeks of training ($p<0.05$). As evident in Figure 3.2., a significant main effect of intervention was shown on muscle maximal strength F (1,15) = 33.429, $p<0.0001$; but no significant main effect of group F (1, 15) =0.007, p=0.934 and no significant interaction (Table 3.3).

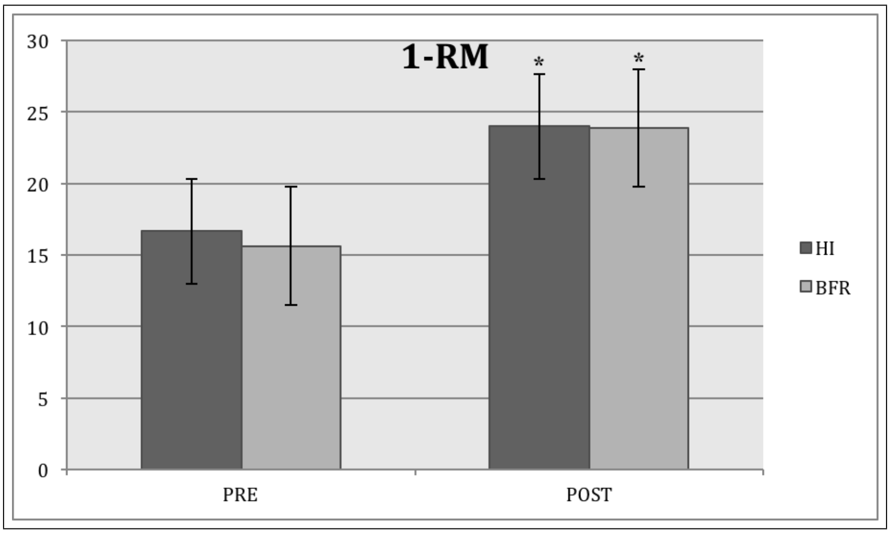

**Figure 3.2** The values for 1-Repetition maximum strength measures before and after training of both groups. Error bars represent standard error (SE). (* $p<0.05$).

**Table 3.3**
The values for 1-Repetition maximum strength measures before and after training of both groups.

| Group | Pre mean±SD (SE) | Postmean±SD (SE) | % change | p |
|---|---|---|---|---|
| HI | 16.66±12.14 (4.05) | 24.00±17.11 (5.7) | 50 | 0.007 |
| BFR | 15.62±10.95 (3.87) | 23.87±16.97 (6) | 48 | 0.011 |
| p | 0.743 | 0.815 | N/A | N/A |

## 3.4 SWE Measurements

For both baseline and post intervention, there were no statistically significant differences between groups for SWE values. There was no statistically significant change in muscle elasticity in either of the groups before and after training ($p>0.05$).

Figure 3.3 shows that measurements using SWE indicates no significant main effect of intervention on muscle stiffness F (1,15) = 0.262, p=0.616, no significant main effect of group F (1, 15) =0.031, p=0.863 and no significant interaction F (1, 15) = 0.032, p=0.860 (Table 3.4).

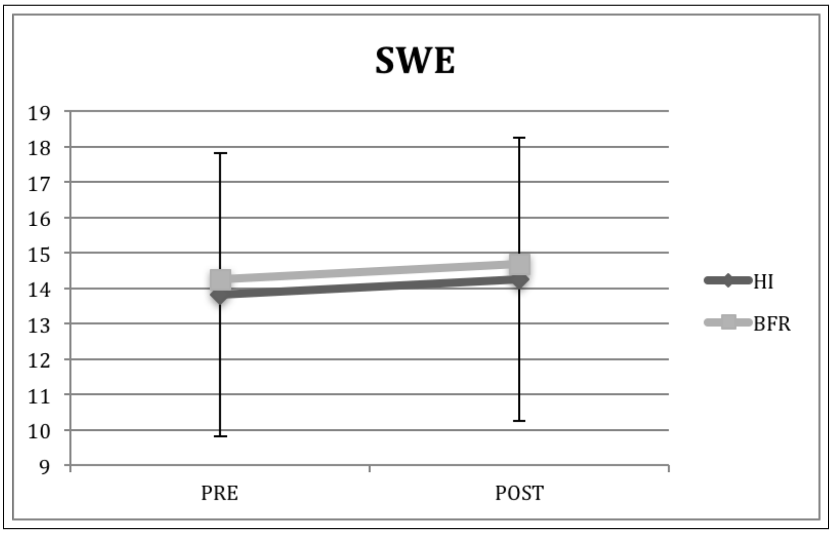

**Figure 3.3** Shear wave elastography measurements (kPa) before and after training of both groups.

**Table 3.4**
Shear wave elastography measurements before and after training of both groups.

| Group | Pre mean±SD | Postmean±SD | p |
|---|---|---|---|
| HI | 13.83±2.49 | 14.72±3.01 | 0.678 |
| BFR | 14.26±3.64 | 14.69±4.87 | 0.889 |
| p | 0.888 | 0.673 | N/A |

## 3.5 Myoton Measurements

Prior to the main study, the intersession reliability of Myoton measurements for biceps brachii muscle was tested in a separate population of 16 healthy volunteers (please see APPENDIX B for details). For both baseline and post intervention, there were no statistically significant difference between groups for Myoton stiffness values. There was no statistically significant change in muscle stiffness in either of the groups before and after training ($p>0.05$).

Measurements using also Myoton indicates no significant main effect on muscle stiffness F (1,15) = 0.001, p=0,987; no significant main effect of group F (1, 15) =0.213, p=0.651 and no significant interaction F (1, 15) =0.862, p=0.368 (Table 3.5).

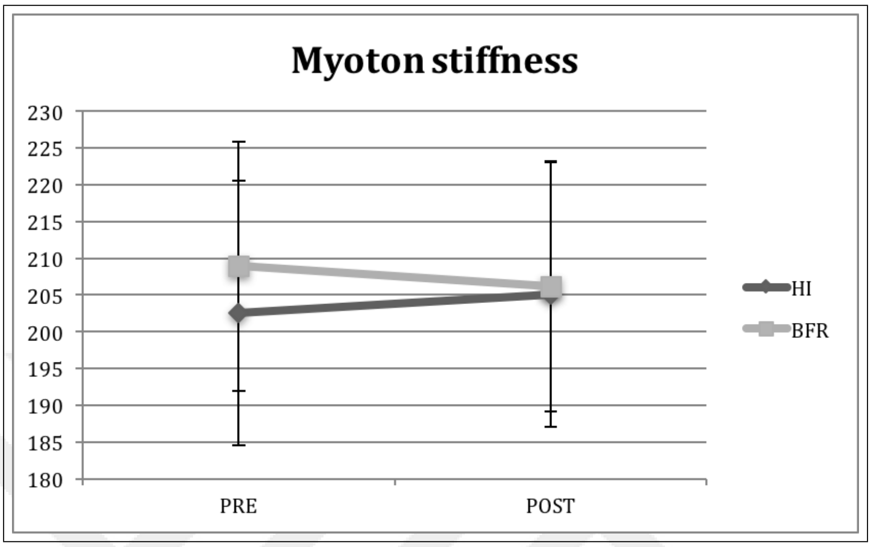

**Figure 3.4** Myoton stiffness (N/m) measurements (averaged) before and after training of both groups.

**Table 3.5**
Myoton stiffness (N/m) metrics for both groups.

| Group | Pre mean±SD | Postmean±SD | p |
|---|---|---|---|
| HI | 202.52±16.42 | 205.12±18.6 | 0.859 |
| BFR | 208.92±19.62 | 206.15±15.52 | 0.779 |
| *p* | 0.541 | 0.606 | N/A |

Note that the outcome of the statistics tests did not change if only the reference point 9 was utilized for pre-post analysis (p>0.05 for both groups).

# 4. DISCUSSION

## 4.1 Myoton Measurements

The stiffness values of biceps brachii muscle found in our study was similar to that of found in previous studies. Agyapong-Badu et al. investigated the normative values and the effects of aging on passive elastic properties of biceps brachii and rectus femoris muscles in both young (n=61, 18-35 years old) and old (n=62, 65-90 years old) sedentary adults. They have found the average stiffness value of biceps muscle in the young group as 213±24 N/m in males (n=34) and 215±28 N/m in females (n=27), with no significant difference between them [30]. Their within session reliability was excellent (ICC 0.97-0.99) whereas good to excellent in between days (ICC 0.72-0.93). The reliability of a previous version of MyotonPRO device (Myoton-3) was studied on biceps brachii of patients with post-stroke both in affected and in unaffected sides. The ICC value for intersession reliability was between 0.87 and 0.91, however there was only 60 minutes in between sessions [34]. Although our intrasession reliability was excellent (ICC 0.96), reliability between days was good (ICC 0.72) when only the reference point was used for calculation, and moderate (ICC 0.66) when the 9-points were averaged for calculation. This showed that deviating even 1 cm from the reference point results with a significant effect so that averaging more assessments provided no improvement, in contrast, diminished the validity of measuring stiffness. We believe that finding the anatomic landmarks in such a sensitive way is not practical, if not impossible, thus questioning the utility of this method between days. Bailey et al. questions finding the true mid-point of the muscle belly further and suggests that anatomical variations in humans, such as biceps brachii sitting more medially on the arms of elderly than on the younger counterparts, may necessitate a compromise from strict landmarking, potentiallly further weakening the between-days reliability of Myoton measurements [35].

## 4.2 SWE Measurements

Young's modulus measurements showed pre exercise values in accordence with previous data obtained with SWE ( 12-17 kPa at resting biceps brachii) [15, 36]. The reliability of muscle shear elastic modulus measurements in various muscles at rest was assessed in a prior study. Except for the small muscles of the hand (e.g., adductor pollicis obliquus), coefficients of variation values were lower than 8%. The muscles studied were tibialis anterior, gastrocnemius medialis, vastus lateralis, rectus femoris, triceps brachii, brachioradialis and biceps brachii [15]. The averaged shear elastic modulus in this study was 3.11 kPa (1/3 of Young's modulus) for biceps brachii, when measured at 90 degrees of elbow flexion. For the intrasession reliability, the mean ICC value was 0.871±0.045; whereas the inter day reliability revealed slightly lower ICC values of 0.815±0.065. Vastus lateralis, triceps brachii and the brachioradialis muscles had ICC values lower than 0.8 (0.740, 0.792 and 0.690; respectively). They also showed that shear modulus was highly dependent on the muscle length and increases with joint angle, i.e. the longer the muscle the stiffer it is, as expected. Thus, only one angle (90 degrees of elbow flexion) was chosen for the study. Our preliminary results of inter day reliability of elastographic measurements revealed moderate reliability (ICC 0.678 [0.13-0.91]). However, we chose random points at a specific length of the muscle belly [37]. Thus, in our main study we marked the measurement point with a skin marker and tried not to deviate from that point.

## 4.3 Strength Gains and Hypertrophy

Both groups' strength gains (50% and 48% for HI and BFR groups, respectively) and muscle thickness changes (8.8% and 8.6% for HI and BFR groups, respectively) were substantial, and similar. Lowery et al. designed a very similar study that utilized BFR with elastic wraps for biceps brachii and measured hypertrophy with ultrasound imaging. The study included 20 participants into 2 groups of HI and BFR training, which interchanged 4 weeks later and trained for 8 weeks in total. Their aim was to investigate the effects of BFR training on muscle hypertrophy when used in combination with a periodized resistance training programme [18]. The volumes of training in both groups were matched in each set, such as when the individual in BFR group did 30 repetitions at 30% of their 1-RM, the high intensity group performed 15 repetitions at 60% of their 1-RM equating to 900 units of volume. This was the aim also in our study, where both groups had 5700 units training volume in total of their 9 sets (Table 2.1). Lowery's study showed that; BFR group resulted in similar hypertrophy gains as high-intensity training, regardless of which was performed first. The muscle thickness in both the BFR-first and high-intensity-first groups increased significantly from baseline to week 4 (6.9% and 8.6%), and from weeks 4 to week 8 (4.1%, 4.0%), respectively [18].

Yasuda compared the strength and size gain effects of HI and BFR training in a 4-group study, consisting of HI group (75% 1-RM), BFR group (30% 1-RM), combined HI and BFR group and a control group. After 6 weeks of bench-press training, increases in 1-RM were similar in HI (19.9%) and combined (15.3%) groups wherease the BFR group experienced a lesser amount of increase, at 8.7% [38]. The training volume in their study was matched between groups at 2250 units per training, which was less than half of which is used in our study. The low volume of training may have contributed the lesser amount of strength gains in their study. Additionally, after 3 weeks, they performed an additional 1-RM testing for HI sessions to re-adjust the new maximal strength, leading to an increase in the used weights for HI sessions of HI and combined groups. This factor may also have contributed the relatively minor difference observed in the BFR group, as they have trained using the constant weight throughout the study. Although it is arguable that bench-press is a multi-muscle activity performed both by pectoralis major and triceps brachii muscles majorly and BFR could have effected triceps brachii only as the wraps were worn on the most proximal part of the arm, their findings provide ability to compare the combined effects of HI and BFR to HI and BFR groups alone. The improvement in muscle strength was significantly greater in the combined group than in BFR group and that was similar to HI group.

Bryk et al. compared the effects of HI and BFR trainings on muscle strength, function of living and pain levels of 34 women who had osteoarthritis and showed that after 6 weeks, quadriceps strength gain in HI group was 30%, whereas this rate was 42% in BFR group [39]. Patients from both groups had a better functional level at the end of the study and an additional benefit was that the patients in BFR group experienced less pain during the training sessions.

The superior strength gains observed in our study for both groups may be associated with increased total volume of the trainings. Most of the studies in the literature have utilized 3 sets of movements each session of exercise, compared to 9 sets used in our study. However, the level of gained hypertrophy was similar compared to other studies.

## 4.4 Stiffness Changes with Training

Studies on muscle stiffness are divided with respect to the measurement methods. Some studies used Myoton whereas others used ultrasound elastography techniques, such as compression elastgoraphy or SWE. Thereafter, results will be discussed in general and details will be provided where relevant.

When a muscle is trained, the percentage of contractile tissue in its structure increases, compared to non-contractile fibro-tendon components [40]. Thus, it can be expected that in long term, muscles of physically active people should become softer than that of a sedentary counterpart. The stiffness measures of 390 athletes with sedentary population and found that athletes had a lower stiffness value (obtained with MyotonPro) than sedentary subjects [40]. Similarly, when stiffness measures of the elderly are compared to the younger age group within the study, elderly people had a higher stiffness value. It was hypothesised that this is due to the relative increase in non-contractile components of the muscle tissue (diminishing of contractile elements) as seen with aging [40, 41]. However, our primary aim was to compare the training effects on muscles and whether it was different in HI and BFR groups due to probable different stresses acting on muscles during both training regimes.

There is much debate on the stress induced by the high intensity training on muscle that whether the imposed stress is beneficial, leading to stimulation of muscle growth, or harmful and causing cell degradation. Opponents of harm claims that the substantial load imposed on muscle during the progressive overload can cause muscle damage and/or injury and therefore it is important to understand to what extent this type of training effects mechanical properties of the muscle [28]. However, the literature investigating muscle damage following an exercise protocol is usually based on extreme eccentric exercise regimes, unlike many high intensity training regimes, purposedly creating a muscle damage and soreness following the exercise [27, 42]. On the other hand, opponents of benefit claim that the reported hypertrophic response from exercise studies is blunted when the eccentric phase is omitted from training [43]. Additionally, it is argued that without muscle damage, satellite cell-mediated compensatory muscle growth is not induced enough [25]. Although the onset of muscle soreness is not deemed necessary for a muscle to be considered as damaged, or the change in muscle stiffness or hardness induced by muscle damage does not necessarily correspond to soreness or other parameters of damage, the hardness is a key mechanical property of materials from material science standpoint. Therefore, the higher hardness indicates the more damage in a muscle. In this sense, Akagi et al. investigated the effects of a six-week resistance training program on shear modulus of triceps brachii muscle using shear wave elastography. Their training intensity was not as high as eccentric-based trainings and consisted of 5 sets of 8 elbow extensions (concentric + eccentric) using a dumbell weight of 80% 1-RM of the participants [28]. After 6 weeks of such training, the shear modulus of triceps brachii did not change significantly, as seen in our results.

One drawback of this study was the evaluation of the shear modulus, which was performed on a transversely oriented probe on the ultrasound scan, which has been shown to demonstrate a lower internal agreement for shear wave speed and elastic modulus measurements [44].

Muscle damage occurs mainly after unaccustomed exercise, particularly if it involves a large amount of eccentric contractions where muscles are forcibly lengthened. Additionally, the initial muscle damage is proportional to the relative load [45]. It is arguable that whether a hypertrophy exercise regime using exercises at lower loads such as BFR creates any damage, not even when the participants are not accustomed [46]. The three most frequently used non-invasive muscle damage masures are subjective soreness scales, strength decrements and alterations in blood proteins such as creatin kinase and lactate dehydrogenase following the exercise. The soreness scales of BFR trainings are reported inferior to that of eccentric trainings (2-3 compared to 7-8, respectively over a 10 point scale), and the increase in creatine kinase is much smaller than those observed in eccentric regimes [45]. Even tough participants in our study experienced some muscle soreness after the first couple of sessions; this was diminished and became absent during the following days. The muscle soreness peaks at 24-72 hours post exercise; and usually subsides as the training continues, thus it is an acute effect of strength trainings. Nevertheless, we performed the post-measurements 72 to 96 hours after the last session at the end of the study, to avoid even the slightest possibility of soreness.

When evaluating the acute effects of strength training on muscle stiffness, one study using compression elastography technique evaluated hardness of biceps brachii after a bout of dynamic arm curl exercise (dumbell weight, approximately 70% of the participants' 1-RM, 5 sets of 8 repetitions, similar to Akagi's protocol), the stiffness index was increased right after the exercise and returned to its initial value 30 minutes later [26]. This study did not aim any muscle soreness or damage, in line with our study, however the assessment method (compression elastography) is relatively subjective. Similar to this, Lacourpaille et al. investigated the time-course effects of exercise induced muscle damage on muscle mechanical properties using SWE. Their exercise regime consisted of 3 sets of 10 repetitions maximal isokinetic eccentric arm flexion, exposing a much higher load to biceps brachii muscle and aiming for muscle damage to occur, and an average increase of 46% in shear elastic modulus was observed 1 hour after the exercise, which has returned to its initial value at 48 hours post exercise [27].

Although the mechanisms of increased stiffness acutely after an exercise bout (such as exercise induced edema and increased intramuscular pressure) are distinctly different than the possible changes expected after chronic exercise, these studies shows that a even after a very high intensity exercise (maximal eccentric), 48 hours of rest is enough to dismiss the acute stiffness increase effects in working muscles.

Blood flow restriction training, in comparison with high-load/intensity training, is generally recognised as safe in terms of muscle damage [25, 45]. It is argued that high-intensity training induces a higher level of mechanical tension and a lower level of metabolic stress than moderate and low intensity exercises with BFR [25]. Metabolic stress (i.e accumulation of metabolic byproducts during exercise), which is magnified under ischemic or hypoxic conditions as seen during BFR trainings, has been shown as being equally important as mechanical tension, if not more, in order to induce muscle growth. This is in contrast with opponents of muscle soreness, considered as a need to induce muscle growth at a desired level. When the mechanical tension of the exercise is kept constant and only metabolic stress is altered, i.e. comparing low-intensity (30-50% 1RM) training with or without the BFR, the hypertrophic effects are significantly greater when there is a blood flow restriction [25]. However it is of our concern that applying the restriction to an extremity over the subjected muscle may also possibly alter mechanical interactions more than it is thought, as questioned by Pearson et al, [25] and myofascial force transmission considering the significant amount of transversely or axially imposed force by the restricting device, or bands. An example of superficial interventions affecting mechanical tension within a muscle is outlined in a kinesiotaping study of Pamuk et al., where a kinesiotape applied on the skin of tibialis anterior muscle caused heterogeneous deformations on the targeted muscle regardless of the tape adhering direction and as well caused heterogeneous deformations on non-targeted muscles [47]. Further studies may investigate the possible mechanical stress of the restriction method itself on muscle tissue underneath the area and also on the whole extremity.

A higher proportion of metabolic stress is not the only advantage of BFR training. There are several other mechanisms by which the BFR training enhances muscle hypertrophy. One of the key features of BFR training, as seen by athletic trainers, coaches and athletes, is the higher percentage of fast-twitch fibers (Type II) recruitment that is seen during the strength trainings, which is thought to be a critical factor responsible for its powerful hypertrophic effects [25]. Under natural conditions, slow twitch (Type I) muscle fibers are recruited first until the intensity of work demands the use of fast twitch fibers. In other words, if the exercise intensity is not high enough, the Type II fibers are relatively spared. However, research on BFR training has demonstrated that Type II fibers are being recruited during vascular restricted conditions even tough intensities are low [25]. The reason behind this phenomena is likely the inadequate oxygen supply for Type I fibers and high metabolite accumulation [25,48]. Although we did not investigate in our study, it is clearly a major benefit of BFR training that may be advantageous in clinical setting such as the utilization of low-intensity trainings post-operatively when patients can not tolerate high loads but in need of strength gains as quick as possible or after a muscle strain that involves fast twitch type fibers. We have no doubt that there will be an abundant number of studies that compare time to return to play after a sustained muscle injury between usual rehabilitations and rehabilitations that utilize BFR training in the close future.

## 4.5 Stiffness and Athletic Performance

It is often argued that ’some’ stiffness is necessary for performance and too much or too little may lead to an injury [40]. However, the stiffness in these studies are referring to an overall stiffness measurement (or model) of an extremity, thus not reflecting the stiffness solely of the involved muscle, and in sharp contrast, this extremity stiffness accounts for the joint moments, multiple series and parallel elastic components (muscles, tendons, ligaments, cartilage, bone) and also involves calculating or estimating the changes in muscle force as a function of contraction velocity [49]. Therefore, the lack of actual relationship between a muscle’s passive stiffness alone and athletic performance exists.

In one study, the relationship between individual muscle stiffness (measured by MyotonPro) of the rectus femoris, biceps femoris and medial gastrocnemius muscle and physical performance variables was assessed. There was a positive correlation between stiffness of only the rectus femoris muscle and sprinting, agility and jump performances [50]. Although highly important for these tasks, stiffness of biceps femoris and gastrocnemius muscles were surprisingly not significantly correlated with these athletic tasks. Moreover, the individual measures of muscular stifness did not correlate with any force measures, such as maximal isometric squat force. Authors have suggested that the lack of a relationship between individual stiffness and maximal force production could be due to the tendon being the key modulator of force velocity and force length relationships rather than the musculature [50]. Akkoç et al. investigated a relationship between passive stiffness of lower extremity muscles (rectus femoris, gastrocnemius lateralis and medialis, soleus) and vertical jump test and shuttle run tests but found no significant relationship in a group of adolescent female basketball players [51]. Further studies are needed in order to establish or disclude any relationship between the muscle stiffness and athletic performance.

## 4.6 Safety Concerns of BFR Training

Although the BFR training is proven to be safe in terms of muscle damage, there have been few cases of muscle wasting syndrome following exercise (rhabdomyolysis) and some concern of the possible systemic or serious side effects due to restricting blood flow for a certain period of time. Authors suggested that there might be problems associated with haemodynamics and ischemic reperfusion injury. A large epidemiological study in Japan reported that these adverse events were very rare and the most commonly seen adverse event is the skin bruising. There have been two cases of rhabdomyolosis after BFR training in one in otherwise healthy ice hockey player after one session of BFR training and the other in an obese sedentary person [19]. In addition to these, there was one reported case of brain hemorrhage during BFR training. Although during BFR training with low loads, the blood pressure raises less than that occur during high-intensity loads, authors put emphasis on general recommendations prior to commencing a strength training, which blood pressure of people who use BFR training ideally should be lower than 160/95 mm Hg, and the training is contraindicated – as well as any physical activity – when the blood pressure is above 180/100 mm Hg [52]. Moreover, the hormones those are responsible from increased heartbeat and blood pressure (catecholamines) tend to increase more in BFR training than exercises without BFR, therefore extra caution or medical examination is recommended for patients with high blood pressure, ischemic or any heart disease or other various systemic diseases before commencing BFR training [52].

## 4.7 Attitudes Towards the Use of BFR Training by the Community

A large community based survey has been conducted in 2016 for the first time since the establishment of KAATSU Training Society in 2004. A web-based questionnaire was distributed to the leaders and instructors of 232 facilities belonging to the society, approximating a total number of subjects in the facilities of 13.000 people. According to the survey, KAATSU training has been applied for numerous kinds of conditions such as health promotion (87% of facilities), diet (85%), beaty and anti-aging (70%), increase of muscle strength (71%), muscle hypertrophy (72%), improvement of sports performance (53%) and rehabilitation (38%) [53]. More than 90 percent of the facilities reported that the training is effective for the majority of people who apply the protocol. They found KAATSU training effective for muscle hypertrophy (77%), increase muscle strength (73%), stiff shoulder improvement (73%), weight loss (73%), beautiful skin (57%), low back pain improvement (57%) and pain improvement (53%).

The symptoms related to blood flow restricted type training were reported as follows: dizziness (37%), subcutaneous hemorrhage (31%), drowsiness (25%), numbness (15%), nausea (15%), itchiness (14%) and others. However, there were no answers about major side effects such as cerebral hemorrhage, cerebral infarction, thrombosis, or rhabdomyolysis [53]. The authors attirbuted the reasons of minor side effects to vagal nerve reflex, as purposed earlier and further analyze of their data revealed that 31% of the surveyed facilities answered ’None’ to the question ’Are you doing regular physical measurements or tests?’. They critisized that these minor side effects can be diminished substantially by close attention of training instructors, measuring the pressure applied in each session and carrying out periodic tests regularly.

## 4.8 Pressure Effects

Our study has utilized practical blood flow restriction, in which an elastic band or wrap is used without the actual measurement of the pressure applied, unlike its predecessor KAATSU training that necessitates automated pressure cuffs. Although knowing the pressure applied during BFR training would provide in-depth information on the level of restriction, this may not as well be a practical approach for most populations owing to the high cost and accessibility of KAATSU systems. Since the first applications of KAATSU training, a more practical approach, as used in our study, has been purposed by Loenneke et al. and widely studied thereafter [24, 54].

This approach uses the subjective pressure scale as a determinant of pressure applied, that do not elicit pain during the occlusion, providing subjective but somehow personalized pressure for an individiual. Setting a pressure across a whole cohort may not restrict blood flow to the same extent in all individuals, as outlined by Hughes et al recently in his meta-analysis [19]. For instance, thigh circumference is an important factor that affects the required pressure to reach the same level of occlusion, with larger limbs requiring a higher pressure, therefore using a guideline in order to obtain a set pressure (such as 1.3 times the systolic blood pressure) may not be effective. Studies varied largely among the pressure applied to extremities, ranging from 60 mmHg to 270 mmHg, reflecting the confusion and lack of consensus on the set pressures [19]. Therefore, using a more practical approach may be beneficial, as Wilson et al showed, that practical BFR training utilizing a subjective pressure scale provided venous but not arterial occlusion, as the training requires, at the pressure level of 7 out of 10 [32].

# 5. CONCLUSION

We have shown that a six-week low intensity resistance training with blood flow restriction induced muscle growth and strength gains as much as classical high intensity resistance training. After six weeks, the stiffness values of both groups did not change from their initial values, suggesting that BFR training did not induce muscle damage or chronic structural change in the biceps brachii muscle and the muscle passive mechanical properties of the biceps were similar in both groups. These findings further support blood flow restriction training as a feasible alternative to high intensity training

# APPENDIX A. Reliability of Ultrasound Measurements

In our prior study [37] for reliability of ultrasound measurements of the biceps brachii muscle, we performed thickness measurements with brightness mode (B-mode) and SWE measurements from a shear-wave cycle on 17 (11 male, 6 female) healthy volunteers in 3 consecutive days, for triple times. The reference point was at 66% distal point of the upper arm of their non-dominant side. Participants were sitting, relaxed and elbows flexed at 90 degrees. Stiffness of biceps brachii was measured by SWE at 3 different close but randomly chosen points, using the same diagnostic ultrasound device (Figure A.1).

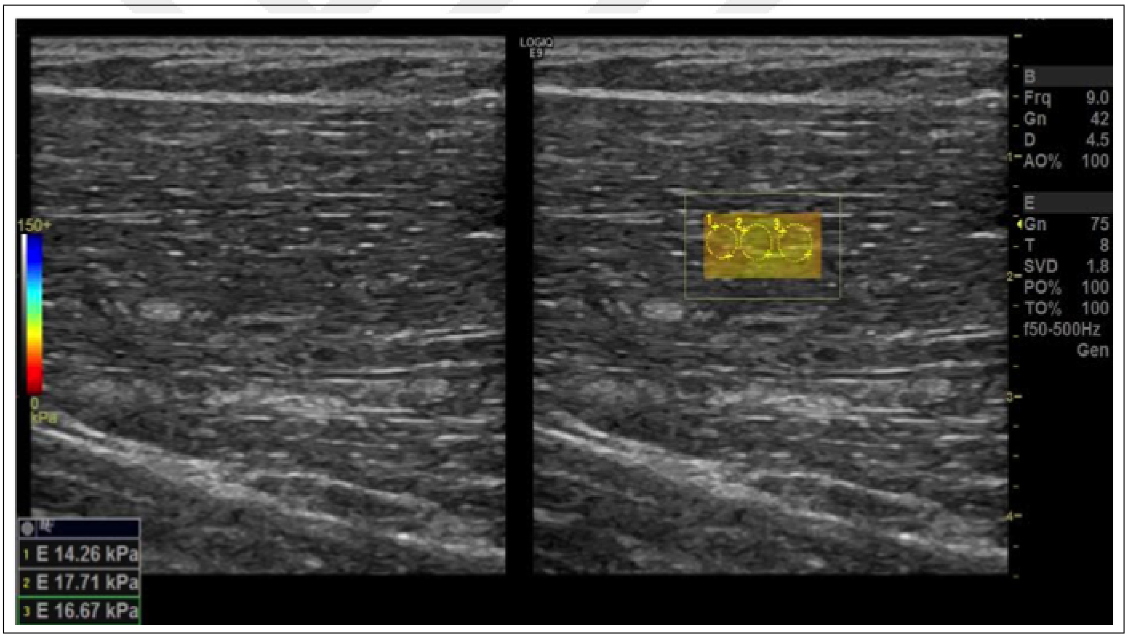

**Figure A.1** Shear wave elastography measurements (kPa) before and after training of both groups.

The inter-sessions thickness measurement reliability was very high r=0.993 (CI: 0.985 to 0.997). No statistically significant difference was found among stiffness measurements of intra-session (p=0.307, p=0.529 and p=0.234 for day 1, 2 and 3 respectively) and of intersessions (p=0.529). However day-to-day stiffness measurements reliability was moderate, r=0.678 (0.13 to 0.91) [37].

As the randomly chosen point for SWE revealed moderate reliability, we used only the exact marked point (corresponding to number 9 at Myoton markings) where we measured the thickness, to measure the stiffness of the muscle for the main study.

# APPENDIX B. Reliability of Myoton Measurements

The Myoton measurements were performed in a separate population of 16 healthy volunteers for two consecutive days for the intersession reliability. Since there were only 24 hours in between sessions, the skin marks (Figure 2.2) that were put on the arms of the subjects were still visible on the majority of the volunteers, thus the measurements were repeated at the very same points. Before applying the ICC test, average values for a session of 9 measurement points for stiffness was calculated (Table B.1). A paired sample T test revealed that the stiffness values of Day1 and Day2 were significanlty different from each other ($p<0.05$). The 95% confidence interval of the difference between days was between 1.53 and 16.78 N/m.

**Table B.1**
Descriptive values of average stiffness measures (of 9 points) obtained by Myoton at two consecutive days.

| Stiffness values | Average (N/m) | Standart deviation (SD) |
|---|---|---|
| Day 1 | 218.49 | 16.66 |
| Day 2 | 209.33 | 13.91 |

The data had a normal distribution for these 16 subjects, for both sessions (Table B.2).

**Table B.2**
Test of normality for stiffness as measured by Myoton.

| | Kolmogorov-Smirnova | | | Shapiro-Wilk | | |
|---|---|---|---|---|---|---|
| | Statistic | df | Sig. | Statistic | df | Sig. |
| Day 1 | .121 | 16 | .200* | .953 | 16 | .545 |
| Day 2 | .146 | 16 | .200* | .952 | 16 | .530 |

Although the skinmarks from Day1 were used for most patients repeatedly, inter session reliability was moderate for the average of 9 points ($r=0.659$, 0.067 to 0.879, 95% CI). When the reliability of only the reference point (point number 9) was calculated, the figure was higher, reaching a higher reliability score ($r=0.719$, 0.234-0.900, 95% CI).

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