# I Executive Summary

Deep Venous Thrombosis, a threatening condition in which large blood clots form in the body's major veins, has received considerable media attention recently because of its significant incidence in passengers on long air flights. The growing popular awareness of "economy class syndrome" in conjunction with the ever-present desire for better in-hospital methods of preventing DVT has shaped the need for a new prophylactic measure.

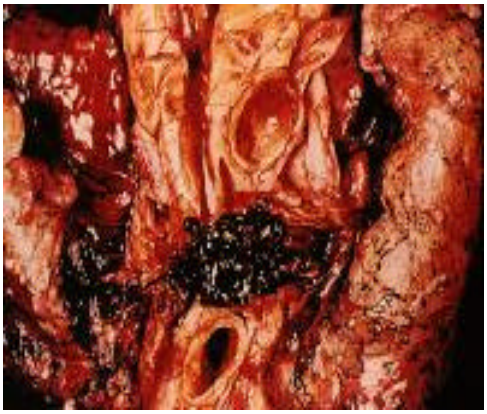

**Figure 1. Deep venous thrombi can break loose from vessel walls and cause potentially deadly obstructions of the pulmonary artery. A thrombus that has led to such a fatal pulmonary embolism is shown in this photo.**

The objective of the ME 282 DVT Team is to produce – by June 25, 2002 - a working prototype of a device that targets the average long-haul flight passenger, while being as effective as current methods in reducing the occurrence of DVT in high-risk individuals. Design specifications and drawings, fabrication instructions, test protocol, and all raw data will be included in a comprehensive report on the design process, which will be presented to the BMI Group at the end of the spring quarter.

During the winter academic quarter, the team established communication with its sponsors, researched the scientific and clinical background for the problem, identified key resources that would be needed for project completion, and determined design requirements. A list of candidate solutions was generated and evaluated, two rough prototypes were constructed, and a single concept - the "electro-stocking" - was selected for primary pursuit. This concept involves developing an electrically conductive graduated compression stocking, and using a small, on-board, fixed-current source to stimulate the calf muscles to contract in a fashion that mimics normal ambulation. In parallel with the development of this

device, the DVT team will pursue proof of principle testing for a concept that utilizes ultrasound as a prevention means.

At the outset of the spring quarter, the team will form subgroups in order to maximize productivity. Two members will take primary responsibility for development of the stimulation circuit/module while the other two members will work to develop the stocking. The ultrasound pathway responsibilities will be similarly divided. One group member will continue to extract relevant information from the literature. Another will attempt to acquire a device to be used in testing. The remaining two members will work on designing a test-paradigm and acquiring the resources needed to conduct testing.

The DVT team is excited by the challenge that this project presents, and feels poised for success in the months ahead.

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# V Background

## 1. *Sponsor Background*

This project is being developed in cooperation with the Stanford Biomedical Technology Innovation Program as a part of the Biodesign initiative. The biomedical technology innovation program is a unique course and project experience designed to provide the knowledge and skills essential for the early development of new biomedical technologies. The program will enhance participants' abilities to identify new opportunities for innovation, to assess clinical needs and market potential and to take the critical first steps in the invention, patenting, early prototyping and development of new concepts. More information about Stanford Biomedical Technology Innovation Program is available on the Internet at http://innovation.stanford.edu.

The current Innovation Fellows (three engineers and two medical graduate students) serve as ad-hoc resources for the ME282 project team. Advisors from different areas of medicine – hematology, pulmonary, vascular surgery – are readily accessible with the help of the fellows.

## 2. *Problem/Need statement*

There has been recent extensive coverage of "Economy Class Syndrome," which attributes a high risk of development of Deep Vein Thrombosis to the prolonged inactivity induced by long airplane flights. Consumer groups such as Airhealth.org and the Aviation Health Institute are raising public awareness in the issue, advocating hydration, flexion of calf muscles, and the use of compression stockings to reduce the risk of DVT. The current state of the art dictates several potential areas for improvement. A new device should be portable, at least as effective as sequential compression and drug therapies, and comparable in cost with compression stockings. Furthermore, the new design should be more comfortable than compression devices and stockings, and easier to use. Finally, a non-invasive, non-pharmaceutical solution, will give the design the distinct advantage of having few potential side effects, such as internal bleeding.

According to the National Institutes of Health 2,000,000 Americans develop DVT each year. Of these, 600,000 are hospitalized for Pulmonary Embolism, 60,000 of which are fatal. Thus, there is a great urgency to produce a device to prevent DVT.

## *3. Market Analysis*

The Stanford BMI group has estimated the potential market for a product that meets the specifications described above to be as high as $500 million. Assuming that the age distribution of air travelers is the same as the age distribution of the US population, this brings the potential at-risk population to about 125 million. This double-counts people making multiple trips, however. So to get a better estimation of the patient population: out of 25 million 2.5 million are at a high risk of DVT, if 6% develop DVT symptoms then there would be 150,000 cases!
The cost of outpatient anticoagulant treatment is approximated to be about $2800. This number implies a total market size of $195 - $420 million. From a legal perspective, potential lawsuits have estimated $700,000 for each victim. Compared to this a $20 preventive device seems very cost effective. These lawsuits abroad and in the US may spur greater education initiatives on the part of airlines and could open an opportunity for easy-to-implement preventative treatments.

## *4. Clinical Background*

Deep Venous Thrombosis (DVT) is a condition in which large blood clots form in major veins within the muscles of the body, usually in the legs and/or pelvis. If thrombi break loose from vessel walls, they can travel upstream and eventually obstruct the pulmonary artery (pulmonary embolism), creating a potentially fatal situation. Even in cases where a DVT does not lead to pulmonary embolism, consequences can be serious. A large deep vein thrombus can damage blood vessel valves, leading to lasting venous insufficiency, and could represent the genesis of chronic swelling and pain.

The development of venous thrombosis is best understood as the activation of clotting factors in areas of reduced blood flow (stasis) (Schreiber, 2001). Among those at high risk for DVT are the elderly, smokers, the obese, people with a history of vascular disease, pregnant women, women taking birth control pills or estrogen, those who have sustained venous trauma (perhaps through limb injury), people who are paralyzed or temporarily immobilized (e.g. post-operative patients), sufferers from inflammatory bowel disease, and thrombophiliacs.

DVT has been dubbed “economy class syndrome” as a result of its significant incidence in passengers (who are relatively immobile for extended periods of time) on long air flights, and several highly publicized cases resulting in pulmonary embolism fatalities have caused considerable public stir.

Accurate clinical diagnosis of DVT is difficult, and thus the exact incidence of the condition is unknown. Approximately one person in twenty develops the DVT in his lifetime, and about 600,000 hospitalizations occur annually in the United States. Pulmonary embolism is the leading cause of preventable in-hospital mortality in the US, causing 200,000 deaths per year (Schreiber, 2001).

***Current Prophylactic Measures Evaluated***

One of the most successful and widely adopted means of DVT prevention in the hospital setting is the sequential pneumatic compression device, which consists of a pair of multi-chambered leg cuffs that are each inflated intermittently in a graded and sequential fashion to produce a "milking" effect, with the largest pressures applied to the lower regions of the leg. Because these devices usually involve bulky compressors and require power from a wall outlet, they are not appropriate for out-of-hospital use. Also, there is a fairly significant degree of noncompliance associated with misuse by staff and (far more frequently) non-tolerance by patients due to lack of comfort.

A relative of the cuff-based system provides intermittent compression to the sole of the foot, which flattens the plantar arch and stimulates the physiologic venous pump in the foot. The mechanism is intended to stimulate the hemodynamic effects of walking. Although one version of the foot compression system has been recommended as a preventive measure for orthopedic patients, additional studies are needed to compare its safety and efficacy with other prophylactic means (Faber, 2000).

Graduated Compression Stockings solve the problems of affordability and portability for the potential out-of-hospital user, but they do so at the expense of efficacy. When worn properly, these leggings provide a static, graded compression that is marginally effective in reducing the risk of DVT. However, if the stockings are applied incorrectly they can actually have a tourniquet effect, increasing venous stasis and the risk of developing a deep vein thrombus.

Anticoagulants and Thrombolytics are the two main drug classes used in treatment and prevention. Anticoagulants, like heparin and warfarin, inhibit the clotting process but do not affect preexisting thrombi. Thrombolytics, like Streptokinase and Alteplase, are clot-dissolving agents, but do not prevent rethrombosis, clot propagation, or embolization. Drawbacks to pharmaceutical solutions include high cost, many contraindications, requirement for doctor monitoring, and potentially severe bleeding complications.

Limb exercise is clearly the simplest means of DVT prevention. Walking, foot dorsiflexion, and other exercises that promote calf muscle action create a pumping action that facilitates venous return, preventing stasis. The degree of DVT protection conferred by limb exercises, however, is directly dependent on how often and thoroughly they can be performed. For many bedridden patients, limb exercises are difficult or impossible, and even the healthy (but at-risk) long distance traveler may not be motivated to move about enough to significantly reduce risk.

## *5. Scientific Background and Motivation*

All oxygen-poor blood is eventually received by the deep venous system on its way to the right atrium of the heart. There are 5 major branches of the deep venous system: two above, and three below the knee. The branches below the knee - the anterior tibial vein (ATV), the posterior tibial vein (PTV), and the peroneal vein, are of most interest to the design team. These branches are the sites of origin for most DVTs. Specifically, most deep thrombi (approximately 80%) are born in the valve sinuses of the soleal plexus veins (which feed into the peroneal and posterior tibial veins) or behind the valve cusps in the PTV and ATV (Faber, 2000).

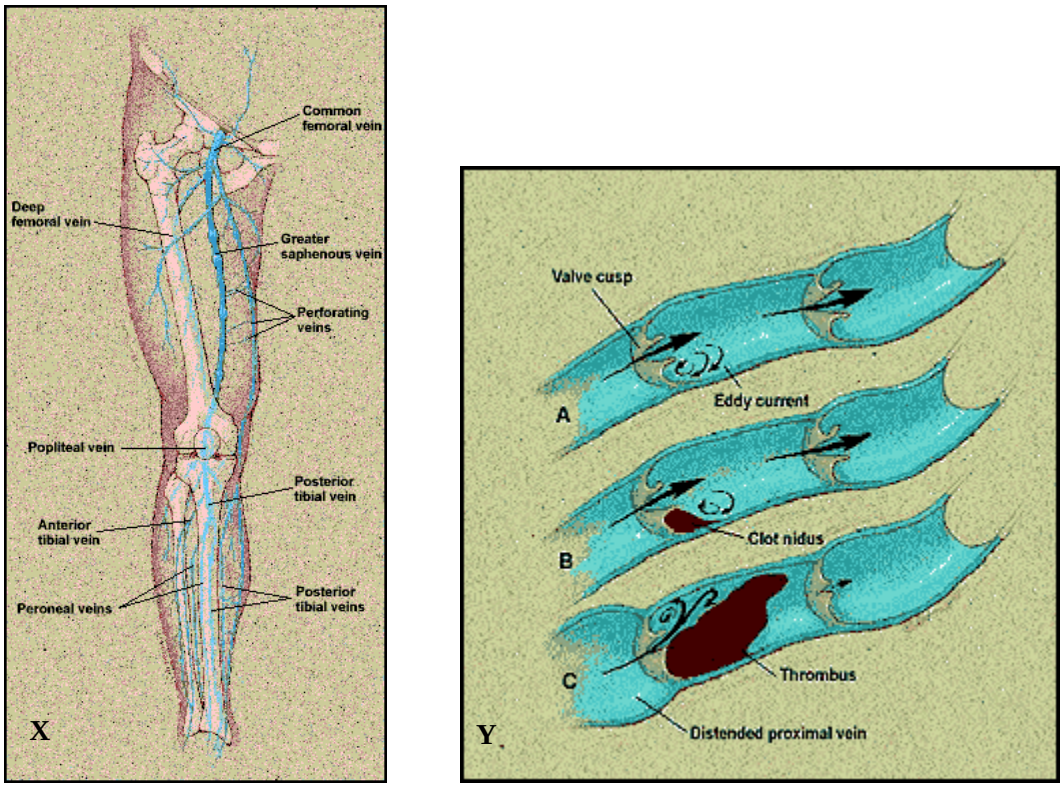



**Figure 2. X. The lower limb veins. The posterior tibial, anterior tibial, and peroneal veins below the knee are of particular importance to the design team. Y. DVT formation. Most deep vein thrombi form behind the valve cusps (as shown here) in the ATV or PTV, or in the valve sinuses of the soleal plexus veins**

So not to be misleading, it should be noted that calf-vein thrombi usually are regarded clinically as non-threatening. Furthermore, it is presumed that many are occult and spontaneously resolved without complication (Schreiber, 2001). The most severely threatening DVTs – the source of 95% of pulmonary emboli, in fact – actually originate in the more proximal deep veins of the lower extremity. So why focus design efforts on the calf area? The answer lies in the importance of the so called "calf muscle pump."

The calf muscle pump, of ten called the peripheral heart, is the body's primary means of returning blood from the leg to the right atrium. Its mechanism is comprised of the calf muscles, the deep venous compartment (pump chamber), a compartment connecting the superficial veins to the deep veins via perforators, and an outflow tract (the popliteal vein) (Feied, 2001). Valves within the pump chamber prevent fluid reflux and permit one-way flow toward the heart.

A particular vein segment, its associated valves, and surrounding muscle constitute a mini pump within the overall system. In normal ambulation, the muscles of the calf contract and relax cyclically. The naturally force-graded muscle contractions act on these serially arranged mini pumps to produce a "milking" of blood cephalad.

something like an airplane seat, for example) for durations of 5 or more hours can significantly increase risk (Giangrande, 2001).

One of the design team's critical assumptions is that it can prevent all deep vein thrombi – those that originate in the calf veins as well as those that originate more proximally – by replicating the action of the normal calf muscle pump, and consequently reducing blood stasis in individuals whose lower-limb movement is constrained. Mimicking of the normal pump can be accomplished in two ways. The first is direct mechanical compression of the calf area. The second is by electrically stimulating the calf muscles to contract. These two strategies will be discussed in more detail later.

Some neuromuscular anatomy is required to approach a potential electrical stimulation solution intelligently. Since the DVT team is pursuing a non-invasive design, only external muscle stimulation via skin-surface electrodes is being considered. Although the lower limb contains several different muscles, it is presumed at the present time that the primary players with regard to the calf muscle pump are the gastrocnemius and soleus muscles. This assumption is based on the relative size of those muscles, their orientation with respect to the veins of concern, their axes of contraction, and an intuitive consideration of their roles in propelling the body forward during walking. Other lower limb muscles such as those that enable knee-joint rotations, ankle rotations, and toe-movements, are viewed as less desirable targets. Additionally, the relatively superficial nature of the gastrocnemius and soleus make tissue impedance a less formidable factor when attempting to stimulate at the skin surface.

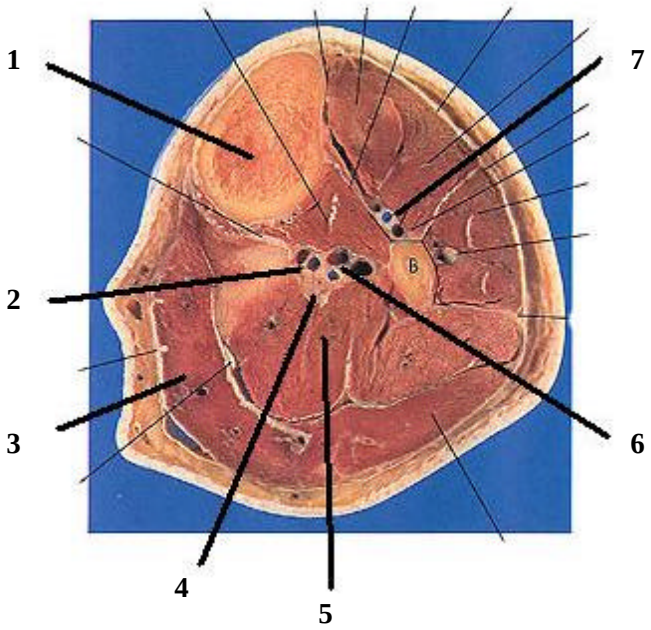



**Figure 4: Cross sectional view of the lower right limb, around the mid-calf level. A-Tibia; B-Fibula; 1-PTV; 2-Gastrocnemius muscle (medial head); 3-Tibial nerve; 4-Soleus muscle; 5-Peroneal vein; 6-ATV**

The gastrocnemius and soleus receive innervation from motor neurons that originate in the ventral horn of spinal segments S1 and S2. These axons are carried into the calf region via the tibial nerve, and distribute terminals throughout the muscles. Neuronal action potentials lead to the release of acetylcholine at the neuromuscular junction. This release triggers a series of chemical responses that ultimately result in muscle action potentials and contraction of the innervated fibers, known as muscle twitch. If neuronal action potentials are produced in sufficiently rapid succession, the resultant muscle twitches will begin to fuse. High enough frequencies can produce sustained contraction, or tetanus.

Stimulating muscles via skin-surface electrodes is not entirely analogous to the situation described above. Since the current source is several millimeters or centimeters of tissue away from the target muscle, higher intensities are required to elicit a given muscle response (over what would be needed if directly stimulating nerve or muscle tissue). Secondly, because the depolarizing stimulus is not localized, twitches of various muscle fibers (in different motor units) may be synchronized. This synchronization, and the associated phenomenon of “reverse recruitment,” hinders the finely graded muscle control that is normally possible. This makes it at least slightly more difficult than one might expect to mimic the contractions that occur during normal walking.

Direct stimulation of muscle fiber requires much higher currents than does stimulation of innervated muscle. As a result, stimulation of muscle by

external electric currents will usually take place most efficiently through neural excitation (Reilly, 1998). By this reasoning, electrodes will be optimally located at the "motor points," (Walthard & Thicaloff, 1971) those sites along the bulk of the muscles that contain the highest density of neuromuscular synapses, or possibly at skin locations above the most superficial parts of the tibial nerve. The DVT team is currently examining the literature to determine optimal electrode location and geometry.

Biphasic stimulation is often used in implanted functional neuromuscular stimulation systems. The "primary" cathodic phase serves to stimulate the excitable tissue while the "secondary" anodic phase performs charge balancing in order to prevent adverse electrochemical reactions from occurring at the electrode tissue interface. Although skin-surface electrodes are not in an extra cellular fluidic environment, the design team feels that it would still be a wise precaution to employ a biphasic pulse. The single caveat is that the anodic current reversal of a biphasic stimulus can act to abolish an action potential developing in response to the cathodic phase; in order to avoid this situation, the two phases should be separated in time by at least roughly 100 μs (Reilly, 1998).

## *6. Benchmarking and Related Technology*

The DVT team has searched periodicals, magazines, patent databases and the Internet for all types of information related to current technology and academic research. In the patent search, the team found that there are three major relevant device categories: mechanical compression devices, electrical stimulation devices, and exercise devices. These three categories reflect the currently available products on the market. The team found that all commercially available DVT prevention devices also fall into the three categories stated above.

***Mechanical compression*** devices are those devices providing compression stress on the calf muscles. Almost all these devices have at least one inflatable fluid chamber and at least a pump or a compressor (US patent No. 6,123,681 uses polymer stripes that contract in accordance with electric stimulus). Most of these mechanical compression devices are boot-like or stocking-like in order to fit a user's calf. Several of them utilize a plurality of inflatable chambers and a controller to provide sequential and graded compression that decreases from the ankle of a user towards the knee of the user. Sequential, graded compression has sound theoretical support on the effect of DVT prevention.

The DVT team visited Stanford Medical Center and examined one of the most clinically popular sequential pneumatic compression devices, the SCD Sequential Compression System produced by Kendall. Inc. The

SCD unit has basically two separate parts. They are a case, which contains a compressor, a control circuit, and four valves; and a pair of compression sleeves. The case weighs around 25 lbs and has a dimension of roughly 10”x8”x4”. The compression sleeves come in different sizes and usually cover about 4/5 of a patient’s leg. The SCD unit is AC powered and not suitable for use on board an aircraft.

Nicolaides et al. suggest that the sequential compression devices are more effective than non-sequential devices in preventing DVT. The studies of Kamm R et al. and Salzman et al support the conclusion of Nicolaides, and Kamm suggests that pure gradation is better than pure sequencing. Flam et al. found that Intermittent Pneumatic Compression (IPC) systems produce a significantly higher venous blood flow than sequential pulse systems when given the same dimension. The mechanical compression is clinically proven to be effective. However, studies by Comerota et al. show that patients usually find the compression devices uncomfortable and sometimes try to remove them when not attended by nurses and doctors.

***Electrical stimulation*** devices are also found applicable in prevention of DVT. In US patent No. 6,226,552 “Neuromuscular Electrical Stimulation in Prevention of Deep Vein Thrombosis,” an electrical stimulating device is disclosed. The device is intended to conduct electrical current to a patient’s limb, contracting the superficial muscles. In US patents No. 6,181,965, No. 6175764, and No. 6,051,017, implantable microstimulators are suggested. The work by Klecker et al. has experimentally proved that electrical stimulation effectively increases venous flow velocity.

Some other devices and methods that ultilize electrical stimulation, though not explicitly indicated for the prevention of DVT, may represent useful technology for the design team (From www.doctorstore.com):

***Electro-Acupuncture***: Characterized by applying to specific acupuncture or trigger points on the body small electrical impulses (milliamp/microamp) through acupuncture needles or with electro-stimulating, hand-held cutaneous probes. The frequency of stimulation may vary from 1 to 1,000 Hz.

***High Voltage Pulsed Galvanic Therapy***: Characterized by high volt, pulsed galvanic stimulation, used primarily for local blood flow stimulation through muscle pumping and through the "polarity effect." Excessive fluid is comprised of negatively charged plasma proteins, which leak into interstitial spaces. By placing a negative electrode over the site and a positive electrode at a distant site, the monophasic high voltage stimulus applies an electrical potential, which disperses the negatively charged proteins away from the site, thereby helping move the excess fluid.

***Interferential Therapy***: Characterized by the crossing of two medium, independent frequencies that work together to effectively stimulate large impulse fibers. These interfere with the transmission of pain messages at the spinal cord level. Because of the frequency, the IF wave meets low impedance when crossing the skin to enter underlying tissue. This deep tissue penetration can be adjusted to stimulate parasympathetic nerve fibers for increased blood flow.

***Microcurrent Therapy***: Characterized by subsensory current that acts on the body's naturally occurring electrical impulses to decrease pain and help facilitate the healing process.

***TENS***: (Transcutaneous Electrical Neural Stimulation) Characterized by biphasic current and selectable parameters. Stimulates sensory nerves to block pain signals, stimulate endorphin production to help normalize sympathetic function distal to the electrodes.

A final category is interactive exercise devices, for example, US patent No. 4,501,421. Exercises are proven to be effective but are not impractical for long-haul air travelers and patients in hospital on DVT prevention.

***Ultrasound***

Research papers indicate that low frequency, high intensity ultrasound is a solution to breaking down clots. The theory behind this belief is that ultrasound helps induce the production of the enzyme tPA (tissue plasminogenic activator) which acts on fibrin and helps to dissolve clots. Another theory that helps explain the dissolution of clots is that it vibrates and shakes off the clots before they form.

At present several devices using ultrasound are available in the market, not only for surface testing and imaging but also for therapeutic purposes. The device that drew our interest and helped generate our concept was the IVUS.

***IVUS***

In recent diagnostic equipments using ultrasound, an Intra-Vascular Ultrasonic (IVUS) imaging system plays an important role to observe the internal structure of blood vessels to diagnose diseases like blood stricture, blood vessel lesion, etc. Currently a new scanning method using a micromotor instead of a mechanical motor has been developed where rotation-transmitting wire was not required. A catheter was developed for this micromotor type IVUS endoscope method and calibrated through phantom experiments. Finally, it was applied to observe the inside of blood vessel by an in vitro experiment.

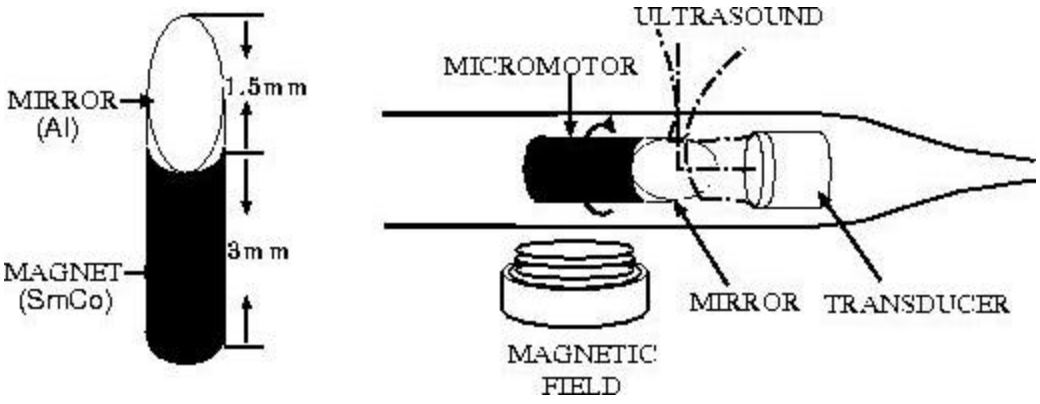
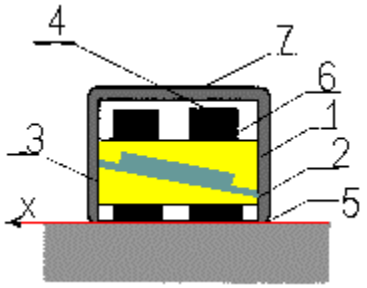



**Figure 5: IVUS**

***Ultrasound Generation***

A directional diagram of how to produce ultrasound is shown below. In all cases, on a surface of ultrasound input it is necessary to create distribution of acoustic pressure. At the same time, ultrasound is transmitted in object only through the area, filled by contact magnetic environment. In turn, the directional diagram depends on amplitude-phase distribution of oscillatory speed of particles on a surface. Thus, operating a magnetic field in the area of acoustic contact there is the opportunity to operate by the directional diagram of acoustic radiator. In this case, measurements were made by a transducer with a corner of a prism 7°. Piezoelectric element was the source of acoustic pressure. The magnetic system was placed in damper and consisted from two permanent magnets in a form of rectangular parallelepiped. The magnetic contact liquid is located in a backlash between surfaces of an acoustical transmittance element (prism) and the investigated object.




1. Piezoelement
2. Magnetic fluid
3. Acoustic prism
4. Magnet
5. Sample
6. Damper
7. Frame

**Figure 6: Principal of ultrasound Generation**

Below are graphs indicating the frequencies generated for different directions of acoustical axis relative to the area of magnetic fluid.

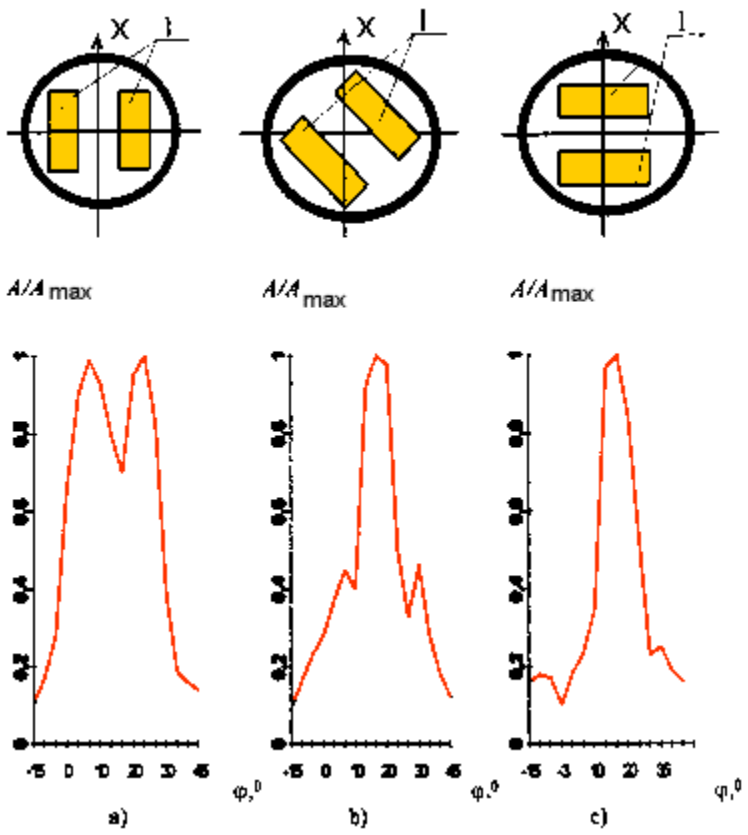



**Figure 7: Types of waveform generated depending on acoustic prism position and magnetic alignment.**

The frequencies generated from this device are 1MHz. The waveforms depend on the alignment of the axis of the acoustic prism with the magnet.

## *7. Project Team*

There are four students on the DVT prevention project design team. They are:

**Justin Blanco** jblanco@stanford. EDU
Justin graduated from Brown University with an ScB in Neuroscience (May 1999). He spent a year teaching chemistry at Deerfield Academy (Deerfield, MA) before interning at Medtronic Neurological, where he worked designing new intrathecal catheters for the company's implantable drug pumps. He is currently pursuing an MS in Mechanical Engineering, with a focus in biomechanical device design. Justin has a strong interest in neural prostheses, and plans to purse an MD after his studies at Stanford. His strengths are problem and design requirement definition, concept generation, and test protocol development.

**Eric Tao** erictao@stanford.EDU
Eric is currently a PhD student in Mechanical Engineering (Design Division). He obtained his BS in Mechanical Engineering from Tsinghua University in Beijing, China. His research is focused on MEMS (Micro-Electro-Mechanical Systems) semiconductor micro-fabrication with biological applications. He has experience in IC fabrication, CAD modeling, rapid prototyping and manufacturing.

**Abha Chinubhai** abhac@stanford.EDU
Abha came to Stanford from LD College of Engineering, India, and has a background in Mechanical Engineering. She is now a part of the Mechanical Engineering MS program with biomechanics as her depth. Abha is an absolute bio-enthusiast. Her excellent analytical skills will be essential in determining the feasibility of alternative design solutions.

**Jay Yin** jayyin@stanford.EDU
Jay graduated from National Taiwan University with a degree in chemical engineering. He worked as a technical consultant for Lee Tsai & Partners for 13 months before coming to Stanford to pursue the MS in Materials Science and Engineering. Jay has experience in patent processing and infringement assessment, and is highly interested in the biology-engineering interface. His strengths are analytical reasoning, data mining, and critical thinking.

Justin Eric Abha Jay

**Figure 8: The DVT Team**

## *8. Project sponsors*

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Josh Makower M.D. Consulting Associate Professor of Medicine
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# VI Design Definition

## *1. Purpose of Design/Model*

The purpose of the design is to develop a DVT prevention device that is suitable for airline environments. The device must be comfortable, light, small, and quiet in operation. It must not be embarrassing to use or wear on board an aircraft. The device should be able to generate at least one type of stimulus that fits the purpose of DVT prevention. The stimulus must be appropriate for users awake and asleep. Furthermore, the stimulus of the device must not introduce harmful chemical or physiological reactions of any kind, even after long durations of. The device should also be enjoyable in order to encourage repeated use of the device.

## *2. Project Goals and Scope*

The project as assigned is very broad in scope. It calls for "either a working prototype or an advanced concept...prophylactic measure to decrease the occurrence of DVT for passengers on long airline flights and for other individuals at high risk."

The "high-risk" group spans several populations with widely divergent need-profiles, and the design team felt the need to focus its conception of the target market in order to select a design pathway. Toward that end, it has defined the long-haul airline passenger as the primary target. However, the team is drawing heavily on input from the hospital setting with the intention of making the final product compatible with both environments. Gathering such feedback also seems a logical approach in light of the fact that hospitals employ the most effective preventative measures currently available.

Because designs intended for installation in aircraft violate the cross-compatibility requirement, such solutions were excluded from consideration.

As per the "nonmedical" customer specification outlined in David Maltz's needfinding document, solutions that were pharmaceutical and/or invasive (i.e. requiring implant) were also excluded from consideration.

Concepts not having sufficient backing in the literature - and thus requiring proof-of-principle and possibly the design of an animal validation model -

were not excluded from consideration. However, it was agreed that a concept of this nature would occupy a secondary pathway in the interest of ensuring the production of a working prototype by year's end.

### *3. External Constraints*

In accordance with Stanford BMI's Customer Needs Analysis Report and project proposal, the DVT team is developing the project under the following constraints, which pertain to the definition of the user and the circumstances under which the product will be used.

- **Marketability**
  In general, the customers of this medical device will not only be healthy long haul air flight passengers (the design team's primary market), but also general hospital patients. The population for whom the device would be useful is large and diverse and will be difficult to target effectively.

- **Ease of acquisition**
  There are several alternatives for users to acquire this medical device. The device may be leased from providers or provided by airlines.

- **Cost**
  The product should be inexpensive (should be in a similar range as compression stockings -- $10-$20) so as to have a lower barrier to enter the targeted market.

### *4. Functional Requirements*

Based on the sponsor's needs statement and market analysis, the DVT team generated a list of design requirements and broke them down into to two major categories, functional requirements and physical requirements.

- **Safe**
  As with all medical devices, the final product should be safe to use under any circumstances. Specifically, there must be little risk for electrical shock or for hampering the circulation. It must be easy to remove/reverse the system in the event of malfunction.

- **Easy to use**
  The device must be as user-friendly as current treatments. Ease of use will be determined through interviewing hospital staff, patients and the general public.

- **Reliable**
  Appropriate reliability testing protocol will be determined during the spring quarter.

- **Effective**
  It will be as effective as sequential compression devices and anticoagulant therapy, which are the most effective solutions currently available.

- **“Nonmedical”**
  There are no potential side effects; noninvasive and nonpharmaceutical.

### *5. Physical Requirements*

- **Compact geometry**
  To maximize portability, the device must be compact. There must be no bulky compressor or external power source. The device should fit inside a typical piece of carry-on luggage (22" x 14" x 9") along with other articles.

- **Ergonomic design**
  Some functions will be customizable/adjustable to make it more comfortable than current GC stockings and compression cuffs.

- **Interchangeability**
  It will be nice to have interchangeability so that users don’t need to differentiate devices for left or right legs.

- **Long running time**
  Considering long flight situation, the device should be able to function for at least 12 hours periodically.

- **Non-toxic, hypoallergenic material**

- **Consistent functionality in temperature range -20 – 120?F at pressures 760 mm-Hg ? 5%**

- **Simple structure (manufacturability)**
  To ensure ease of use, as well as to improve portability, the system needs to have limited number of parts.

- **Low weight**
  It will be nice if the entire system weighs less than 3 lbs to improve the portability.

- **Adjustability**
  The device must accommodate the average range of variability in limb girth.

- **Quietness**
  The whole system should function at less than 60 db, which is the approximate intensity level for normal conversation.

The design team ranked each of the above requirements on a 1 to 10 scale (10 indicating most crucial). These rankings were later employed in Pugh Analysis of solution concepts.

**Table 1: Design requirements importance ranking**

| Requirements/Goals | Importance(1-10) |
|---|---|
| Marketability | 7 |
| Ease of acquisition | 5 |
| Cost | 7 |
| Safe | 9 |
| Easy to use | 8 |
| Reliable | 9 |
| Effective | 7 |
| "Nonmedical" | 9 |
| Compact geometry | 8 |
| Ergonomic design | 8 |
| Alternative power source | 6 |
| Long running time | 7 |
| Material | 9 |
| Simple structure | 8 |
| Adjustability | 7 |
| Interchangeability | 7 |
| Low weight | 7 |

## *6. Regulatory Considerations*

If the team decides to use pneumatic sequential compression, the device will be classified as class II and will be regulated by Sec. 870.5800 "Compressible limb sleeve." If the team stays with electrical stimulation, the device will be a class II device and will be regulated by Sec. 890.5850 "Powered muscle stimulator." However, if the team chooses to use ultrasound, the device probably belongs to class III since the device will provide stimulation other than deep heat (regulated by Sec. 890.5860 "Ultrasound and muscle stimulator").

### *7. Other Constraints on Design/Model*

Eventually, the device produced by the DVT team may be marketed to airline travelers. If it requires a prescription to buy the device, the sale is likely to be to limited to airline travelers who have DVT history and specifically request the prescription. The DVT team has to take the pertinent FDA regulatory issues into careful consideration in order to avoid inadvertently shrinking its market.

# VII Design Development

## *1. Vision/Strategy*

The DVT team's design strategy is summarized in the flow chart below.

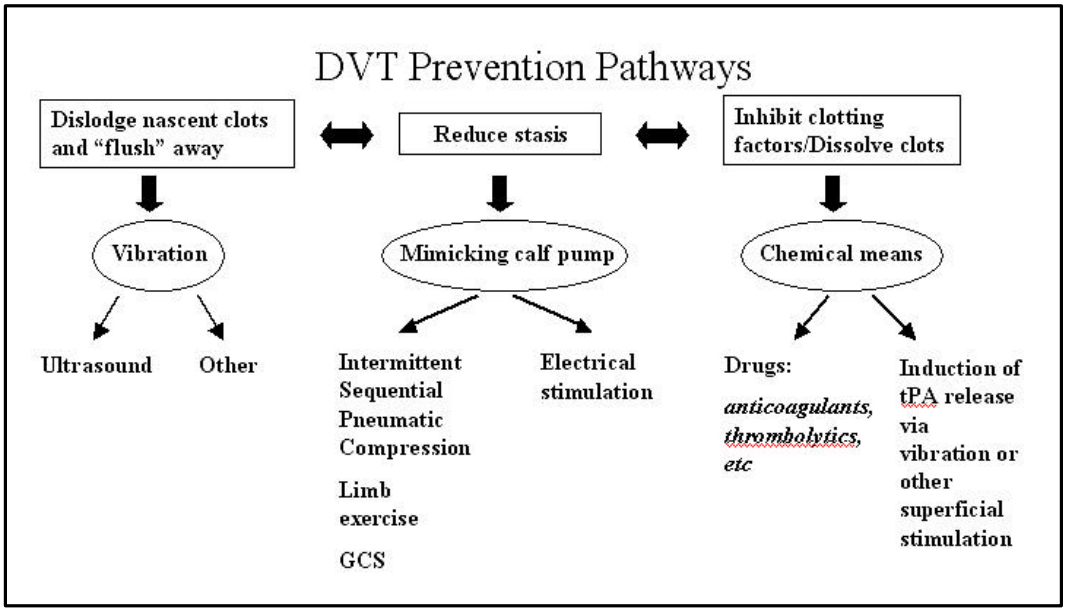


**Figure 9: Design strategy**

An investigation of the scientific basis of the problem, which included discussions with physicians and a thorough literature search, suggested three broad pathways by which to approach prevention/treatment of DVT: 1) dislodging embryonic clots from vessel walls before they reach potentially threatening size, thus facilitating natural thrombolysis; 2) reducing blood stasis; and 3) Inhibiting clotting factors and directly dissolving clots. Notably, the stasis reduction pathway is not exclusive of the other two; there is some evidence that shear stresses on vessel walls may lead to the release of anticoagulant or thrombolytic agents, and the kinetic energy accompanying increased flow could well be sufficient to dislodge early clots.

Mechanisms by which each of these particular pathways could be realized were then determined, and general solution categories were generated on the basis of these mechanisms. Next, those solution categories were filtered using sponsor input and other project scope considerations. Finally, the team then developed a list of design opportunities in each of

the candidate solution categories, and on the basis of those opportunities produced five specific design concepts.

## *2. Overview of Work Completed*

The DVT team generated five different solution concepts: two involving compression, two involving electrical stimulation, and one involving ultrasound. All will be described in detail below. Since the compression concepts offered the opportunity for construction of quick mock-ups, two preliminary prototypes were produced and evaluated. Once design requirements were finalized, they were weighted and used as criteria in a Pugh Analysis of all five of the candidate solutions. The results of this analysis and the lessons learned from the prototyping process have motivated the DVT team to focus its design efforts on developing the "electro-stocking" concept. As a secondary and parallel pathway, the team will pursue its ultrasound concept.

## *3. Design Concepts Generated*

The design team generated concepts from three areas: mechanical compression, electrical stimulation and ultrasound. Detailed concepts and alternatives in each category are described below.

### *Sequential pneumatic compression*

#### *Design Specifications*

Based on literature research and available products applying pneumatic compression, the DVT team generated design specifications for a compression device. First, the device needs to cover from ankle through knee but still permit flexion of the knee. Second, compression should be sequential, graded, and intermittent. Third, cycle parameters should be:

**Rise time** in each chamber (time to 2/3 max. pressure): 0.5 s
**Delay** (time between onset of pressurization in individual chambers): 0.5 s
**Total** compression period (beginning of first chamber on to deflation): 10 s
**Deflation time** (uncontrolled, all chambers off simultaneously): 50 s

Fourth, the maximum pressure applied on ankle is 60 mmHg, on calf is 50 mmHg and on knee is 40 mmHg.

#### *Multi-lumen tubing*

The sequential pneumatic compression concept is the most widely applied technology in DVT prevention products. The basic idea behind those devices is to generate milking motion cycles from ankle to knee along the calf with gradient compression. Figure 10 describes the actual compression

distribution with time. The pressure gradient is realized by different pressure values at each covering segment, and each portion begins to pressurize at a different time. The ankle portion is applied the most pressure while knee portion is applied the least. Thus, if a device undergoes this pressurization process, it will be able to generate the desired milking motion. The pressures in the different compartments will peak simultaneously, and the whole system releases so as to finish one working cycle. As the working cycle continues, the prevention of DVT can be achieved by generating a periodic blood flow in deep veins.

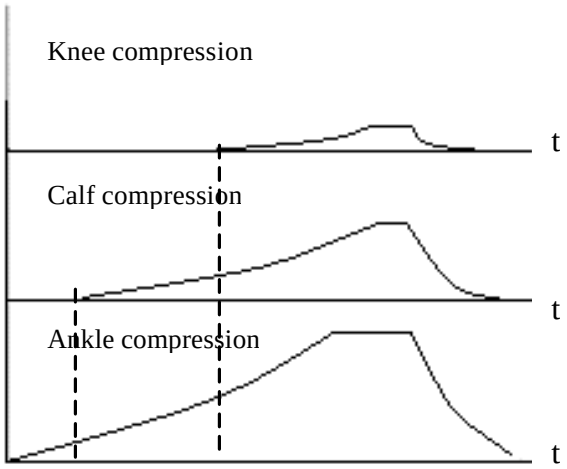


**Figure 10: "Milking" motion pressurization process**

In order to achieve the pressure gradient, which is crucial to prevent DVT effectively, the design team came up with a multi-lumen tubing idea. As shown in Figure 11, a specially made tubing system is wrapped around the user's calf when the DVT prevention device is used. The tubing contains three lumens with different lengths (the shortest covers the ankle area and the longest covers the knee area). Thus, when all three chambers are pressurized, the ankle area achieves the highest pressure (the sum of the three chamber pressures), while the knee area achieves the lowest pressure.

An air pump is employed to fill the lumens. An electrically controlled rotational connector ensures that the device follows the pressurization diagram in Figure 10. The rotational connector links the air pump and tubing. The three lumen ends are fastened in the connector cylindrically. A thin metal flywheel that can only open one lumen with the other two closed is controlled to rotate inside the connector. Thus, when air is pumping in, three lumens can be pressurized individually.

There is a more rigid band covering the outer side of the tubing system while the inner side of the system is more elastic, so that the pressure inside the lumen can be pushed against calf more effectively.

One drawback of this concept is that users still need to wind the device around their legs before using it. Considering the difference of individual's calf in size, the actual pressure applied on individuals could vary substantially, limiting the performance of the device.

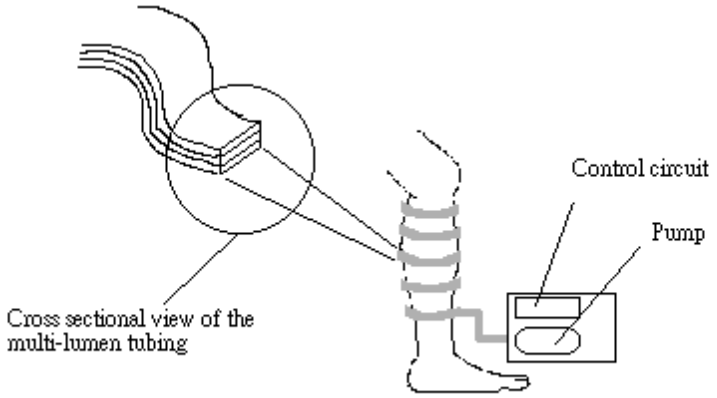


**Figure 11: Multi-lumen tubing concept for pneumatic compression**

An alternative idea that addresses some of the shortcomings of the idea described above is shown in Figure 12. Instead of winding tubing around when using it, the pre-wind tubing system is "snaked" into a cuff. Again, a connector connects air pump and all lumens in the fabric band. In this design, users don't need to carefully wrap tubing around the leg. In addition, it's easier for users to adjust appropriate tightness of the cuff.

The design team decided to follow the latter concept for its initial prototype. Instead of a full size device, they made a smaller scale tubing system with a regular fabric cuff.

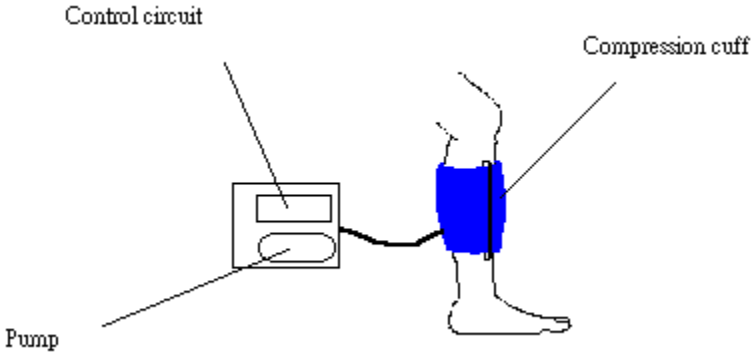


**Figure 12: Second compression concept. Multi-lumen tubing (not shown) is snaked within the thickness of the cuff**

## *Electrical Stimulation*

### *Design Specification*

For electrical stimulation, it is the current that produces the stimulation required, and a constant current signal source is used for the electro-stocking design concept. The current output range is 1 to 10 mA (Dillner) . A square waveform will be used in a first prototype because of its ease of implementation using a DC source. The team would also like the signal wave to be biphasic and symmetric because in this way the occurrence of unwanted chemical reactions is minimized. Since the team already chose external skin-surface electrodes to provide the electrical stimulation, oxidation reactions of metal electrodes are unlikely, so the biphasic pulse is really just an extra-precautionary measure.

The stimulation signal will be right-left alternating so as to mimic ambulation. Considering the pace of the average gait, the burst duration, which is the period when stimulation is on a given leg, will be about 0.5 to 1 second. The pulse frequency is chosen to be about 50 to 100 pulses per second because these are the minimum required frequency for the effects of multiple stimuli to sum and create a low-ripple contraction.

### *Electro-Stocking*

Figure 13 shows the electro-stocking (1), a modified graduated compression stocking (GCS). A stimulation signal generator (2) is selectively mountable on the stocking by snaps (6). The signal generator transmits via electrodes (3) that are woven into the fabric of the stocking. The woven-in electrodes (3) are made of compliant materials and are electrically conductive. They conduct the stimulation signals to a user's calf muscles when the user wears the stocking and turns on the stimulation signal generator. The signal generator (2) is provided with a screen (4) to show signal parameters and modes that can be modified through manipulation of a button set (5).

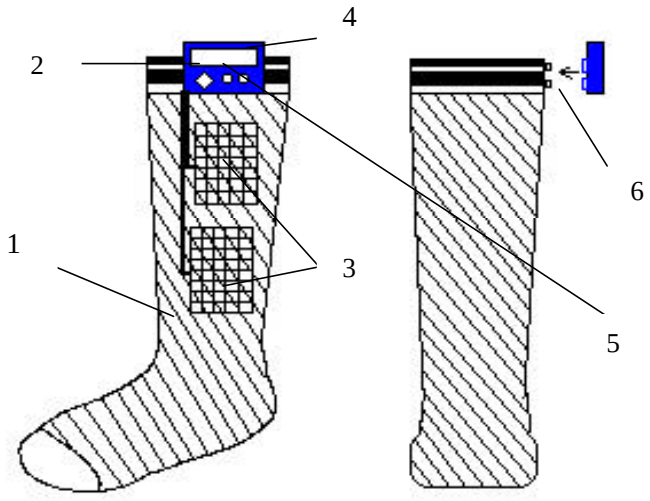


**Figure 13: Electro-stocking with a woven-in electrodes and a stimulation signal generator**

Users can put on the stocking before boarding on an airplane. When the user wants to turn on the generator, he may simply demount the unit, adjust the setting, and click it back into place. The stimulation signal is such selected that it can induce the same muscle contraction as in ambulation. When the user puts on one electro-stocking for each leg, the stimulation signal can be left-right alternating to further mimic the left and right movement of legs in ambulation.

**Music Amplifier**

Please refer to Figure 14. An audio output (7) is installed in an airline chair (8). A connector (9) receives the signal from the audio output and passes it on to a music amplifier (10), which amplifies the signal from the audio output and sends it to a calf unit (11). The calf unit (11) is in the shape of an earphone with two electrodes extending along the calf muscles. When a user puts the calf unit around the user's calf and turns on the music, the calf muscles will contract to the music.

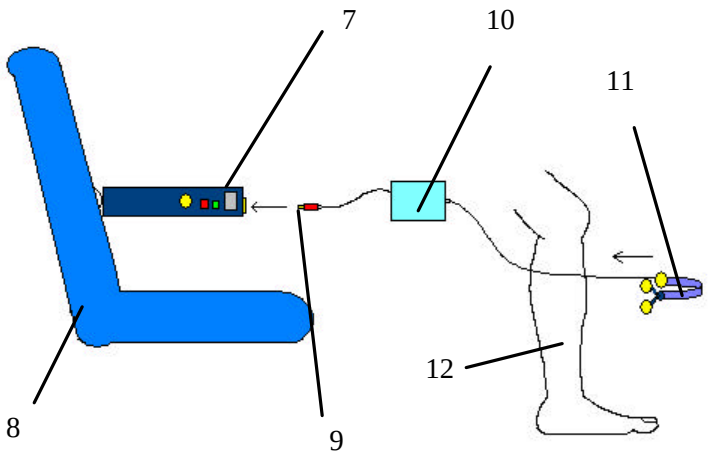


**Figure 14: the setup of a music amplifier concept on airline**

The setup shown in Figure 14is represented in the block diagram shown in Figure 15. The circuit within the dotted line is shown in Figure 16. The circuit is composed of an amplifier circuit and a filter circuit. Please note the circuit shown in Figure 16 is only a simplified version, not a realized one.

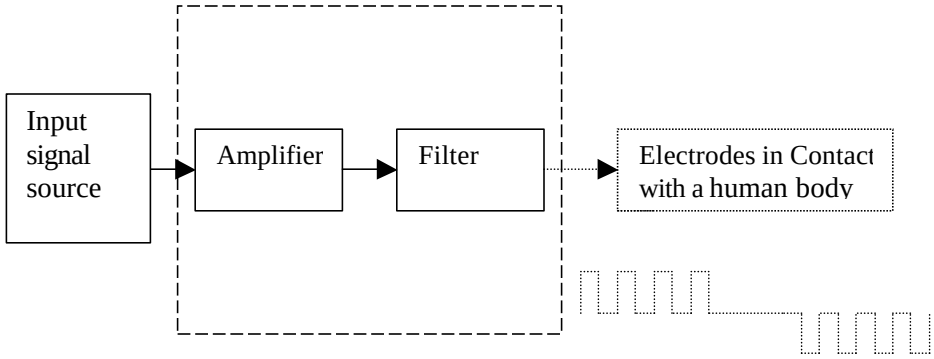


**Figure 15: A block diagram of the music amplifier**

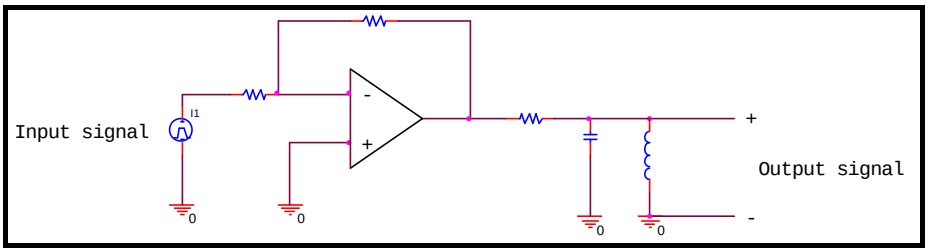


**Figure 16: Detailed design of the circuit within the dotted line portion in Figure 15**

### *Ultrasound*

This concept uses a transducer that can be clipped onto the leg just above the ankle. It would have an inlet for the ultrasound generator that could be provided by the airline (ie. kept on board) and it could be passed to all the patients at specific intervals so that it is effective. Ultrasound energy is transmitted to tissue through the tibia. Below is a diagram of our concept.

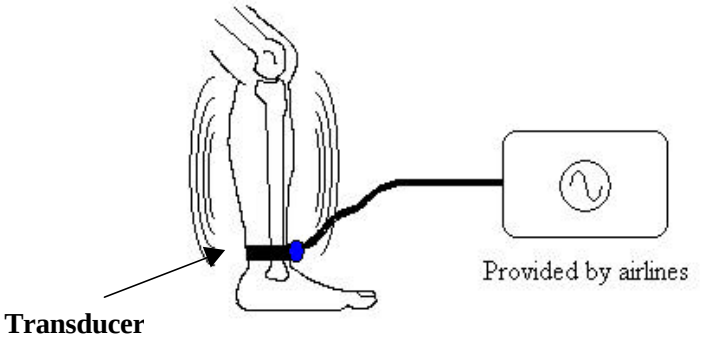


**Figure 17: Ultrasound concept**

## *4. Evaluation of Designs*

We have evaluated our design concepts and prototypes on the basis of our design specifications and requirements. The concepts were:

1) Sequential pneumatic compression (tubing)
2) Sequential pneumatic compression (bladder)
3) Electrical stimulation (music amplifier)
4) Electrical stimulation (electro-stocking)
5) Ultrasound

The main categories in our Pugh analysis to evaluate these concepts were: potential side effects (in regular use), weight, volume, manufacturability, aesthetic appeal, trendiness and ease of use. Weighing all the concepts we reached the conclusion that “electro-stocking” would be the path pursued. We have also decided to keep working at the

ultrasound device until we are in a better position to evaluate it against a built prototype.

Please refer to the Pugh analysis in the appendices section for details.

## *5. Initial Prototypes*

As mentioned, the DVT team made two prototypes for concepts they generated from two categories (sequential pneumatic compression and electrical stimulation).

### Tubing Set

The DVT team made a miniaturized prototype for the pneumatic compression tubing concept. Figure 18 is a schematic drawing of tubing concept. Three latex tubes are coiled in parallel, and are stacked together. The lower portion with three tube-layers is used to cover the ankle region, which requires the highest pressure. The top portion, with a single layer of tubing is used for the knee region. The stacked tubes are inserted into a hollowed-out blood pressure cuff.

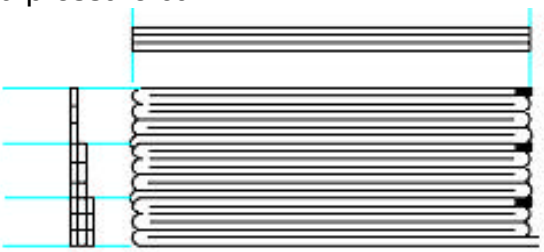

**Figure 18: Rubber tubing setup**

As a simpler alternative, the DVT team used bladders in different sizes instead of coiled tubes. The basic bladder concept is shown in Figure 19.

**Figure 19: Rubber bladder setup**

Please refer to Figure 20. Tubing set (1) is composed of a first curved tube (2), a second curved tube (3) and a third curved tube (4), stacked one

above another. Each of the curved tubes has one end air-sealed and the other connecting to a three-way valve. In this manner, the DVT team is able to inflate the tubing set (1) by connecting a pump to the three-way valves.


**Figure 20: 3 layers of rubber tubing**

Please refer to Figure 21. The tubing set in Figure 20 is inserted in the compartment of a commercial blood pressure cuff (5). In Figure 21, one of the DVT team members tries to wrap the blood pressure cuff (5) around his leg. Note that the curved tubes are stacked along the normal of leg surface in order to achieve a graded compression.


**Figure 21: Pressurized tubing system**

Please refer to Figure 22 now. When an elastic tube is bent to near 180 degrees, kinking takes place and inhibits total pressurization throughout the curved tubes. In Figure 23, tubes kink even when bent to about 95 degrees. This fact implies kinking could happen when one wraps the tubes around his legs.

**Figure 22: Kinking problem when winding tubing around**

**Figure 23: Representation of kinking problem when device is attached to calf**

Figure 24 reveals two other problematic encountered while fabricating the prototype. These were sealing and connecting issues. Stretches and twists during inflation and wrapping may cause the tubing setting to leak. It was better to apply adhesives or sealants on the contact surfaces when trying to dead-end a tubes or connects it to a valve.

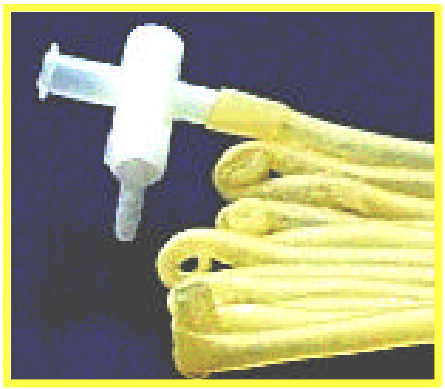

**Figure 24: sealing and connecting issues for tubing set**

## Music Amplifier

Between the electro-stocking and the music amplifier, the DVT team chose to produce the function prototype of the music amplifier simply because the materials were easier to acquire in the given time frame.

Please refer to Figure 25. A housing (13) contains the circuit required to generate stimulation signals. A connector (14 ) is for retrieving the audio signal from an audio output. An AC plug (15) is used to power the DC

circuit after the AC power is converted by an AC/DC converter inside the housing. A push button (16) serves as the switch of the amplifier. A user can vary the gain by turning a knob (17). The audio signal received from the connector is then amplified and outputted to electrodes (18).

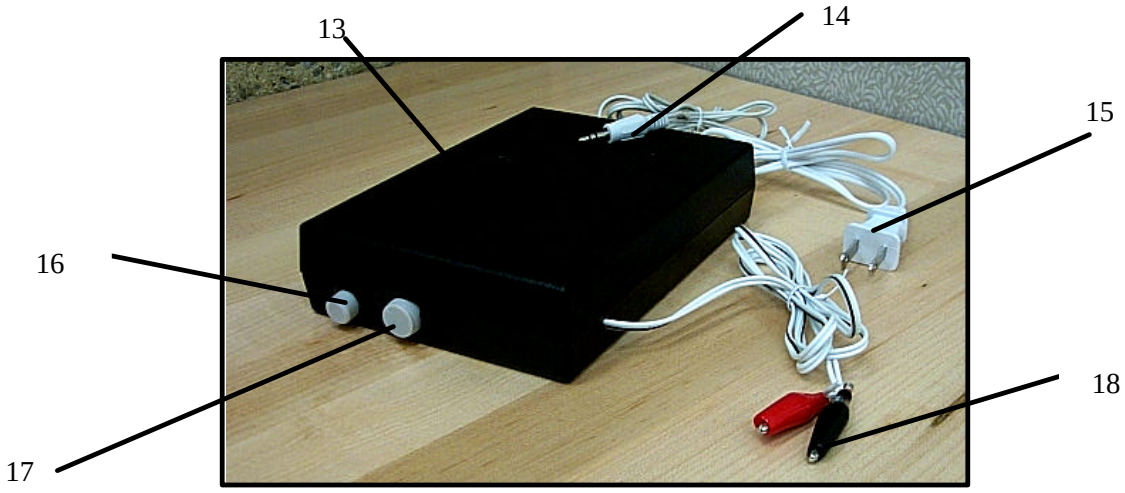


**Figure 25: The prototype of the music amplifier**

Figure 26 shows the circuit inside the housing (13). We put two amplifying circuits in series in order to achieve a larger gain. The AC/DC converter is not clearly shown in Figure 26.

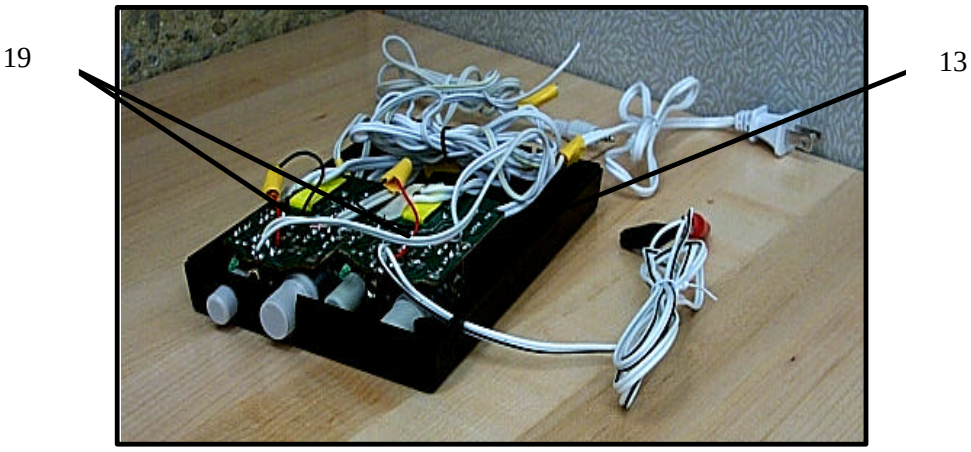


**Figure 26: Details of the prototype of the music amplifier**

# VIII Project Plan

## *1. Overview*

This project is a very open-ended one. One of the challenges the design team has faced is selecting a clear design concept from numerous potential solutions in time (by the end of winter quarter) to make functional prototype and test it. During the winter quarter, the DVT team generated three categories of concepts (pneumatic compression, electrical stimulation and ultrasound) and made several prototypes to evaluate them. After Pugh analysis, the team finalized the solution so that it could focus on functional prototyping in spring quarter. Meanwhile, the design team must leave enough time for testing after prototyping for a better evaluation of the concept and further development.

The basic plan is to develop a functional device and other potential concepts to prevent DVT. Along the development in the coming spring quarter, some design processes such as literature research, benchmarking, and brainstorming are still necessary. Also, a good communication with sponsor team, teaching team is needed to keep the development on the right track.

## *2. Deliverables*

The DVT team will build a working electrical stimulation prototype that will be accompanied by detailed drawings and specifications. The team will also design, conduct, and report the results of appropriate reliability and validation tests for the prototype. Potential regulatory pathways will be assessed. In addition, the feasibility of an ultrasound solution will be tested, and this concept will be carried as far as time permits. A final document will be produced that outlines the entire design and fabrication process. This document will contain a level of detail necessary to convey the scientific/clinical background utilized and the design rationale employed, and enable the replication of any testing procedures and the fabrication of the device.

### *3. Methodology (Future Plans)*

In the final quarter, the team will divide and work on tasks in parallel. There are three major pathways needing attention. The first is development of the electrical stimulation circuit. The second is development of the conductive stocking component of the design. The third is the pursuit of the ultrasound concept.

The team will quickly determine whether the stimulation circuit is one that needs to be built from scratch, or whether an existing product can be modified. In accomplishing the build or modification, the team will draw on circuit-design texts, electrical engineering professors, and several electrical engineering graduate students who are lab-mates of one of the team members.

The initial steps in accomplishing the second task will be to purchase an "electromesh" sock (Thera Tech Equipment, Inc.) and a graduated compression stocking, and to integrate the two into a crude prototype. Materials and manufacturing issues with regard to these two products will be compared, and a "combination" design will be produced and outsourced for manufacture.

By mid-quarter, the first two paths will converge, and an integrated prototype suitable for testing will be produced.

Unless sufficient supporting literature for the ultrasound concept can be found very shortly, the final pathway consists of acquiring an ultrasound system suitable for feasibility testing, and designing and carrying out the tests. Dr. Paul Yock has provided contact information for a local company that may be useful for acquiring an ultrasound unit. He also has access to equipment that can be used for measuring blood flow rate. The team will meet with Dr. Yock at the start of the quarter to determine whether that equipment will be available, and to decide whether a human or animal model is required/appropriate for proof of concept testing.

By the quarter's end, the DVT team will have produced a working prototype of the electro-stocking design, and will have assessed the feasibility of the ultrasound concept. If time permits, a prototype for the latter concept will be generated.

### *4. Reliability and Validation*

The design team decided to make different miniaturized prototypes for different concepts to prove the initial ideas. After that, the DVT team will

focus on one concept and make the function prototype and start testing. To evaluate the effectiveness to prevent DVT, design team might need to utilize animal model to monitor blood flow when applying the prototype onto the animal model. Also, to apply on human for testing is necessary to get conceptual feedback. The DVT team will generate a process to test fatigue and other mechanical properties with given facilities, as well as characterization of electrical circuit and power supply.

## *5. Major hurdles*

### *Electrical Stimulation ("Electro-stocking")*

The major hurdles for our "electro-stocking" concepts are listed below:

1. Need to research on the right kind of material to enable the desired effect.
2. The circuit needs to be prototyped
3. Validation and testing of the prototype

The potential show stopper here is the validation and testing aspect. If that were to not meet the mark then we would have a problem on our hands. The DVT team will be required to acquire basic knowledge on the circuits and electronics that go into the "electro-stocking". Most circuits books will give us the desired basic knowledge.

**Ultrasound Potential Problems**

Due to limited research we need to prove our concept, find out whether it is safe and then implement it to make our prototype. Ultrasound has several problems regarding its use. It can cause burns and if high intensity high frequency ultrasound is used instead of low frequency ultrasound, and in some studies has actually been shown to induce clot formation. The design team still needs to find out the safe frequency range of operation as too low a frequency affects the auditory system and too high a frequency induces clots.

The DVT team needs to be well versed with the ultrasound, its background, the threshold frequencies to be effective and yet not cause any damage. The design team intends to get in touch with TIMI system 3, a company that makes ultrasound cardiovascular device, and help get the required data regarding the threshold frequency and energy needed to be applied per square centimeter.

## *6. Timeline*

For the coming quarter the team has decided to go along with the "electro-stocking" concept which rates best in the Pugh analysis and for a

secondary pathway, develop the ultrasound concept. Mid-quarter we plan to come up with detailed prototype of the electro-stocking concept, which we will then test. The latter part of the quarter is dedicated to refining and testing of the prototype to make it as effective and appealing as possible.

**Table 2: Project plan timeline**

| **Winter Quarter** | **14 January - 15 March** |
|---|---|
| | |
| Background research | 14 Jan – 24 Jan |
| Benchmarking | 20 Jan – 15 Mar |
| Concepts generation | 20 Jan – 15 Feb |
| Hospital Interviews | 10 Feb – 20 Feb |
| Critical function prototyping | 20 Feb – 1 Mar |
| Concepts evaluation/selection | 1 Mar – 10 Mar |
| Documentation | 11 Mar – 15 Mar |
| | |
| **Spring Quarter** | **2 April – 6 June** |
| | |
| Material selection/Purchase | 2 April – 26 April |
| Ultrasound research | 2 April – 30 April |
| Testing for both concepts | 2 April – 30 May |
| Concept evaluation | 8 May – 28 May |
| Final prototyping | 23 May – 10 June |
| Documentation | 5 June – 10 June |

## *7. Individual responsibilities of team members*

### *Winter Quarter*

The DVT team faced a fairly open-ended project. Right after the presentation of Stanford BMI group, the DVT team members agreed on keep on brainstorming. The team decided to search for benchmarks in parallel. There are three places we could find relevant technologies and researches, which are the Internet, periodical literatures and patents. Eric and Abha took the responsibility of browsing the Internet. Justin volunteered to look up into periodicals since he has solid biological and neurological background. Jay volunteered to search the patent database of USPTO because he was a technical consultant in a law firm.

The team members kept on comparing and combining their brainstorming results and benchmarks. The design scope was narrowed down to electrical stimulation, pneumatic sequential compression and ultrasound according to efficacy consideration and whether there were enough research supporting that idea. The team decided that a preliminary Pugh analysis might be useful but not sufficiently evident to exclude any of the

design ideas. To explore the value of the ideas in detail, the team needed to build critical function prototypes or at least models for each of the ideas. Justin and Jay were assigned to build prototypes for the electrical idea. Eric and Abha were assigned to work on prototypes for the compression idea. Eric and Abha successfully developed two design concepts for pneumatic compression and built a functional prototype for each of the concepts. Jay and Justin developed two design concepts for electrical stimulation and built a prototype for one of the design concepts. With these prototypes and information, the team evaluated all design concepts and found that the “Electro-stocking” concept has the highest rating.

***Spring Quarter***

The main tasks of the DVT team for the coming quarter are building the stimulation circuit, looking for the right material for electrodes, embedding (weaving) the electrodes into stocking, testing and validating the prototype, preparing documentation, and preparing the final report and presentation. Jay and Justin will work on the circuit since they both have taken electronics courses before. Abha and Eric will develop the conductive stocking. The four team members will work together on the validation and testing processes. Documentation will be collected along the path. At the end of the spring quarter, the DVT team members will prepare slides and paragraphs according to their assigned responsibilities. Eric will coordinate the editing of the final powerpoint file and the word file since he is the best at these two application programs on the DVT team.

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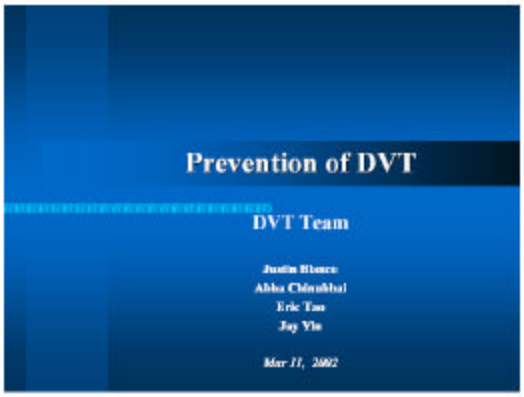
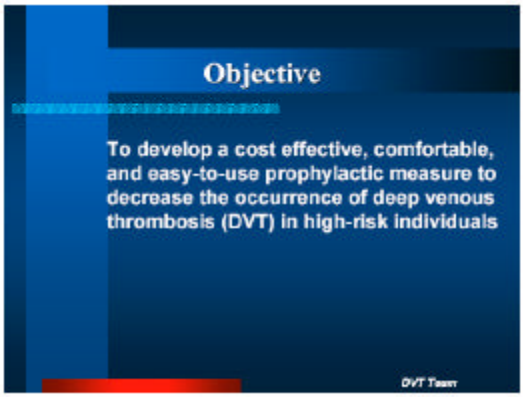
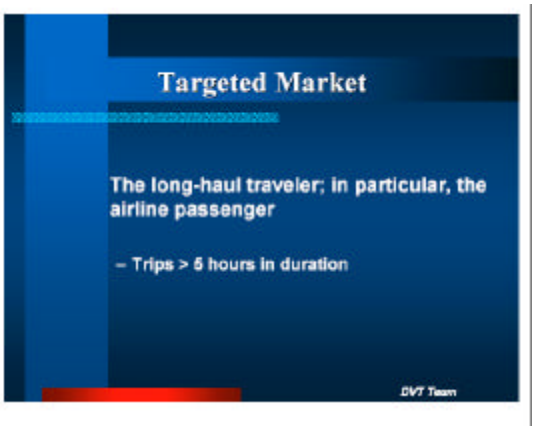
# X Appendices

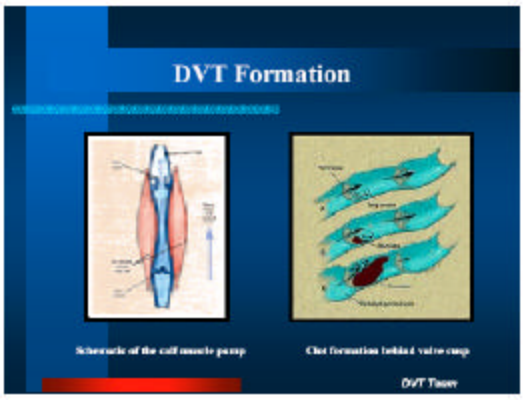
## 1. Presentation slides

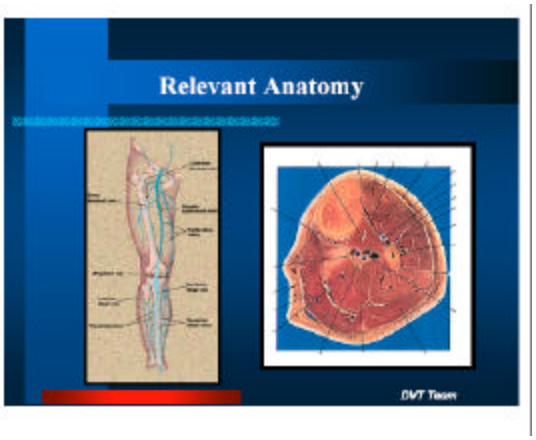






## Design Rationale

DVT Prevention Pathways

Dislodge nascent clots and "flush" away ⟷ Reduce stasis ⟷ Inhibit clotting factors/Dissolve clots

- Dislodge nascent clots and "flush" away
  - Vibration
    - Ultrasound
    - Other
- Reduce stasis
  - Mimicking calf pump
    - Intermittent Sequential Pneumatic Compression
    - Electrical stimulation
    - Limb exercise
    - GCS
- Inhibit clotting factors/Dissolve clots
  - Chemical means
    - Drugs: anticoagulants, thrombolytics, etc
    - Induction of tPA release via vibration or other superficial stimulation

DVT Team

## Design Opportunities

| Sequential Pneumatic Compression | Electrical Stimulation | Vibration, Ultrasound, Magnetic, Thermal, Other |
|---|---|---|
| •Increase comfort | •Use in the non-surgical setting is somewhat novel | •Fairly novel technologies (increased patentability?) |
| •Make portable: do away with multi-tube inputs; have on-board power supply and pump | •Tailor stimulus parameters to mimic normal ambulation | •Potential increased efficacy |
| •Make more appealing to the healthy consumer | •Integrate into GCS | •Customer appeal ("Sharper Image" Factor) |
| | •Low noise, discrete | |
| | •Enjoyable | |

DVT Team

## Design Specifications

**Optimal Characteristics: Sequential Pneumatic Compression Device**

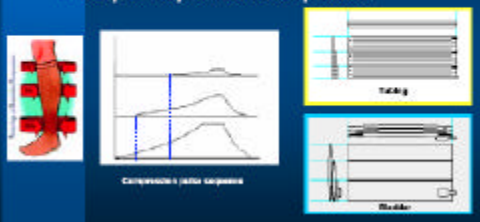
- Knee high (ankle to knee coverage)
- Permits flexion of knee
- Compression should be sequential, graded, and intermittent
- **Rise time** in each chamber (time to 2/3 max. pressure): 0.5 s
- **Delay** (time between onset of pressurization in individual chambers): 0.5 s
- **Total compression period** (beginning of first chamber on to deflation): 10 s
- **Deflation time** (uncontrolled, all chambers *off* simultaneously): 50 s
- For a 3-chamber model:

| Chamber | Max Pressure (mmHg) |
|---|---|
| 1 (ankle) | 60 |
| 2 (calf) | 50 |
| 3 (knee) | 40 |

DVT Team

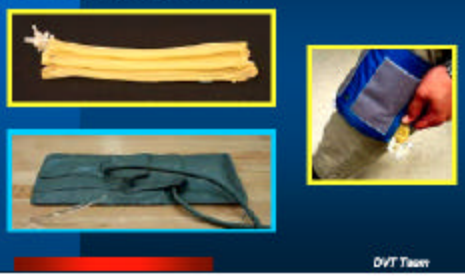
## Design Concepts

- Sequential pneumatic compression




DVT Team

## Critical Functional Prototypes



DVT Team

## Critical Functional Prototypes

Potential problems

- Kinking
- Sealing
- Connecting

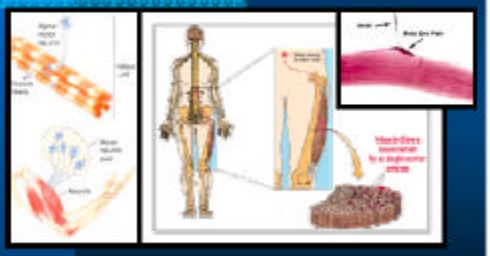
DVT Team

## Design Opportunities

| Sequential Pneumatic Compression | Electrical Stimulation | Vibration, Ultrasound, Magnetic, Thermal, Other |
|---|---|---|
| •Increase comfort | •Use in the non-surgical setting is somewhat novel | •Fairly novel technologies (increased patentability?) |
| •Make portable: do away with multi-tube inputs, have on-board power supply and pump | •Tailor stimulus parameters to mimic normal ambulation | •Potential increased efficacy |
| •Make more appealing to the healthy consumer | •Integrate into GCS | •Customer appeal ("Sharper Image" Factor) |
| | •Low noise, discrete | |
| | •Enjoyable | |

DVT Team

## More Relevant Anatomy



DVT Team

## Design Specifications

Optimal Stimulus Characteristics: Electrical Stimulation

- Source: constant current
- Waveform: square
- Polarity: biphasic, symmetrical
- Right-left alternating
- Burst Duration (stimulus on time): ~ 0.5-1 s
- Pulse Duration: 0.1-0.3 ms
- Pulse Repetition Rate: 50-100 pulses/sec
- Amplitude: 1 -10 mA


DVT Team

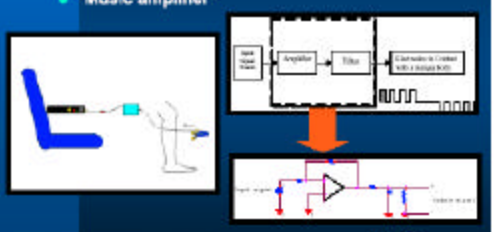
## Design Concepts

- Electro-stocking

DVT Team

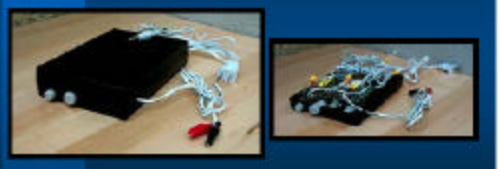
## Design Concepts

- Music amplifier



DVT Team

## Critical Functional Prototype



DVT Team

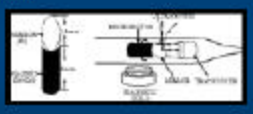
## Design Opportunities

| Sequential Pneumatic Compression | Electrical Stimulation | Vibration, Ultrasound, Magnetic, Thermal, Other |
|---|---|---|
| •Increase comfort<br>•Make portable: do away with multi-tube inputs; have on-board power supply and pump<br>•Make more appealing to the healthy consumer | •Use in the non-surgical setting is somewhat novel<br>•Tailor stimulus parameters to mimic normal ambulation<br>•Integrate into GCS<br>•Low noise, discrete<br>•Enjoyable | •Fairly novel technologies (increased patentability?)<br>•Potential increased efficacy<br>•Customer appeal ("Sharper Image" Factor) |

DVT Team

## Ultrasound Background

- Ultrasound solution



Frequency: 1MHz
Source: permanent magnets

- Intra-Vascular Ultrasound (IVUS)
- Generates 20MHz and transducer has diameter 1.2mm

DVT Team

## Design Concepts

Works by breaking up fibrin, a protein component of clots

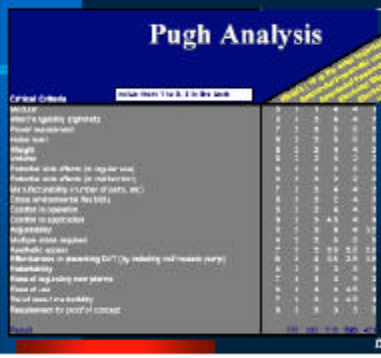
Activates tPA, a naturally occurring enzyme that helps dissolve clots

Helps aid and regulate blood flow

Some hurdles


DVT Team

## Pugh Analysis



DVT Team

## Future Plan

- Primary Pathway
  - Prototype stimulation circuit
  - Investigate "electromesh" garments and attempt to incorporate technology into GSC
  - Gait analysis/muscle force measurements to refine stimulus parameters
- Secondary Pathway
  - Continue to explore ultrasound
  - Proof of concept prototype
- Continue to refine ideas using Pugh Analysis

DVT Team

## Thank you !

DVT Team

## *2. Expenses*

**Table 3: Expenses details**

| | Description | Date | Value($) | Balance($) |
|---|---|---|---|---|
| 1 | Office supply | 1/22/02 | 90 | 4910 |
| 2 | AB energizer | 1/30/02 | 71 | 4839 |
| 3 | Pressure cuff with E. readout | 2/02/02 | 69 | 4770 |
| 4 | Large size blood cuff | 2/02/02 | 20 | 4750 |
| 5 | Earphone | 2/02/02 | 50 | 4700 |
| 6 | Ear piece | 2/20/02 | 2 | 4698 |
| 7 | Speaker #1 | 2/20/02 | 8 | 4690 |
| 8 | 12V DC Recap | 2/28/02 | 10 | 4680 |
| 9 | Universal test leads | 2/28/02 | 10 | 4670 |
| 10 | Pipe tape | 3/02/02 | 1 | 4669 |
| 11 | Adhesive | 3/02/02 | 5 | 4664 |
| 12 | Glue | 3/02/02 | 3 | 4661 |
| 13 | Plastic fuser | 3/02/02 | 2 | 4659 |
| 14 | Wire stripper | 3/04/02 | 10 | 4649 |
| 15 | Core solder | 3/04/02 | 10 | 4639 |
| 16 | Speaker wire | 3/04/02 | 7 | 4632 |
| 17 | Solid wire | 3/04/02 | 6 | 4626 |
| 18 | Vinyl electrical tape | 3/04/02 | 3 | 4623 |
| 19 | Large ABS housing | 3/04/02 | 8 | 4615 |
| 20 | Small ABS housing | 3/04/02 | 7 | 4608 |
| 21 | Weller soldering iron | 3/04/02 | 10 | 4598 |
| 22 | Physics Lab expenses | 3/05/02 | 60 | 4538 |

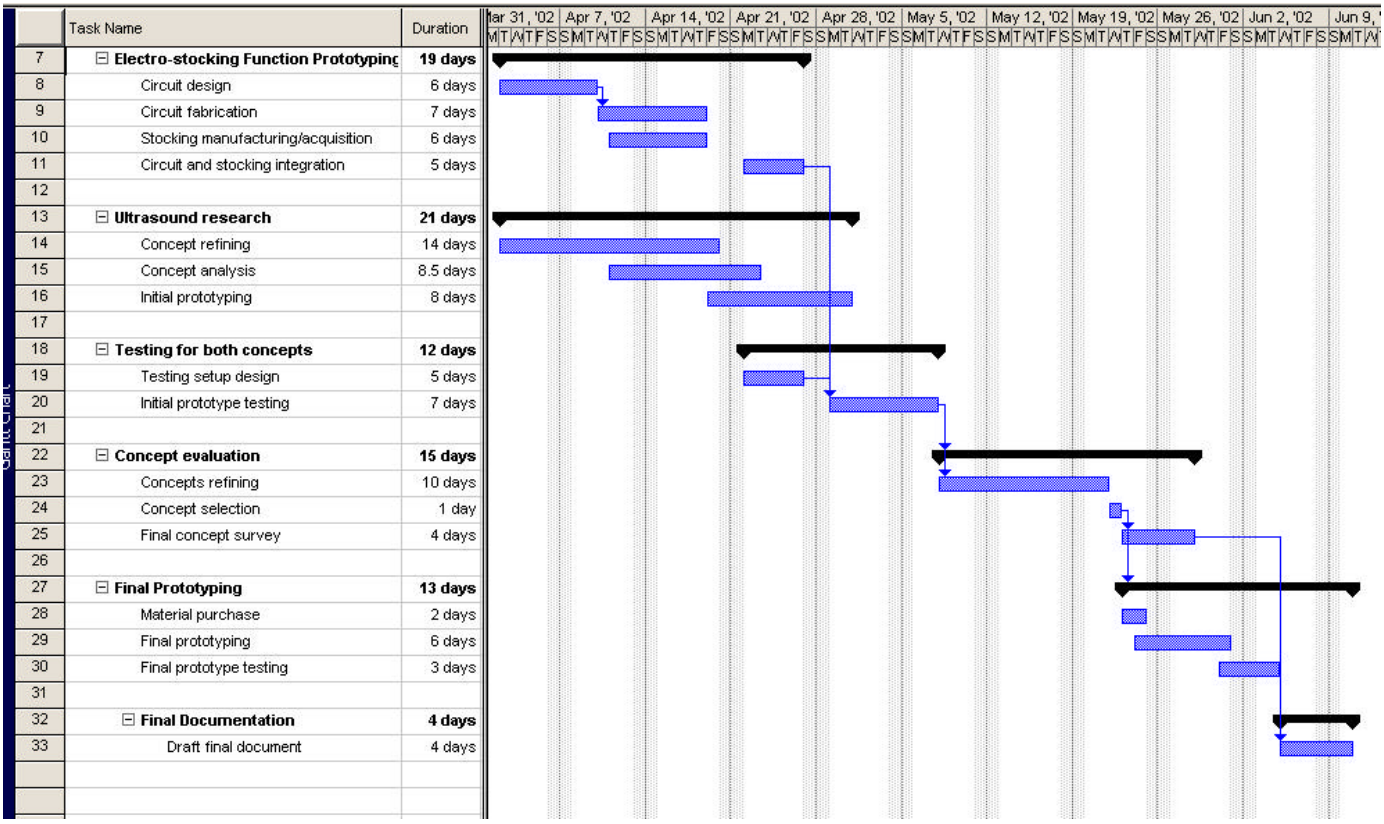
## *3. Resources*

The resources that have been used thus far include the Stanford Biomedical Innovation Fellows, the ME 282 teaching team, several Stanford physicians (Dr. Yock, Dr. Zehnder, Dr. Nayak, Dr. Berenson, and Dr. Fowler), the Stanford Medical Center, and the Lane Medical and Terman Engineering libraries at Stanford.

In the coming quarter, the team will need access to a laboratory in which it can conduct gait analysis and muscle force measurement testing. If an arrangement can be worked out, Stanford's Biomotion Lab seems appropriate. Dr. Yock and the Stanford Medical Center will continue to be important resources for carrying out the development of the ultrasound concept. The assistance of professors and students with electrical engineering expertise will be needed to build the stimulation circuit. A resource for purchasing the required soldering equipment, components,

breadboards, etc. will also be required. Lastly, a resource for fabricating the final electro-stocking will be needed. This has not yet been located.

### *4. Gantt Chart*



| | Task Name | Duration |
|---|---|---|
| 7 | **Electro-stocking Function Prototyping** | **19 days** |
| 8 | Circuit design | 6 days |
| 9 | Circuit fabrication | 7 days |
| 10 | Stocking manufacturing/acquisition | 6 days |
| 11 | Circuit and stocking integration | 5 days |
| 12 | | |
| 13 | **Ultrasound research** | **21 days** |
| 14 | Concept refining | 14 days |
| 15 | Concept analysis | 8.5 days |
| 16 | Initial prototyping | 8 days |
| 17 | | |
| 18 | **Testing for both concepts** | **12 days** |
| 19 | Testing setup design | 5 days |
| 20 | Initial prototype testing | 7 days |
| 21 | | |
| 22 | **Concept evaluation** | **15 days** |
| 23 | Concepts refining | 10 days |
| 24 | Concept selection | 1 day |
| 25 | Final concept survey | 4 days |
| 26 | | |
| 27 | **Final Prototyping** | **13 days** |
| 28 | Material purchase | 2 days |
| 29 | Final prototyping | 6 days |
| 30 | Final prototype testing | 3 days |
| 31 | | |
| 32 | **Final Documentation** | **4 days** |
| 33 | Draft final document | 4 days |

## *5. Pugh Analysis Chart*

| Critical Criteria | Weight ( 10 is the most important) | Sequential Pneumatic compression (tubing) | Sequential Pneumatic compression (bladder) | Electrical Stimulation (music amplifier) | Electrical Stimulation (electrode stocking) | Ultrasound |
|---|---|---|---|---|---|---|
| Modular | 5 | 1 | 1 | 4 | 4 | 1 |
| Interchangability (right/left) | 3 | 3 | 3 | 4 | 4 | 3 |
| Power requirement | 7 | 2 | 3 | 5 | 5 | 2 |
| Noise level | 8 | 2 | 2 | 5 | 5 | 5 |
| Weight | 8 | 2 | 2 | 4 | 4 | 2 |
| Volume | 8 | 2 | 2 | 3 | 2 | 2 |
| Potential side effects (in regular use) | 9 | 3 | 3 | 2 | 2 | 2 |
| Potential side effects (in malfunction) | 8 | 3 | 3 | 2 | 2 | 2 |
| Manufacturability (number of parts, etc) | 7 | 2 | 3 | 4 | 4 | 3 |
| Cross environmental flexibility | 6 | 3 | 3 | 2 | 4 | 3 |
| Comfort in operation | 8 | 2 | 2 | 4 | 4 | 3 |
| Comfort in application | 8 | 3 | 3 | 4.5 | 4 | 4 |
| Adjustability | 5 | 3 | 3 | 4 | 4 | 3.5 |
| Multiple sizes required | 4 | 2 | 2 | 5 | 5 | 5 |
| Aesthetic appeal | 7 | 2 | 2 | 3.5 | 3.5 | 3.5 |
| Effectiveness (by imitating calf muscle pump) | 9 | 4 | 4 | 3.5 | 3.5 | 3.5 |
| Patentability | 4 | 2 | 2 | 3 | 3 | 4 |
| Ease of regulatory compliance | 7 | 4 | 4 | 3 | 3 | 2 |
| Ease of use | 8 | 4 | 4 | 4 | 4.5 | 3 |
| Trendiness / marketbility | 7 | 2 | 2 | 4 | 4.5 | 4 |
| Requirement for proof of concept | 8 | 3 | 3 | 3 | 3 | 2 |
| Result | | 378 | 392 | 518 | 526 | 421 |

## *6. Patent Search Information*

### By Searching Criteria

First Search (Spec/deep, Spec/venous, spec/thrombosis, spec/vein, spec/clot, and not (ttl/method), ttl/device)

| | PAT. NO. | Title | Summary | Assignee |
|---|---|---|---|---|
| 1 | 6,123,681 | Anti-embolism stocking device | It is a stocking with electric stimulus operated polymer stripes. The stripes can cause separate, segmental compression to a body wrapped by the stocking. | Global Vascular Concepts, Inc. |
| 2 | 5,022,387 | Antiembolism stocking used in combination with an intermittent pneumatic compression device | It is a boot stocking with separate fluid chambers that can apply decreasing pressure on a patient's limb from ankle to the top of the stocking. | The Kendall Company |
| 3 | 4,669,722 | Antistasis device | It is a pair of foot exercise device having a rigid panel and a flexible, spring operated pedal. | Rangaswamy; Avvari |

Second Search (Spec/deep, Spec/venous, spec/thrombosis, spec/vein, spec/clot, andnot (ttl/method), ttl/apparatus)

| | PAT. NO. | Title | Summary | Assignee |
|---|---|---|---|---|
| 1 | 6,290,662 | Portable, self-contained apparatus for deep vein thrombosis (DVT) prophylaxis | It is portable device to prevent DVT. It has an electric powered air pump and an inflatable bladder. | Morris; John K. |
| 2 | 6,007,559 | Vascular assist methods and apparatus | A device with a plurality of inflatable chambers that apply static as well as dynamic compression to limb. | ACI Medical |
| 3 | 5,358,513 | Parameter selection | A system and method to use electrical current to | Medtronic, Inc. |

| | | | | |
|---|---|---|---|---|
| | | and electrode placement of neuromuscular electrical stimulation apparatus | stimulate the common peroneal nerve transcutaneously. | |

Third Search (Spec/deep, Spec/venous, spec/thrombosis, spec/vein, spec/clot, andnot (ttl/method), ttl/appliance)

| | PAT. NO. | Title | Summary | Assignee |
|---|---|---|---|---|
| 1 | 5,584,798 | Medical inflatable cuff appliance | A device which performs tourniquet action on the distal calf portion of a log to treat abnormal blood circulation | Novamedix Limited |

Fourth search (Spec/deep and Spec/vein and spec/thrombosis and spec/foot andnot (ttl/method))

| | PAT. NO. | Title | Summary | Assignee |
|---|---|---|---|---|
| 1 | 6,319,215 | Medical device for applying cyclic therapeutic action to a subject's foot | A boot having at least three different compartment | Medical Dynamics USA, LLC |
| 2 | 6,296,617 | Gradient sequential compression system for preventing deep vein thrombosis | A device improving venous blood flow in a limb by applying sequentially established compressive forces to the limb | KCI Licensing, Inc. |
| 3 | 6,129,688 | System for improving vascular blood flow | A device applying compression on foot as well as on limb | ACI Medical |
| 4 | 6,064,912 | Orthotic/electrotherapy for treating contractures due to immobility | A device that conducts electrical current to skeletal body parts when there is a joint especially when the body parts are immobile. | Kenney; John P |

| | | | | |
|---|---|---|---|---|
| 5 | 6,047,700 | Systems and methods for electrosurgical removal of calcified deposits | A device that conduct electrical current to a patient's heart to remove calcified deposits | ArthroCare Corporation |
| 6 | 5,931,797 (5840049) | Medical pumping apparatus | A device having bladders to provide fluid pressure to a plurality of bags, in order to compress a patient's limb. | Kinetic Concepts, Inc. |
| 7 | 5,782,893 | Neuromuscular electrical stimulator for deep vein thrombosis treatment | A neuromuscular electrical stimulator for the prevention of deep vein thrombosis (DVT) | J.D. Medical, Inc. |
| 8 | 5,769,801 (5443440) | Medical pumping apparatus | A device having bladders to provide fluid pressure to a plurality of bags, in order to compress a patient's limb. | NDM Acquisition Corp. |
| 9 | 5,711,760 | Self-inflating venous boot | A compression boot having at least two air chambers. | Englewood Research Associates |
| 10 | 5,671,751 | Medical pumping apparatus | Provides a sensing and control circuitry other than the bladder-bag system | LRC Holding Company, Inc. |
| 11 | 5,468,217 | Lower extremity phlebo pump | A pair of electric pedals that passively exercise a patient's foot. | Prevent Products Inc. |
| 12 | 5,396,896 | Medical pumping apparatus | Provides a sensing and control circuitry other than the bladder-bag system | Chrono Dynamics, Ltd. |
| 13 | 5,263,473 | Compression device for the limb | A compression device providing periodic compression cycles | The Kendall Company |
| 14 | 5,186,163 | Compression device | A compression device providing periodic compression cycles with the foot portion applying the highest compression | The Kendall Company |
| 15 | 5,117,812 | Segmented compression device for the limb | A compression device that apply compression in segments | The Kendall Company |

| | | | | |
|---|---|---|---|---|
| 16 | 5,046,487 | Therapeutic leg elevator | A device elevating a patient's leg | Scott; James W. |
| 17 | 4,938,208 | Full length compressible sleeve | A multiplayer sleeve that compress the leg | The Kendall Company |
| 18 | 4,928,958 | Exercise device | Pneumatic pedals that help a patient exercise his foot. | Medical College of Ohio |
| 19 | 4,745,917 | Therapeutic stocking | Stocking that provides large pressure gradient | The Kendall Company |
| 20 | 4,206,751 | Intermittent compression device | A device to provide compression to a patient's limb. | 3M |
| 21 | 4,153,050 | Pulsatile stocking and bladder therefor | A device applying pulsatile compression to a patient | Alba-Waldensian, Incorporated |

Fifth search(spec/deep and spec/venous and spec/thrombosis and spec/foot andnot (ttl/method))

| | **PAT. NO.** | **Title** | **Summary** | **Assignee** |
|---|---|---|---|---|
| 1 | 6,226,552 | Neuromuscular electrical stimulation for preventing deep vein thrombosis | A system provides a series of electrical pulses to instigate muscle twitch to prevent occurrence of deep vein thrombosis. | Stryker Instruments |
| 2 | 6,010,468 | Foot flexion device | A pair of foot pedals powered by inflatable bellows. | The Discovery Group, LLC |
| 3 | 5,782,893 | Neuromuscular electrical stimulator for deep vein thrombosis treatment | A neuromuscular electrical stimulator for the prevention of DVT | J.D. Medical, Inc. |
| 4 | 5,007,411 | Device for applying compressive pressures against a patient's limb | A device having a plurality of chambers to apply pressure against a patient's limb | The Kendall Company |
| 5 | 6,175,764 | Implantable | An implantable system | Advanced |

| | | | | |
|---|---|---|---|---|
| | | microstimulator system for producing repeatable patterns of electrical stimulation | producing repeatable patterns of electrical stimulation in order to contract one or more muscles | Bionics Corporation |
| 6 | 4,501,421 | Foot and leg exercising device | A portable foot and/or leg exercising apparatus having two pedals | Kane; James G. |
| 7 | 4,299,206 | Foot exerciser | Two pedals reciprocating by means of electric motor | World Medical Marketing Corporation |
| 8 | 6,051,017 | Implantable microstimulator and systems employing the same | An implantable system producing repeatable patterns of electrical stimulation in order to contract one or more muscles | Advanced Bionics Corporation |

**By Category**

1. Mechanical Compression
6,123,681, 5,022,387, 6,290,662 , 6,007,559, 5,584,798, 6,319,215, 6,296,617, 6,129,688, 5,931,797(5840049), 5,769,801(5443440), 5,711,760, 5,671,751, 5,396,896, 5,263,473, 5,186,163, 5,117,812, 4,938,208, 4,745,917, 4,206,751, 4,153,050, 5,007,411

2. Electrical stimulation
5,358,513, 6,064,912, 6,047,700, 5,782,893, 6,226,552, 5,782,893, 6,175,764(6,181,965), 6,051,017

3. Exercise devices
4,669,722, 5,468,217, 5,046,487, 4,928,958, 6,010,468, 4,501,421, 4,299,206(4,294,236, 4,280,486, 4,276,887, 4273,113)

## *7. Original Sponsor Descriptions*

**Biomedical Product Design and Evaluation** **ME 282A/B**
**2002** **Project Description**

***Title:***

**Prevention of Deep Venous Thrombosis ("Economy Class Syndrome")**

***Sponsor:***

**Stanford Program in Biomedical Technology Innovation**

***Type of Project:*** New Design

***Design Description***

Deep venous thrombosis (DVT) is a serious and relatively common condition in which large blood clots form in the veins of the leg. The clots can break loose and travel to the heart and lungs, causing pulmonary embolism (leading to destruction of lung tissue and, in severe cases, death).

DVT has received a great deal of popular attention because there is a significant incidence on long air flights, even in normal individuals. Because the condition is related to immobilization on the flight it has been dubbed the "Economy Class Syndrome". Unfortunately the problem is often difficult to diagnose, which contributes to its great danger. DVT also occurs in patients who have undergone major surgery and are immobile for long periods in recovery. Elderly individuals with restricted activity are also targets for DVT.

There is no effective means of prevention for this condition. In air travelers the incidence is not high enough to warrant widespread anticoagulation by medicine, which would carry its own risks. The only reasonably safe prophylaxis – the use of compression stockings— represents an inconvenient, marginally effective and expensive solution for the average traveler.

The challenge is to develop a workable and cost effective prophylactic measure to decrease the occurrence of DVT for passengers on long air flights and for other individuals at high risk for this problem. The solution should be easy enough to use or wear that it could be adopted by the average healthy traveler; but it should also be applicable in the hospital environment or the nursing home.

## ***Goals of Project – Final Deliverables***

The deliverable can be a working prototype or advanced concept. Depending on the concept, testing in an animal model may be appropriate. Comfort and ease of use should be demonstrated on volunteers. Reasonable confidence in the manufacturability of the solution is important.

## ***Resources Available***

This project has been developed in cooperation with the Stanford Biomedical Technology Innovation Program as a part of the Biodesign initiative. The current Innovation Fellows (three engineers and two medical graduate students) will serve as ad-hoc resources for the 282 project team. Advisors from different areas of medicine – hematology, pulmonary, vascular surgery – will be provided. If animal testing is appropriate, this will be arranged through the Division of Cardiovascular Medicine

## ***Resources Needed***

Depending on the nature of the solution(s) proposed, special prototyping capabilities may be required. These will be located on campus if possible; otherwise within the local medical technology industry.

## ***Project Sponsor Contacts***


?? Name Paul Yock, Josh Makower
?? Title Professor of Medicine, Consulting Associate Professor of Medicine
?? Address
?? Phone 736-1160
?? e-mail pyock@cvmed.stanford.edu; jmakower@transvascular.com

## *8. Checklists from Executive Committees*

**Regulatory and Standards Checklist**

### ***1. What is your project?***

Please briefly describe the project you are working on:
To develop a non-invasive medical device which will be used to decrease the occurrence of deep venous thrombosis.

Please describe potential solutions that you are considering for your project:
1. Using pneumatic sequential compression to apply pressure on the leg.
2. Using ultrasound to stimulate the muscles to relax and contract.
3. Using electrical stimulation to imitate exercise.

List and briefly describe any potential solutions that have biological or chemical components.
None.

List and briefly describe any solutions that emit radiation.
None.

### ***2. Project Scope***

List which solutions involve developing a completely new device.
Solution #2

List solutions reusing a known technology, approach, or process.
Solutions #1 and #3

Are any solutions based on other devices?
Yes

If so which devices?
Pneumatic Sequential Compression Device.

Were the device(s) developed before 1976?
Yes. (patent filed before 1976)

How are they similar?
Both are applying sequential compression on muscles.

Does your solution pose any new risks?
None that we foresee.

Utilize any new technologies?
A compression solution might use a continuous length of material to create a graded compression, or might involve valves.

Are any of your solutions used with other devices or treatments?

None.

If so, what devices or treatments?

N/A.

Are they life critical?

N/A.

## ***3. Safety***

Does you project pose any dangers to patients, physicians, or others?

Not if used correctly

If so, how?

Is it life threatening?

## ***4. Sponsor recommendations***

What classification does your sponsor want your group to aim for?

Class II.

What premarket approval process do they envision for your project?

## ***5. Assuming your project is a device:***

This last section of the checklist is intended to help start your project's FDA identification/ classification process and to document your progress. In order to guide you through this process, this document utilizes the FDA website's device advisor (see step 1). Note: at various points along the process the website offers more information to help you answer questions; these questions/links are not in this checklist.

Steps:

1) Open http://www.fda.gov/cdrh/devadvice/31.html
2) Does the product emit radiation? Yes / No
3) Does Your Product Meet the Definition of a Medical Device? Yes / No
4) Do you know the class of your device?
    a. If yes jump to 5
    b. If no:
        i. Read section on "How to determine Classification"
        ii. Use the Classification Database or the Device Panels (circle which you used)
5) Record the following information:

Device: Sequential compression

Medical Specialty: Cardiovascular

Product Code: JOW

Device Class: Class II

510(k) exempt?: No

Regulation Number (7 digit): 870.5800

Device Description: A compressible limb sleeve is a device that is used to prevent pooling of blood in a limb by inflating periodically a sleeve around the limb.

6) Which are required: 510k / PMA / Exempt
(circle which apply – known from the above classification)

7) The next steps in the regulatory process depend greatly on your specific project. See the regulatory team for guidance if you are uncertain of your next steps.