The Standard of Care for Lymphedema: Current Concepts and Physiological Considerations

In discussing the broad concept of the standard of care for lymphedema it is useful to delineate four major focus areas; risk reduction, early detection, phase I therapy and phase II therapy. In this presentation I will discuss these sequentially although not to the same depth. Although I mainly focus on the patient who is at-risk for or who has developed breast cancer treatment-related lymphedema, the concepts, suitably modified, apply to those who have or are at-risk for secondary lymphedema arising from treatment complications related to gynecological, prostate or melanoma surgery or radiation.

Risk Reduction

By this term I refer to things that the surgeon, caregiver and the at-risk patient can do to minimize or blunt the development of lymphedema. High on this list are items that result in an informed and educated patient; the earlier the better. Since it is the surgeon that likely has the earliest contact, it initially falls to them to alert the patient to possibilities of lymphedema complications and to provide information as to precautionary do's-and-don'ts and things to look for, either directly or by pointing to reliable sources, of which there are now many. This is not to say that such do's-and-don'ts all have scientifically based underpinnings, they do not. Many are common sense approaches and it is important not to encumber and over-whelm the patient with non-relevant or over-blown precautions. Future research may be able to better define the most useful. Some good sources of relevant educational information may be found in the literature[1] and at various web sites.

An informed patient may or may not heed recommended precautions, may or may not recognize early symptoms and may or may not seek a timely consult and therapy. It is my belief that if an initial consult with a therapist, skilled in lymphedema therapy and education, were done as part of standard care, either prior to surgery or soon after, then patient mind-set, compliance and eventually outcomes could be improved. This brings me to the issue of early detection.

Early Detection

We have long be taught that the lymphedematous condition, left untreated, will progressively become worse[2]. So it makes sense that the earlier lymphedema is detected and properly treated the better will be the outcome[3]. By better, I mean a more complete normalization of a swollen limb or an edematous trunk and a greater chance of minimizing or avoiding significant complications including fibrosis, infection, pain, range of motion limitations, reduced body image and an array of life-activity-limiting sequels. An important component of the early detection process is the patient's own early recognition of symptoms and her timely action to seek therapy. Too often symptoms are either unrecognized or disregarded resulting in a patient seeking therapy at a more advanced stage when the ability of therapy to 'arrest and reduce' the developing lymphedema is more limited. As noted, patient education and informed awareness can improve this situation but, even under these favorable conditions, self-referral may be unnecessarily too long delayed.

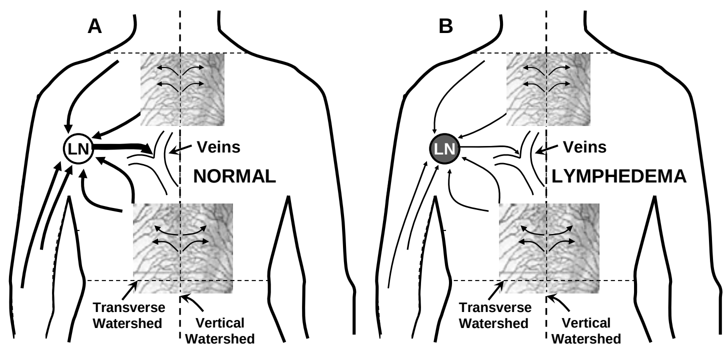
Thus, there have been efforts to achieve earlier, possibly pre-clinical detection, of incipient lymphedema using quantitative methods that may detect early changes in tissue water in limbs by electrical impedance[4,5], changes in limb volume[6] or by changes in tissue dielectric constant values that importantly can be measured anywhere on the body surface[7,8]. Although these approaches are promising, they are limited by the absence of a standard accepted criteria of pre-clinical lymphedema and the fact that a patient must be evaluated at the clinic, preferably prior to their surgery, and then at continuing follow-up intervals after surgery if early pre-clinical lymphedema is to be detected. This again emphasizes the importance and utility of having, as a standard of care, an early pre-surgical consult and evaluation with a lymphedema therapist. It is encouraging that this concept of pre-surgical assessment with periodic follow-ups is beginning to be recognized and implemented[9].

Phase I Therapy

Once lymphedema is suspected or detected patients are usually referred to a lymphedema therapy clinic staffed by certified therapists. The standard of care for this phase I, intensive, but short term therapy sequence is referred to by several names including; Complete Decongestive Physiotherapy (CDP) or Complex Decongestive Therapy (CDT). The goals of CDP are to arrest lymphedema progression, reduce lymphedema volume and to train patients for their subsequent life-long phase II in-home self-care and educate them in risk reduction considerations. Phase II is needed to maintain and possibly improve upon gains made during Phase I.

The standard of care of phase I CDP therapy includes manual lymphatic drainage (MLD), short stretch compression bandaging, decompression exercises, skin care and sometimes the use of intermittent pneumatic compression (IPC). The details of the various CDP components and their utility to achieve initial reductions in lymphedema are well documented by earlier literature[3,10-12] and more recent reviews[13-16]. However, because MLD is central to the Phase I therapeutic processes, and self-MLD is used in Phase II, it is instructive to consider its physiological basis and role more closely. To illustrate, I will use as an example upper extremity lymphedema.

To set the stage it is helpful to recognize that the lymphatic system consists of an enormous number of lymphatic vessels, punctuated with lymph glands (nodes) that course through the body in association with blood vessels. Movement of lymph through these vessels is directed toward specific entry points into the venous system. For drainage of the upper extremity under normal healthy conditions (**figure 1A**), axillary lymph nodes (LN) receive most upper extremity lymph fluid via superficial and deep lymphatic channels and the ipsilateral trunk quadrant via multiple pathways. Lymph also drains from the arm to and through the supra – and infraclavicular nodes bypassing the axillary nodes. Lymph enters the nodes via afferent channels and exits via efferent channels. It is collected by lymphatic vessels that join major trunks to empty into the venous system via junctions within the venous angle as schematized in the **figure 1**.



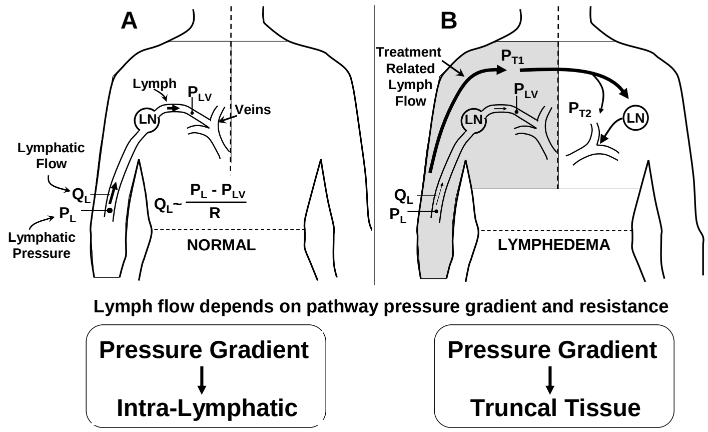
Lymph flow and drainage determined by normal physiological processes and lymphatic pathways

Lymph flow through normal pathways *reduced or absent* due to nodal or lymph vessel obstruction and dysfunction

If nodes are removed as part of breast cancer treatment, or channels damaged by radiation, then the ability of upper extremity lymphatic channels and all truncal tributaries to move lymph out of their respective territories is reduced (**figure 1B**). This reduction depends on the number of lymph nodes removed, their prior share of the overall drainage load and other effects associated with surgery and therapeutic radiation. Subsequent effects depend on the extent of lymphatic channels with direct connections to the venous system, the presence of anastomotic lymph collectors connecting the affected quadrant to the contralateral axillary and supraclavicular nodes, and on differences of upper extremity lymph flow features that affect subsequent arm lymphedema patterns. If, the reduction in lymph drainage capacity is large enough, lymphedema develops.

MLD and IPC effectiveness, when used, depends on stimulating lymphatic flow in a way that facilitates lymph movement through alternative pathways so that lymph is moved from lymphedematous regions circumventing damaged or obliterated normal pathways. Key to effective therapy is the recognition of the underlying physiological processes, anatomical features and physical principles governing the lymph movement. These collectively indicate that one essential element is the treatment of truncal lymphatics to provide optimally effective lymphedema therapy.

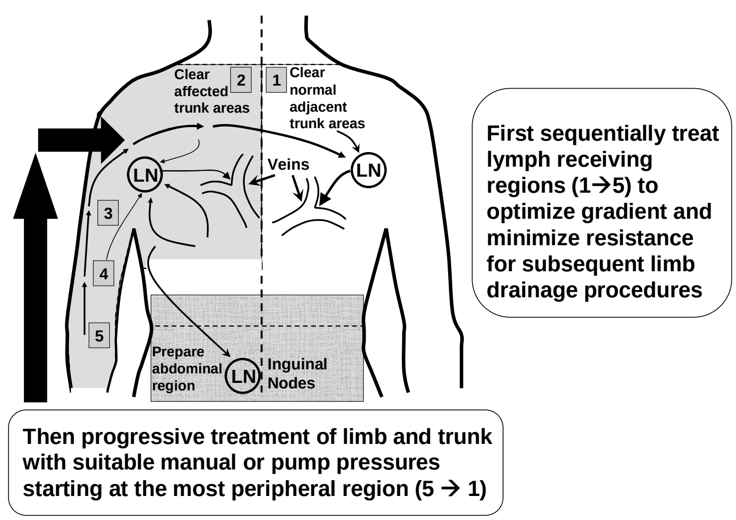
This concept may be amplified and clarified by considering the physical and physiological factors involved (f**igure 2**). Lymph movement within and then out of lymphatic territories is determined by (1) normal contractile activity of lymphatic vessels, (2) the associated dynamic pressures that are developed and (3) the resistance to lymph flow attributable to the overall network of lymphatic vessels and nodes. Dynamic pressures, in turn, depend on distension of smooth muscle within lymph vessel walls as influenced by their lymph volume or load. An optimal therapeutic approach should facilitate lymph flow into cleared areas and then flow within and then out of these cleared regions, ultimately emptying into the venous circulation.



I consider first normal lymph transport from a limb to and through lymph nodes and lymph collectors and conduits terminating at junctions with the venous system (**figure 2A**). Three major physical factors affect this process; 1) dynamic propulsive pressures developed by contracting lymphatic vessels located within the limb (P_L), 2) resistance to lymph flow between limb and venous junction (R_L), and 3) pressures within the network of lymphatic vessels linking nodes to the venous system (P_{LV}). These factors determine lymph flow (Q_L) from the limb as described by following functional relationship; [1] $Q_L \sim (P_L - P_{LV}) / R_L$. It compactly states that lymph flow is proportional to the pressure gradient between intra-lymphatic vessels and lymph-venous conduits divided by the lymphatic network resistance that lies between them.

In the *lymphedematous condition*, lymph movement through normal channels and out of lymphedematous regions is reduced due to increased R_L, (node removal and injury to lymphatic vessels and tissues) and reduced P_L within lymph vessels in the lymphedematous regions[17]. Promotion of lymph flow out of lymphedematous areas, parlty by bypassing higher resistance pathways, as is the strategy with MLD and some advanced IPC devices, now depends on the pressure gradient ($P_L - P_T$) in which P_T conceptually represents the truncal tissue pressure (**Figure 2B**). Thus, the importance and basis for preparatory truncal clearance, in which truncal pressure and volumes are reduced *prior to* attempting to drain lymphedematous regions is evident. It facilitates lymph flow through remaining 'normal' pathways by reducing P_{LV} and P_T thereby optimizing the gradient and facilitating treatment related lymph movement through alternate pathways.

From the forgoing it is hopefully clear that the standard of care should include a treatment process that begins with a thorough truncal clearance phase and progresses in a manner schematically shown in **figure 3.** This approach is needed to minimize volume and pressure within lymphatic territories that will subsequently collect lymph fluid drained from lymphedematous tissue regions. Thus the prepared normal truncal region serves as an optimized pathway for the adjacent affected quadrant and the prepared affected truncal region serves as an optimized pathway for draining the lymphedematous arm. A similar proximal clearance requirement and analysis applies to lower extremity lymphedema.



Phase II Therapy

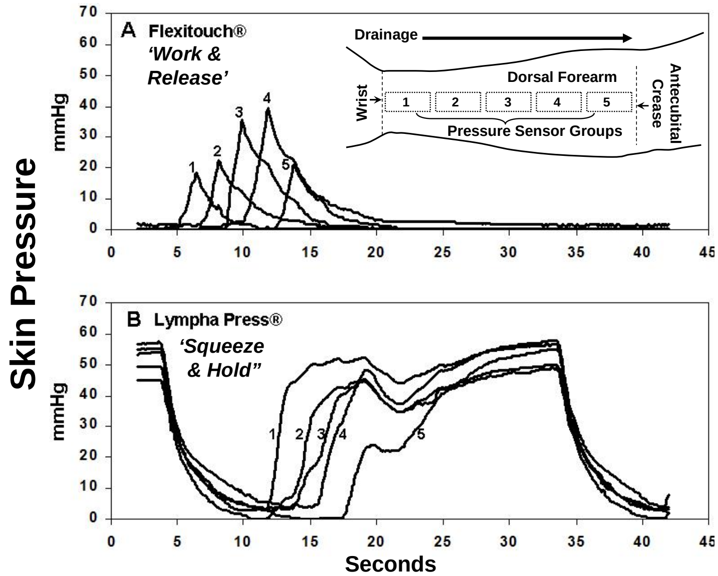
The goals of home self-care are to maintain or improve edema reductions achieved during phase I and to reduce risks of complications. Conservative self-care in the home includes elements of the following: self-MLD, skin care, self-examination to detect diagnostic hallmarks of cellulitis, consistent wear and fitting and care of garments, weight control, and exercise. As defined by the Centers for Medicare and Medicaid Services, conservative in-home self-care may include a compression bandage or garment system. Only after a 4-week trial of conservative in-home care with no improvement are IPC devices covered and then only the older generation pumps. This is unfortunate since as discussed subsequently, a newer advanced pump approach provides the already mentioned needed preparatory truncal clearance and also provides patient-customized programming to meet individual patient special needs such as those dictated by ulcer presence and areas that are too painful to treat.

It has been determined[14] that lack of compliance in performing the various home self-care elements is a major factor contributing to the loss of gains so diligently achieved during phase I. Such losses and in fact reversals may trigger related complications including fibrosis, inflammation, cellulitis, diminished range of motion and pain. Lack of compliance, especially with respect to self-MLD and bandaging may be attributable to a number of factors. The affected areas may be difficult to reach because of impaired mobility, or because of their location, such as the back. The location of the affected area also complicates application of compression bandaging, which can be much more difficult to apply to the trunk than to the extremities. Further, self-care is emotionally challenging, because of the daily time required. Self-MLD also requires the patient's complete attention, as well as placing upon the patient physical demands. These demands are being made more difficult to meet in light of the longevity of aging cancer-survivors and their declining physical prowess. Self-MLD to be effective must also be done consistently and correctly which for many patients is a significant challenge. This self-care regimen may also lead to repetitive stress injuries of the already compromised limb or unaffected limb.

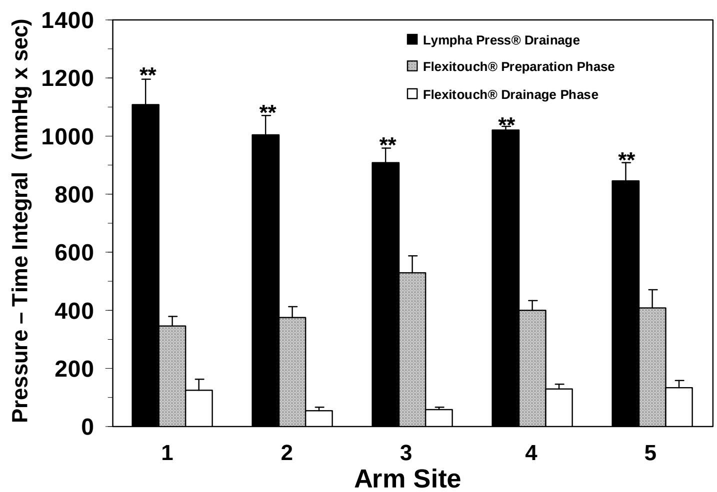
Together these factors can discourage compliance, particularly as the patients are coping with cancer and its aftermath. As a result, many patients who make initial diligent efforts to adhere to the in-home treatment regimen experience exacerbations of the lymphedema or infections and require further rounds of in-clinic treatment including CDP. While the specialized attention provided by therapists is often psychologically supportive to patients, the costs associated with cycling through multiple sessions of CDP mount. Some third-party payers do not cover repeated CDP sessions, creating financial burdens for patients. A treatment improvement approach that can ease the physical and emotional burdens of in-home self-care while maintaining or improving the lymphedematous condition is available via the use of at least one advanced IPC device. Use of such effective IPC devices, such as the Flexitouch® system should be seriously considered as a component of standard home self-care and suitably supported by third-party payers as an early adjunctive component. Its features and effectiveness have been previously described[18-21]

In considering adjunctive IPC use in the home care setting or as a component of phase I treatment, it is important to define a minimum set of features required to provide safe and effective therapy consistent with underlying physiological principles. As already noted the capacity to provide automated initial truncal or proximal clearance is essential. Without it, not only are attempts to drain lymphedematous regions inefficient and less effective, but may also result in injury. In a recent survey of 50 certified lymphedema therapists conducted by the author, their greatest concerns about using or recommending IPC was that it would cause truncal or genital edema or produce fibrotic cuffs. Each of the these is indeed a concern with 'older generation' pumps that do not have truncal or proximal clearance preparation phases, further indicating the importance of using advanced IPC devices .

Another IPC feature consideration is the pattern and magnitude of the pressure delivered to the skin by the segmented chambers in contact with the skin. With respect to the pattern of compression, most IPC devices use what I call a "squeeze and hold" pattern whereas newer advanced approaches use a "work and release" pattern that, during drainage progresses distal to proximal in way that more closely emulates the established effective pattern used in MLD. The differences are well illustrated in **figure 4** that shows arm drainage pressures measured for an advanced IPC device (Flexitouch®) in comparison to an 'older generation' device using the "squeeze and hold" approach (Lympha Press®). In the aforementioned survey of experienced therapists one of the most important IPC compression feature was to have an IPC that operated with the "work and release' approach.



Besides the compression pressure pattern, the magnitude and duration of pressure applied to the skin should be considered. The literature alerts us to the possibility of lymphatic vessel injury if too high a pressure for too long a time is used. Interestingly, too high a pressure was also a prime concern of surveyed therapists regarding IPC use. Thus it is important that pressures delivered to skin be in accord with the pressure settings, either via manual or programmed methods. Literature has indicated that in 'older generation' IPC pumps this calibration is not accurate[22]. The combined pressure magnitude and action duration can be captured using the pressure-time integral that takes into account the actual time dependent pressure profile delivered to the skin. When applied to "work and release" vs. "squeeze and hold" patterns, the "work and release' approach yields a significantly less pressure-time integral as shown in **figure 5.** This fact suggests that efficient and safe therapy are features of the "work and release" method used in advanced IPC devices.



To succinctly sum up the main points:

- The standard of care for lymphedema embraces a broad spectrum of considerations that include 1) reducing risk for those who are at-risk, 2) early, potentially pre-clinical detection, 3) early and intensive initiation of therapy (phase I) and 4) maintenance and improvements upon phase I gains via long-term in-home self-care (Phase II).
- Risk reduction can be enhanced by suitable early education of patients and when possible coupled with pre-surgical and follow-up evaluations
- Historically and generally accepted phase I therapy includes MLD, short stretch compression bandages, decompression exercise and skin care in some cases supplemented with IPC use.
- Phase II consists of a long-term possibly life-long in home self-care program including self-MLD, use of an elastic garment, compression bandaging, exercise and skin care.
- Significant Phase II compliance issues that may negate Phase I gains may be countered or preempted by the use of IPC devices preferably by an IPC device that provides truncal clearance, programmable patient-customized treatment patterns and calibrated pressures, and a pressure pattern that emulates the well established and physiologically based "work and release" method.

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Figure Legends

Figure 1. Schematized lymph drainage of right arm and trunk quadrant: Normal vs. Lymphedema. LN represents lymph node. (A) Normal drainage from arm and ipsilateral and contralateral trunk quadrants. Lymph normally drains away from the watershed into nodes in the corresponding quadrant (B) LN removal or lymph vessel injury renders normal pathways deficient or absent thereby reducing lymph drainage from arm and ipilateral quadrant. Lymph flow can be directed across the watershed into the contralateral quadrant with proper applied therapy.

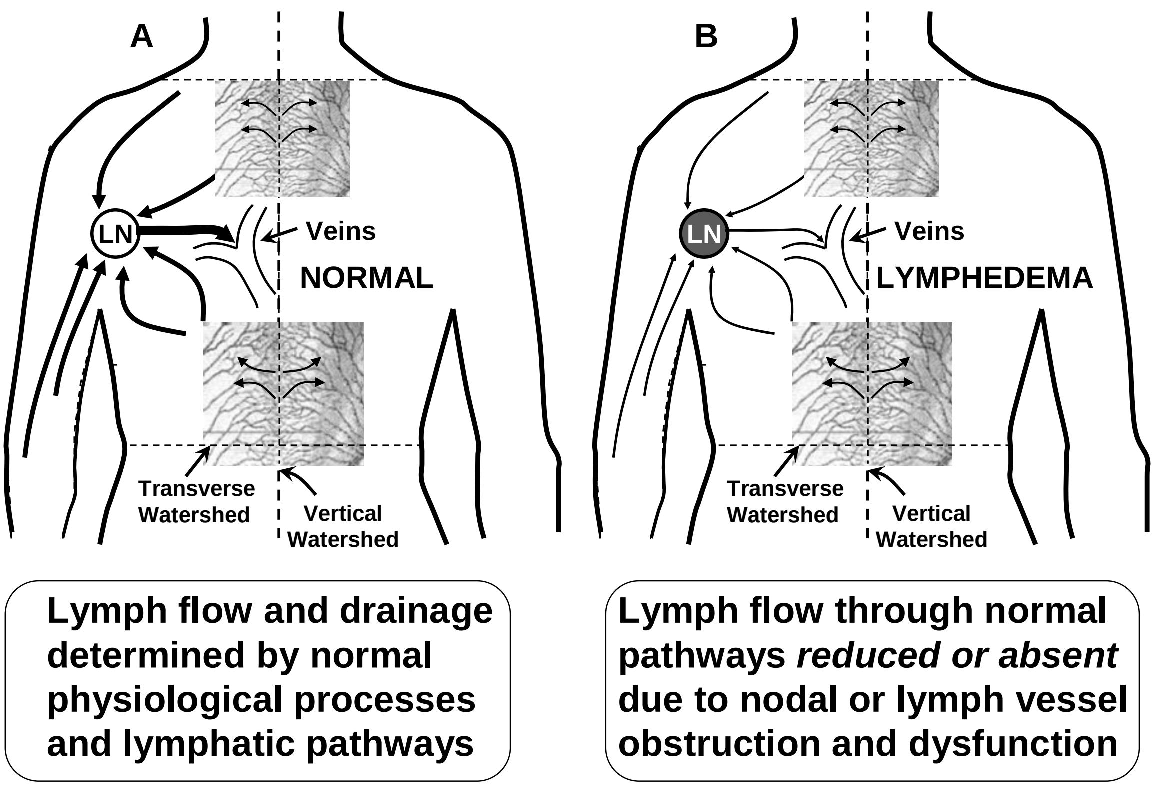


Figure 2. Main physical determinants of lymph flow from the arm: Normal vs. Lymphedema.

P_L is the dynamic propulsive pressure developed by contracting lymphatic vessels and P_{LV} is the pressure in the network of lymphatic vessels linking the nodes to the venous system. (A) Normally the lymph flow (Q_L) depends on the gradient between P_L and P_{LV} and on the resistance of the normal lymphatic pathways between arm and venous junction. (B) When normal pathways are lost therapy seeks to use alternate ones. The effective pressure gradient now depends truncal tissue pressures (P_T) of both the contralateral and ipsilateral quadrants. Effective therapy seeks to reduce P_T to maximize the lymph perfusion gradient (P_L – P_T).

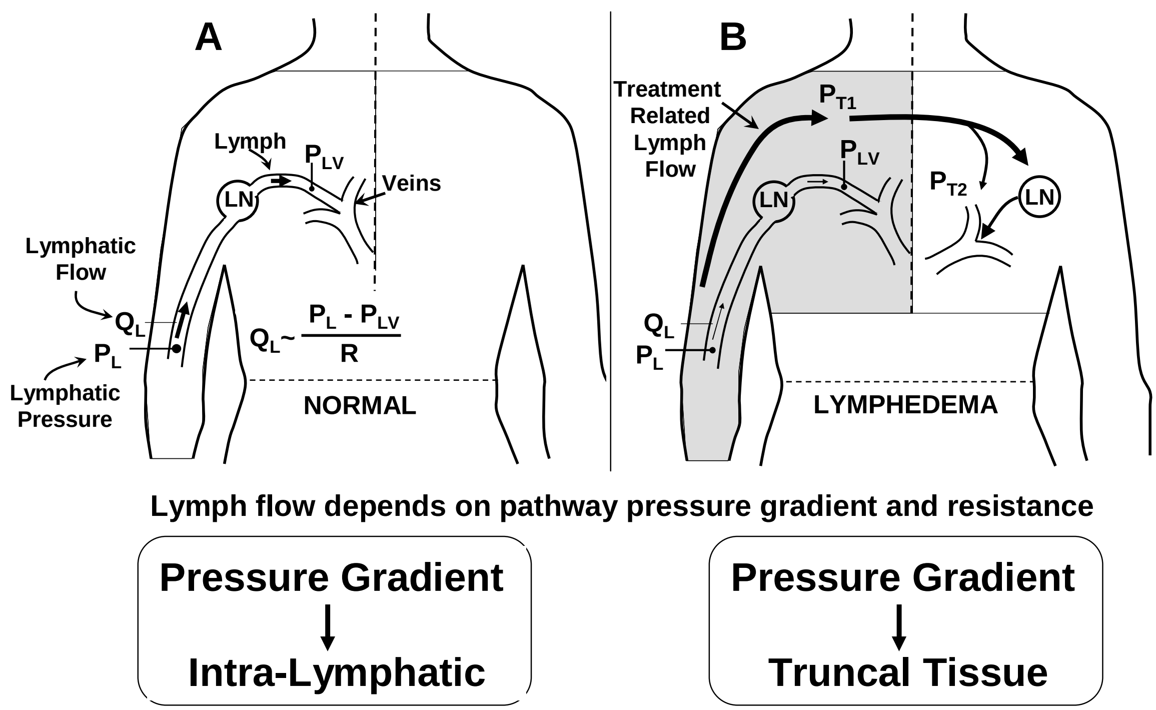


Figure 3. Schematized depiction of effective truncal-limb treatment

Normal flow pathways are reduced or absent. Truncal clearance reduces P_T and P_{LV} in ipsilateral and contralateral quadrants and augments normal lymphatic vessel pumping actions prior to attempting limb drainage therapy. Treatment related lymph flow is thus optimized. See text for further discussion The numbers show the sequential order in which applied therapeutic decongestion or clearance is most appropriate and effective. The main emphasis is on preparing the truncal regions prior to treating the affected limb. The physiological basis for this approach is discussed in detail within the text.

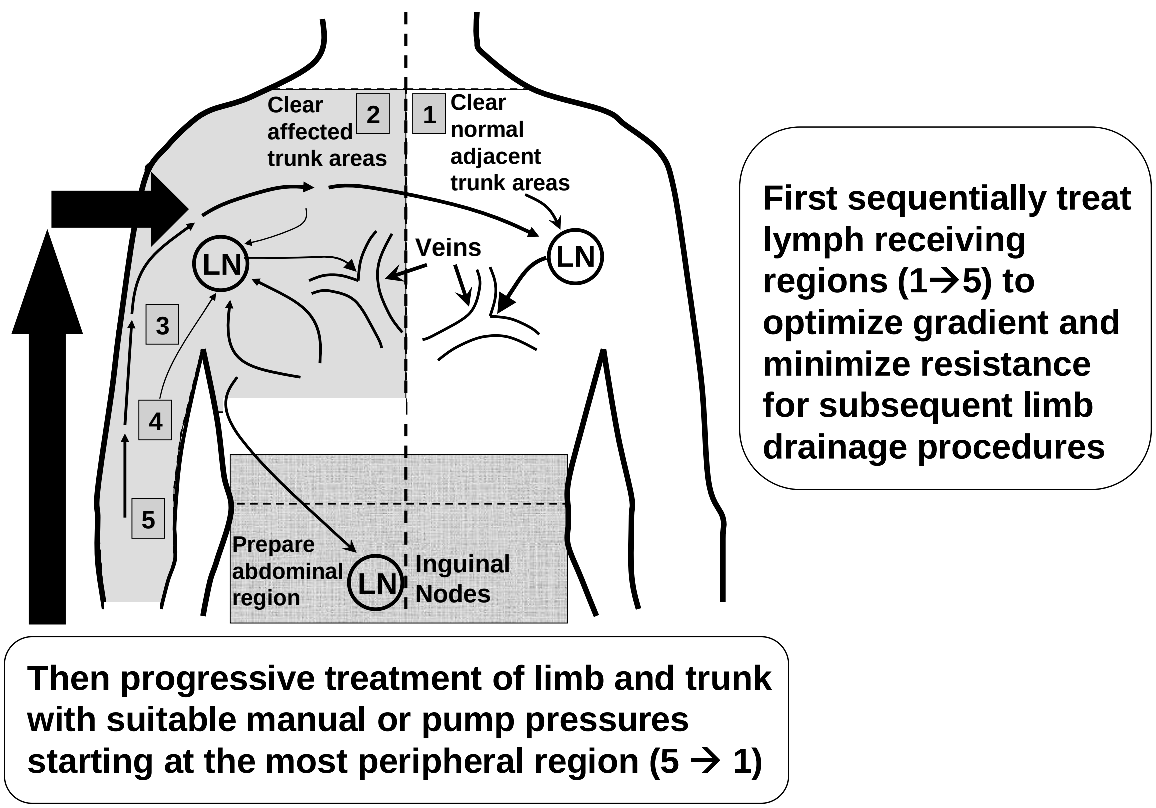
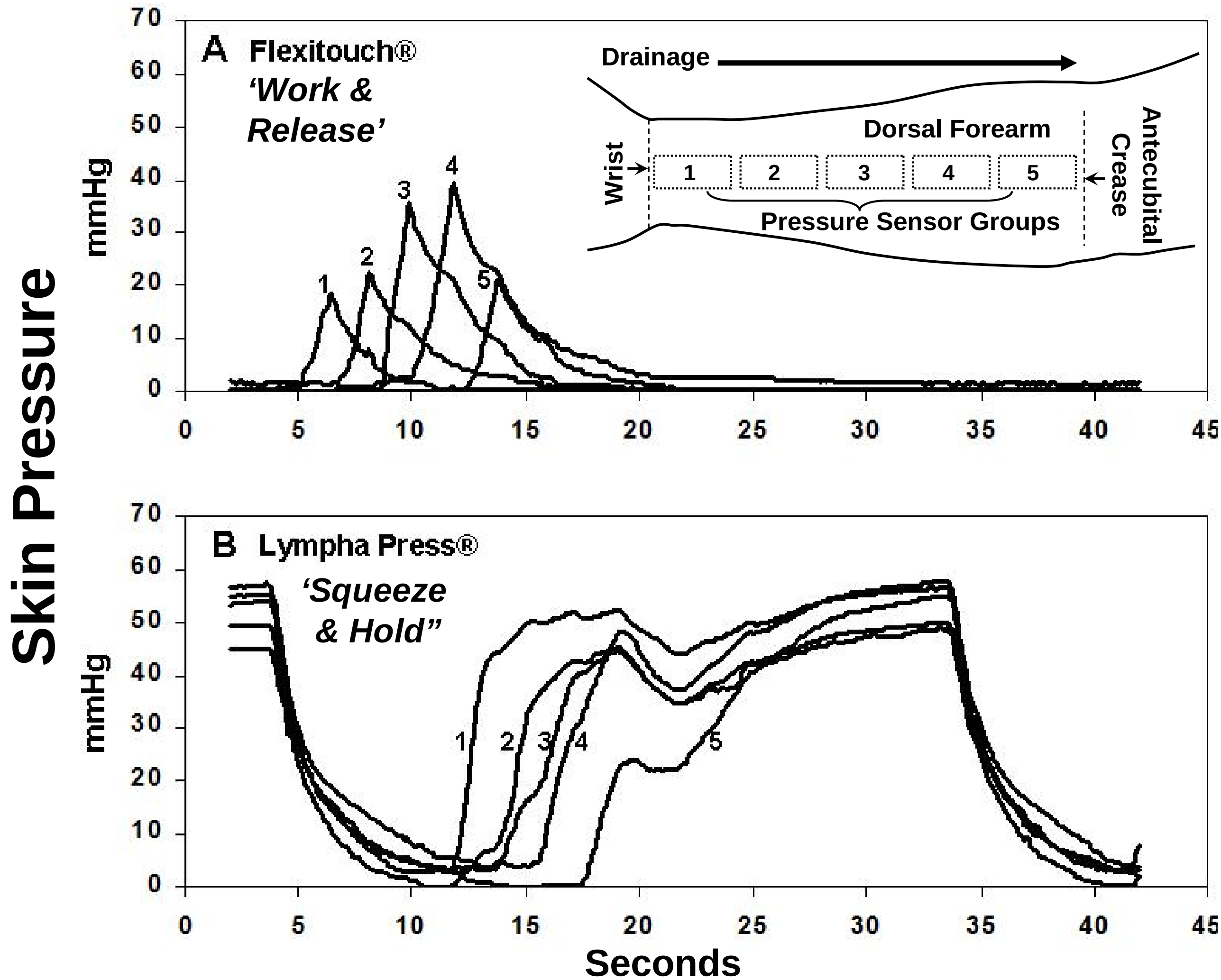


Figure 4. Differences in skin pressure-time patterns associated with IPC pump types.

Numbers (1-5) correspond to pressure sensor groupings on the forearm and the sequential pressures measured as the IPC chambers on the arm sequentially inflate and deflate. Skin pressures are the instantaneous average pressures of multiple sensors within each grouping. On complete drainage cycle is shown for each of the devices. A) Flexitouch® - drainage cycle, B) Lympha Press®



Figures 5. Comparison of pressure-time integrals associated with different IPC devices.

Data is mean and SD of measurements on 10 subjects. At all forearm sites the Lympha Press® device resulted in pressure-time integrals that were significantly greater (** $p<0.001$) than for the Flexitouch® device. (Data from reference 19).

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