Lymphoedema microsurgery: are we re-inventing the wheel yet again?

Ramin Shayan MBBS PhD FRACS1−5

1 O’Brien Institute
St Vincent’s Institute for Medical Research
Fitzroy, Victoria, AUSTRALIA
2 Plastic, Hand and Faciomaxillary Surgery
Alfred Hospital
Fitzroy, Victoria, AUSTRALIA
3 Plastic and Reconstructive Surgery Department
Royal Melbourne Hospital
Parkville, Victoria, AUSTRALIA
4 Department of Plastic Surgery
St Vincent’s Hospital Melbourne
Fitzroy, Victoria, AUSTRALIA
5 St Vincent’s Lymphoedema Clinic
St Vincent’s Hospital Melbourne
Fitzroy, Victoria, AUSTRALIA

Microsurgery as a treatment for lymphoedema is not new. Indeed, the late Bernard O’Brien first described the suite of surgical techniques that are used today in 1976,1 the year of this author’s birth! Nevertheless, despite extraordinary growth in the number of publications relating to lymphovascular anastomoses and free lymph node transfer, it is still important to ask ourselves how far we have actually come in the past four decades and whether, in this latest burst of enthusiasm, we are merely re-inventing the wheel. Apart from an interesting technical exercise in which microsurgeons challenges themselves to anastomose smaller and smaller vessels, how realistic is it to expect these tiny vessels to drain a whole limb?

In assessing the efficacy of the surgical approaches used in lymphoedema, it is worthwhile recalling the principles upon which O’Brien originally based his description of techniques—lymphovascular anastomosis (LVA), free lymph node transfer and limb liposuction. These principles were based on improvement of limb function, aesthetics and volume; and reduced infection risk and symptoms of heaviness and discomfort. It is vital to remind ourselves why it is that we are undertaking the surgery in the first place and what we are hoping to achieve for each patient and whether these goals are realistic. Generally, the goal of the microsurgical approaches to lymphoedema is to restore physiology, whereas liposuction aims to reduce symptoms through debulking—which is not in itself curative.

Isao Koshima, the great Japanese microsurgeon who coined the term ‘super-microsurgery’, and who must himself take much credit for re-popularising
lymphatic microsurgery, has described O’Brien as the ‘father of lymphoedema surgery.’ However, O’Brien’s successor at the institute that bears his name, Wayne Morrison, recalls that at the time of his untimely passing, O’Brien remained vexed by the unpredictability of the results of the surgical approaches available, and that after having produced the largest ever published Australian series of LVAs, O’Brien was ultimately disappointed with the results.³

Citing the findings of this seminal 1990 publication³ and lamenting the poor predictability and seemingly random nature of the limb volume reduction results obtainable in many patients, Australian plastic surgeons have traditionally viewed lymphoedema surgery with a healthy dose of Aussie skepticism, if not outright negativity. Apart from the difficulty in assessing which patient will benefit from what treatment, this view has been further fueled by several factors: the ‘too-hard basket’ in which many doctors often place lymphoedema patients by the bedside; the desperation of this patient cohort and a propensity to sometimes embrace often alternative treatments; and, finally, the difficulty in meaningfully assessment of outcomes and having objective markers by which to report them.

So what then, has really changed? Why do we find ourselves coming full circle to embrace a set of techniques that was (perhaps rightly) largely abandoned many years ago?

Hopefully, it can be said that, in the four decades since O’Brien devised the lymphoedema surgical techniques, we have learnt to learn from our mistakes and have learned to employ several key advances.

Firstly, the tools that we now use to study lymphatics have improved, and consequently, so has our biological understanding of their physiology and role in disease. Our improved knowledge of the hierarchy of anatomically and functionally distinct lymphatic vessel subtypes, along with the recent advent of molecular techniques that enable identification of lymphatics in tissue, have shown each lymphatic vessel subtype to boast a unique molecular profile and responsiveness to growth factor cues.⁴ Enhanced histological markers enable researchers to manipulate the growth and development of the lymphatics (lymphangiogenesis) as well as the generation of abnormal lymphatics in pathological conditions, as mediated by mechanisms such as vascular endothelial growth factor (VEGF) proteins. Physiologically, the lymphatic system is now better understood as an intricate vessel network that regulates interstitial fluid balance, lipid metabolism and immune cellular trafficking, thereby allowing surgical strategies to be designed to focus on any or several of these parameters depending on the aetiology, chronicity and secondary effects of the disease.

Indeed, the lymphatic system is implicated in several key diseases encountered by plastic surgeons. Functional inadequacy at draining lymph from peripheral tissues, resulting in local fluid accumulation that we know as lymphoedema, may be ‘acquired’ after physical trauma, surgery, irradiation or parasitic infection. It is now known, however, that lymphoedema may also occur congenitally due to deficient or defective developmental processes in lymphatics.⁴

Recently, and as an indicator of its key role in development and function, it has emerged that the lymphatic system has been highly preserved across species and throughout evolution. It has been found that there are tightly controlled, very specific genes that modulate spatial relationships between lymphatic vessels, valve formation and integrity and the characteristics of lymphatic absorption and propulsion.⁵ For example, Milroy disease is caused by point mutation in a gene coding for the VEGFR-3 protein—the receptor for VEGF-C and VEGF-D on lymphatics.⁵ A further array of genes such as SOX-18, FOXC2 and CCBE1, to name a few, have been implicated in clinical lymphoedema syndromes.⁵ While this opens doors for potential future gene-based treatments, it also suggests that we may be able to undertake patient selection for surgical procedures based on gene profile and the likely source of abnormality in the lymphatic system and, therefore, whether and how much they are likely to benefit from each respective modality of surgical treatment.
Conversely, in malignancy, lymphatics may be overly proficient—transporting cancer cells from a primary tumor around the body, facilitating unwanted lymphogenous metastasis and systemic dissemination. Similarly, unwanted overgrowth of lymphatics is seen in lymphatic malformations and Kaposi’s sarcoma, as well as in rheumatoid arthritis. Wounding interrupts lymphatic drainage, leading to local tissue swelling or lymphoedema that further impairs healing. This understanding, along with the potential availability of lymphangiogenic agents and inhibitors, paves the way toward future therapeutic targets in diseases such as lymphoedema and cancer metastasis. Clearly, the future plastic surgeon offering lymphatic surgery will need an appreciation of this enhanced biological understanding.

Secondly, microsurgery has come a long way since O’Brien had his microsutures manufactured by hand by a pair of Melbourne watchmakers. The improved magnification provided by modern microscopes and an increased familiarity with perforator-level dissections and anastomoses have heralded an era of further refinement and evolution in perforator-to-perforator free flap surgery and super-microsurgery. Imaging techniques have also improved with the advent of magnetic resonance (MR) lymphangiography using lymphatic-specific tracers, as well as the more widespread availability of indocyanine green (ICG) and patent blue v dyes with which to visualise lymphatics clinically.

In conclusion, lymphoedema microsurgery has once again become a hot topic in plastic surgery. However, it is important to look to the past and ask whether our results will be any different from those of the original pioneers. The average plastic surgeon knows little about the complex biology behind the lymphatic system, but in order to perform optimal patient assessment, surgical selection and informed consent, it is imperative that surgeons offering lymphoedema surgery are aware of the biological implications of the options available for a given patient and that they are able to offer their patients meaningful statistics and justification for the management decisions taken. Otherwise, there is the risk that the cavalier and ineffective application of these surgical techniques may once again tarnish the reputation of microsurgery in treating lymphoedema in Australia, and potentially, again banish it into obscurity for another three decades—or worse, that the damage done to the credibility of these surgical techniques may this time be irreparable.

Disclosure
The author has no financial or commercial conflicts of interest to disclose.

References