



GUIDELINES

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Viewpoint

Rewiring the Brain: The Next Frontier in Supermicrosurgery

In this article, we would like to share our recent progress in exploring the therapeutic potential of lymphatic reconstruction for the treatment of Alzheimer disease. Our team at Cleveland Clinic has made significant strides in exploring the lymphatic system's role in brain disorders and the possibility of treating brain conditions previously considered untreatable.¹

Our research on lymphedema reconstruction of the arms, legs, and trunk led us to observe the catchment effect² and systemic effect.³ These effects demonstrate that the lymphatic system responds to surgical treatment as a unified organ, which means that lymphatic surgery remains effective whether it is done at the problem site or elsewhere. Combining these observations

with the discovery of glymphatic⁴ and meningeal lymphatic⁵ dysfunction in Alzheimer disease and other neurodegenerative proteinopathies, we hypothesized that extracranial supermicrosurgical lymphatic reconstruction may “de-clog” the brain to improve the above conditions.

We were pleased to find that we were not alone in our thinking. Dr. Qingping Xie has explored similar hypotheses and has successfully performed 50 cases of such reconstruction on patients with Alzheimer disease, with a mean follow-up period of 9 months. He observed remarkable improvements in behavior, cognitive function, and memory, as demonstrated by the Minimum Mental State Examination and Montreal Cognitive Assessment. [See **Video (online)**, which shows the postsurgery recovery of an 84-year-old bedridden man with Alzheimer disease. The patient's preoperative condition and progress at 3 days, 6 months, and 8 months are shown.] Although impressive, we recognize the need for more objective, quantitative evidence, including biomarker measurements, imaging studies, and neuropsychological evaluations, to support the efficacy of this procedure.

We are currently conducting animal studies to assay Alzheimer disease biomarkers before and after extra-anatomic supermicrosurgical lymphatic reconstruction using an established murine Alzheimer disease model (hospital ethics committee approval no. 330103009-202100003). These studies will provide critical evidence on whether lymphatic reconstruction can indeed treat Alzheimer disease. In parallel, Dr. Xie will continue his institutional review board–approved study on human subjects, following a protocol developed jointly with our multidisciplinary team, which includes lymphatic supermicrosurgeons, neuroscientists, neurologists, neuroradiologists, and neurosurgeons. By combining data from basic science and animal and human studies, we hope to arrive at a more definitive conclusion in the near future.

Our findings have significant implications for both plastic surgeons and humanity. For plastic surgeons, this means expanding our scope of practice to brain disorders, creating new procedures, and establishing the new subspecialty of brain lymphatic reconstruction surgery. For humanity, we will likely be able to treat conditions previously considered untreatable, providing hope and help to a patient population with limited options.

We acknowledge that our findings are preliminary, and the study is still ongoing. However, we remain committed to pursuing this research with rigor and diligence, and we are optimistic about the promise of lymphatic reconstruction for brain disorders.

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DISCLOSURE

None of the authors has a financial interest in products, devices, or drugs mentioned in the article.

PATIENT CONSENT

The patient or guardian provided written informed consent for use of the patient's images.

REFERENCES

1. Louveau A, Smirnov I, Keyes TJ, et al. Structural and functional features of central nervous system lymphatic vessels. *Nature* 2015;523:337–341.
2. Lin CH, Ali R, Chen SC, et al. Vascularized groin lymph node transfer using the wrist as a recipient site for management of postmastectomy upper extremity lymphedema. *Plast Reconstr Surg*. 2009;123:1265–1275.
3. Kukreja-Pandey S, Al-Malak M, Ku Y, Duarte-Bateman D, Chen WF. D40. Effects of lymphaticovenular anastomosis in contralateral leg in patients with acquired bilateral leg lymphedema [Abstract]. *Plast Reconstr Surg Glob Open* 2023;11:81–82.
4. Rasmussen MK, Mestre H, Nedergaard M. The glymphatic pathway in neurological disorders. *Lancet Neurol*. 2018;17:1016–1024.
5. Da Mesquita S, Louveau A, Vaccari A, et al. Functional aspects of meningeal lymphatics in aging and Alzheimer's disease. *Nature* 2018;560:185–191.