Leksell’s Posteroventral Pallidotomy 1992–2022: Quo Vadis?

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Dear Editor,

In their 2017 publication titled “The Changing Landscape of Surgery for Parkinson’s Disease,” Lozano et al.\textsuperscript{[1]} discussed “The Rise and Fall, Re-emergence, and Re-decline of Pallidotomy for PD.” Indeed, pallidotomy heralded the era of stereotactic surgery for various movement disorders, including Parkinson’s disease: Spiegel and Wycis, Narabayashi, Cooper, Talairach, Guiot, Leksell, Krayenbühl, Bertrand, Gillingham, and others used as surgical target various parts of the globus pallidus. With exception of Leksell, most surgeons aimed at the anterior, anteromedial, or dorsal parts of the globus pallidus\textsuperscript{[2]}. Toward the late 1950s and early 1960s, pallidotomies declined altogether in favor of ventrolateral thalamotomy because of the latter’s more robust effect on tremor.

The “Re-emergence” mentioned by Lozano et al. did not concern just any kind of “pallidotomy” but specifically Leksell’s posteroventral pallidotomy (PVP) that was rediscovered by Laitinen in 1992\textsuperscript{[3]}. That procedure was first published in 1960, i.e., before the L-dopa era, by neurologist Svennilson et al.\textsuperscript{[4, 5]}. Following personal meeting and discussion between Leksell and Laitinen in 1984 (Fig. 1), the first PVP of the post-L-dopa era was performed in January 1985 in Umeå, Sweden, by Laitinen assisted by one of the present authors, who was his resident at that time. The first series of patients was eventually published in the seminal paper of Laitinen et al. in 1992\textsuperscript{[3]}. The manuscript had been rejected several times until Laitinen asked Thoralf Sundt Jr, the previous editor of \textit{The Journal of Neurosurgery} to kindly review himself the manuscript. According to Gildenberg, this 1992 publication marked the renaissance of surgery for Parkinson’s disease\textsuperscript{[6]}, and Laitinen’s 1992 paper became a citation classic\textsuperscript{[7–9]}, reaching 1354 citations (Google Scholar, February 9, 2022). As this year marks 30 years since the “renaissance” of PD surgery, the authors, working at the University Hospital of Northern Sweden in Umeå, the very cradle of that “renaissance,” aim to mark this anniversary by highlighting selected publications from the rich pallidotomy literature of the last 30 years, and to venture a tentative prediction concerning the future place of posteroventral pallidotomy in the surgical armamentarium of movement disorders.

**Pallidotomy versus STN DBS: Very Long-Term Outcome**

A publication from 2001 reported the 10-year follow-up of the first PVP patients operated on by Laitinen between 1985 and 1990, and concluded that “The long-term
effect of PVP on dyskinesias was not only curative but also appeared to be prophylactic. Contralateral tremor was improved in the majority of patients...Further progression of axial and akinetic symptoms, and an eventual decline in cognition together with other concomitant illnesses, contributed to increased disability in several patients” [10]. In 2003, Krack et al. [11] published the 5-year follow-up of bilateral STN DBS of the Grenoble patients and concluded that there was “…worsening of akinesia, speech, postural stability, freezing of gait and cognitive function between the first and the fifth year…”. In 2011, Zibetti et al. [12] published the beyond 9-year results of STN DBS and stated that “Beyond 9 years from STN surgery patients’ performances in the ADL worsened considerably, likely because of the progressive development of L-dopa unresponsive axial symptoms, together with cognitive decline and…comorbidity”. There is a striking similarity between these three statements, especially in relation to progression of akinetic symptoms, cognitive decline, and the presence of comorbidities at long-term follow-up after surgery, be it a pallidotomy or STN DBS [13].

### Medium-Term Follow-Up in Pallidotomy and DBS Trials

How about results of pallidotomy versus DBS at a 2–4 years follow-up? In 1997, Lang et al. [14] published results of PVP in advanced PD with a mean off-med UPDRS III score of 44 at baseline. They reported about 25–28% improvement in off-med motor scores at 2 years. In 2003, Vitek and the Atlanta group published the 2-year follow-up of patients randomized to either best medical therapy or PVP, and who had a mean off-med UPDRS III score at baseline of 39 [15]. The surgical group showed a sustained 25% improvement in off-medication motor scores. In 2006, the Amsterdam group published a randomized study of PVP versus STN DBS. The patients had a mean off-med UPDRS III score of 46.5 at baseline. The PVP cohort showed a 31% improvement in off-med motor scores at 1 year [16] and 27% at 4 years [17]. Valdeoriola et al. [18] from Barcelona evaluated patients with a UPDRS III score of 51.4 at baseline. Four years after pallidotomy, UPDRS III scored 39.6 (23% improvement) [18]. A study from Houston on patients scoring 58.3 points on UPDRS III off-med at baseline reported at a mean of 5 years after PVP a score of 44.3 (24% improvement) [19].

In 2010, Follett et al. [20] published a large multicenter randomized study comparing the 2-year results of DBS in the globus pallidus internus (GPI) versus DBS in the STN. At baseline, the mean off-med UPDRS III score was 42 for patients receiving GPI DBS and 43 for patients receiving STN DBS. Postoperatively, there was no significant difference in improvement of off-med motor scores between GPI DBS patients (28%) and STN DBS patients (25%).

If we compare the pallidotomy studies mentioned above with the DBS paper of Follet et al. [21] – and granting that the moderate results of DBS in that paper may not be a benchmark of the true efficacy of DBS – we notice that the mean off-med UPDRS III scores at baseline were similar for the patients receiving pallidotomy and those receiving DBS, indicating a similar severity of disease, and the percentual motor improvement after pallidotomy or DBS was also similar at 2 years (and at 4–5 years for pallidotomy patients). Additionally, there were less adverse events in the pallidotomy cohorts compared to the DBS cohorts, confirming a previous observation of Blomstedt et al. [22] about safety of ablative surgery compared to DBS. Hence, one cannot but agree with Gross [23] from Emory University that “unilateral pallidotomy is a relatively safe operation, compared with the benefits that can be expected. On its own merits, it is unlikely that modern pallidotomy would have been abandoned based on an excessive rate of adverse effects”.

### Laitinen’s Posteroventral Pallidotomy as Inspiration for DBS in Dystonia

Andres Lozano is probably the first neurosurgeon who performed in 1997 simultaneous bilateral PVP for generalized dystonia [24]. Soon after, the posteroventral palli-
dum became the target of choice for DBS in dystonia, a procedure that was pioneered in 1999 by three neurosurgeons from Montpellier, Bern, and Toronto, respectively, independently of each other [25–27]. It is interesting to notice that in the seminal publication of Krauss on Gpi DBS for pallidal dystonia published in The Lancet in 1999 [26], he wrote: “Quadrupolar electrodes were implanted bilaterally into the posteroverentral lateral globus pallidus internus.” Also when Coubes on 26 November 1996 was about to perform DBS in more or less emergency on his first dystonia patient who had been for several weeks in status dystonicus (SD) in intensive care [25], his assistant inquired from one of the authors about the exact coordinates of Laitinen’s pallidotomies (Nathalie Vayssière, personal communication, 1996).

Hence, it was the excellent results of Laitinen’s PVP on the dystonia and dyskinesias of post-L-dopa PD that triggered the use of the pallidum as target for lesioning and subsequently for DBS in patients with non-PD dystonia. Yet, in a recent editorial in Movement Disorders Journal [28], it was written: “… Laitinen et al. [3] providentially published their 1992 article that described his long and solo experience with pallidotomy … Unexpectedly but highly welcomed, it became obvious that levodopa-induced dyskinesias were abolished by pallidotomy. Such observation was not advanced by Laitinen et al. [3]…”. It is unfortunate to read that statement when in fact “Such observation” was plainly stated by Laitinen et al. [3] in the 1992 paper, both in the abstract where one can read “The L-dopa-induced dyskinesias and muscle pain had greatly improved or disappeared in most patients” and in the Results section of the paper where it is written “Pallidotomy had a very good effect on involuntary movements induced by Ldopa and on painful muscular spasms” [3].

**What Future for Posteroventral Pallidotomy?**

From browsing the scholarly literature of the last 5–10 years, it seems that Leksell-Laitinen’s posteroventral pallidotomy is a “die-hard” surgical procedure, not only managing to survive under the overwhelming shadow of DBS publications, but even re-re-emerging slowly again, this time to treat, among others, patients suffering from a new syndrome labelled “DBS withdrawal syndrome.” This new and sometimes fatal syndrome can occur in some parkinsonian patients after long-term STN DBS [29–31] or in some dystonia patients after long-term Gpi DBS [32], when battery is suddenly depleted and no replacement is available or affordable, or when hardware is explanted due to infection. In cases where such patients have been fortunate enough to receive a pallidotomy thanks to the neurosurgeons having been trained to perform this procedure, the sudden post-DBS deterioration was reversed by the PVP [33]. Isn’t this a testimony to the resilience and efficacy of PVP, even unilateral, when it manages to reverse the medication-resistant deterioration of patients who become suddenly severed from several years of bilateral DBS in either pallidum (for dystonia) or STN (for PD)? Pallidotomy has also been performed through implanted DBS electrodes in patients with SD [34] or as a rescue procedure prior to explanting an infected DBS lead [35–37].

PVP may be re-re-emerging also as a primary procedure in some countries such as Japan [38–42] and primarily thanks to the skills and confidence of neurosurgeons who had been trained or are being trained in performing PVP. Furthermore, even bilateral pallidotomy, especially for dystonia, is being revisited: last year a paper titled “Bilateral Pallidotomy for Dystonia: A Systematic Review” was published in Movement Disorders Journal by a Dutch team from Groningen [43]. These authors conducted a systematic review of individual patient data concerning a total of 100 patients from 33 articles, including 25 patients with SD in 23 of whom SD resolved after the bilateral pallidotomy. They concluded that “Given the burden of dystonia, bilateral pallidotomy should be regarded a viable tool in the armamentarium of the neurosurgeon in the treatment of dystonia, particularly for patients with contraindications for DBS or if the severity of the dystonic symptoms outweighs the risk of permanent speech disorders.”

PVP seems thus to be reported more and more in single cases or small case series, to treat dystonic storm [43, 44], including in pediatric patients [45], or other refractory conditions beyond the classical generalized or cervical dystonia or PD, such as embouchure dystonia [40] camptocormia [41], abdominal dystonia [46], hemichorea-ballism [47], or Meige syndrome [48]. Recently, PVP has even shown beneficial effect on the postherpetic neuralgic pain of a patient who had received a pallidotomy primarily for PD [49].

These reports, however, may be perceived today as anecdotic when compared to publications from the hey days of PVP in the 1990s and early 2000, and they do not receive the same attention that DBS publications received and are still receiving among movement disorder neurologists and the new generation of functional neurosurgeons. In fact, one of the main reasons for the slumbering life of pallidotomy in today’s DBS-dominated practice,
and indeed the reason for fatalities in patients with “DBS withdrawal syndrome” [29, 30, 32], may well be that younger generations of movement disorder practitioners, whether neurologists or neurosurgeons, are only familiar with DBS and have not been exposed to, or trained in, the art of pallidotomy [50], even though radiofrequency (RF) pallidotomy has officially been declared “efficacious” by the International Movement Disorders Society on several occasions [51, 52]. Another obstacle affecting training in RF pallidotomy and its swift re-re-emergence is that the two main companies that used to dominate the business of RF generators no longer market these products for lack of enough profit, given that most stereotacticians had shifted to using DBS instead of lesioning. Hence, a situation akin to a vicious circle may take place, which would shift from RF generators to DBS, including a renewed interest in the good old RF thermocoagulation pallidotomy, and hence a new incentive among the young and future generations of functional neurosurgeons to learn its skills.

**Conflict of Interest Statement**

The authors have no conflict of interest to declare.

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**Author Contributions**

Both authors contributed equally to this letter.

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