SUPPLEMENTARY MATERIAL

Aggregate Data Analysis

The random effects meta-analysis showed an estimated mean 3D error of 1.89 mm (95%CI 1.42-2.36) (supplementary figure 1), an estimated mean X error of 0.83 mm (95%CI 0.68-0.98]) (supplementary figure 2), an estimated mean Y error of 0.93 mm (95%CI 0.61-1.25) (supplementary figure 3) and an estimated Z error of 1.23 mm (95%CI 0.74-1.73) (supplementary figure 4). All covariates showed high heterogeneity.

Regarding the response variables, the estimated mean on-medication DBS improvement was 29.1% (95%CI 11.8-46.4) (supplementary figure 5), while the estimated mean percentage change in LEDD was 43.1% (95%CI [35.1-50.9]) (supplementary figure 6) and the estimated mean postoperative stimulation amplitude was 2.6 V (95%CI 2.3-3.0) (supplementary figure 7). All response variables showed high heterogeneity. Funnel plots and Egger's test did not show indications of publication bias for any of the secondary outcome measures.

The meta-regression analysis showed that 3D error was not significantly related to the degree of DBS motor improvement ($p = 0.54$). Furthermore, X error and Y error were not correlated to DBS motor improvement ($p = 0.76$ and $p = 0.11$, respectively). However, Z error was positively correlated with DBS motor improvement ($p < 0.001$), but just 9 studies were included in this analysis, which should be considered when interpreting its results (supplementary figure 8). All models showed considerable heterogeneity after adjustment for the covariates.

The meta-regression analysis showed that radial error was not correlated to on-medication DBS motor improvement ($p = 0.20$). Radial error had a borderline significant negative effect on average percentage change in LEDD; on average, for each millimeter increase in radial error, percentage change in LEDD decreased with 13.9% (95%CI -29.9-0.18) (supplementary figure 9). Also, radial error was positively correlated with postoperative stimulation amplitude ($p = 0.003$), but just 7 studies were included in this analysis, which should be considered when interpreting its results

(supplementary figure 10). On average, for each millimeter increase in radial error, postoperative stimulation amplitude increased with 0.3 V (95%CI 0.10-0.49). Except for the model for amplitude, considerable heterogeneity remained after adjustment for radial error.

Individual Patient Data Meta-Analysis

The estimated means and confidence intervals for the secondary DBS lead placement accuracy outcomes (covariates) and secondary response variables according to the random intercept models are described in supplementary table 4 and 5, respectively.

The mixed effects model showed no effect of any of the secondary covariates on DBS motor improvement. Effect estimates and corresponding confidence intervals are described in supplementary table 6. Radial error in the right hemisphere was negatively correlated to on-medication DBS motor improvement, for each millimeter increase in right hemisphere radial error, on-medication DBS motor improvement decreased with 78.6% (95%CI -158.6-1.50). However, just 18 patients were included in the analysis. Radial error was not correlated to on any other response variable (supplementary table 7).

Supplementary Figure Legend

Supplementary figure 1: Forest plot showing averages (black boxes) and confidence intervals for 3D error for all studies contributing mean and standard deviation. The dotted line represents the prediction interval for the mean estimate from the random effects model.

Supplementary figure 2: Forest plot showing averages (black boxes) and confidence intervals for X error for all studies contributing mean and standard deviation. The dotted line represents the prediction interval for the mean estimate from the random effects model.

Supplementary figure 3: Forest plot showing averages (black boxes) and confidence intervals for Y error for all studies contributing mean and standard deviation. The dotted line represents the prediction interval for the mean estimate from the random effects model.

Supplementary figure 4: Forest plot showing averages (black boxes) and confidence intervals for Z error for all studies contributing mean and standard deviation. The dotted line represents the prediction interval for the mean estimate from the random effects model.

Supplementary figure 5: Forest plot showing averages (black boxes) and confidence intervals for on-medication DBS motor improvement for all studies contributing mean and standard deviation. The dotted line represents the prediction interval for the mean estimate from the random effects model.

Supplementary figure 6: Forest plot showing averages (black boxes) and confidence intervals for percentage change in Levodopa Equivalent Daily Dose (LEDD) for all studies contributing mean and standard deviation. The dotted line represents the prediction interval for the mean estimate from the random effects model.

Supplementary figure 7: Forest plot showing averages (black boxes) and confidence intervals for postoperative stimulation amplitude for all studies contributing mean and standard deviation. The dotted line represents the prediction interval for the mean estimate from the random effects model.

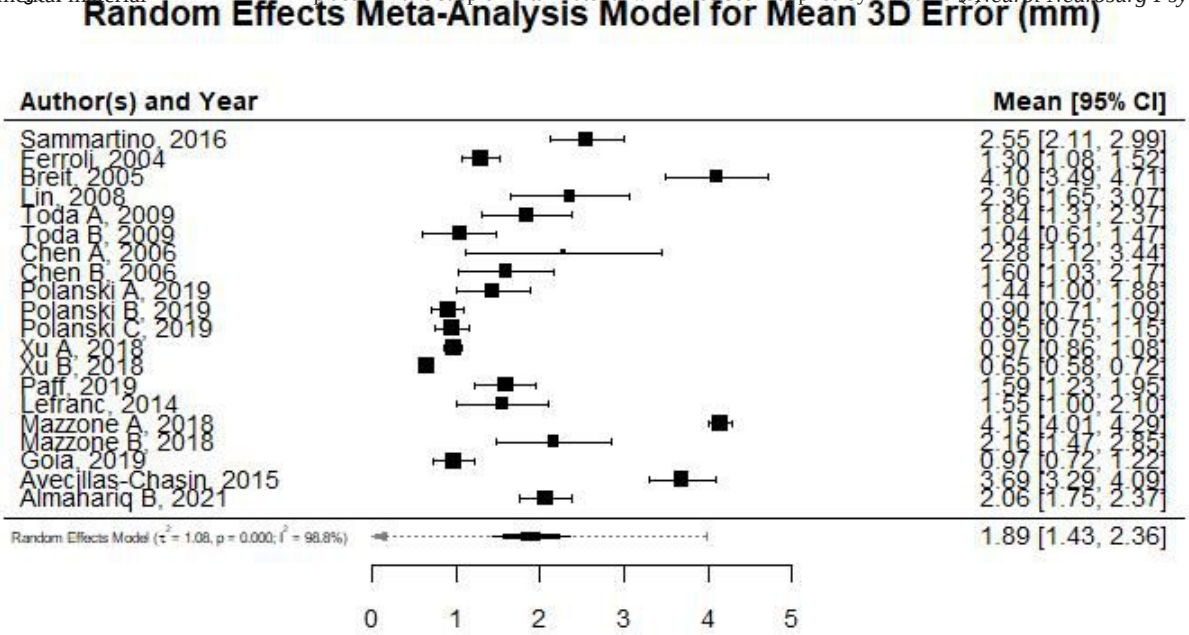
Supplementary figure 8: Bubble plot showing mean DBS motor improvement of the individual studies plotted against their mean Z error. The symbol sizes are related to the weights of the studies in the analysis (symbols are proportional to the inverse of the sum of within study variance and the variance

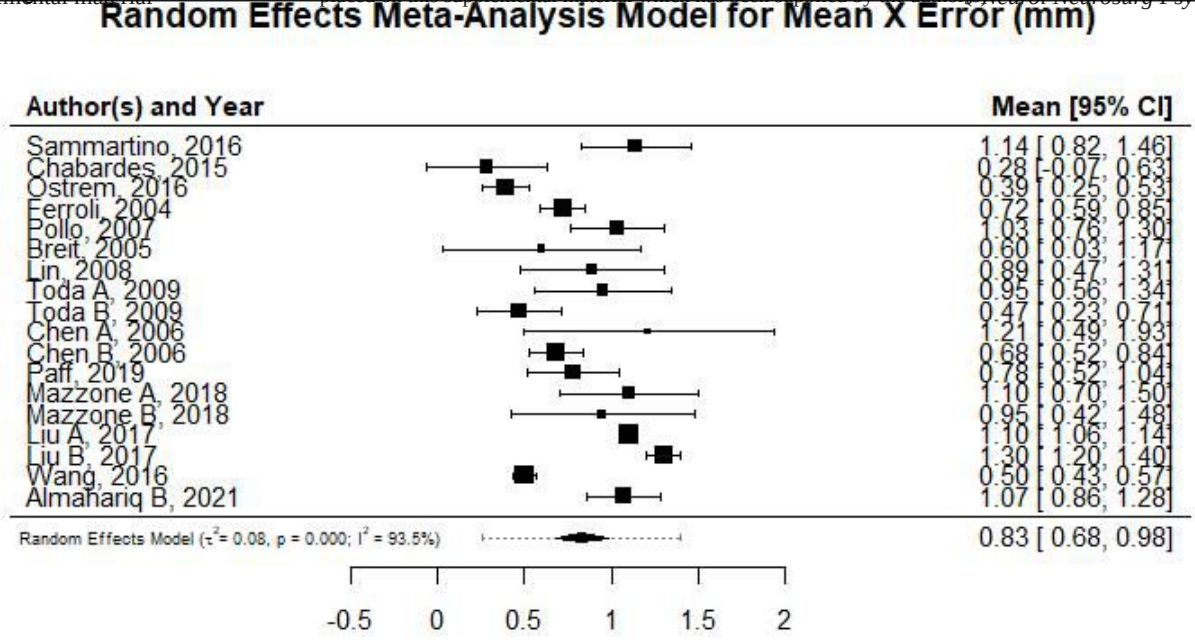
between the studies, larger and more precise studies correspond to larger diamonds). Based on the meta-regression random-effects model, the predicted average mean DBS motor improvement as a function of the covariate Z error is added to the plot (line) with corresponding 95% confidence interval bounds (dotted line).

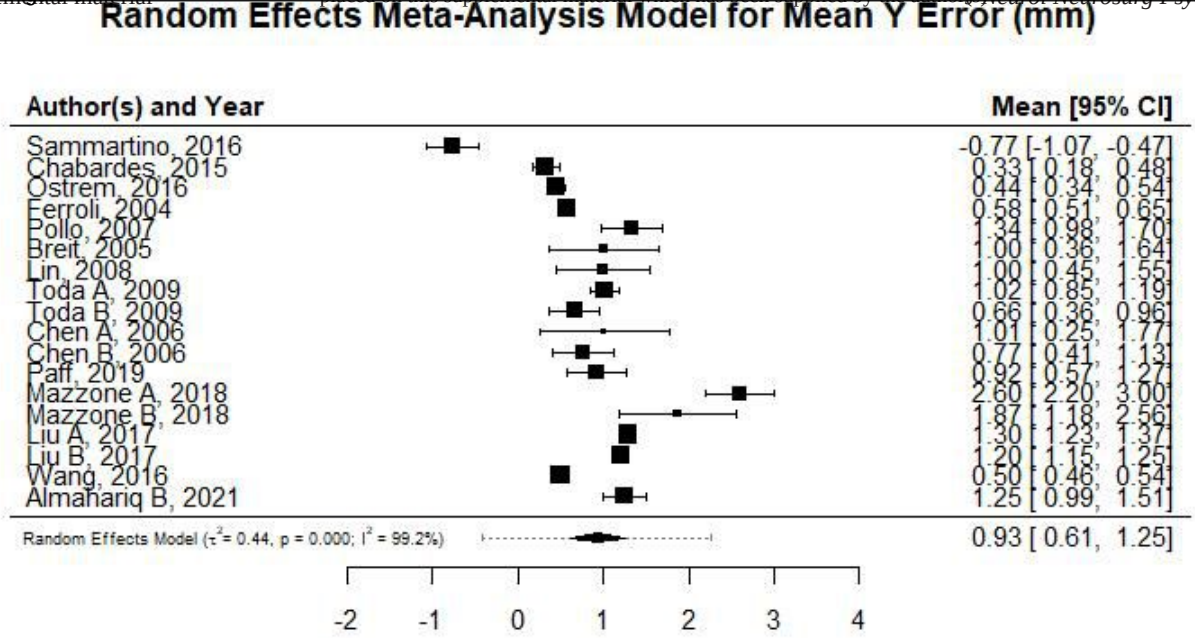
Supplementary figure 9: Bubble plot showing mean percentage change in Levodopa Equivalent Daily Dose (LEDD) of the individual studies plotted against their mean radial error. The symbol sizes are related to the weights of the studies in the analysis (symbols are proportional to the inverse of the sum of within study variance and the variance between the studies, larger and more precise studies correspond to larger diamonds). Based on the meta-regression random-effects model, the predicted average mean percentage change in LEDD as a function of the covariate radial error is added to the plot (line) with corresponding 95% confidence interval bounds (dotted line).

Supplementary figure 10: Bubble plot showing mean postoperative stimulation amplitude of the individual studies plotted against their mean radial error. The symbol sizes are related to the weights of the studies in the analysis (symbols are proportional to the inverse of the sum of within study variance and the variance between the studies, larger and more precise studies correspond to larger diamonds). Based on the meta-regression random-effects model, the predicted average mean postoperative stimulation amplitude as a function of the covariate radial error is added to the plot (line) with corresponding 95% confidence interval bounds (dotted line).

Figure 1


Random Effects Meta-Analysis Model for Mean 3D Error (mm)
Author(s) and Year
Mean [95% CI]
Sammartino, 2016
Ferroli, 2004
Breit, 2005
Lin, 2008
Toda A, 2009
Toda B, 2009
Chen A, 2006
Chen B, 2006
Polanski A, 2019
Polanski B, 2019
Polanski C, 2019
Xu A, 2018
Xu B, 2018
Paff, 2019
Lefranc, 2014
Mazzone A, 2018
Mazzone B, 2018
Goia, 2019
Avecillas-Chasin, 2015
Almahariq B, 2021
2.55 [2.11, 2.99]
1.30 [1.08, 1.52]
4.10 [3.49, 4.71]
2.36 [1.65, 3.07]
1.84 [1.31, 2.37]
1.04 [0.61, 1.47]
2.28 [1.12, 3.44]
1.60 [1.03, 2.17]
1.44 [1.00, 1.88]
0.90 [0.71, 1.09]
0.95 [0.75, 1.15]
0.97 [0.86, 1.08]
0.65 [0.58, 0.72]
1.59 [1.23, 1.95]
1.55 [1.00, 2.10]
4.15 [4.01, 4.29]
2.16 [1.47, 2.85]
0.97 [0.72, 1.22]
3.69 [3.29, 4.09]
2.06 [1.75, 2.37]
Random Effects Model (τ^2 = 1.08, p = 0.000; I^2 = 98.8%)
1.89 [1.43, 2.36]
0
1
2
3
4
5


Random Effects Meta-Analysis Model for Mean X Error (mm)
Author(s) and Year
Mean [95% CI]
Sammartino, 2016 1.14 [0.82, 1.46]
Chabardes, 2015 0.28 [-0.07, 0.63]
Ostrem, 2016 0.39 [0.25, 0.53]
Ferroli, 2004 0.72 [0.59, 0.85]
Pollo, 2007 1.03 [0.76, 1.30]
Breit, 2005 0.60 [0.03, 1.17]
Lin, 2008 0.89 [0.47, 1.31]
Toda A, 2009 0.95 [0.56, 1.34]
Toda B, 2009 0.47 [0.23, 0.71]
Chen A, 2006 1.21 [0.49, 1.93]
Chen B, 2006 0.68 [0.52, 0.84]
Paff, 2019 0.78 [0.52, 1.04]
Mazzone A, 2018 1.10 [0.70, 1.50]
Mazzone B, 2018 0.95 [0.42, 1.48]
Liu A, 2017 1.10 [1.06, 1.14]
Liu B, 2017 1.30 [1.20, 1.40]
Wang, 2016 0.50 [0.43, 0.57]
Almahariq B, 2021 1.07 [0.86, 1.28]
Random Effects Model (τ^2= 0.08, p = 0.000; I^2 = 93.5%) 0.83 [0.68, 0.98]
-0.5
0
0.5
1
1.5
2


Random Effects Meta-Analysis Model for Mean Y Error (mm)
Author(s) and Year
Mean [95% CI]
Sammartino, 2016 -0.77 [-1.07, -0.47]
Chabardes, 2015 0.33 [0.18, 0.48]
Ostrem, 2016 0.44 [0.34, 0.54]
Ferroli, 2004 0.58 [0.51, 0.65]
Pollo, 2007 1.34 [0.98, 1.70]
Breit, 2005 1.00 [0.36, 1.64]
Lin, 2008 1.00 [0.45, 1.55]
Toda A, 2009 1.02 [0.85, 1.19]
Toda B, 2009 0.66 [0.36, 0.96]
Chen A, 2006 1.01 [0.25, 1.77]
Chen B, 2006 0.77 [0.41, 1.13]
Paff, 2019 0.92 [0.57, 1.27]
Mazzone A, 2018 2.60 [2.20, 3.00]
Mazzone B, 2018 1.87 [1.18, 2.56]
Liu A, 2017 1.30 [1.23, 1.37]
Liu B, 2017 1.20 [1.15, 1.25]
Wang, 2016 0.50 [0.46, 0.54]
Almahariq B, 2021 1.25 [0.99, 1.51]
Random Effects Model (τ^2 = 0.44, p = 0.000; I^2 = 99.2%) 0.93 [0.61, 1.25]
-2
-1
0
1
2
3
4

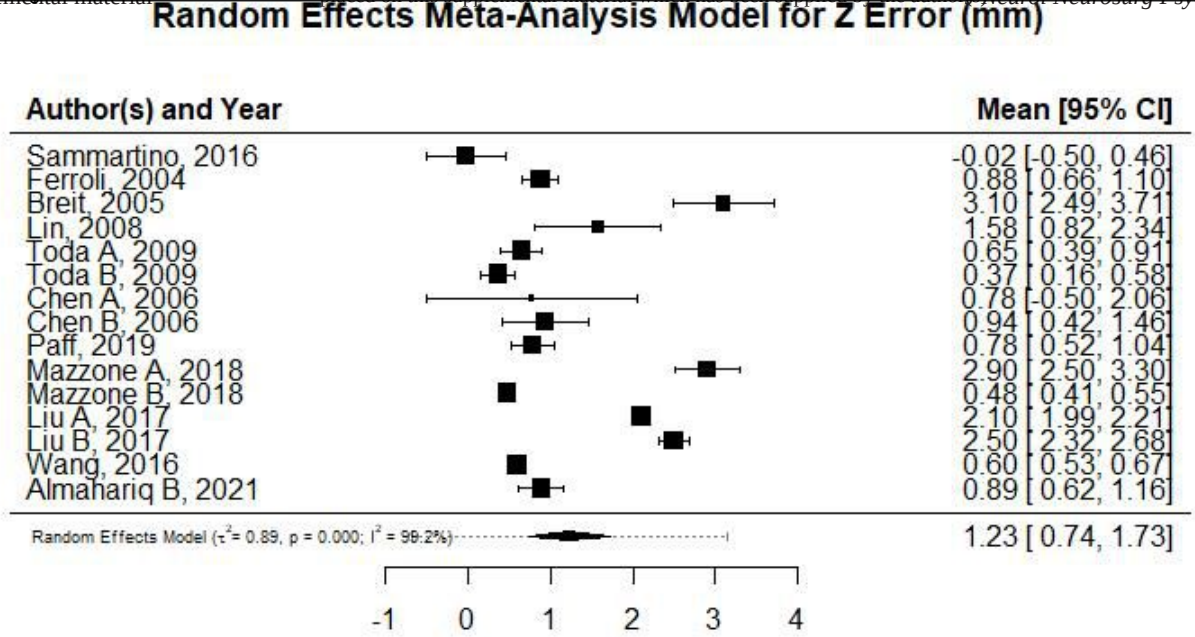
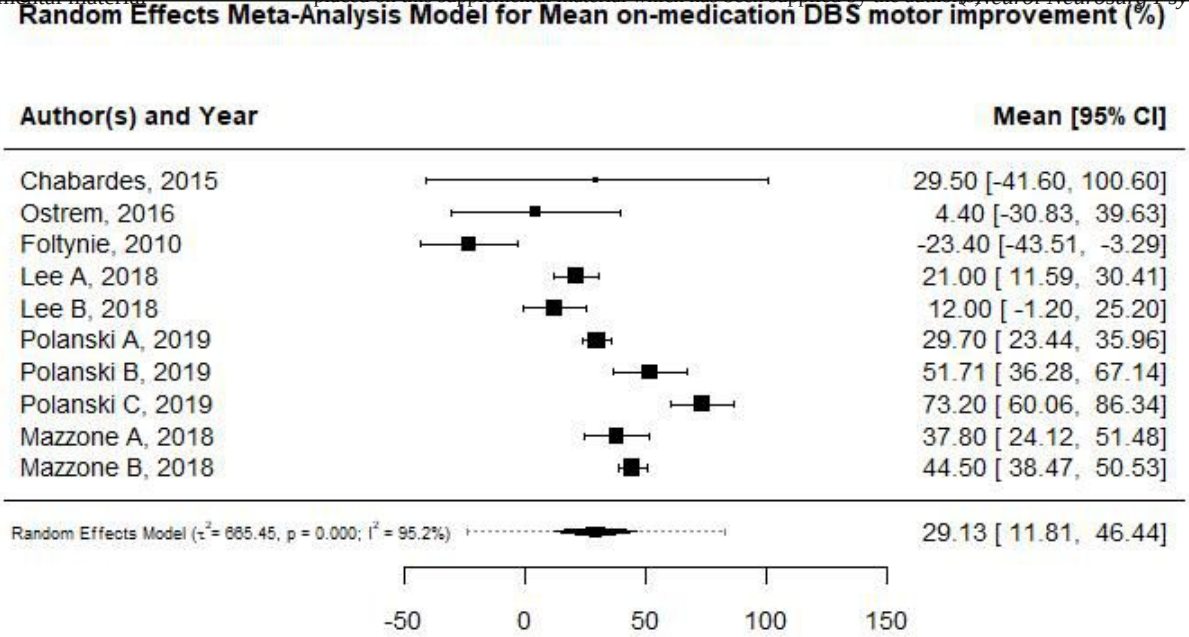

Random Effects Meta-Analysis Model for Z Error (mm)
Author(s) and Year
Mean [95% CI]
Sammartino, 2016 -0.02 [-0.50, 0.46]
Ferroli, 2004 0.88 [0.66, 1.10]
Breit, 2005 3.10 [2.49, 3.71]
Lin, 2008 1.58 [0.82, 2.34]
Toda A, 2009 0.65 [0.39, 0.91]
Toda B, 2009 0.37 [0.16, 0.58]
Chen A, 2006 0.78 [-0.50, 2.06]
Chen B, 2006 0.94 [0.42, 1.46]
Paff, 2019 0.78 [0.52, 1.04]
Mazzone A, 2018 2.90 [2.50, 3.30]
Mazzone B, 2018 0.48 [0.41, 0.55]
Liu A, 2017 2.10 [1.99, 2.21]
Liu B, 2017 2.50 [2.32, 2.68]
Wang, 2016 0.60 [0.53, 0.67]
Almahariq B, 2021 0.89 [0.62, 1.16]
Random Effects Model (τ^2 = 0.89, p = 0.000; I^2 = 99.2%) 1.23 [0.74, 1.73]
-1
0
1
2
3
4

Figure 5


Random Effects Meta-Analysis Model for Mean on-medication DBS motor improvement (%)
Author(s) and Year
Mean [95% CI]
Chabardes, 2015
29.50 [-41.60, 100.60]
Ostrem, 2016
4.40 [-30.83, 39.63]
Foltynie, 2010
-23.40 [-43.51, -3.29]
Lee A, 2018
21.00 [11.59, 30.41]
Lee B, 2018
12.00 [-1.20, 25.20]
Polanski A, 2019
29.70 [23.44, 35.96]
Polanski B, 2019
51.71 [36.28, 67.14]
Polanski C, 2019
73.20 [60.06, 86.34]
Mazzone A, 2018
37.80 [24.12, 51.48]
Mazzone B, 2018
44.50 [38.47, 50.53]
Random Effects Model (τ^2= 665.45, p = 0.000; I^2 = 95.2%)
29.13 [11.81, 46.44]
-50
0
50
100
150

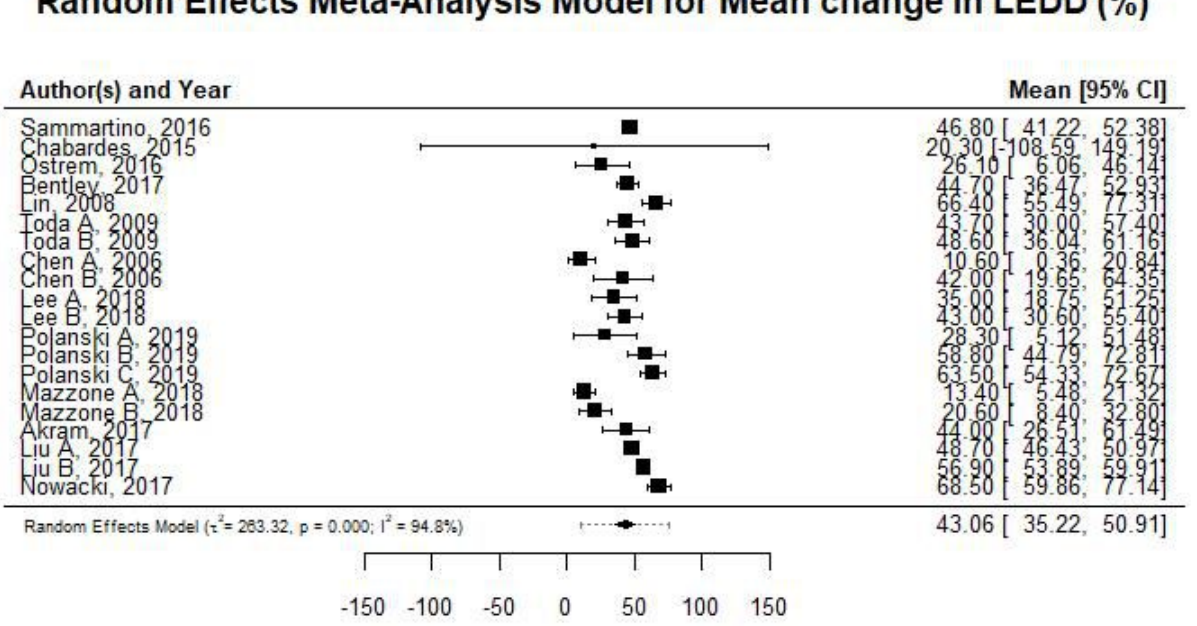
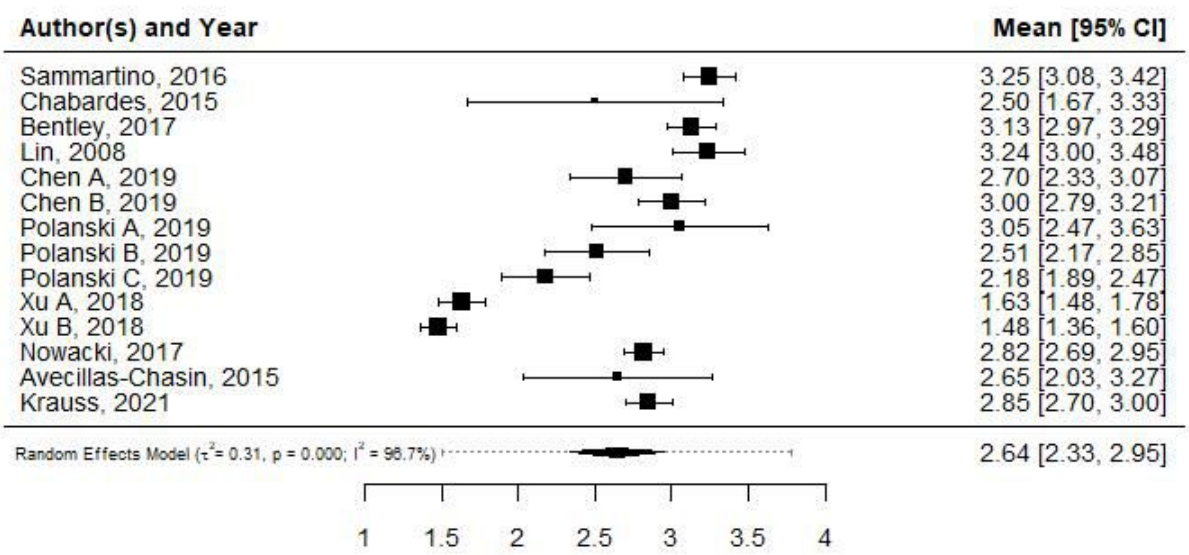
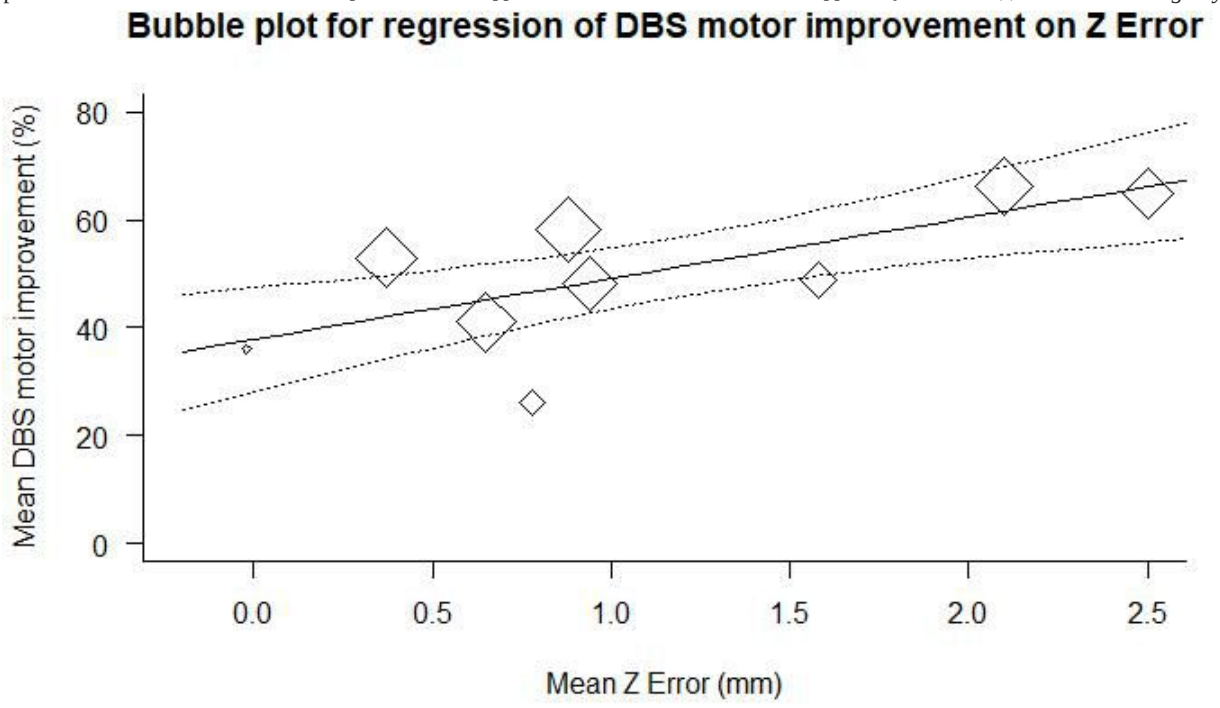
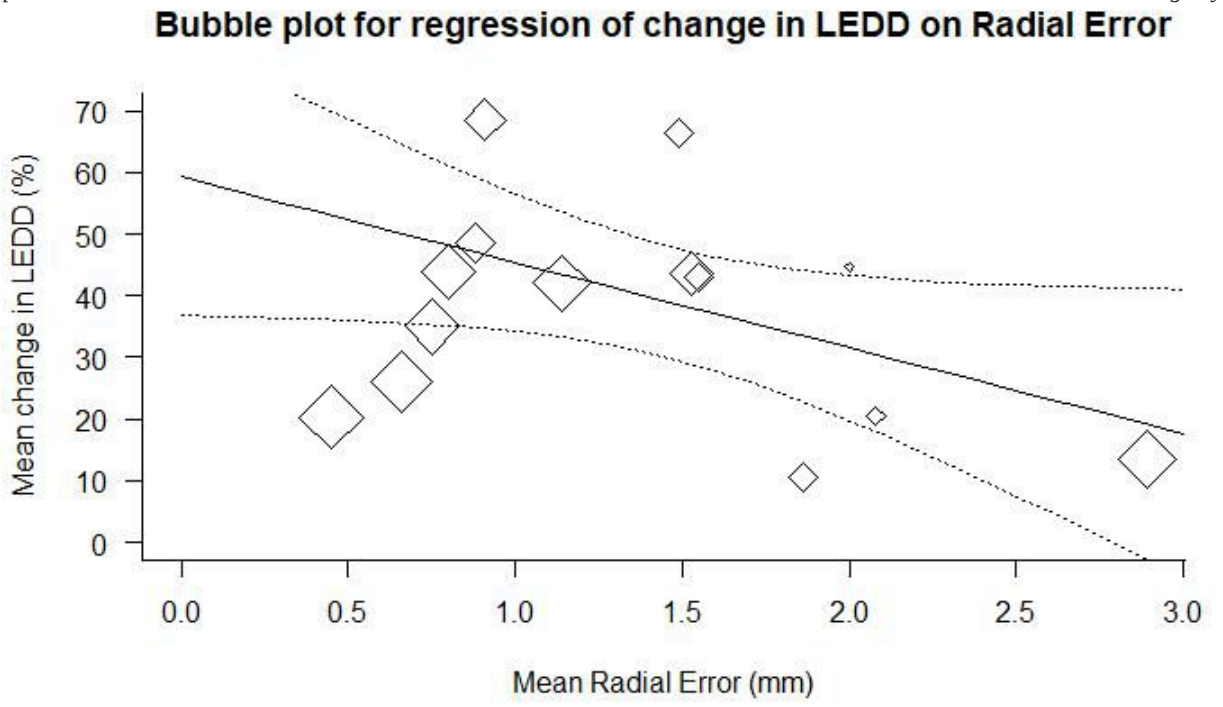
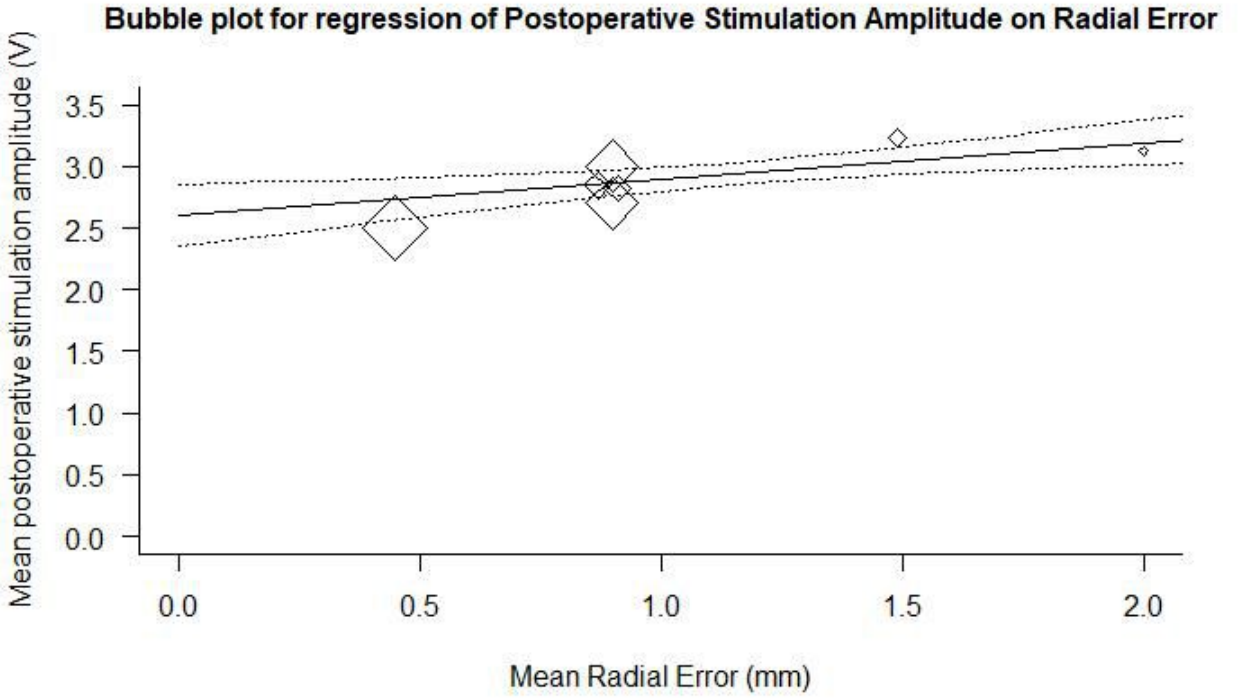

Random Effects Meta-Analysis Model for Mean change in LEDD (%)
Author(s) and Year
Mean [95% CI]
Sammartino, 2016 46.80 [41.22, 52.38]
Chabardes, 2015 20.30 [-108.59, 149.19]
Ostrem, 2016 26.10 [6.06, 46.14]
Bentley, 2017 44.70 [36.47, 52.93]
Lin, 2008 66.40 [55.49, 77.31]
Toda A, 2009 43.70 [30.00, 57.40]
Toda B, 2009 48.60 [36.04, 61.16]
Chen A, 2006 10.60 [0.36, 20.84]
Chen B, 2006 42.00 [19.65, 64.35]
Lee A, 2018 35.00 [18.75, 51.25]
Lee B, 2018 43.00 [30.60, 55.40]
Polanski A, 2019 28.30 [5.12, 51.48]
Polanski B, 2019 58.80 [44.79, 72.81]
Polanski C, 2019 63.50 [54.33, 72.67]
Mazzone A, 2018 13.40 [5.48, 21.32]
Mazzone B, 2018 20.60 [8.40, 32.80]
Akram, 2017 44.00 [26.51, 61.49]
Liu A, 2017 48.70 [46.43, 50.97]
Liu B, 2017 56.90 [53.89, 59.91]
Nowacki, 2017 68.50 [59.86, 77.14]
Random Effects Model (τ^2= 263.32, p = 0.000; I^2 = 94.8%) 43.06 [35.22, 50.91]
-150 -100 -50 0 50 100 150

Figure 7 **Random Effects Meta-Analysis Model for Mean Postoperative Stimulation Amplitude (V)**




Bubble plot for regression of DBS motor improvement on Z Error
Mean DBS motor improvement (%)
80
60
40
20
0
0.0
0.5
1.0
1.5
2.0
2.5
Mean Z Error (mm)


Bubble plot for regression of change in LEDD on Radial Error
Mean change in LEDD (%)
0
10
20
30
40
50
60
70
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Mean Radial Error (mm)


Bubble plot for regression of Postoperative Stimulation Amplitude on Radial Error
Mean postoperative stimulation amplitude (V)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.0
0.5
1.0
1.5
2.0
Mean Radial Error (mm)

Study	1	2	3	4	5	6	7	8	10	11	12	Total
Sammartino et al., 2016	2	2	1	2	0	2	0	0				9/16
Chabardes et al., 2015	1	1	0	2	0	2	2	0				8/16
Chang et al., 2011	2	2	1	1	0	2	2	0				10/16
Ostrem et al., 2016	2	1	2	2	0	2	1	2				12/16
Foltynie et al., 2010	2	2	2	2	0	2	2	0				12/16
Ostrem et al., 2012	2	2	2	2	0	2	1	0				11/16
Bentley et al., 2017	2	2	2	2	0	2	1	0				11/16
Caire et al., 2014	2	0	0	1	0	1	2	0				6/16
Derrey et al., 2008	2	2	0	2	0	2	2	0				10/16
Sidiropoulos et al., 2016	2	0	1	2	0	2	2	0				9/16
Ferroli et al., 2004	2	2	1	1	0	0	2	0				8/16
Pollo et al., 2007	2	1	0	2	0	2	2	0				9/16
Breit et al., 2005	2	0	0	2	0	2	0	0				6/16
Lin et al., 2008	2	0	1	1	0	2	2	0				8/16
Toda et al., 2009	2	2	0	1	0	1	1	0	2	2	2	13/22
Chen et al., 2006	2	2	1	2	0	1	2	0	2	1	1	14/22
Lee et al., 2018	2	2	1	1	0	1	1	0	2	2	2	14/22
Chen et al., 2019	2	2	2	2	0	2	1	2	2	2	2	19/22
Rasouli et al., 2017	2	1	1	2	0	2	0	2				10/16
Polanski et al., 2019	2	0	0	1	0	1	0	0	1	1	2	8/22
Xu et al., 2018	2	0	1	1	0	1	2	0	1	2	2	12/22
Paff et al., 2019	2	2	1	1	0	2	1	0				9/16
Lefranc et al., 2014	2	2	0	2	0	2	0	0				8/16
Vesper et al., 2002	2	1	0	1	0	2	0	0				6/16
Mazzone et al., 2018	2	0	0	1	0	2	0	0	0	1	1	7/22
Starr et al., 2002	2	2	0	2	0	1	0	0				7/16

Akram et al., 2017	2	1	0	1	0	2	0	0				6/16
Liu et al., 2017	2	0	1	1	0	2	2	0	0	2	2	12/22
Nowacki et al., 2017	2	1	1	2	0	2	1	0				9/16
Wang et al., 2016	0	0	1	2	0	2	2	0				7/16
Park et al., 2017	2	1	1	1	0	2	0	0				7/16
Goia et al., 2019	2	2	0	2	0	2	1	0				9/16
Rampini et al. 2003	1	0	0	1	0	1	0	0				3/16
Avecillas-Chasin et al., 2015	2	1	1	2	0	1	2	0				9/16
Longhi et al., 2015	2	2	1	2	0	2	2	0	0	0	1	12/22
Engelhardt et al., 2020	2	2	2	2	2	2	1	1	2	1	2	19/22
Krauss et al., 2021	2	2	1	2	0	2	0	0				9/16
Piacentino et al., 2021	2	2	1	1	0	2	2	0	1	0	2	13/22
Almahariq et al., 2021	1	2	1	1	0	1	0	0				6/16
Chen et al., 2021	2	1	1	2	0	2	0	0	1	2	2	13/22

Supplementary table 1: Methodological quality assessment of the included studies using MINORS. 1) a clearly stated aim; 2) inclusion of consecutive patients; 3) prospective collection of data; 4) endpoints appropriate to the aim of the study; 5) unbiased assessment of the study endpoint; 6) follow-up period appropriate to the aim of the study; 7) loss to follow-up less than 5% and 8) prospective calculation of the study size. Additional four items for comparative studies: 9) an adequate control group, 10) contemporary groups, 11) baseline equivalence of groups and 12) adequate statistical analysis. The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate).

	Average target coordinates relative to MCP		
	X	Y	Z
Sammartino et al., 2016	11.3 ± 0.9	-3.6 ± 1.8	-7.7 ± 1.6
Chabardes et al., 2015	11.3 ± 0.4	-2.3 ± 0.3	-3.2 ± 0.3
Pollo et al., 2007	12.0 ± 1.2	-2.3 ± 1.4	-5.9 ± 1.6
Breit et al., 2006	11.8 ± 1.3	-2.7 ± 1.5	-5.7 ± 1.3
Lin et al., 2008	11.3 ± 0.6	-3.4 ± 0.7	-5.7 ± 0.6
Chen et al., 2006	9.7 ± 1.3	-4.0 ± 0.9	-5.5 ± 1.3
Rasouli et al., 2018	11.5 ± 1.2	-2.9 ± 1.1	-4.5 ± 0.9
Lefranc et al., 2014	11.4		-4.3
Starr er al., 2002	12.9	-3.5	-5.3
Nowacki et al., 2018	11.6 ± 0.9	-3.2 ± 0.5	-4.4 ± 1.6

Supplementary table 2: Average intended target coordinates (in mm) in relation to the mid-commissural point (MCP). Average coordinates of left and right hemispheres were pooled when both reported in the study. The target Y coordinate for Lefranc et al. is missing due to reporting relative to the post-commissural (PC) line instead of MCP. No standard deviations were reported in Lefranc et al. and Starr et al. X: mediolateral axis, Y: anteroposterior axis, Z: supero-inferior axis. Positive values: lateral, anterior and superior. Negative values: medial, posterior and inferior.

Study	No. of patients included	No. of leads implanted	Age (years)	No. women (%)	Disease duration (years)	Follow-up duration (months)	Anesthetic technique	Stereotaxy method	Uni-/ bilateral	MER	Test stimulation†	Imaging modality ‡	Software
Sammartino et al., 2016	76	152	58 (7.2)	26	.	12	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	MRI	Framelink (Medtronic)
*Chabardes et al., 2015	2	4	69 (2.8)[c]	50[c]	14.5 (3.5)[c]	12	General	Frame-less (Smartframe)	Bilateral	No	No	iMRI	Clearpoint
Chang et al., 2011	23	46	57	57	.	19.6	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	MRI	Leksell SurgiPlan (Elekta)
*Ostrem et al., 2016	16[c]	32[c]	61.6 (7.5)[c]	25[c]	12.1 (3.6)[c]	12	General	Frame-less (Clearpoint)	Bilateral	No	No	iMRI	Framelink (Medtronic)
Foltynie et al., 2010	79	158	57.3 (7.7)	38	13.4 (7)	14	Both local and general	Frame-based (Leksell)	Bilateral	No	Yes	iMRI	Framelink (Medtronic)
Ostrem et al., 2012	17	34	59.8 (4.8)	47.1	11.1 (4.4)	6	General	Frame-less (Nexframe)	Bilateral	No	No	MRI	.
Bentley et al., 2017	73	146	62.3 (7.7)	30	9.9 (5.3)	6	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	CT	Framelink (Medtronic)
*Caire et al., 2014	15	29	54	.	11.4	3	Local	Frame-based (Leksell)	Both	Yes	Yes	iCT (O-arm)	NeuroMate (Renishaw)
Derrey et al., 2008	20	40	56.5	45	10.8	6	Both local and general	Frame-based (Riechert-Mundinger)	Bilateral	Yes	Yes	iX-Ray	Stereoplan software + Framelink (Medtronic)
Sidiropoulos et al., 2016	6	11	63.7 (6.3)[c]	33.3[c]	12.3 (3.8)[c]	13.5	General	Frame-less (Nexframe)	Both	No	No	iMRI	Clearpoint + iPlan (BrainLab)
*Ferroli et al., 2004	6	12	59.7 (5.7)[c]	50[c]	.	.	Local	Frame-based (Leksell)	Bilateral	No	Yes	MRI	Framelink (Medtronic)
Pollo et al., 2007	31	62	63 (8)	41.9	.	26.3	Local	Frame-based (CRW)	Bilateral	Yes	Yes	MRI	UCLF software (Radionics)
Breit et al., 2005	30	60	.	.	.	12	Local	Frame-based (CRW)	Bilateral	Yes	Yes	MRI	Stereoplan (Radionics)

													+ Neuromate (ISS)
*Lin et al., 2008	10	20	58.9 (9.9)	20	8.8 (3.7)	6	General	Frame-based (Leksell)	Bilateral	Yes	No	CT/MRI	VectorVision (BrainLab)
*Toda et al., 2009[a]	13	22	61.5 (6.2)[c]	30.8[c]	13.8 (4.1)[c]	2-3 weeks	Local	Frame-based (Leksell)	Both	Yes	Yes	MRI	Framelink (Medtronic)
*Toda et al., 2009[b]	13	25	58.7 (8.4)[c]	53.8[c]	14 (11.1)[c]	2-3 weeks	Local	Frame-based (Leksell)	Both	Yes	Yes	MRI	Framelink (Medtronic)
*Chen et al., 2006[a]	6	12	59.3 (11.3)	50	13 (4.7)	7.8	Local	Frame-based (Leksell)	Bilateral	No	No	MRI	VectorVision (BrainLab)
*Chen et al., 2006[b]	5	10	52.8 (8.6)	20	10.2 (4.5)	5.6	Local	Frame-based (Leksell)	Bilateral	Yes	No	MRI	VectorVision (BrainLab)
Lee et al., 2018[a]	21	42	64.9 (9.9)	.	.	7.7	General	Frame-less (Clearpoint)	Bilateral	No	No	iMRI	Clearpoint + iPlan (BrainLab)
Lee et al., 2018[b]	24	48	66.3 (6.6)	.	.	9.2	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	MRI	iPlan (BrainLab)
Chen et al., 2019[a]	14	28	63.1 (10.1)	35.7	8.6 (4.6)	6	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	iCT	Framelink (Medtronic)
Chen et al., 2019[b]	41	82	64.6 (8.2)	29.3	7.5 (3.4)	6	General	Frame-based (Leksell)	Bilateral	No	No	iCT	Framelink (Medtronic)
Rasouli et al., 2017	25	50	68 (7)	28	.	12	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	iCT	Framelink (Medtronic)
*Polanski et al., 2019[a]	10	20	65.8	30	11.8	3	Local	Frame-based (Inomed)	Bilateral	Yes	Yes	CT	BrainLab
*Polanski et al., 2019[b]	10	20	63.1	40	9.1	3	Local	Frame-based (Inomed)	Bilateral	Yes	Yes	CT	BrainLab
*Polanski et al., 2019[c]	10	20	59.9	30	10.4	3	Local	Frame-based (Inomed)	Bilateral	Yes	Yes	CT	BrainLab
Xu et al., 2018[a]	33	65	64.7 (9.2)	51.5	9.4 (2.6)	10 weeks	.	Frame-based (Leksell)	Both	Yes	Yes	CT	ROSA
Xu et al., 2018[b]	38	75	65 (11.1)	52.6	9 (2.5)	10 weeks	.	Frame-based (Leksell)	Both	Yes	Yes	CT	ROSA
Paff et al., 2019	20	39	63.5 (11)	40	10.6 (4.7)	6	General	Frame-based (Leksell)	Both	Yes	Yes	CT	ROSA
Lefranc et al., 2014	8	16	.	.	.	6	General	Frame-based (Leksell)	Bilateral	Yes	Yes	iCT (O-arm)	ROSANA (MedTech)

Vesper et al., 2002	38	76	55.6	31.6	13	6	General	Frame-based (Riechert-Mundinger)	Bilateral	Yes	Yes	CT	.
*Mazzone et al., 2018[a]	6	12	65 (1.5)	33.3	8.2 (2.6)	12	General	Frame-less (Nexframe)	Bilateral	No	No	CT/MRI	Framelink (Medtronic)
*Mazzone et al., 2018[b]	8	16	63 (3.4)	37.5	8.6 (2.7)	12	General	Frame-less (Nexframe)	Bilateral	No	No	CT/MRI	Framelink (Medtronic)
Starr et al., 2002[a]	44	76	60.5	.	.	3	Local	Frame-based (Leksell)	Unilateral	Yes	Yes	MRI	Framelink (Medtronic)
Starr et al., 2002[b]	44	76	60.5	.	.	12	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	MRI	Framelink (Medtronic)
Akram et al., 2017	20	40	56.3 (10.2)	20	11.2 (4.3)	12	General	Frame-based (Leksell)	Bilateral	No	Yes	MRI	Framelink (Medtronic)
Liu et al., 2017[a]	76	141	62 (7.7)	43.4	.	12	Local	Frame-based (Leksell)	Both	Yes	Yes	iMRI	.
Liu et al., 2017[b]	61	113	63 (4.5)	50.8	.	12	Local	Frame-based (Leksell)	Both	No	Yes	iMRI	.
*Nowacki et al., 2017	46	92	61.9 (9)[c]	43.5[c]	8.8 (2.9)[c]	12	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	CT	iPlan (BrainLab)
Wang et al., 2016	79	156	61 (10.7)	44.3	5.5 (2.3)	6	Local	Frame-based (Leksell)	Both	Yes	Yes	CT	iPlan (BrainLab)
*Park et al., 2017	24	48	58.4 (10.4)	58.1	.	12	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	CT/MRI	Framelink (Medtronic)
Goia et al., 2019	24	44	62	29.2	9	12	General	Frameless	Both	No	No	iCT (O-arm)	ROSANA (Zimmer-Biomet)
Rampini et al. 2003	11	22	62.6 (3.3)	45.5	11.1 (1.8)	3	Local	Frame-based (CRW)	Bilateral	Yes	Yes	MRI	.
*Avecillas-Chasin et al., 2015	6	12	58.8 (8)[c]	33.3[c]	.	7.2 (4.5)[c]	Local	Frame-less (Nexframe)	Bilateral	Yes	Yes	CT	Framelink (Medtronic)
Longhi et al., 2015	14	28	56	25	11.6	12	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	CT	Leksell SurgiPlan (Elekta)
Engelhardt et al., 2020[a]	20	40	60	30	12	6	General	Frame-based (Leksell)	Bilateral	No	No	iCT (O-arm)	NeuroMate (Renishaw)
Engelhardt et al., 2020[b]	9	18	63	33	10	6	Local	Frame-based (Leksell)	Bilateral	Yes	Yes	iCT (O-arm)	NeuroMate (Renishaw)

Krauss et al., 2021	101	202	62.4 (9.2)	41.6	11.4 (5.2)	6	General	Frame-based (Riechert-Mundinger)	Bilateral	Yes	Yes	iCT	Framelink (Medtronic)
Piacentino et al., 2021[a]	25	50	61	45.7	.	6	Local	Frame-based (CRW/Leksell)	Bilateral	Yes	Yes	CT	Framelink (Medtronic)
Piacentino et al., 2021[b]	23	46	61	45.7	.	6	Local	Frame-based (CRW/Leksell)	Bilateral	Yes	Yes	CT	Framelink (Medtronic)
Almahariq et al., 2021	33	66	62.3 (7)	21.2	13.7 (6.3)	3	Local	Frame-based (Leksell)	Bilateral	No	Yes	CT	Framelink (Medtronic)
Chen et al., 2021[a]	19	38	54.4	47.4	9.3	12	Local	Frame-less (Nexframe)	Bilateral	Yes	No	iCT	Stealthstation (Medtronic)
Chen et al., 2021[b]	9	18	58.7	33.3	10.6	12	Local	Frame-less (Nexframe)	Bilateral	Yes	No	CT	Stealthstation (Medtronic)

Supplementary table 3: Characteristics of the 40 included studies. Values are described as mean (standard deviation). MER: micro-electrode recording; iMRI: intraoperative Magnetic Resonance Imaging; iCT: intraoperative Computed Tomography; iX-ray: intraoperative X-ray; CRW: Cosman-Roberts-Wells; ROSA: Robot Stereotactic Assistance.

[c] Calculated based on individual patient data

* Individual patient data available

† To assess the clinical effect and the occurrence of side effects; either via the DBS electrode, macro-electrode or micro-electrode

‡ Used to assess DBS lead accuracy relative to the intended target

. Not reported

	Right hemisphere	Left hemisphere
	Mean, mm (Confidence interval)	
3D error	1.69 (1.19; 2.19)	1.76 (1.18; 2.34)
X error	0.63 (0.43; 0.84)	0.78 (0.50; 1.06)
Y error	0.83 (0.62; 1.04)	0.70 (0.46; 0.94)
Z error	0.81 (0.36; 1.26)	0.89 (0.57; 1.21)

Supplementary table 4: Means and confidence intervals for the secondary lead placement accuracy outcomes (covariates) (individual patient data).

		Mean (Confidence interval)
On-medication DBS motor improvement (%)		38.7 (20.0; 57.4)
Percentage change in LEDD		38.7 (27.0; 50.4)
Postoperative stimulation amplitude (V)	Right hemisphere 2.8 (2.6; 2.9)	Left hemisphere 2.8 (2.6; 3.0)

Supplementary table 5: Means and confidence intervals for the secondary response variables (individual patient data). LEDD: Levodopa equivalent daily dose.

	Right hemisphere	Left hemisphere
	Effect estimate, mm (Confidence interval)	
3D error	0.45 (-4.33; 5.23)	1.23 (-3.12; 5.58)
X error	-6.00 (-14.73; 2.70)	-3.51 (-11.17; 4.15)
Y error	-3.31 (-12.03; 5.41)	3.76 (-4.21; 11.74)
Z error	0.62 (-5.29; 6.43)	0.96 (-5.05; 6.96)

Supplementary table 6: Effect estimates and confidence intervals for the secondary covariates on DBS motor improvement (individual patient data).

	Radial error right hemisphere		Radial error left hemisphere	
	Effect estimate (Confidence interval)			
On-medication DBS motor improvement (%)	-78.6 (-158.6; 1.5)		1.9 (-126.8; 130.5)	
Percentage change in LEDD	-4.8 (-14.7; 5.2)		-2.0 (-11.7; 7.7)	
Postoperative stimulation amplitude (V)	Right hemisp.	Left hemisp.	Right hemisp.	Left hemisp.
	-0.03 (-0.17; 0.12)	0.13 (-0.10; 0.35)	-0.03 (-0.24; 0.18)	0.11 (-0.22; 0.44)

Supplementary table 7: Effect estimates and confidence intervals for radial error on the secondary response variables (individual patient data). LEDD: Levodopa equivalent daily dose. Hemisp.: hemisphere.