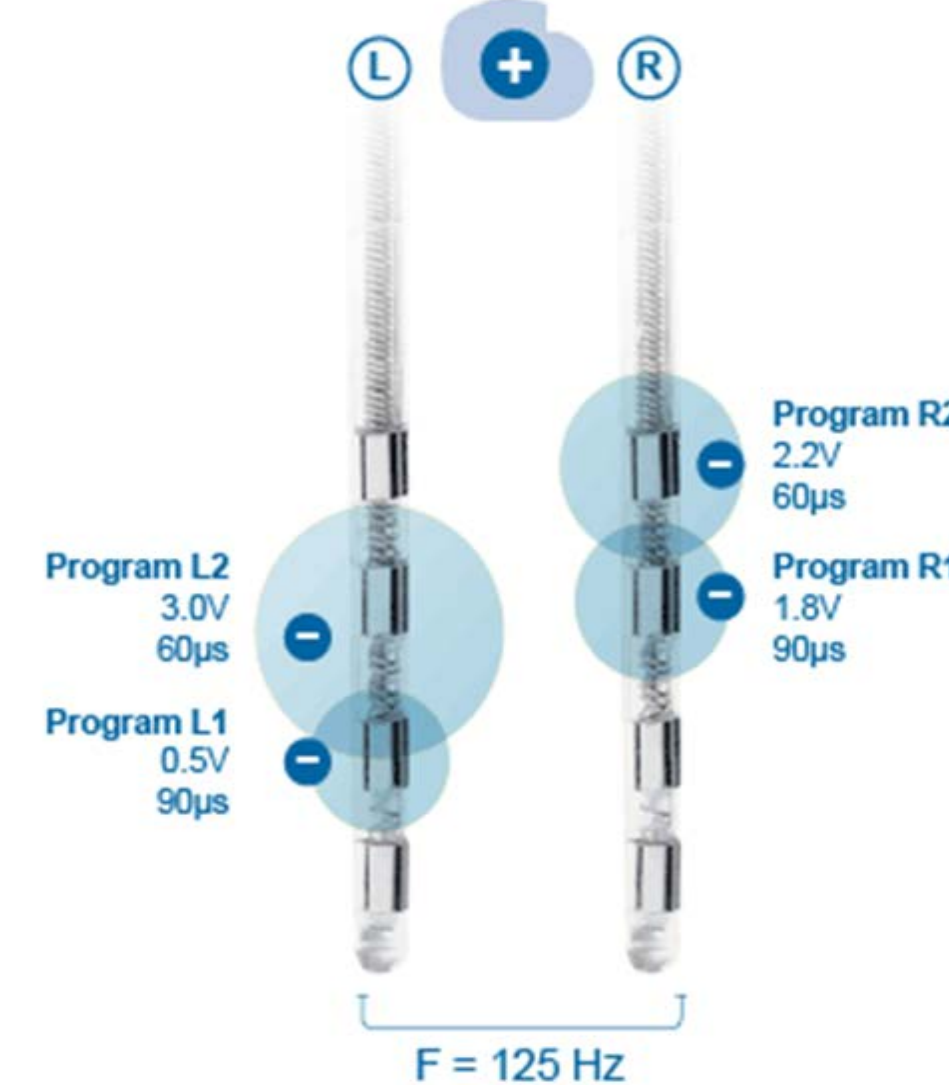


Olga Waln, MD¹; Joohee Jimenez-Shahed, MD²

Methodist Neurological Institute, Department of Neurology, Houston, TX, USA;¹
Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, TX, USA²

Background

- Interleaving - advanced DBS programming proposed to improve the stimulation effect when other programming options failed (suboptimal benefit or intolerable side effects)
- Interleaving is achieved by rhythmic automatic switching of current between two groups of DBS parameters on the same electrode at a maximum frequency of 125Hz. Amplitude and pulse width (PW) can be different between the interleaved programs.
- No study has directly compared the effectiveness of interleaving to other DBS programming options in patients with different movement disorders.¹⁻⁵
- There are no evidence-based guidelines regarding patient selection for interleaving.
- Study objectives:
 - To compare efficacy and side effects of interleaved DBS versus conventional DBS programming.
 - To describe characteristics of patients with DBS who may be candidates for interleaving.



Methods

- Retrospective review – Chart review of patients currently treated with interleaving and those who failed it to analyze the indications for interleaving and reasons for failure.
- Prospective evaluation – Direct comparison of effectiveness of interleaved DBS vs non-interleaved stimulation in the same patients.
- Evaluation / video done in 5 conditions:
 - Interleaved DBS ON;
 - DBS ON with non-interleaved stimulation (Program 1 of two interleaved: monopolar or bipolar)
 - DBS ON with non-interleaved stimulation (Program 2 of two interleaved: monopolar or bipolar).
 - DBS ON and both contacts used for interleaved stimulation programmed in a double monopolar or bipolar configuration (if applicable).
 - DBS OFF (baseline of the disease-specific rating scale).
- All side effects from stimulation and effectiveness on cardinal disease-specific symptoms were documented

Results

- 9 patients identified in retrospective chart review (Table 1)
 - 7 were still using interleaving at the time of study
 - 2 failed and were switched to non-interleaved settings.
- Reason for interleaving failure:
 - Suboptimal lead position eventually requiring revision (n=1);
 - Tremor improves better with higher stimulation frequency (>125 Hz) (n=1)
- 6 out of 9 patients participated in prospective study:
 - 2 patients were excluded (1 had electrode revision and no longer interleaved; 1 had impending IPG failure that required exchange)
 - 1 lost to follow up.

Results, continued

Table 1. Demographic and clinical data of study patients

	Retrospective study (n=9)	Prospective study (n=6)
Age	51 - 89	51 - 89
Gender	4 F, 5 M	2 F, 4 M
Diagnosis	2 PD, 6 ET, 1 ET+PD	2 PD, 4 ET
DBS target	3 STN (2 b/l, 1 uni), 6 VIM (all b/l)	2 STN (1 b/l, 1 uni), 4 VIM (all b/l)
Interleaved side	8 uni, 1 b/l	5 uni, 1 b/l (VIM)
Reason for interleaving	1. Good effect from monopolar / bipolar configuration but AEs (n=6) 2. Suboptimal effect and AEs from higher settings, including ET+CIDP with tremor habituation (n=2), suboptimal lead placement (n=1)	1. Best symptom control with interleaving + no / least AEs (n=4); 2. Same / slightly worse ET control + no / least AEs (n=2) -- (all 6 pts had AEs from non-interleaved stimulation)

PD – Parkinson's disease; ET – essential tremor, STN – subthalamic nucleus; VIM – ventral intermedus nucleus; CIDP – chronic inflammatory demyelinating polyneuropathy; AE – adverse effect

Table 2. Prospective clinical evaluation

Diagnosis DBS target	Interleaved programs (electrode configuration; Amp, PW, freq)	Effect of interleaved stimulation (total / contralateral score), AEs	Non-interleaved programs (electrode configuration; Amp, PW, freq)	Effect of non-interleaved stimulation (total / contralateral score), AEs	Advantages of interleaving
57 ET F b/l VIM	10-11+; 3.2,100,125/ C+9-; 1.8,80,125	TETRAS: 5.5/ <u>5.5</u> , no AEs	C+9-; 1.8,80,170 10-11+; 3.2,100,150 11+10-9-; 1.5,80,150	TETRAS: 7.5 / <u>6.5</u> , dysarthria, dizzy TETRAS: 7 / <u>7</u> , mild dysarthria TETRAS: 8 / <u>8</u> , dysarthria	Best tremor control, no AEs
89 ET M b/l VIM	C+0-; 2.4,160,125 / C+1-2-; 2.0,180,125	TETRAS: 22.5/ <u>14.5</u> min dysarthria	C+0-; 2.4,160,180 C+1-2-; 2.0,180,180 C+0-1-2-; 2.0,180,180	TETRAS: 24 / <u>15</u> , L face pulling TETRAS: 26 / <u>17</u> , at 2.5V more dysarthria TETRAS: 23.5 / <u>15.5</u> , dysarthria, L face pulling	Best tremor control, least AEs
60 ET M b/l VIM	3+2-; 2.5,100,110 / C+2-; 1.7,60,110	TETRAS: 19.5/ <u>7</u> no AEs	C+2-; 1.7,60,170 3+2-; 2.5,100,170	TETRAS: 16.5 / <u>7.5</u> , dysarthria TETRAS: 17 / <u>7</u> , dysarthria	Min worse tremor control, no AEs
81 ET M b/l VIM	L: 0-1+ 2.3,60,125 / C+0- 2.4,60,125 (b/l interleaved) R: C+3- 1.7,60,125 / C+2-2.1,60,125	TETRAS: 27.5/ <u>13</u> TETRAS: 27.5/ <u>11.5</u>	0-1+; 2.3,60,180 C+0-; 2.4,60,180 C+2-; 2.1,60,180	TETRAS: 31 / <u>14</u> , worse balance; 3.0V - dysarthria, R hand pain TETRAS: 25.5 / <u>8.5</u> , worse balance TETRAS: 29 / <u>12.5</u> , dysarthria, spasmodic dysphonia TETRAS: 28.5 / <u>13</u> , spasmodic dysphonia, 2.5V-face pull TETRAS: 30.5 / <u>15</u> , spasmodic dysphonia, L leg heavy	Tremor control OK, least AEs
61 PD M L-STN	1+2- 4.3,100,120 / C+2- 1.5,70,120	MDS UPDRS 31/ <u>6</u> no AEs	C+2-; 1.5,70,130 1+2-; 4.3,100,130	MDS UPDRS: 47 / <u>19</u> , at 2.0V dysarthria, 2.5V R arm tingling MDS UPDRS: 41 / <u>14</u> , dysarthria	Best PD control, no AEs
51 PD F b/l STN	2+3-; 0.6,60,125 / C+3-; 1.6,60,125	MDS UPDRS 38/ <u>14</u> no AEs	C+3-; 1.6,60,130 2+3-; 0.6,60,130	MDS UPDRS: 42 / <u>15</u> , dizzy, on 2.0V dysarthria MDS UPDRS: 44 / <u>16</u> , on 2.5V dysarthria	Best PD control, no AEs

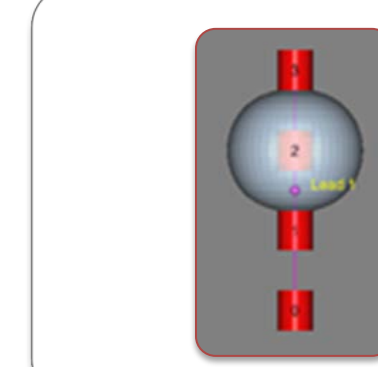
Amp – amplitude; PW – pulse width; freq – frequency; TETRAS – The Essential Tremor Rating Assessment Scale; MDS UPDRS – Movement Disorder Society Unified Parkinson's Disease Rating Scale, motor part

Case Examples

Case Example #1

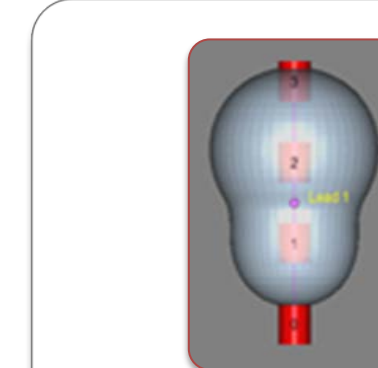
61 yo M with PD L-STN Activa PC

→ Rapid alternating activation of two programs with the same active electrode provides better symptom control and no side effects as opposed to separate use of each of 2 programs



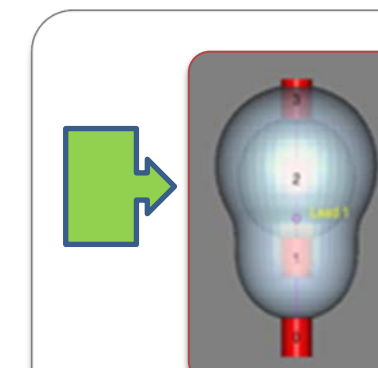
Monopolar C+2-; 1.5, 70, 130

- Reasonable improvement of R-sided symptoms (MDS UPDRS 19 for R side)
- Side effects at 2.0V (dysarthria) and 2.5V (R arm tingling)
- Field too broad with attempt to increase Amp



Bipolar 1+2-; 4.3, 100, 130

- Better control of R-sided symptoms (contralateral MDS UPDRS 14)
- Side effects (dysarthria)
- Field too broad



Interleaved programming 1+2- 4.3,100,120 / C+2- 1.5,70,120

- Best symptoms control (MDS UPDRS 6 for R side)
- No side effects
- Field focused

Case Example #2

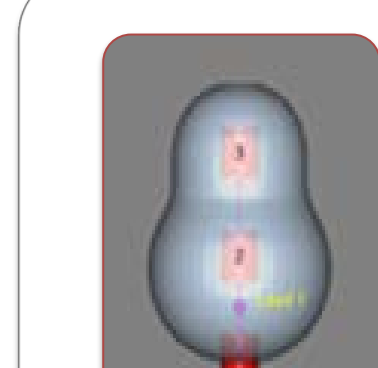
57yo F with ET B/l VIM Activa PC

→ Interleaving of bipolar and monopolar programs with different active contacts provides best effect on tremor with no side effects



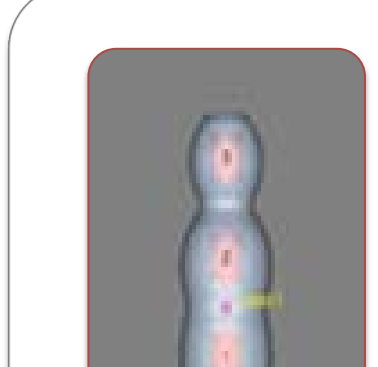
Monopolar C+9-; 1.8, 80, 170

- Good tremor control
- Side effects (dysarthria and dizziness)
- Field too broad



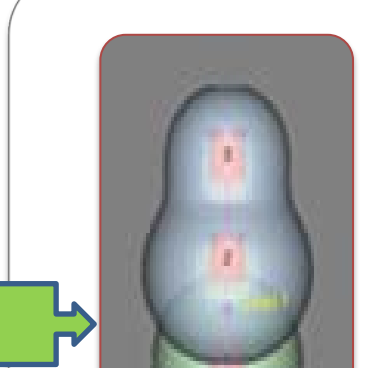
Bipolar 10-11+; 3.2, 100, 150

- Good tremor control
- Side effects (mild dysarthria)
- Field too broad



Double bipolar 11+10-9-; 1.5, 80, 150

- Less effective for tremor control
- Side effects (mild dysarthria)
- Field too narrow



Interleaved programming 10-11+; 3.2, 100, 125 / C+9-; 1.8, 80, 125

- Best tremor control
- No side effects
- Field focused

Discussion

- Interleaved DBS programming might be a good troubleshooting option (early or late post-implant management; initial Activa device or converted from older devices) when conventional programming options:
 - Are not sufficient to control cardinal disease symptoms and / or
 - Cause intolerable side effects
- Interleaving might be less successful in cases where:
 - Adequate symptom control requires higher frequency
 - Electrode location is suboptimal (however, in some cases interleaving can still improve symptoms better than any other programming option → prevent / delay surgical electrode revision)
- Advantages of interleaving (better effect on disease symptoms and fewer side effects) can be mediated by shaping the field to focus / spread electrical stimuli with different intensity within the field.
- Further studies are needed to define selection criteria for patients who would benefit from interleaved programming:
 - larger numbers of patients
 - post-op CT to check electrode location and correlate with effects / side effects of interleaved vs. non-interleaved stimulation fields

Conclusions

- Interleaved DBS can be used in patients unable to tolerate conventional programming due to side effects, or in whom satisfactory control of disease-specific symptoms could not be achieved.
- Evidence-based guidelines for patient selection and methodology of achieving interleaved programming should be defined to assist clinicians treating patients with DBS.

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