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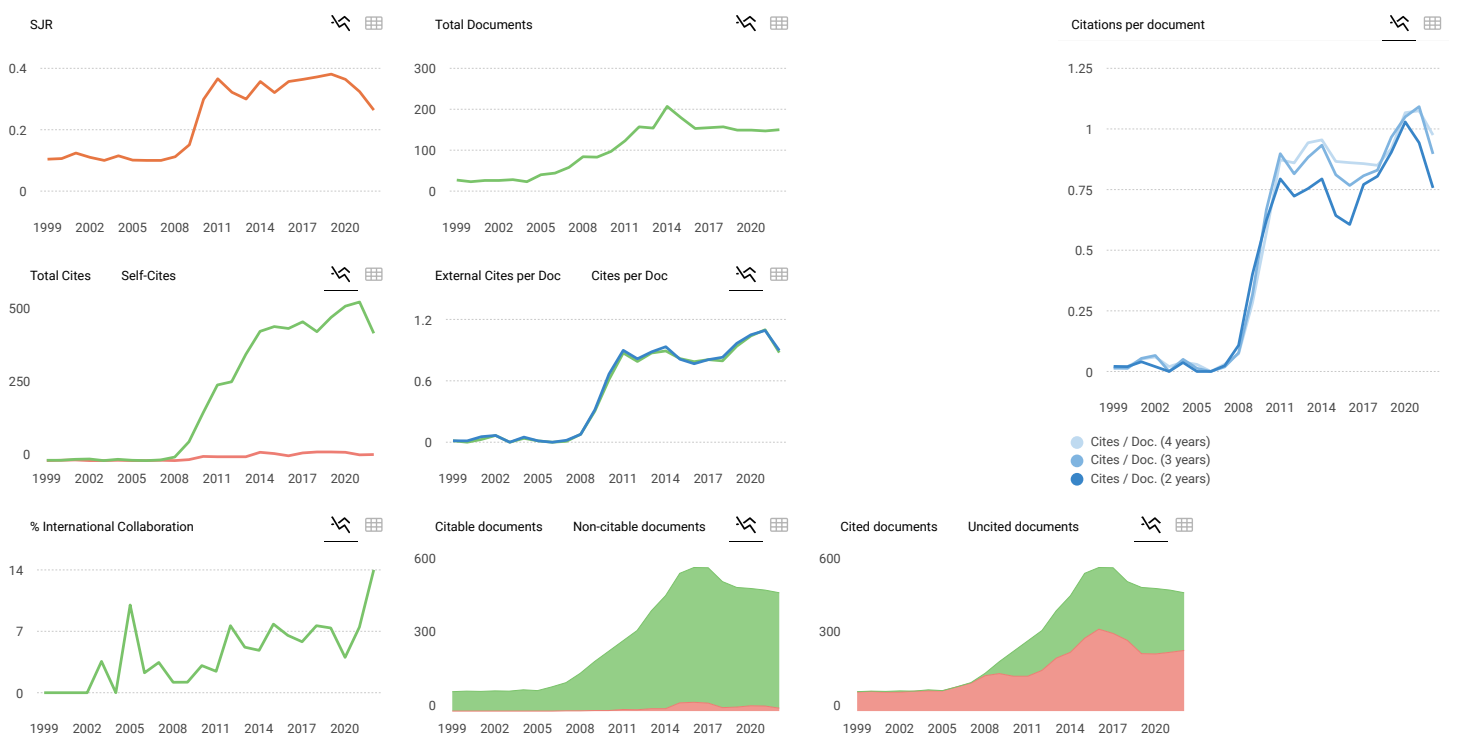
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# VIM Line Technique for Determining the Ventral Intermediate Location

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## ABSTRACT

**AIM:** To prove that VIM line technique created by using a mathematical model, can be used to identify the location of the ventral intermediate nucleus of the thalamus (VIM)

**MATERIAL and METHODS:** Eleven patients with Parkinson's disease (PD) were assessed. To determine the VIM location, 3-T magnetic resonance imaging and stereotactic protocol 128-slice computed tomography were used. The VIM line technique was performed by drawing a line from the end-point of the right external globus pallidus to that of the left external globus pallidus in the intercommissural plane. PD severity was measured using the Unified Parkinson's Disease Rating Scale (UPDRS).

**RESULTS:** A mathematical model was constructed to describe the VIM line technique for determining the VIM location. UPDRS scores before and after thalamotomy showed a significant decreasing trend ( $p=0.003$ ).

**CONCLUSION:** The VIM line technique using the mathematical model can be considered a referential method to determine the VIM location. Its effectiveness was demonstrated by decreased UPDRS scores in patients after VIM thalamotomy.

**KEYWORDS:** Thalamotomy, Ventral intermediate location, VIM line technique

**ABBREVIATIONS:** **AC:** Anterior commissure, **AC-PC:** Intercommissural plane, **CST:** Cerebrospinal tract, **CT:** Computed tomography, **d:** Distance, **DBS:** Deep brain stimulation, **DTI:** Diffusion tensor imaging, **DRT:** Dentatorubrothalamic, **GPeL:** Left external globus pallidus, **GPeR:** Right external globus pallidus, **MRI:** Magnetic resonance imaging, **PD:** Parkinson's disease, **PC:** Posterior commissure, **ROI:** Region of interest, **UPDRS:** Unified Parkinson's Disease Rating Scale, **VIM:** Ventral intermediate nucleus of the thalamus

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## INTRODUCTION

The ventral intermediate nucleus of the thalamus (VIM) is a very important area that plays a vital role in the tremor mechanism in Parkinson's disease (PD). The dentatorubrothalamic (DRT) tract is located in the VIM area and serves as a connection between the areas that regulate tremors (4,10). Determining the VIM location using imaging modalities is difficult; 3-T magnetic resonance imaging (MRI) is unable to distinguish the nucleus of the thalamus by showing homogeneous images of the thalamus. Unclear VIM location might be considered the cause of tremor recurrence and side-effect occurrence in patients after VIM thalamotomy (1,6,10,11,12,18).

Resting tremor is one of the complaints of patients with PD. The prevalence of PD has been continuously increasing. In 2016, approximately 6.1 million people had PD, with male predominance (1.7:1.2), especially those aged >50 years (5). PD as one of the most common diseases in the elderly greatly affects various aspects of life (15). For patients with PD, the cost of care is mainly derived from direct costs for medication, care, and caregivers as well as indirect costs of economic abstinence of patients (14,17).

PD also affects daily activities of living because of the inability to perform them independently. Patients with PD have difficulties in running, engaging in social interaction, showing emotional changes, and performing recreational activities. Most restrictions are derived from disruptions in body movement, such as tremor, stiffness, and slowness, with wearing clothes being the most commonly disrupted daily activity of living (9).

PD management is currently performed using two approaches: medical therapy and surgery. Suboptimal medical therapy of PD can be combined with surgery (2). A systematic review explained that a combination of surgery and medical therapy can significantly decrease the medication dosage compared with the optimal dosage of medication alone (7,16). The combination of medical therapy and surgery was shown to improve the quality of life of patients with PD (13). Deep brain stimulation (DBS) implantation and VIM thalamotomy have been performed for reducing PD tremors (8,12).

VIM thalamotomy is a surgical procedure that involves the creation of a lesion at VIM (12). In this study, the VIM line technique was used to determine the VIM location. MRI and computed tomography (CT) were used as guides to determine this location. Coordinate-based methods such as Schaltenbrand–Wahren, Guiot's, and diffusion tensor imaging (DTI)-based techniques have been previously used to determine this location (6,10,12). These methods require high accuracy and precision. Inaccurate determination of the target can lead to tremor recurrence as well as side effects. The currently used techniques have considerable variation in determining the target's location.

## MATERIAL and METHODS

This study was approved by the Research Ethics Committee.

The study included 11 patients who were well informed of the study risks. All participants provided informed consent. The lesion location was determined based on the patients' dominant tremor symptoms. If the dominant tremor symptoms were on the right side, a left VIM lesion was performed; if the dominant tremor symptoms were on the left side, a right VIM lesion was performed.

This study aimed to determine the treatment outcomes in patients with PD before and after stereotactic thalamotomy surgery using the VIM line technique in the form of the Unified Parkinson's Disease Rating Scale (UPDRS) scores. Assessment of UPDRS scores was performed by a neurologist preoperatively, during the on period (under the influence of the drug) and during the off period (when the effect of the drug diminished).

### Surgical Procedure

Thalamotomy was initiated with a brain MRI using a slice thickness of 1 mm without spaces and without overlapping. MRI was performed in several sequences: T1, T2, T2 FLAIR, and SWAN. Subsequently, the patient was administered local anesthesia in the area where the stereotactic frame would be attached. After anesthetizing the area, an inomed ZD® stereotactic frame was placed on the patient's head, followed by a CT scan. MRI and CT results along with their fusion were included in the stereotactic software (Framelink®).

Stereotactic software is very useful in terms of target planning (determination of target points). The standard target for tremor surgery at the VIM is 25% of the length of the anterior commissure (AC)–posterior commissure (PC) line in front of the PC and 13–15 mm lateral from the midline (11 mm lateral from the third ventricular wall) and was located in the axial intercommissural plane (AC–PC line). This point was shown on MRI and CT images, but caution was advised for individual variations of the thalamus. The VIM line technique was used with a mathematical model to determine the VIM location. This system provided three-dimensional images of the brain (along with MRI and CT images), with a common reference point and coordinate system.

This study was conducted using a mathematical model of the VIM line technique to determine DRT in the VIM area. The VIM line technique was performed by drawing a line from the posterior end-point of the right external globus pallidus (GPe<sub>R</sub>) to the posterior end-point of the left external globus pallidus (GPe<sub>L</sub>) over the AC–PC line. The mathematical model was as follows:

$$\begin{aligned} & (x_{VIM_L}, y_{VIM_L}, z_{VIM_L}) \\ &= (x_{GPe_L}, y_{GPe_L}, z_{GPe_L}) - \frac{d(GPe_L CST) + 1.5 \text{ mm}}{d(GPe_R CPe_L)} \frac{GPe_R GPe_L}{GPe_R GPe_L} \end{aligned}$$

for the left side and

$$\begin{aligned} & (x_{VIM_R}, y_{VIM_R}, z_{VIM_R}) \\ &= (x_{GPe_R}, y_{GPe_R}, z_{GPe_R}) + \frac{d(GPe_R CST) + 1.5 \text{ mm}}{d(GPe_R CPe_L)} \frac{GPe_R GPe_L}{GPe_R GPe_L} \end{aligned}$$

for the right side.

The AC and PC points as well as the medial reference

point were determined so that all images were in the same position. Next, the posterior points of the  $GPe_R$  and  $GPe_L$  were determined, which was performed between two points known as the VIM line. To determine the VIM point for thalamotomy, the right and left corticospinal tracts (CST) were cut off by the VIM line. The VIM point was located 1.5 mm to the medial area of the VIM line from the CST boundary (Figure 1). The entry point from the head bone to the VIM point was determined by avoiding the existing blood vessels and the ventricular system of the brain. The VIM location and its entry point were identified by considering its coordinates (x, y, and z).

VIM point coordinates were determined using the VIM line technique, the patient's hair was shaved in the planned entry point area, and the operating area was disinfected and narrowed using a sterile cloth. Local anesthesia was induced in the area of the planned incision. After the anesthetic was induced, a 3–4 cm-long straight incision was made at the entry point. A hole was made in the bone at the specified entry point; then, an incision was made at the dura mater. After the dura mater was devascularized and opened, the arachnoid was coagulated, and a small incision was made on the arachnoid. The stereotactic arc was mounted on the stereotactic frame. Then, the electrode was inserted based on the coordinates specified in the stereotactic software. Macrostimulation was performed at 1–2 mA, 130 Hz, and 60 ms using the Cosman® radiofrequency machine while evaluating the patient's clinical response on the contralateral side. If good results were achieved and no side effects occurred, a temporary lesion was created by heating on the 45°C electrode tip (4-mm active tip with 1.1-mm diameter) for 30 s. If good results were achieved and no side effects occurred, the procedure was then performed on permanent lesions by heating 70°C for 30 s, with 3–4-mm-diameter lesions. After removing the

electrodes and bow, evaluation was performed for bleeding. The surgical wound was sutured layer by layer and covered with a sterile gauze and plaster.

The frame attached to the patient's head was removed after the thalamotomy procedure, and the wound where the frame was attached was then covered with a sterile gauze. Brain MRI was performed to evaluate the accuracy of the thalamotomy and the possibility of side effects, such as bleeding and pneumocephalus.

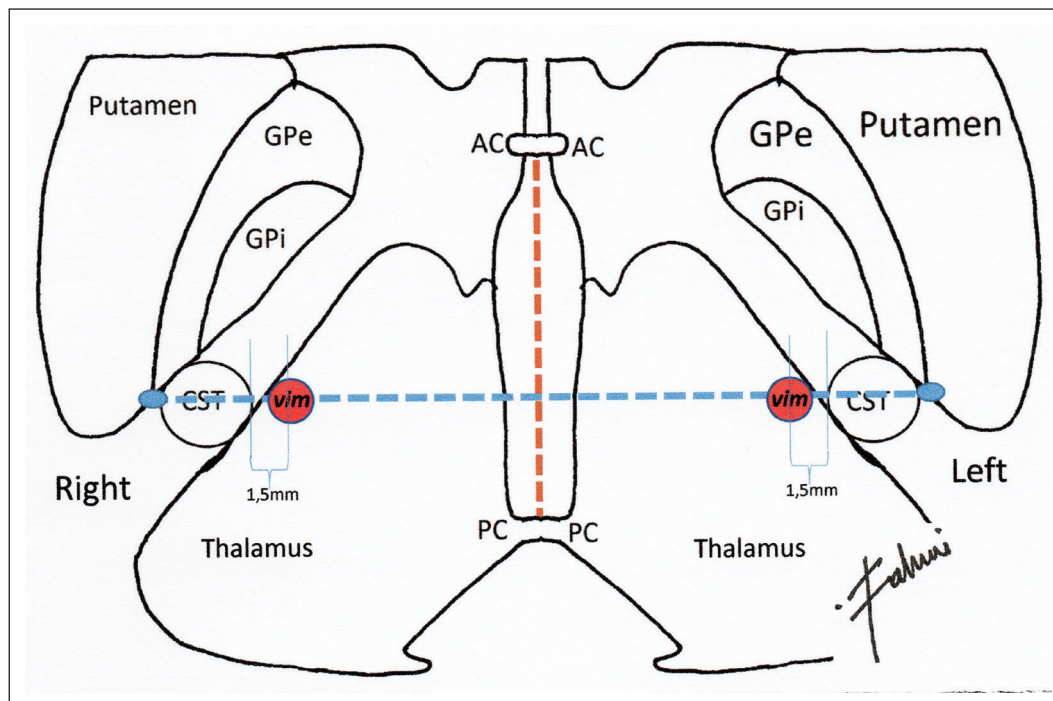
### Statistical Analysis

IBM SPSS statistics version 19 software was used for data analysis. The Shapiro–Wilk test and Wilcoxon test were performed. The significance level was set at  $p \leq 0.05$  with 95% confidence interval.

## RESULTS

The majority of patients were men (72.73%), with an average age of  $50.81 \pm 8.52$  (range, 32–59) years. Two patients were aged <40 years, two were aged between 40 and 50 years, and seven were aged >50 years. Three (27.27%) patients had left dominant tremors with lesions on the right VIM and eight (72.73%) had right dominant tremors with lesions on the left VIM (Table I).

UPDRS data before and after thalamotomy after performing the Shapiro–Wilk normality test showed that data were nonnormally distributed. Thus, the Wilcoxon test was performed, with  $p = .003$ . Significant differences in the UPDRS scores of patients were observed before and after thalamotomy (Table II).



**Figure 1:** Schema of VIM point determination using the VIM line technique. Visible lines connecting the right and left GPe that intersect the CST. The VIM point is set at 1.5 mm medial from the medial CST limit in the AC–PC line. **GPe:** external globus pallidus, **GPi:** internal globus pallidus, **AC:** anterior commissure, **PC:** posterior commissure, **CST:** corticospinal tract, **VIM:** ventral intermediate nucleus of the thalamus.



**DISCUSSION**

The VIM line technique is an alternative method for determining the VIM location. To standardize this technique, a mathematical model should be established. In general, the CST diameter is 9–12 mm. The VIM line technique was performed by drawing a line from the posterior end-point of the  $GPe_R$  and the posterior end-point of the  $GPe_L$  in the AC–PC line (Figure 1). An MRI image using the VIM line technique to determine DRT in VIM is shown in Figure 2A-E.

**Mathematical Formula of the VIM Line Technique**

First, existing points and lines were created and established by the doctor performing surgery to manually determine the VIM point used for the mathematical model of the VIM line technique. The steps to create a mathematical model are described as follows:

$(x_{GPe_R}, y_{GPe_R}, z_{GPe_R})$  is the coordinate of the posterior end-point of the  $GPe_R$ , and  $(x_{GPe_L}, y_{GPe_L}, z_{GPe_L})$  is the coordinate of the posterior end-point of the  $GPe_L$ .  $(x_{VIM_R}, y_{VIM_R}, z_{VIM_R})$  is the right VIM point coordinate based on the vim line technique, and  $(x_{VIM_L}, y_{VIM_L}, z_{VIM_L})$  is the left VIM point coordinate based on the VIM line technique.

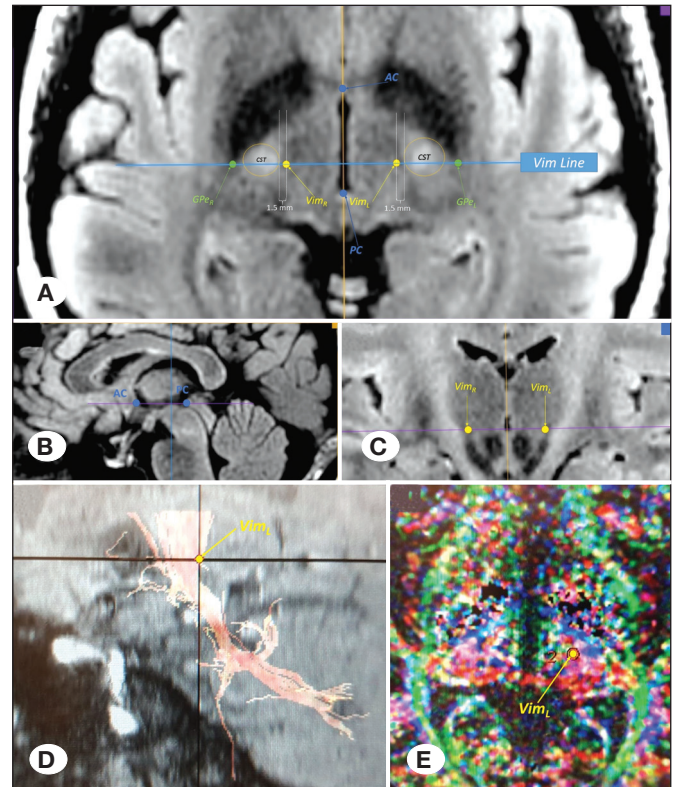
**Table I:** Patient Characteristics (n=11)

| Variables  | n (%)     | Remarks                  |
|------------|-----------|--------------------------|
| Age, years |           | 50.81 ± 8.52 (Mean ± SD) |
| <40        | 2 (18.18) |                          |
| 40–50      | 2 (18.18) |                          |
| >50        | 7 (63.63) |                          |
| Sex        |           |                          |
| Male       | 8 (72.73) |                          |
| Female     | 3 (27.27) |                          |
| Lesion     |           |                          |
| Right      | 3 (27.27) |                          |
| Left       | 8 (72.73) |                          |

**Table II:** Unified Parkinson’s Disease Rating Scale (UPDRS) pre- and Post-Thalamotomy

| Observation period | UPDRS     |        |       |        | P      |             |
|--------------------|-----------|--------|-------|--------|--------|-------------|
|                    | Mean      | SD     | Min   | Max    |        |             |
| On period          | Pre       | 17.27  | 12.64 | 6.00   | 45.00  |             |
|                    | Post      | 6.09   | 10.63 | 0.00   | 35.00  |             |
|                    | ΔPre-post | -11.18 | -2.01 | -6.00  | -10.00 | <b>.003</b> |
| Off period         | Pre       | 48.36  | 28.56 | 12.00  | 119.00 |             |
|                    | Post      | 21.27  | 24.00 | 2.00   | 86.00  |             |
|                    | ΔPre-post | -27.09 | -4.56 | -10.00 | -33.00 |             |

The VIM line was assumed to begin at  $(x_{GPe_R}, y_{GPe_R}, z_{GPe_R})$  to  $(x_{GPe_L}, y_{GPe_L}, z_{GPe_L})$ .  $\vec{GPe_R GPe_L}$  is the beginning vector of  $GPe_R$  and endpoint of  $GPe_L$ , whereas,  $\vec{GPe_R GPe_L} = (x_{GPe_L} - x_{GPe_R}, y_{GPe_L} - y_{GPe_R}, z_{GPe_L} - z_{GPe_R})$ .



**Figure 2:** VIM point determination in MRI (T2 flair sequences) using the VIM line technique. **A)** axial; **B)** sagittal; **C)** coronal; **D)** dentatorubrothalamic track in diffusion tensor imaging (DTI)/diffusion-weighted imaging (DWI) sequence; **E)** region of interest (ROI) placement in DTI sequence. AC: anterior commissure, PC: posterior commissure, CST: cerebrospinal tract,  $GPe_L$ : left external globus pallidus,  $GPe_R$ : right external globus pallidus,  $VIM_L$ : left ventral intermediate nucleus of the thalamus,  $VIM_R$ : right ventral intermediate nucleus of the thalamus.

$d(GPe_R GPe_L)$  is the distance between  $GPe_R$  and  $GPe_L$ , where

$$d(GPe_R GPe_L) = \sqrt{(x_{GPe_L} - x_{GPe_R})^2 + (y_{GPe_L} - y_{GPe_R})^2 + (z_{GPe_L} - z_{GPe_R})^2}.$$

$d(GPe_CST)$  is the manually determined distance between GPe and CST.

Therefore, the calculation of  $(x_{VIM_R}, y_{VIM_R}, z_{VIM_R})$  can be extrapolated to formula (1), and the calculation of  $(x_{VIM_L}, y_{VIM_L}, z_{VIM_L})$  can be extrapolated to formula (2):

$$(1) \frac{(x_{VIM_R}, y_{VIM_R}, z_{VIM_R}) = (x_{GPe_R}, y_{GPe_R}, z_{GPe_R}) + \frac{d(GPe_R CST) + 1.5 mm}{d(GPe_R GPe_L)} \overrightarrow{GPe_R GPe_L}}$$

$$(2) \frac{(x_{VIM_L}, y_{VIM_L}, z_{VIM_L}) = (x_{GPe_L}, y_{GPe_L}, z_{GPe_L}) - \frac{d(GPe_L CST) + 1.5 mm}{d(GPe_R GPe_L)} \overrightarrow{GPe_R GPe_L}}$$

The UPDRS data were significantly decreased in the comparison of scale results before and after thalamotomy. Thalamus VIM destruction of an accurate thalamotomy procedure reached the target according to plan and successfully inhibited thalamus excitation toward the motor cortex (3).

Thalamotomy itself is a procedure that primarily aims to overcome tremor, and the VIM is a standard stereotactic target of thalamotomy for tremor control (12). PD dominant tremor is a good indication for VIM thalamotomy as long as tremor is a major complaint and there are no complaints of other Parkinson's symptoms. Furthermore, essential and dystonic tremors can serve as good indications for thalamotomy (12). DBS is also used in PD to reduce tremors with its adjustable features (8). Patients should understand that thalamotomy does not increase dopamine levels and is not adjustable. Selection of candidates for thalamotomy is important because the procedure is intended for those refractory to levodopa treatment or who have reached the maximum dose of available medical management.

## CONCLUSION

The VIM line technique can be used to determine the VIM location, with differences in UPDRS scores after thalamotomy indicating its effectiveness.

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