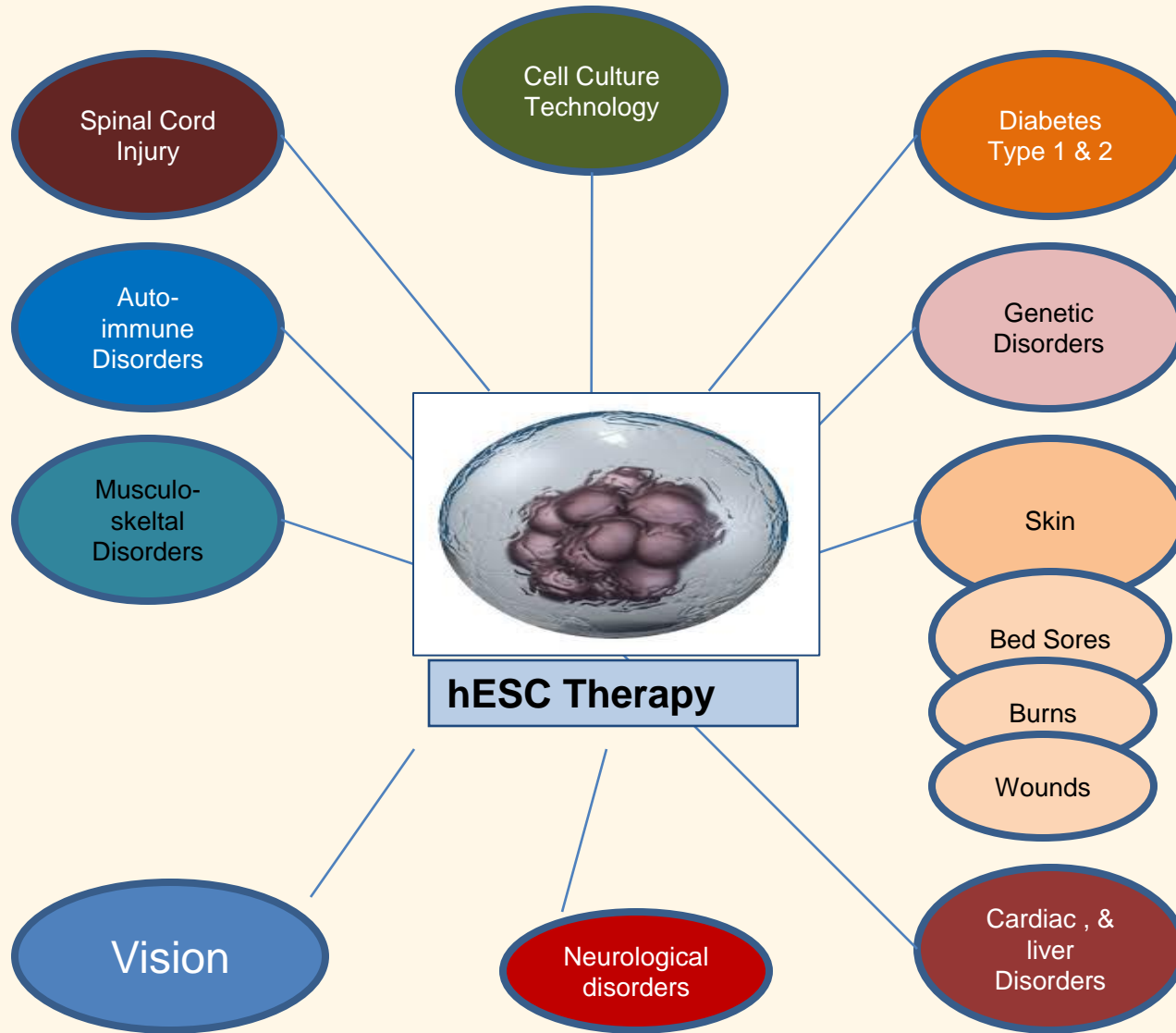




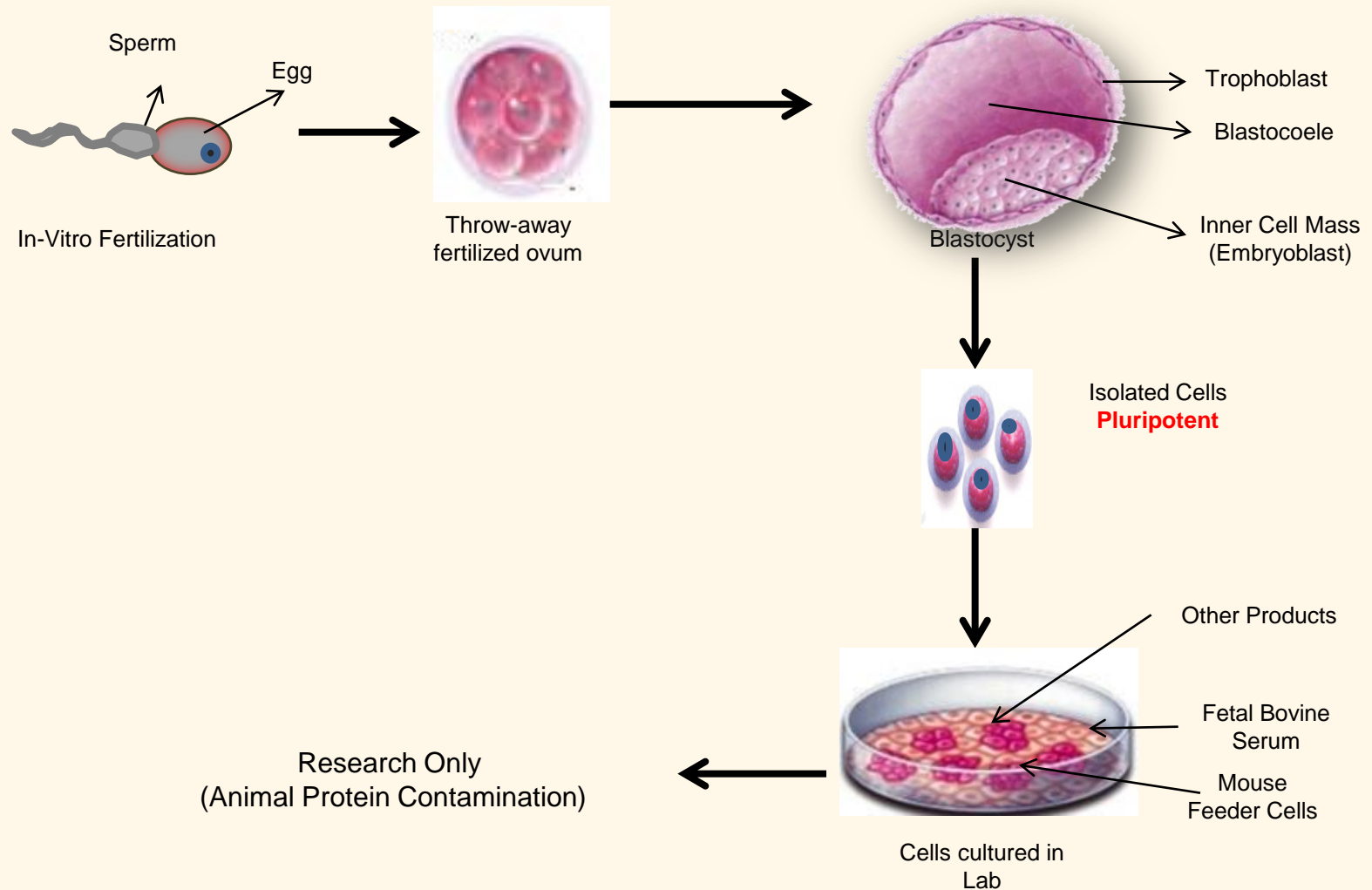
# **USE OF HUMAN EMBRYONIC STEM CELLS IN THE TREATMENT OF PARKINSON'S DISEASE**

**Dr. Geeta Shroff  
Founder and Medical Director,  
Nutech Mediworld**

# CONDITIONS TREATED



# CONVENTIONAL DERIVATION METHODS



## Disadvantages

Antigen-antibody reactions  
Immunosuppressants required

Teratomas formed  
Chromosomal instability

# HESC: WE CULTURE THEM DIFFERENTLY

Day

0

1

2

3

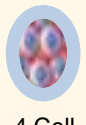
4

5

6



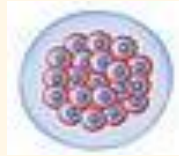
2- Cell



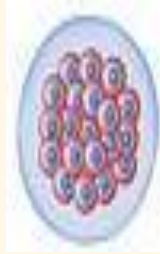
4 Cell



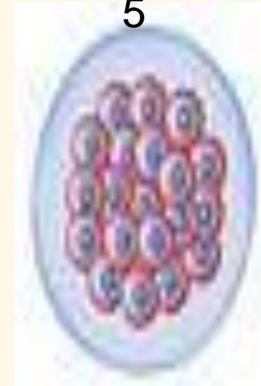
8- Cell



16- Cell



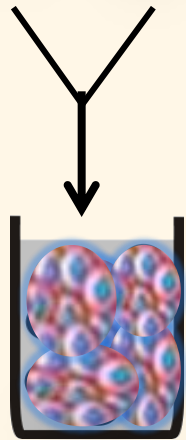
32- Cell



64- Cell

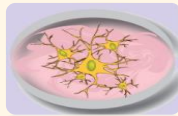


128- Cell



No Feeder Layer  
No Animal Product

Neuronal cell



Non-neuronal cell

Incubated

Re-incubated  
Stored

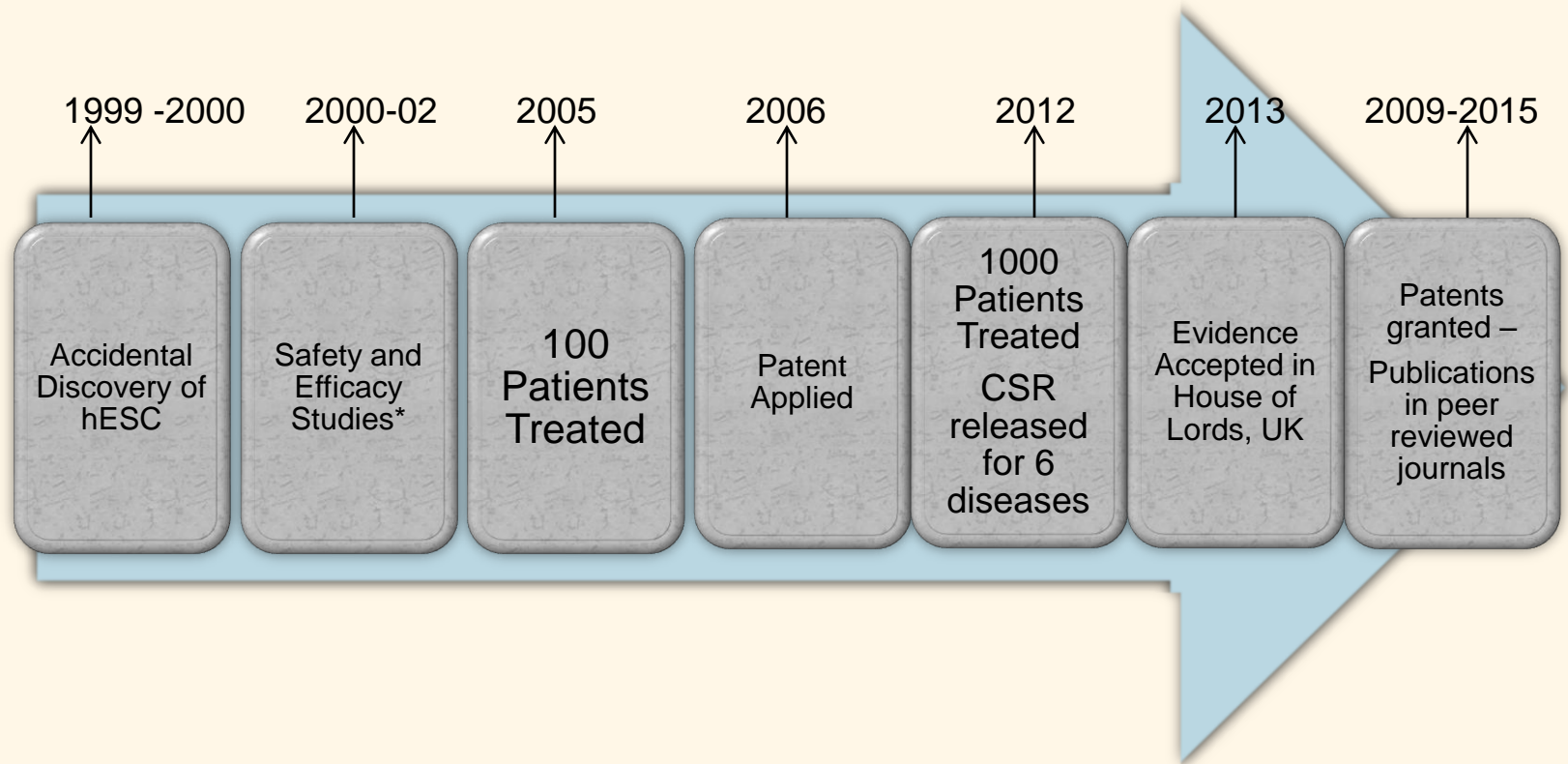
Re-incubated

Stored

Ready to use Cell Cultures

Ready to use Cell Cultures

# OUR HISTORY



\*Shroff G et al. Annals of Neurosciences. 2015;22(3).

# TECHNOLOGY HIGHLIGHTS

- Patented technology<sup>1,2</sup>
- In-house cultured hESC from a Single Fertilized Ovum
- Non- contaminated
- Free of animal products
- Karyotypically stable cell lines upon 4000 passages<sup>3</sup>
- Viable and ready-to-use product form
- Simple, Cost-effective and Scalable
- No immunosuppressants needed
- No significant adverse event in over 13 years of therapeutic usage

1. <http://patentscope.wipo.int/search/en/WO2007141657>

2. Shroff G, International Journal of Recent Scientific Research

3. Paper communicated

# PARKINSON'S DISEASE: BACKGROUND

- Central nervous system (CNS) disorder
- Progressive in nature
- Caused by a genetic defect and/or environmental factors
- In Europe, affects every 1 in 100 persons
- Women have longer life expectancy





# PARKINSON'S DISEASE SYMPTOMS

## Motor Symptoms

- Bradykinesia (slowness)
- Tremor
- Stiffness
- Shuffling gait
- Postural instability
- Lack of facial expression

## Non-motor Symptoms

- Depression
- Anxiety
- Constipation
- Dysautonomia
- Sleep disturbances
- Hallucinations

# PATHOLOGICAL MANIFESTATION

- Degeneration of neurons (DA) in substantia nigra pars compacta (SN) and the nigrostriatal (dopaminergic) tract<sup>1</sup>
- Presence of biomarkers such as  $\alpha$ -synuclein positive Lewy bodies in the brain<sup>2</sup>

<sup>1</sup>Braak *et al Neurobiology of aging*. 2003, 24: 197-211

<sup>2</sup>Marsden *et al J Neural Transm Suppl*. 1983, 19: 121-141

# CONVENTIONAL TREATMENTS

## Drug Therapy

- Levodopa
- MAO-B inhibitors: Selegiline
- Dopamine agonists: Pramipexole, Ropinirole

## Surgical treatment

- Deep Brain Stimulation
  
- No treatment can cure or can reverse the condition

## CELL TRANSPLANTATION STUDIES (ELSEWHERE)

- hESC derived DA neurons promoted partial function recovery in parkinsonian rat models<sup>1</sup>
- Human embryonic DA neurons transplanted into 40 patients (34 to 75 yr) showed clinical benefits in younger patients only<sup>2</sup>
- A phase I trial to assess the safety of using hESC in the treatment of amyotrophic lateral sclerosis, inferring that this therapy could show a potential therapeutic effect in the treatment of PD, multiple sclerosis and Alzheimer's disease patients  
(<http://www.michigandaily.com/news/new-treatments-als-reach-phase-ii-trial>)

<sup>1</sup>Roy *et al* *Nature medicine*. 2006, 12: 1259-1268

<sup>2</sup>Freed *et al* *NEW ENGL J MED*. 2001, 344: 710-719

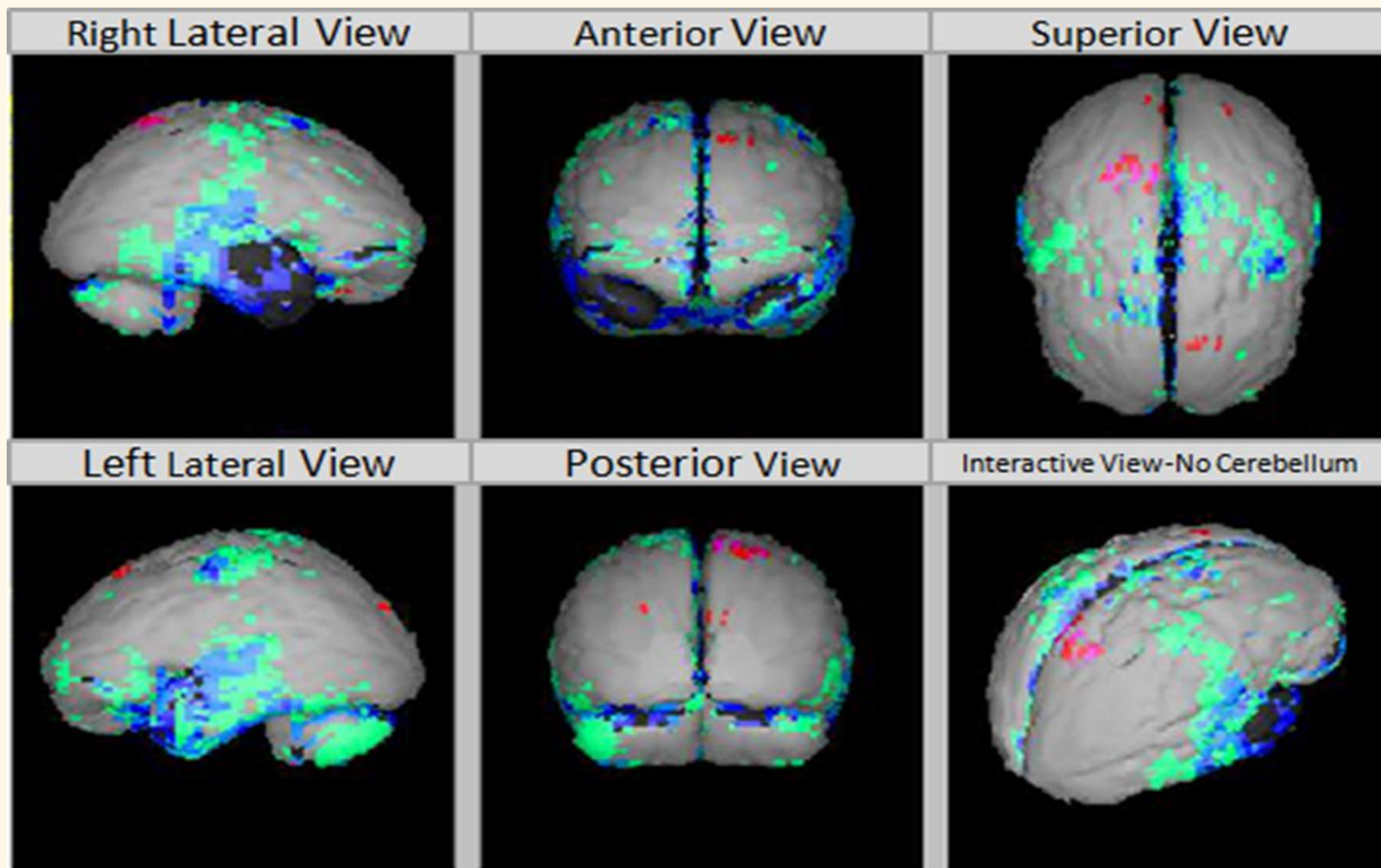
# HESC THERAPY: PARKINSON'S DISEASE

- We are the first to report the safe and effective transplantation of hesc in PD
- Till date, we have treated 30 patients with PD with significant clinical improvements.

# CASE PRESENTATION

- A 65-year old male patient
- Admitted on 19 November 2012
- Complaints of :
  - Resting tremors
  - Back and neck stiffness
  - Bradykinesia
  - Muscle rigidity
  - Unclear speech
  - Micrographia
  - Imbalanced walking
  - Urinary urgency with incomplete voiding
  - Pain in shoulder
  - Numbness in his hand and legs

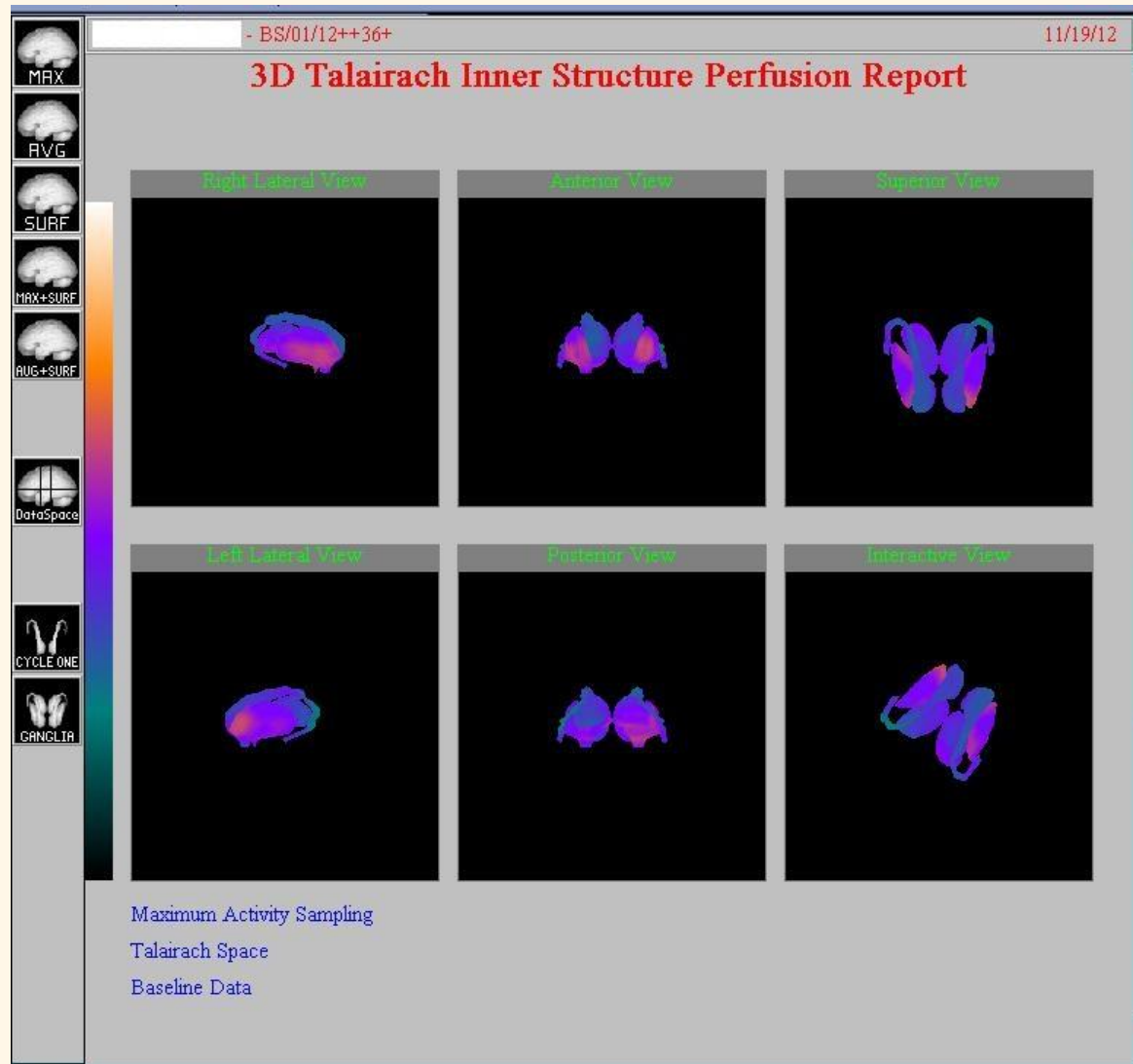
# SPECT BEFORE TREATMENT (20 Nov 2012)



Grey: Normal; Red, pink and white: above normal (+2, +3,+4 of standard); Hypoperfused Regions: Green: -2 of standard; Light blue: -3 of standard; Dark blue: -4 of standard; black: -5 of standard

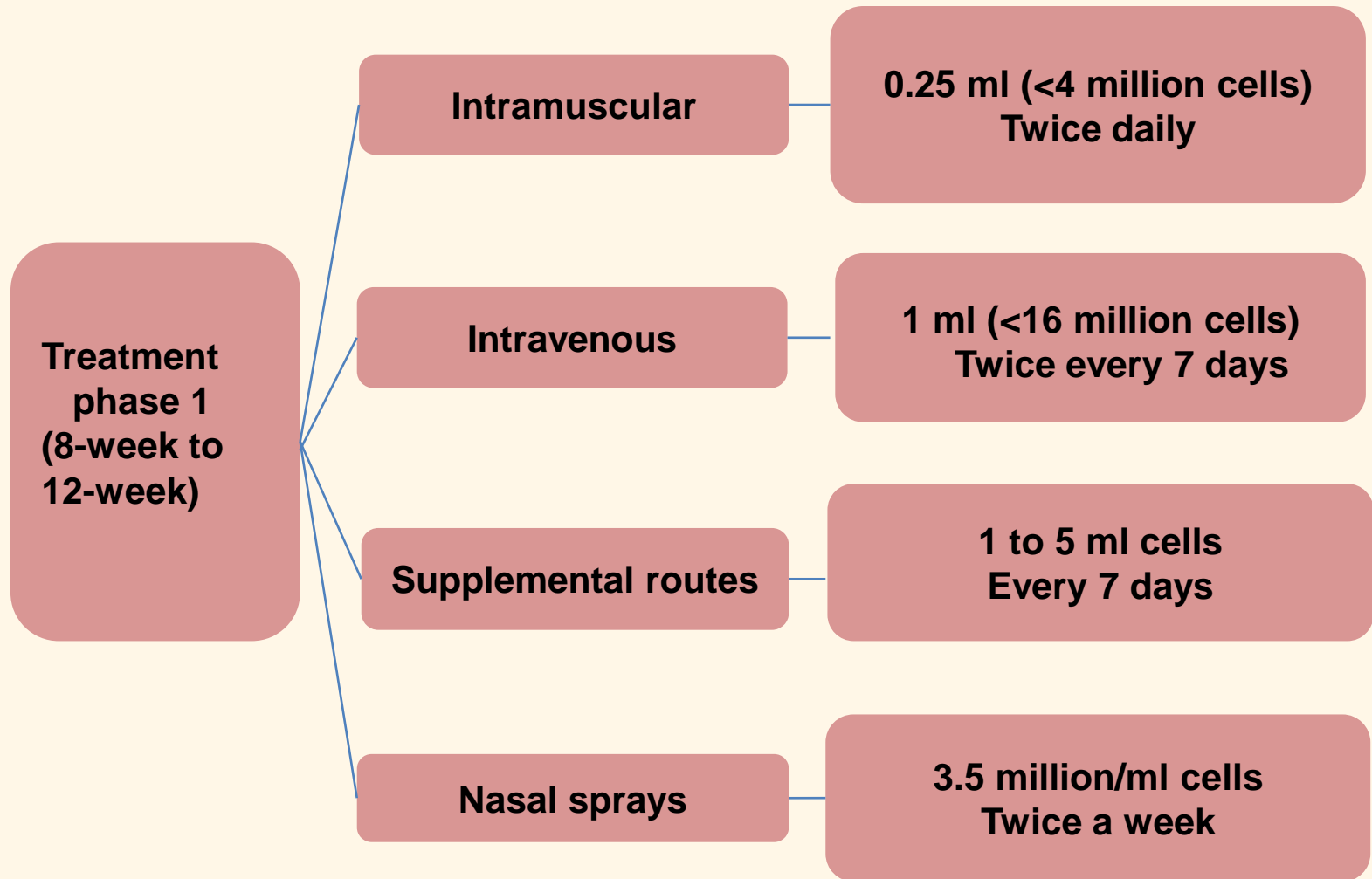
Moderate hypoperfusion in bilateral parieto-temporal regions and moderate to severe hypoperfusion in bilateral basal ganglia and bilateral cerebellar regions

# BEFORE





# TREATMENT PLAN



# CONTD...

## Main therapy

hESC therapy

## Other therapy

Occupational therapy  
Physiotherapy

## Medications

Rasagilin (Azilect), 1 mg OD;  
(Taj Pharmaceuticals Ltd.)  
Pramipexole, 1 mg OD;  
(Taj Pharmaceuticals Ltd.)  
Meloxicam, 7.5 mg OD  
Cymbalta, 30 mg OD;  
(Eli Lilly and Co. Pvt. Ltd.)  
Amlodipine, 5 mg OD;  
(Pfizer Inc.)

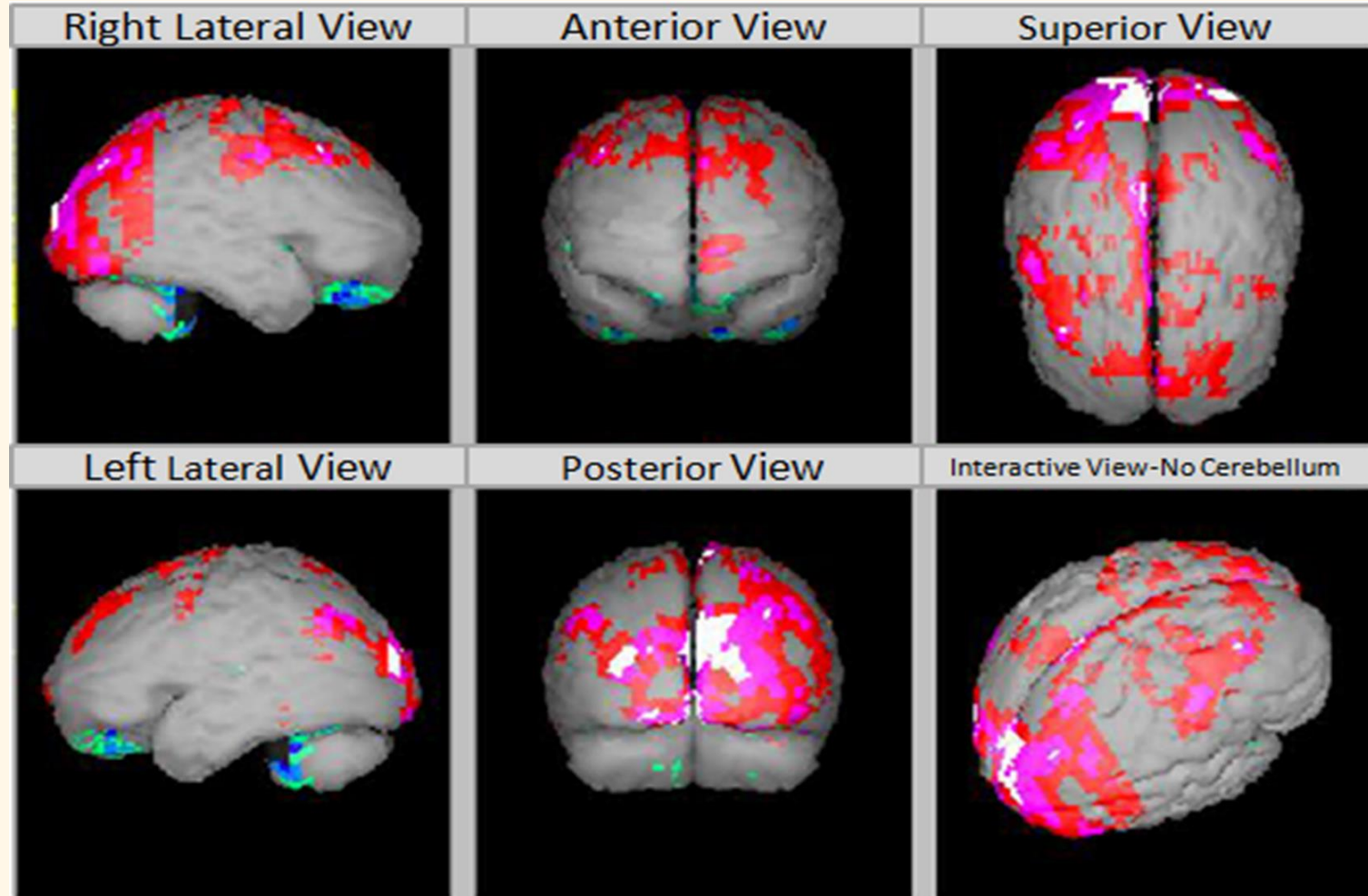
# CLINICAL IMPROVEMENT: AFTER THERAPY

Before Therapy	After Therapy
Resting tremors	Reduction in tremors
Muscle rigidity	Reduction in muscle rigidity
Bradykinesia	Reduction in bradykinesia
Imbalanced walking	Able to balance himself again while walking
Shuffling gait present	Shuffling gait disappeared
Back and neck stiffness	Had reduction in pain and stiffness in the neck and a better ability to turn it around
Pain in shoulder	Had a reduction of shoulder pain
Numbness in his hand and legs	Reduction in numbness in his left (lt) hand and in both of his legs

# AFTER



# SPECT AFTER TREATMENT (20 Nov 2014)



Grey: Normal; Red, pink and white: above normal (+2, +3,+4 of standard); Hypoperfused Regions: Green: -2 of standard; Light blue: -3 of standard; Dark blue: -4 of standard; black: -5 of standard

Normal hypoperfusion in the cerebral region and a significant improvement (> 60%) occurred in the degree of perfusion in the cerebellar regions

# REPORT

## **Examination Performed**

SPECT imaging of the brain performed following injection of 99m Tc-HMPAO intravenously. Imaging performed using a high resolution collimator on a dual head gamma camera.

## **Findings**

SPECT images reconstructed in transaxial, sagittal and coronal axes show minimal hypoperfusion in right basal ganglia.

Homogenous and symmetrical perfusion seen to the rest of the cortical and sub cortical regions.

Bilateral cerebellar uptake is normal.

## **IMPRESSION**

- **Minimal hypoperfusion noted in right basal ganglia.**
- **Compared to the previous scan done on Dec 3<sup>rd</sup>, 2012 the degree of perfusion seen in the cerebral and cerebellar regions has significantly improved.**

**Please correlate clinically.**

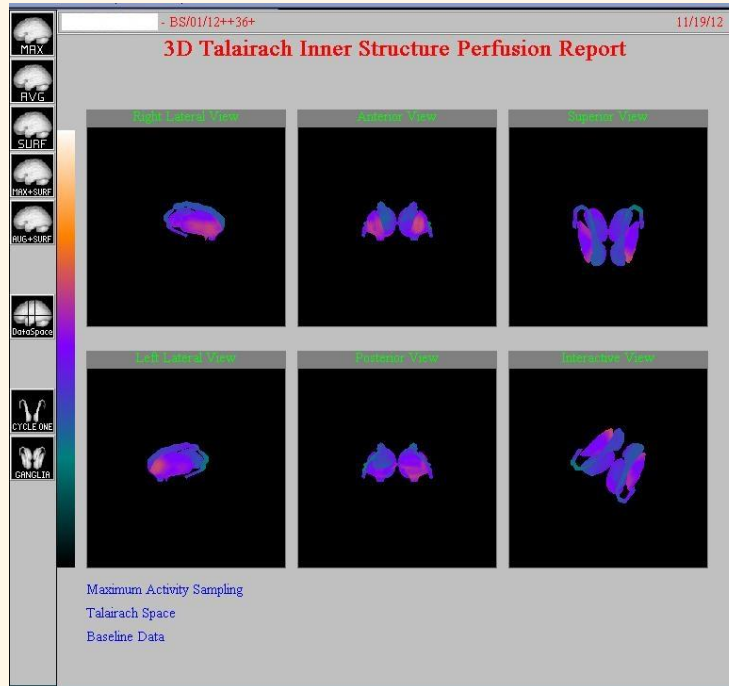
## **N.B.**

10%- 30% change—Mild improvement

30%- 60% change---Moderate improvement

> 60% change--- Significant improvement

# BEFORE



# AFTER



# CURRENT STATUS

- Currently off all medications
- Has a mild resting tremor in his right hand as the only persisting symptom
- Is back at work and has an improved quality of life



# NINE PATIENTS WITH PD TREATED TILL DATE

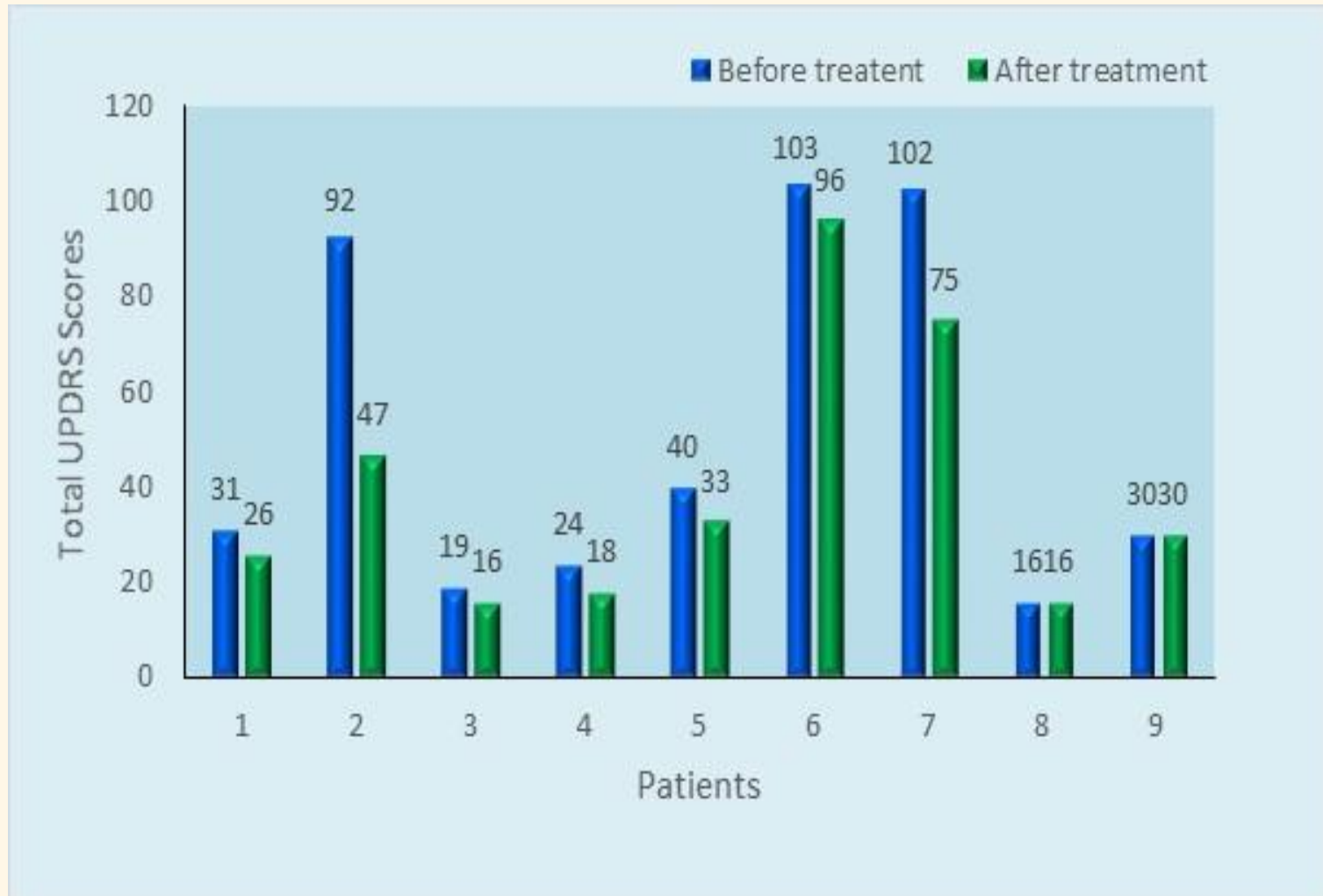
9 most recent PD patients are evaluated here. An independent neurologist examined the patients.

- All patients were scored for 42 symptoms with the Unified Parkinson's Disease Rating Scale (UPDRS) both before and after therapy
- Of the total 9 patients, 7 showed improvement when scored with UPDRS . Their medications were halved

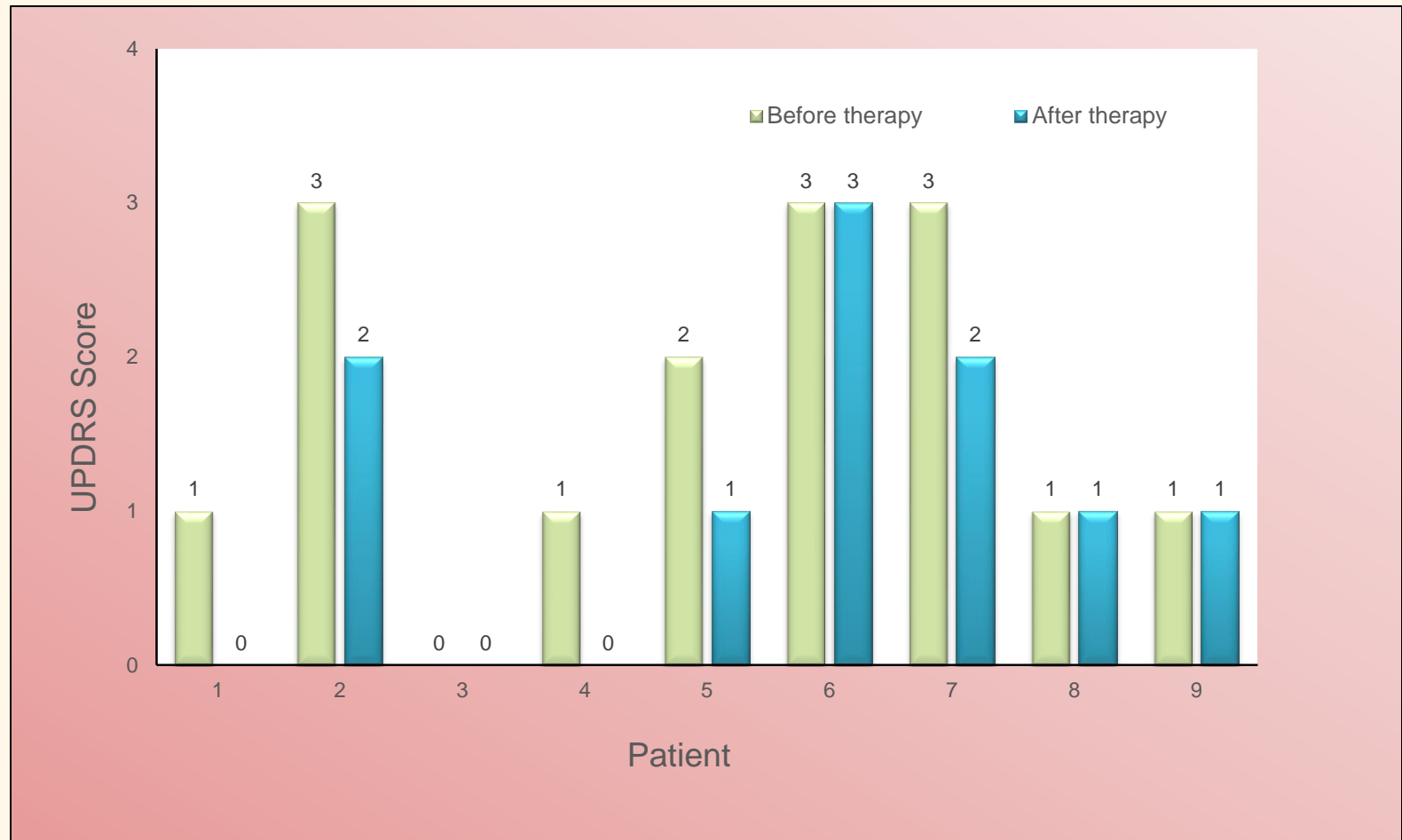
# UNIFIED PARKINSON'S DISEASE RATING SCALE

- UPDRS scale scores symptoms as 0 to 4 in direction good → bad
- For example: Walking is graded as:
  - 0 = Normal
  - 1 = Mild difficulty. May not swing arms or may tend to drag leg
  - 2 = Moderate difficulty, but requires little or no assistance
  - 3 = Severe disturbance of walking, requiring assistance
  - 4 = Cannot walk at all, even with assistance

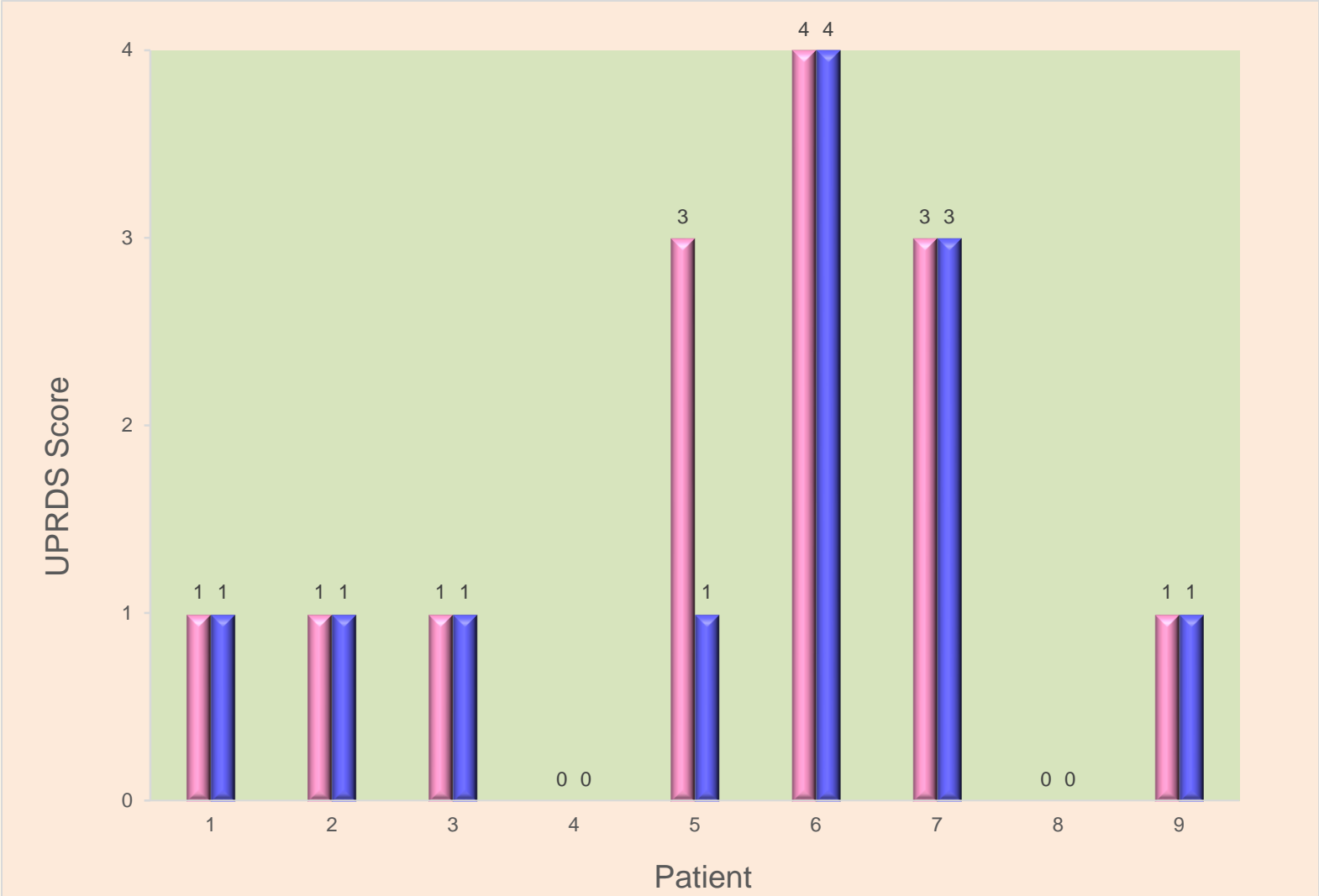
# UPDRS SCORES BEFORE AND AFTER TREATMENT(3 MNTHS )



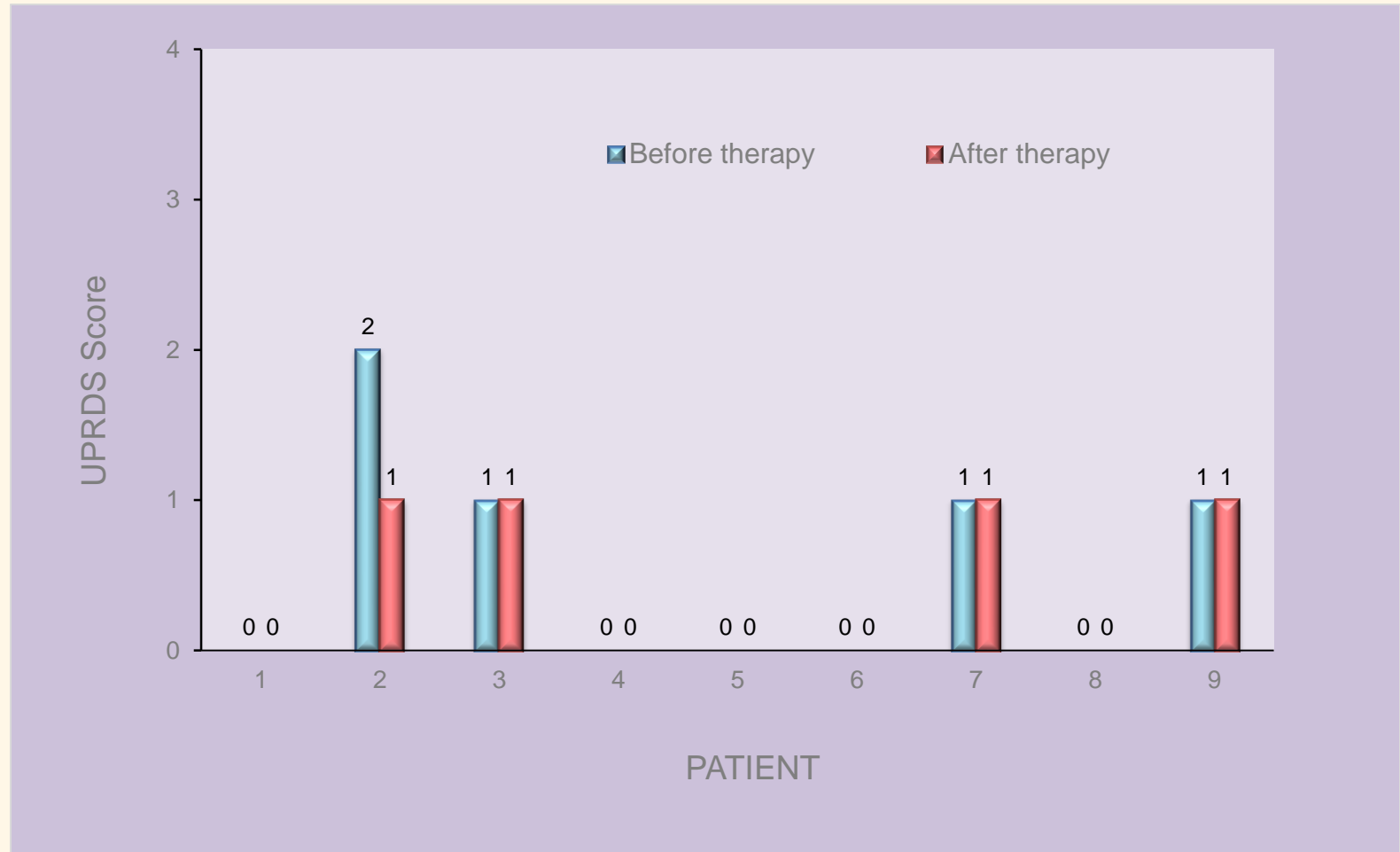
# UPDRS SCORES SHOWING IMPROVEMENT IN WALKING AFTER THERAPY



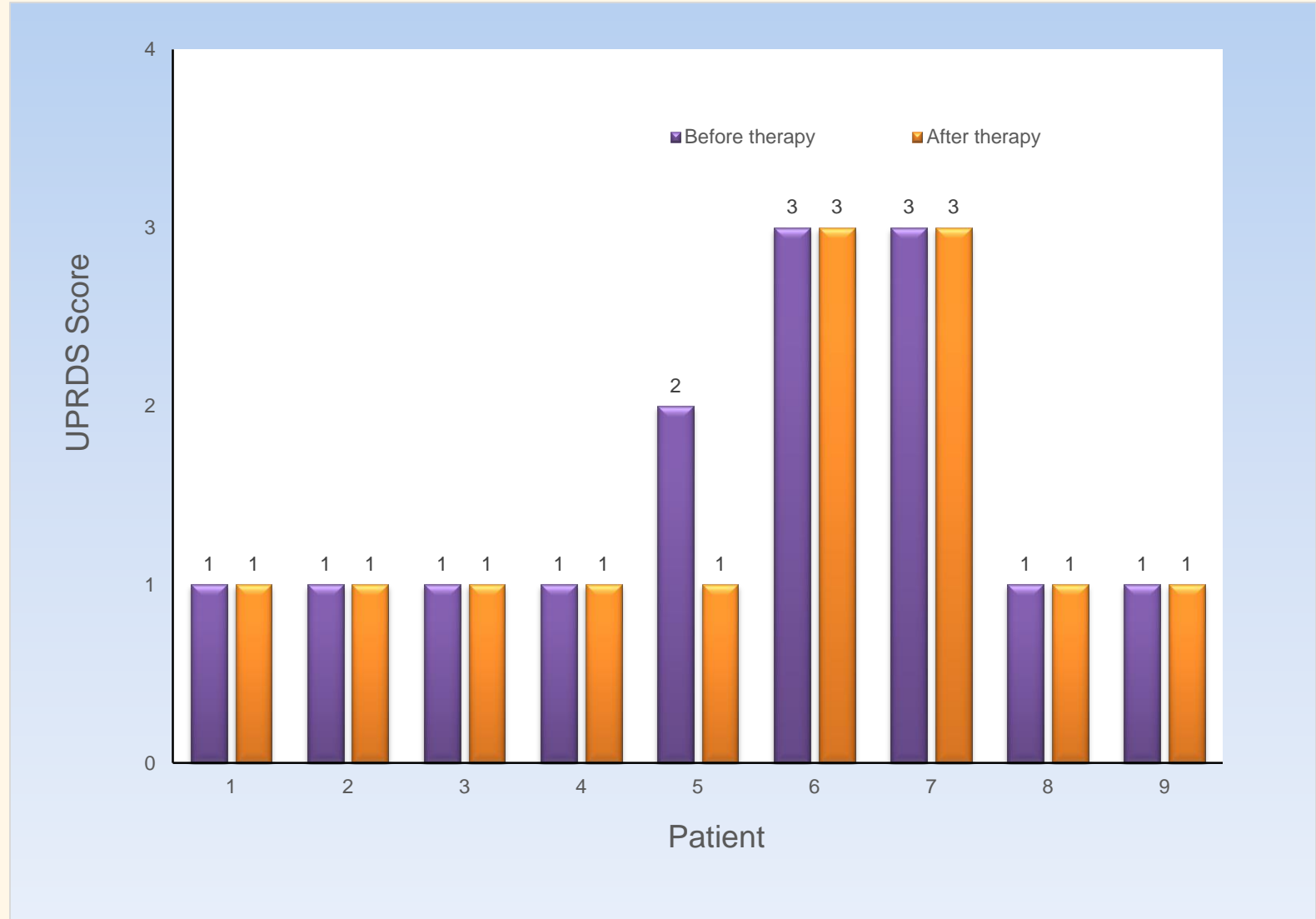
# UPDRS SCORES SHOWING IMPROVEMENT IN POSTURAL STABILITY AFTER THERAPY



# UPDRS SCORES SHOWING FOR TREMOR AFTER THERAPY



# UPDRS SCORES SHOWING FOR BODY BRADYKINESIA AFTER THERAPY



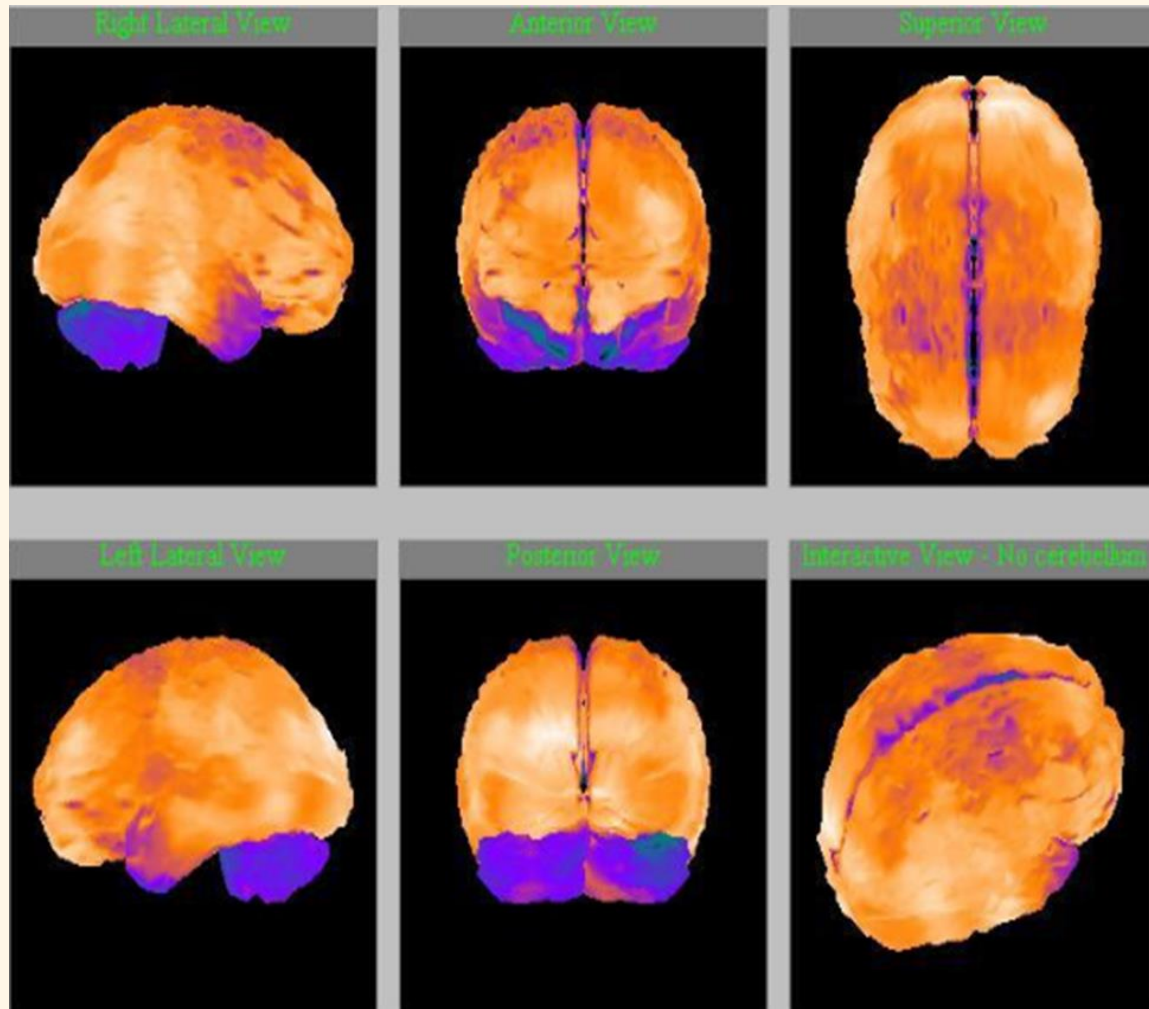
# HESC IN SPINOCEREBELLAR ATAXIA\*

- A 59-year old male doctor
- Chief complaints:
  - Difficulty in speech and sleep since last 28 years
  - Difficulty in maintaining balance since last 25 years
  - Difficulty in writing since last 14 years
  - Difficulty in walking since 19 years
  - Memory loss since 3 months
  - Has stopped his practice since

\*Shroff G. *Clin. Case. Rep.* 2015; 5:1



# SPECT SCAN: BEFORE THERAPY

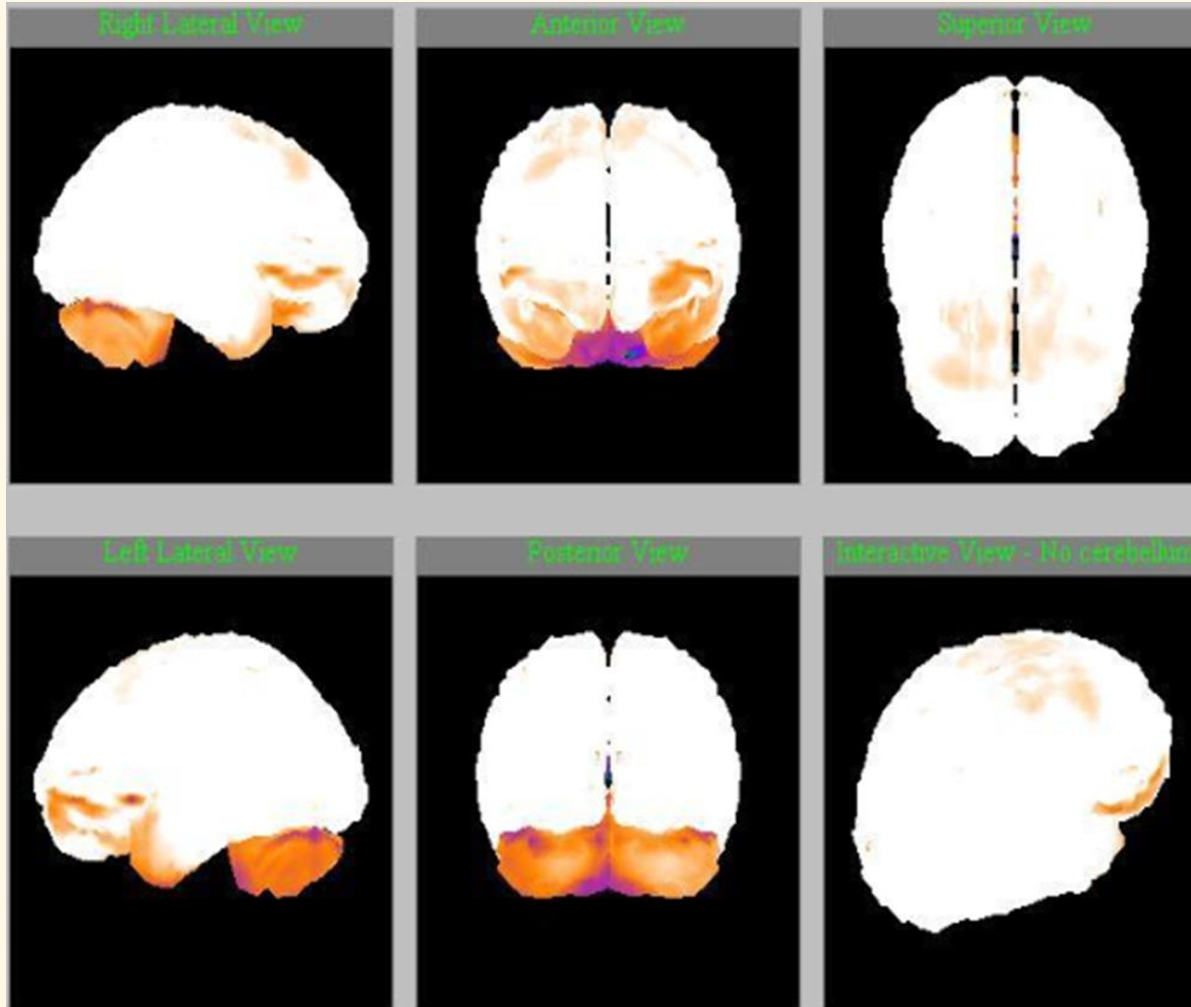


Shows large areas of hypoperfusion (darker areas)

## AFTER THERAPY:

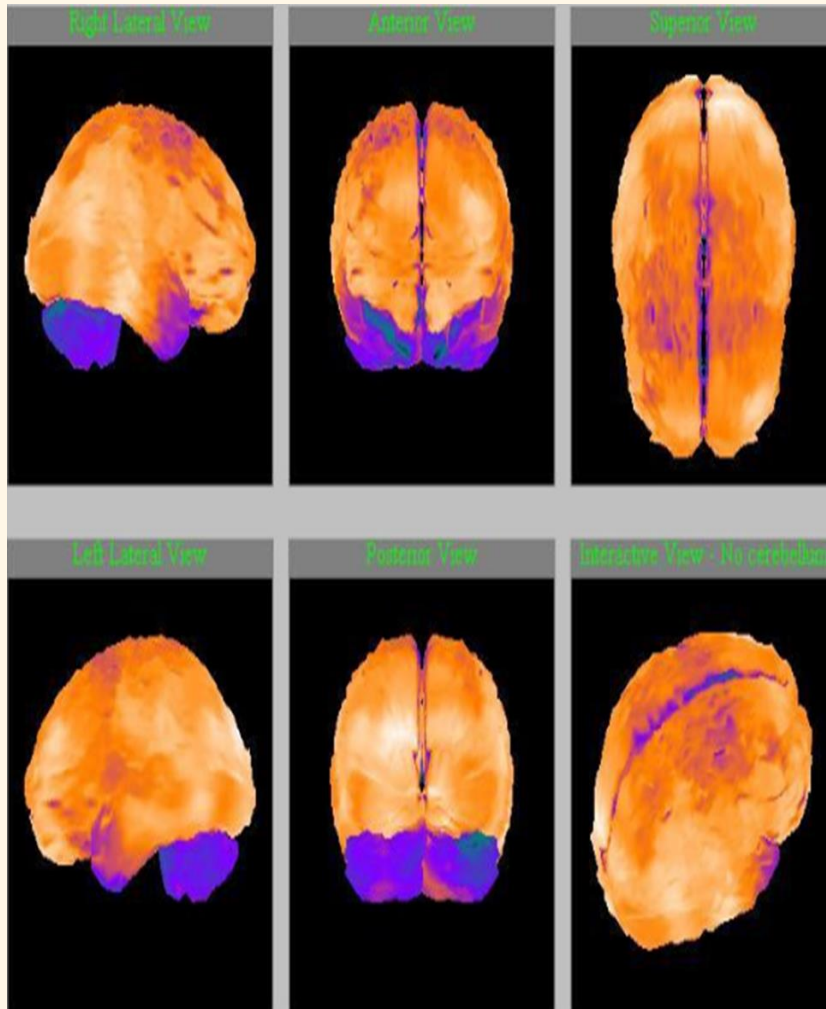
- Patient was able to walk independently (only few steps)
- Showed improvement in the strength of bilateral UL and LLs, balancing, stamina, endurance and coordination
- Better control over trunk and legs.
- Could start writing
- His speech was clearer

# SPECT SCAN: AFTER THERAPY

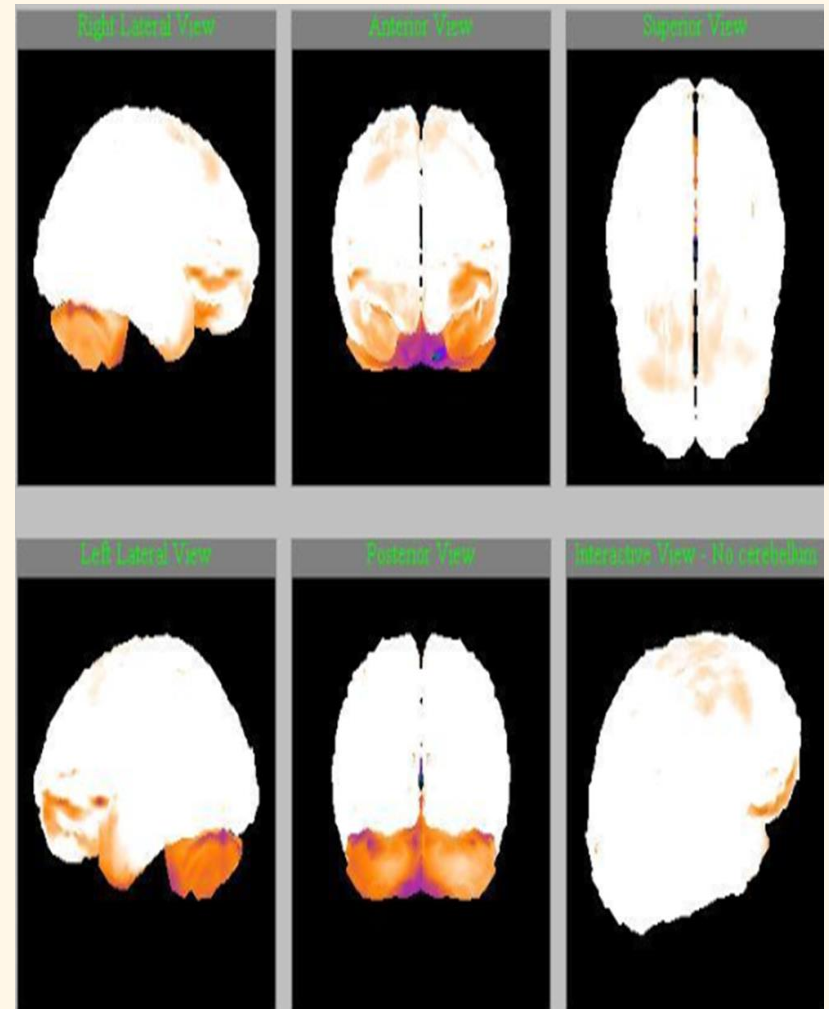


Shows reduction in hypoperfusion (darker areas)

## BEFORE THERAPY



## AFTER THERAPY



Shroff G. *Clin. Case. Rep.* 2015; 5:1

# SUMMARY

- hESC therapy is an effective and safe tool in treating patients with PD
- No adverse events and teratoma formation was seen in the patients
- UPDRS, an internationally used scoring system showed improvement in patients after therapy. Patients had improvement in major symptoms associated with PD including bradykinesia, tremor, rigidity, postural stability and walking
- hESC therapy for PD might become a potential therapeutic option in the future

# PUBLICATIONS

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2. Shroff G. A novel approach of human embryonic stem cells therapy in treatment of Friedrich's Ataxia. *Int J Case Rep Images.* 2015;6:261–266.
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5. Shroff G, Barthakur JK. Safety and Efficacy of Human Embryonic Stem Cells for the Treatment of Cerebrovascular Accident: A Case Series. *Global Journal of Medical Research.* 2015. In Press.
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12. Shroff G, Barthakur JK. Safety of Human Embryonic Stem Cells in Patients with Terminal Conditions. *Annals of Neurosciences.* 2015;22(3).
13. Shroff G, Barthakur JK, Mohan P, Mahajan H. Single Photon Emission Computed Tomography Scan as a Diagnostic Tool in Children with Cerebral Palsy Treated with Human Embryonic Stem Cells. *Journal of Nuclear Medicine and Therapy.* 6 (3), 1.
14. Nutech Functional Score (NFS), a New Scoring System to Assess the Level of Impairment in Patients with Cerebral Palsy. *International Archives of Medicine.* 2015; 8: 117
15. Shroff G. Establishment and Characterization of a Neuronal Cell line derived from a 2-cell Stage Human Embryo: Clinically Tested Cell-based Therapy for Neurological Disorders. *International Journal of Recent Scientific Research* 2015;6(4):3730-8.
16. Shroff G, Gupta R, Makhija LK. Evaluation of Wound Healing Ability with Human Embryonic Stem Cells in Patients with Non-Healing Wounds: A Case Series. *Journal of Pigmentary Disorders* 2015; 2:7.



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18. Shroff G. Use of Human Embryonic Stem Cells in the Treatment of Age-Related Macular Degeneration. J Clin Exp Ophthalmol 2015; 6:446.
19. Shroff G, Barthakur JK, Mohan P, Mahajan H. Single Photon Emission Computed Tomography Scan as a Diagnostic Tool in Children with Cerebral Palsy Treated with Human Embryonic Stem Cells. J Nucl Med Radiat Ther 2015, 6:3.
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21. Barthakur IK, Shroff G. Natural Selection of Gender of the Baby at Conception: Proposing a Scientific Hypothesis. Science Journal of Public Health 2015; 664-668
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# THANK YOU