HBOT2018
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"*Advancing Hyperbaric Medicine Globally in the 21st Century*"

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Hyperbaric Oxygen Therapy in Neurodegenerative Disease with Case Presentations of Alzheimer's Disease

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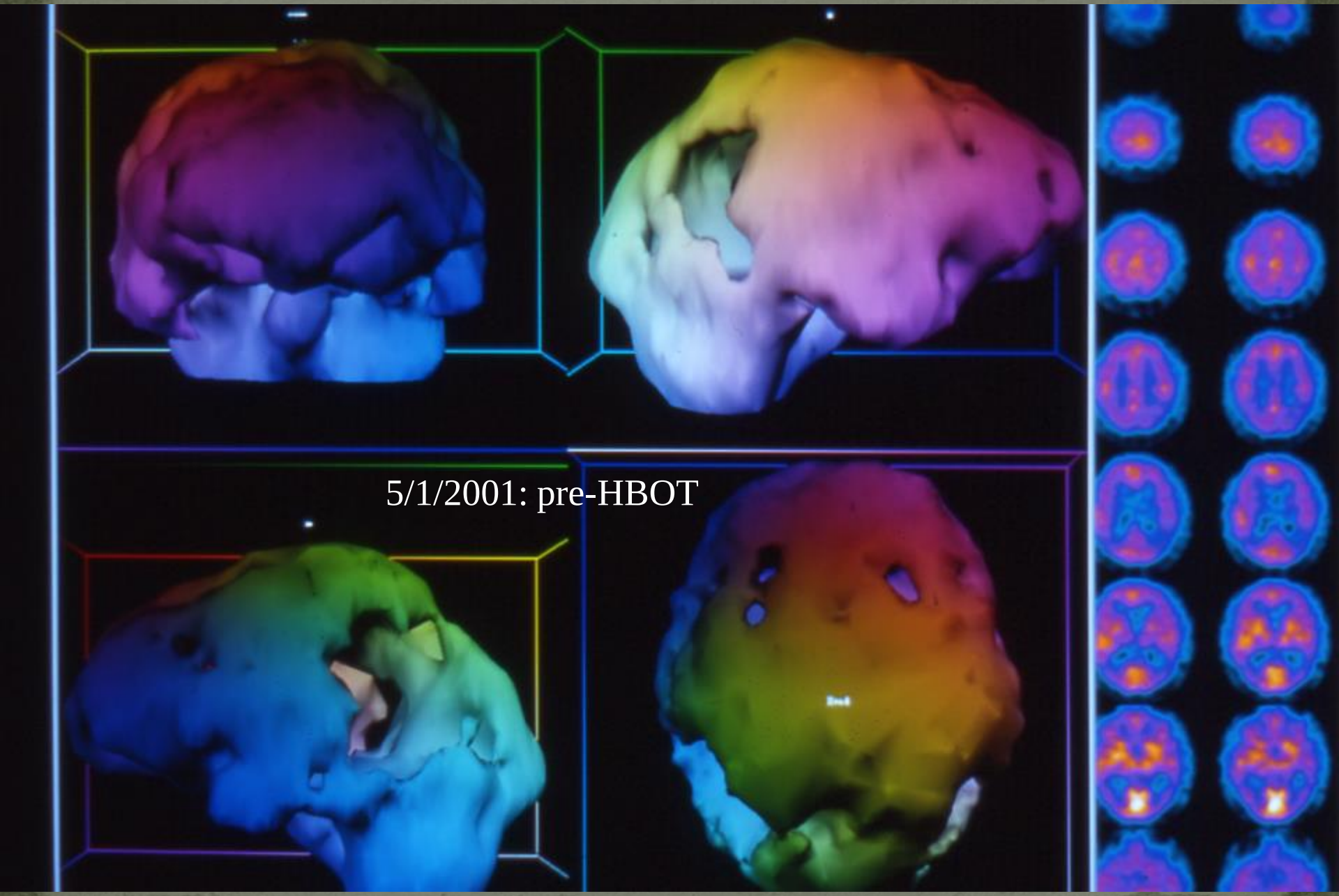
Most, if not all, of the applications of HBOT discussed today will be FDA off-label, i.e., the practice of hyperbaric medicine according to the 2000 year old Hippocratic Oath.

Case Presentation
Alzheimer's Disease

- 58 year old male. Decline in work & memory 8 years before HBOT.
- Alzheimer's diagnosis 5½ years before HBOT; started on Aricept.
- Continued decline over next 3 years.
- Failure Neotrophin and Exelon
- Begins CPAP 1/01 for 10 year history of sleep apnea. Wife notes improvement in cognition & behavior.
- 89 HBOT treatments in blocks: 5/1/01-9/14/01:
  Progressive slow improvement in cognition/behavior.
  Generalized improvement in memory scores.
  Symptomatically better.
  Patient taken off Exelon subsequently due to side effects.
  Periodic HBOT in small doses. Transient improvement in affect.
  Slow deterioration cognitively.
  Re-institution of Exelon and additional medications.

Harch PG. Townsend Letter, April, 2018:417:30-34



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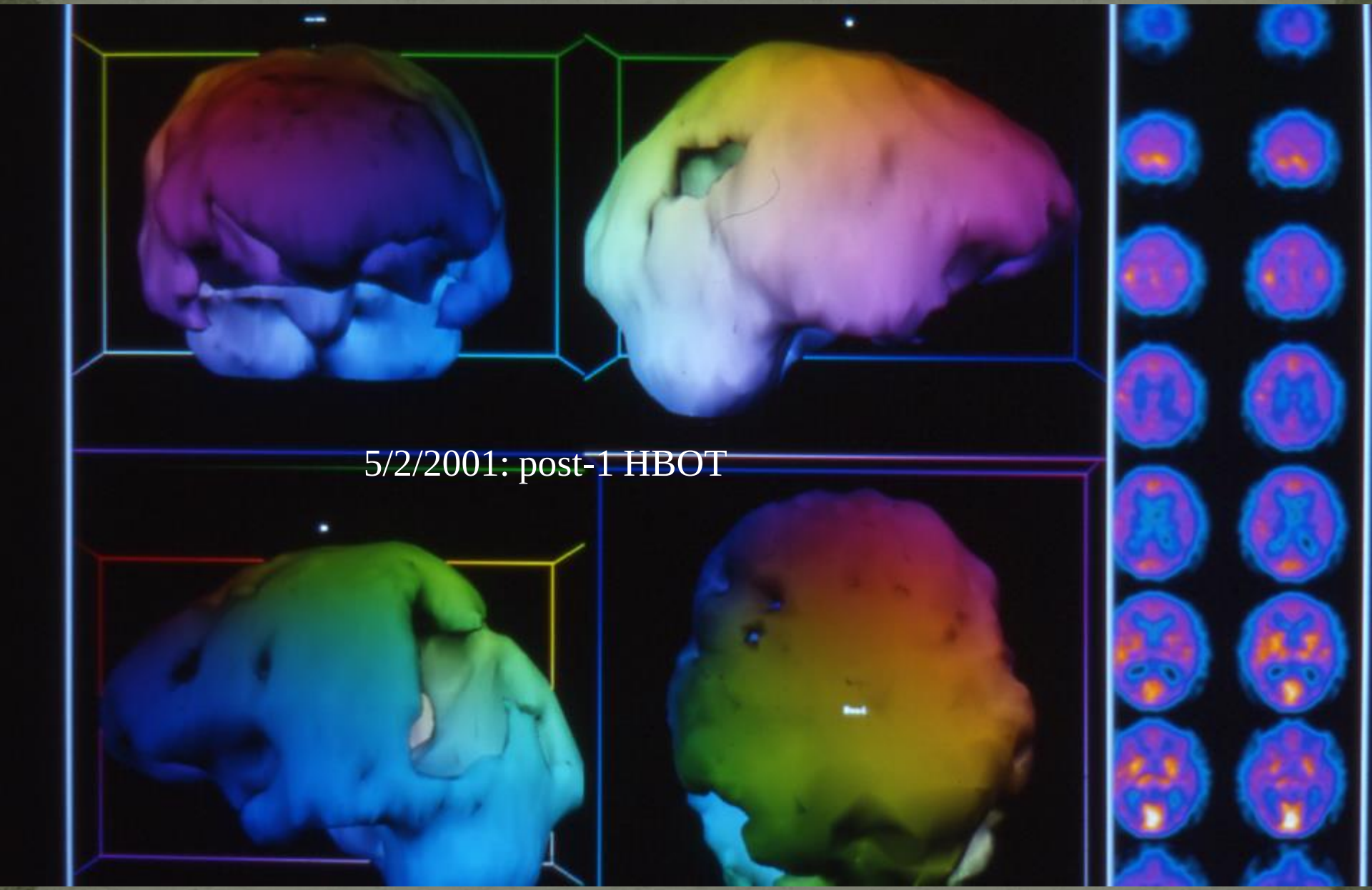

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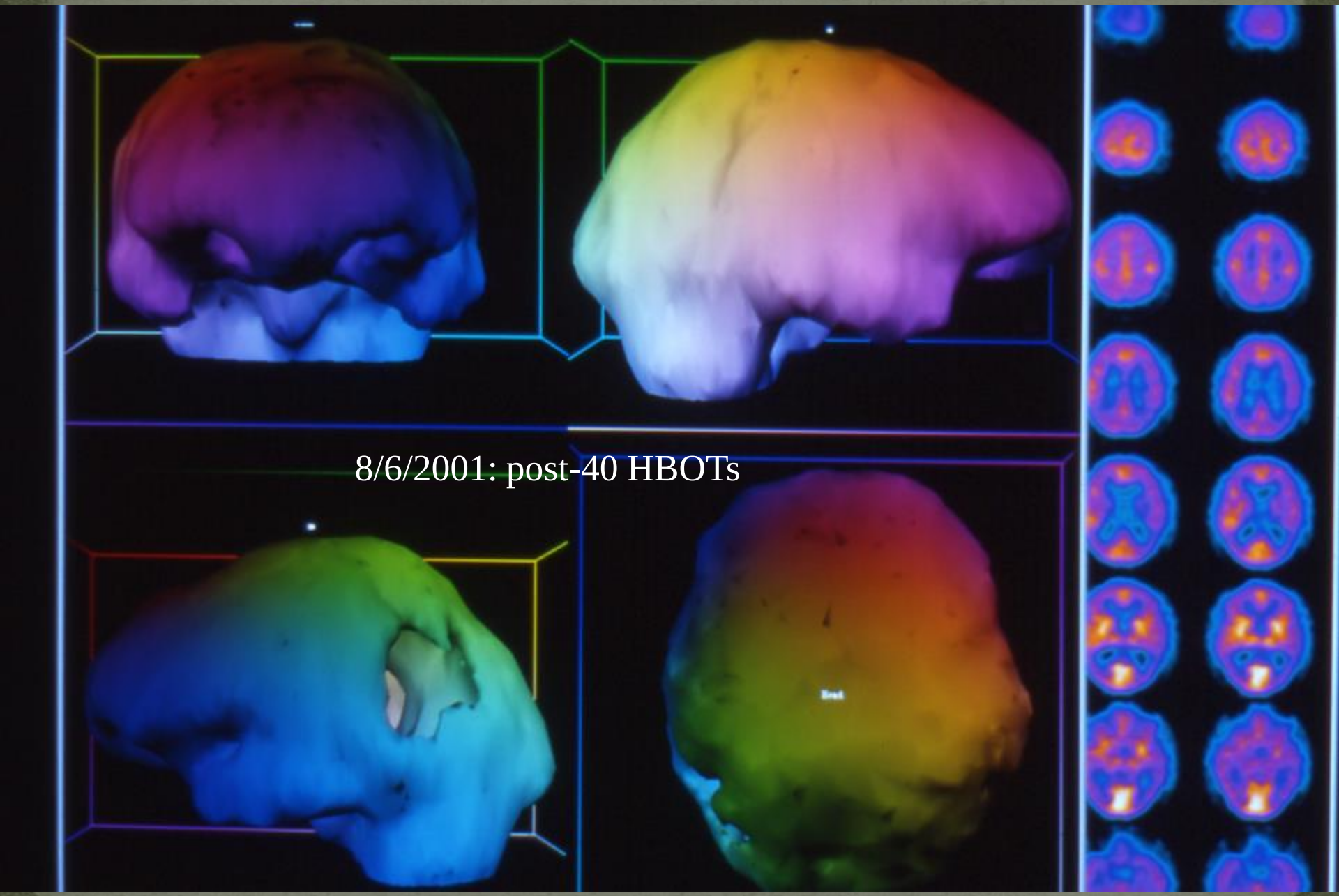

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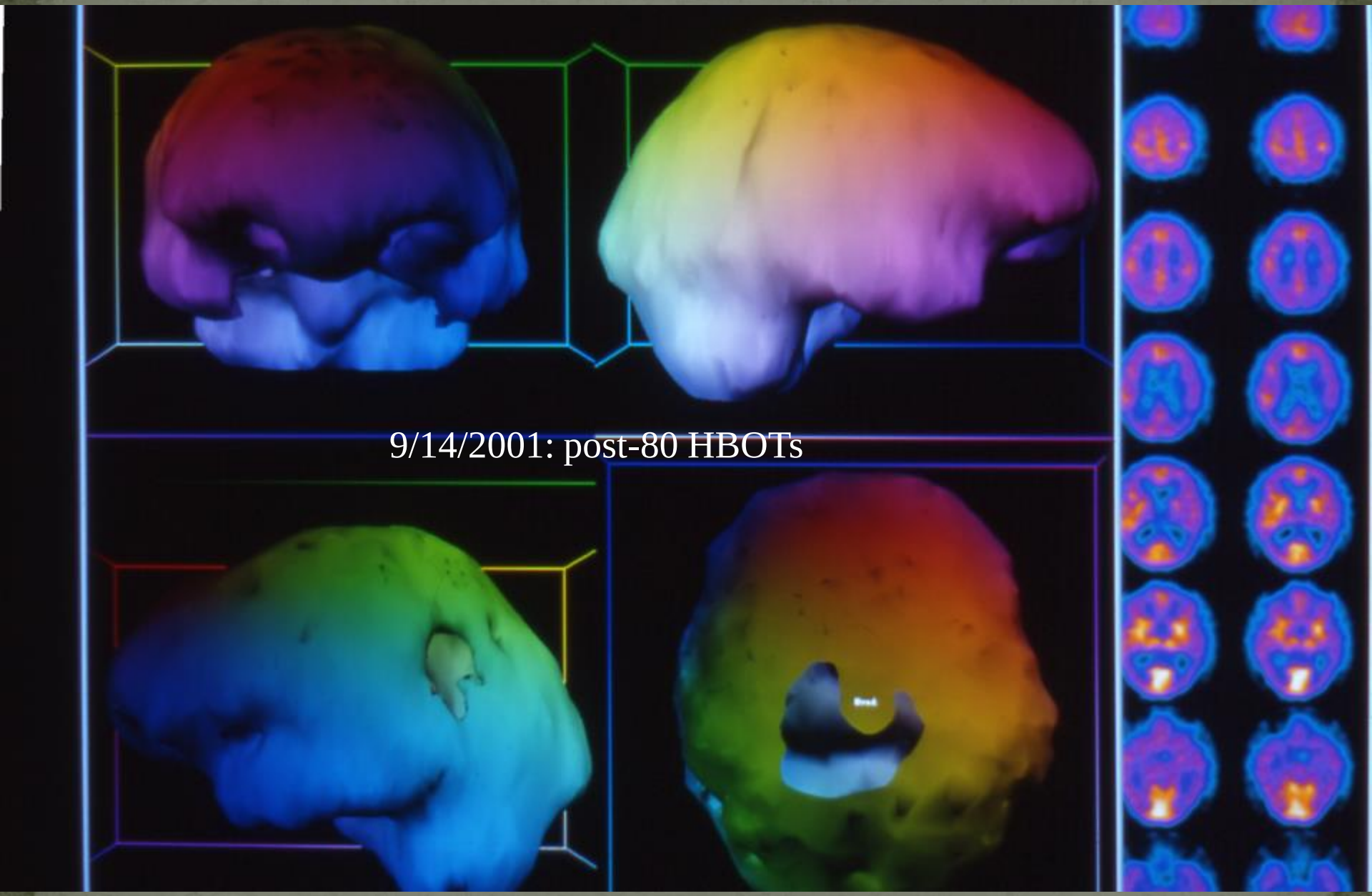


Harch PG. Townsend Letter, April, 2018:417:30-34

WHAT IS HYPERBARIC OXYGEN THERAPY?

Physiologic Definition of HBOT

Hyperbaric Oxygen Therapy is the use of increased…pressure and increased oxygen… as DRUGS to treat pathophysiologic processes of diseases.[1]

1. HBO Therapy in Global Cerebral Ischemia/Anoxia and Coma. Chapter 20. Textbook of Hyperbaric Med., 6th Edition, K.K. Jain (Ed.), 2017.

HBOT as a Drug

"A Re-appraisal"

The basis of HBOT:

The Physiology and Biology of Intermittent Hyperoxia and Hyperbaric Pressure

Human blood vessel cells

Godman CA. Cell Stress and Chaperones, DOI 10.1007/s12192-009-0159-0 (Courtesy Dr. Philip James)

A single HBOT:

8,101 genes turned on or turned off.

Turned on Genes:

Growth and Repair Genes,

Anti-inflammatory Genes.

Turned off genes:

Inflammatory Genes

Cell death Genes

HBOT: Scientific Foundation and Applications to Neurodegenerative Disease

What is Neurodegeneration?

Neurodegenerative Disease

Neurodegeneration corresponds to any pathological condition primarily affecting neurons.

Neurodegenerative diseases represent a large group of neurological disorders with heterogeneous clinical and pathological expressions affecting specific subsets of neurons in specific functional anatomic systems; they arise for unknown reasons and progress in a relentless manner. (A disease of neurons).

Does not include those diseases with neuronal death due to known causes such as hypoxia, poison, metabolic defects, or infections.

????

Przedborski S. J Clin Invest, 2003;111(1):3-10

Neurodegenerative Disease

Hundreds of different neurodegenerative disorders, the more common of which are:

AD, PD, HD, ALS, CTE, Lewy Body Dementia, Prion disease, Motor Neuron Disease,Spinocerebellar ataxia, Spinal muscular atrophy, cortico-bg degen., FT dementia, others.

By 2040 WHO estimates that neurodegenerative diseases will be the second leading cause of death after cardiovascular disease in developed countries.[1]

Katharine Gammon. Neurodegenerative Disease: Brain Windfall. Nature, 2015:515:299-300.

Neurodegenerative Disease Biology:

Apoptosis, oxidative stress, mitochondrial dysfunction.[1,2]

Persistent inflammation and oxidative stress are crucial factors of ongoing cell damage.[3]

Essentially, Neurodegenerative Diseases are partially characterized by persistent wounding.

1. Przedborski S. J Clin Invest, 2003;111(1):3-10
2. Jomova K. Mol Cell Biochem, 2010;345:91-104.
3. Miller E. Frontiers in Bioscience, Elite, 2017;9:214-234.

Neurodegenerative Disease

Biology: Reminder

Wounding in the body and central nervous system can occur by any number of different insults:

(ischemia, hypoxia, toxin, mechanical, electrical, etc.)

all of which generate the dominant
SECONDARY INJURY

(reperfusion injury, inflammation, edema, ischemia, hypoxia)

Neurodegenerative Disease Etiology:

With few exceptions, the causes of NDD are essentially unknown. Even when identified, the mechanisms…remain, at best, speculative:

Genetic factors: 10% of PD, AD, and ALS are unequivocally familial.[1]

For "sporadic" NDD cases, the vast majority of NDD patients, genetic contribution is minimal. Toxic environmental factors may be the prime suspects, but sporadic cases may result from a combination of genetic and environmental causes.[1]

EXAMPLE: Inhaled particulate matter may significantly contribute to neurodegenerative disease through neurotoxic effects (Inflammation, ROS/oxidative stress, disturbance of protein homeostasis/neurotransmitters)[1]

1. Przedborski S. J Clin Invest, 2003;111(1):3-10
2. Wang Y. J Applied Toxicology, 2017; (wileyononlinelibrary.com) DOI 10.1002/jat.3451

Neurodegenerative Disease Treatment:

For the most part, none.

Symptom modulation.

Minimizing oxidative stress.

Antioxidant and redox therapies: Vitamin C, Vitamin E, glutathione, Lipoic acid, Flavenoids (catechins-green tea, curcumin), ginkgo biloba, Coenzyme Q_{10}, selenium, Omega-3 fatty acids, melatonin, cannabinoids, physical exercise.[1,2]

1. Jomova K. Mol Cell Biochem, 2010;345:91-104.
2. Miller E. Frontiers in Bioscience, Elite, 2017;9:214-234.

Neurodegenerative Disease

Treatment:

Hyperbaric oxygen therapy?

Neurodegenerative Disease Treatment:

HBOT Paradox:

NDD is caused?/propagated by oxidative stress.

HBOT causes oxidative stress.

Oxidative stress is necessary for the beneficial effects of HBOT.[1]

Too much oxidative stress is harmful.

Yet, the net effect of HBOT is reduction of oxidative stress and inflammation.

Solution:

Achieving the right amount of oxidative stress through proper dosing of HBOT

1. Thom, SR, et al. J Neurobiol, 2002;51:85-100.
2. Poff A, et al. Compr Physiol, 2017;7:213-234.

HBOT-Dosing in Neurodegenerative Disease

- The benefits of HBOT are in the proper dosing of oxidative stress (Harch, 1998).
- Joseph Priestly, 1774: "Though pure dephlogisticated air (oxygen) might be useful as a medicine, it might not be so proper for us in the usual healthy state of the body: for as a candle burns out much faster in dephlogisticated than in common air, so we might, as may be said, live out too fast and the animal powers be too soon exhausted in this pure kind of air."

Neurodegenerative Disease

Remember:

HBOT Gene Effects:

1. Godman, et al: Anti-inflammatory genes upregulated, pro-inflammatory and apoptotic genes down-regulated
2. Kendall, et al: Inflammatory and apoptotic genes down-regulated.
3. Chen, et al: Neuro-protective and anti-oxidant genes up-regulated.

Neurodegenerative Disease

Remember:

Multiple studies of HBOT effects on inflammation, oxidative stress, and apoptosis in acute global ischemia/anoxia and coma.[1]

Chronic study:

HBOT effects on degenerative human intervertebral disc cells: 2.5 ATA/120 mins. qod x 3.

HBOT suppressed inflammatory signaling and mitochondrial apoptotic pathways.[2]

1. Harch PG. Chapter 20, Textbook of Hyperbaric Medicine, ed. K.K. Jain. 2017.
2. Niu C-C, et al. J Orthop Res, 2013;31:204-209.

Neurodegenerative Disease

HBOT Effects on Mitochondrial Function (A primary biological dysfunction in NDG Dis):

1. Daily hyperbaric oxygen therapy for life improves mitochondrial function and delays onset of motor disease in Wobbler mice (ALS model). Dave KR, et al. Neuroscience, 2003;120:113-120. 2 ATA/60 minutes/d x 30.
2. Oxygen-Induced Mitochondrial Biogenesis in the Rat Hippocampus. Gutsaeva DR, et al. Neuroscience, 2006;137:493-504. 3 or 5 ATA/45 minutes TDT.
3. Endurance performance is enhanced by intermittent hyperbaric exposure via up-regulation of proteins involved in mitochondrial biogenesis in mice. Suzuki J. Physiol Rep. 2017;5(15): e13349, https://doi.org/10.14814/phy2.13349. 1.3 ATA air/60 minutes TDT, qd, 6d/week, x 24.

HBOT in Neurodegenerative Disease: Dementia

- Definition: Dementia is the loss of cognitive functioning—thinking, remembering, and reasoning—and behavioral abilities to such an extent that it interferes with a person's daily life and activities.[1]
- Types: Alzheimer's (60-70%), Vascular (25%).[2]

- 1. https://www.cdc.gov/chronicdisease/resources/publications/aag/alzheimers.Htm
- 2. Perng C-H. Psychopharmacology, 2018;235:1571-1580.

HBOT in Dementia

- Literature Review: HBOT in Vascular dementia

9 human studies on vascular dementia, all in inaccessible Chinese journals.

Multiple case reports of HBOT in post-CO dementia.

- Cochrane Review, 2012 (Xiao Y, et al. Cochrane Database Syst Rev, 2012;7:Art. No.: CD009425.
  - Single article: Wang SP, et al. Chinese Journal of Physical Med & Rehab, 2009;31(7):478-80.
  - RCT, 64 patients, vascular dementia.
  - Donepezil, 5mg qd +/- HBOT: 2 ATA (97% O2)/60 qd x 24 consecutive days, 6d rest, x 3 or 72 HBOTs
  - Measure: Mini Mental Status and Hasegawa's Dementia Rating Scale
  - Results: Significant improvement both measures in HBOT group vs. Controls (6.2 vs. 3.2 points on MMSE and 7.2 vs. 3.7 points on Hasegawa)
  - Cochrane conclusion: Insufficient evidence to support HBOT as an effective treatment for patients with vascular dementia.

1. Xiao Y. Cochrane Database of Systematic Reviews, 2012;7:Art. No.: CD009425. www.cochranelibrary.com

HBOT in Dementia

- Literature Review: HBOT in Dementia
- Studies with positive results:
  - Edwards AE. J Am Geriat Soc, 1974;22:376-379.
  - Boyle E. Proc. 5th Int HBO Conf, W.G. Trapp (Eds.), Simon Fraser Univ., Canada, 1974; pp. 432-438.
  - Jacobs EA. J Geriat Psychiatr., 1972;5:107-136.
  - Jacobs EA. NEJM, 1969;281:753-57.
  - Jacobs EA. Current Psychiatric Therapy, Vol. II, H Masserman (Ed.), Grune and Stratton, Phila, 1971: pp. 100-106.
  - Jacobs EA. Proc. 5th Int HBO Conf., WG Trapp (Eds.), Simon Fraser University, Canada,;1974; pp. 439-445.
  - Ben-Yishay Y. NY State J Med, 1973;73:2877-2880.
  - Ben-Yishay Y. Proc. 5th Int HBO Conf, WG Trapp (Eds.), Simon Fraser University, Canada, 1974; pp. 424-431.
  - Ben-Yishay Y. NY State J Med, 1978;78:914-919.

Schmitz GF. Evaluation of HBOT for Senility. HBO Review, 1981;2(4):231-250.

HBOT in Dementia

- Literature Review: HBOT in Dementia
- Studies with negative results:
  - Thompson LW. J Gerontol, 1976;31:23-28.
  - Raskin, A. Arch Gen Psychiatry, 1978;35:50-56.
  - Goldfard AI. J Gerontol, 27:212-217.
- Conclusions:
  - "At the present time there is no basis for claiming that hyperbaric oxygen is beneficial in reversing senility or any other central nervous system deficit which occurs in the aged. There is a lack of scientifically sound data on this topic."

Schmitz GF. Evaluation of HBOT for Senility. HBO Review, 1981;2(4):231-250.

HBOT in Dementia

- Literature Review: HOWEVER!
  - Meta-analysis on treatment of dementia
  - Review of literature 2000-2016
  - 235 studies, 44,854 patients, vascular, Alzheimer's dementia, mild cognitive impairment, and mixed.
  - Reviewed 5 types of treatments:
    - Antipsychotic drugs and cognitive enhancers
    - Symptomatic treatment drugs for Vascular Dementia (piracetam, nimodipine, aniracetam, flunarizine, vinpocetine, HBOT, oxiracetam, or EGB761).
    - Behavioral therapy (exercise, music, reminiscence, rehab, cog, PT
    - Adjunctive therapy (Chinese herbal and medicine, decoctions
    - Other alternative treatments: scalp acupuncture, Premarin, statin, butylphthalide soft capsules, donepezil, huperzine A, and lithium

Perng C-H. Psychopharmacology, 2018;235:1571-80.

HBOT in Dementia

- Literature Review:
  - Results:
    - Treatment 1 lowest efficacy.
    - Treatment efficacy increases with publication year and decreases with age of the patient.
    - Treatment 2 and Treatment 4 had the highest efficacy for treating cognitive dysfunction
    - Vascular Dementia patients had the greatest cognitive improvement.
    - Treatment 2 and Treatment 5 had the highest efficacy vs. other treatments (p=.010 and .001) in relatively young patients with vascular dementia.
    - Alternative therapies are effective in the treatment of dementia.

Perng C-H. Psychopharmacology, 2018;235:1571-80.

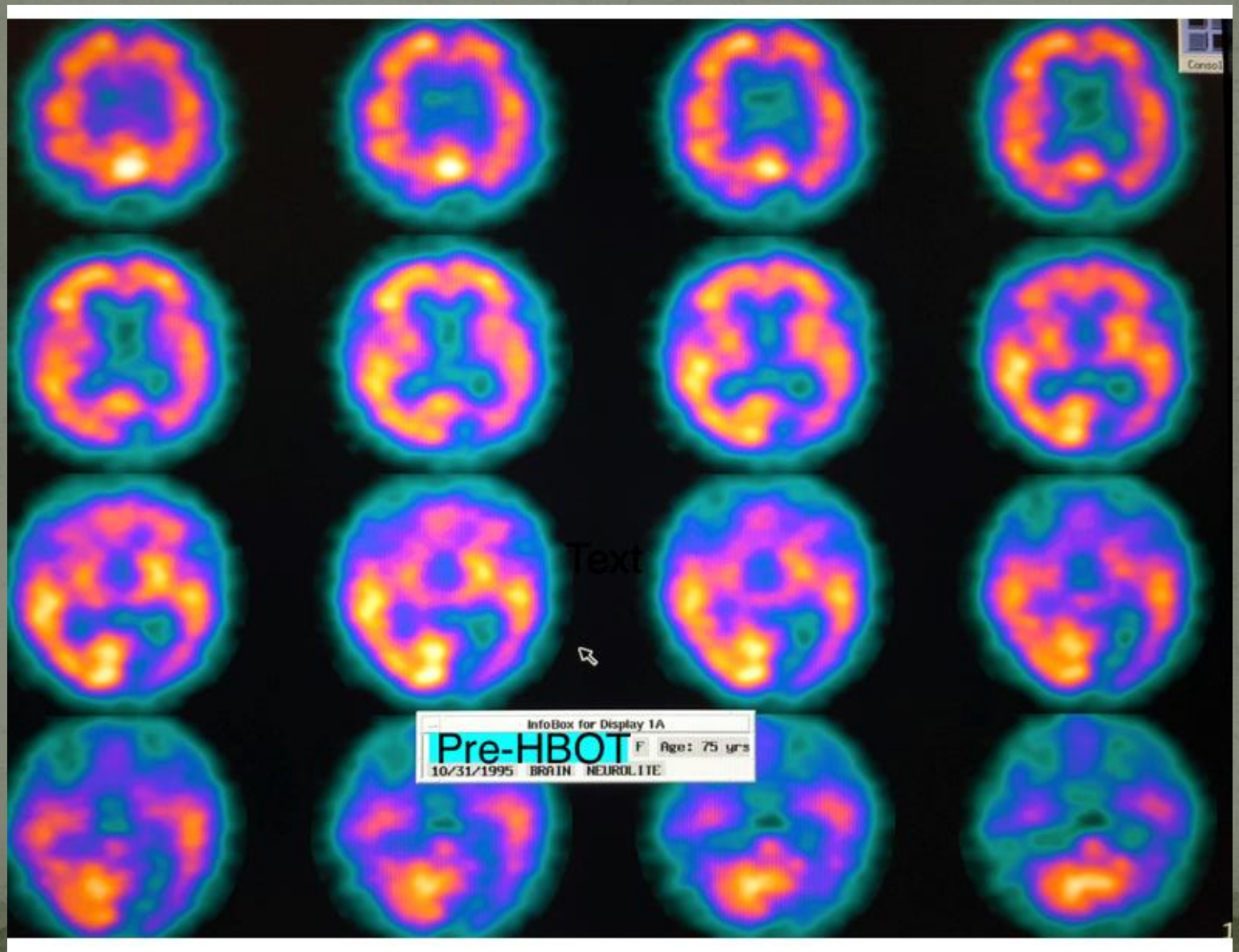
HBOT in Dementia-Case #1

- Lecturer's personal experience:
  - First case in 1995.
    - 75 y.o. female, urosepsis/shock in 1992, coma x one week, progressive decline in mental function noted by treating physicians, disputed by husband.
    - Repetitive falls 1-3/1994 without TBI, RSD LUE due to injury.
    - 24h nursing care.
    - 9/1994: fall, subdural hematoma, accelerated decline in mental status.
    - 10/1995: evaluation in New Orleans
      - Incontinence, hostility, blind right eye, wheelchair-bound, depressed, disorient, blank stare.
      - MRI: 8/95: atrophy + multiple small CVAs (right caudate, corona radiata, internal capsule, left occiput).
      - Neuropsych testing: "failed."
      - PMH: RA, DM.
      - Folstein: 11, after 3rd HBOT.
      - SPECT, dive, SPECT.
      - 38 HBOTs, 1.5/60, 11-12/1995, bright, alert, increased ADL's, Folstein 13

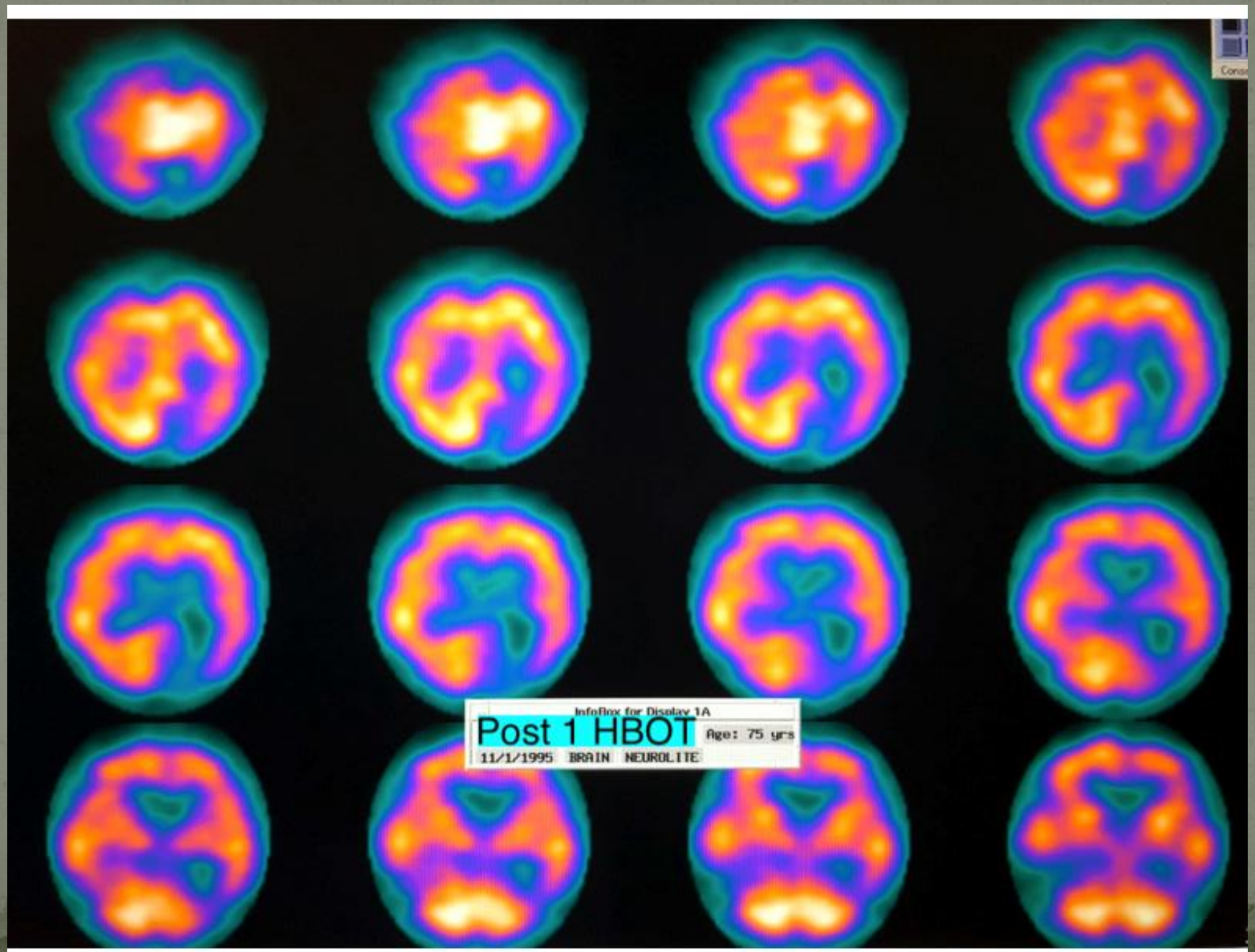
HBOT in Dementia-Case #1

- Lecturer's personal experience:
  - First case in 1995.
    - 30 HBOTs 1-3/1996, total 68 HBOTs. peak improvement at 19, total 57, mild deterioration afterward.
    - Clinically improved: conversational, not combative, feeding self independently, incontinence decreased, diaper frequently dry and signals that needs to use bathroom, watching TV and reacting appropriately to events/news.
    - PEx: bright alert, follows commands, gets out of chair unassisted, unassisted gait.
    - Husband made non-profit donation that funded TBI animal study: human protocol of HBOT in chronic TBI, became first and only improvement of chronic animal brain injury in history of science.
    - Repeat SPECT after 57th HBOT.
    - Second case (vide supra): 2001, presented to congress 2002.

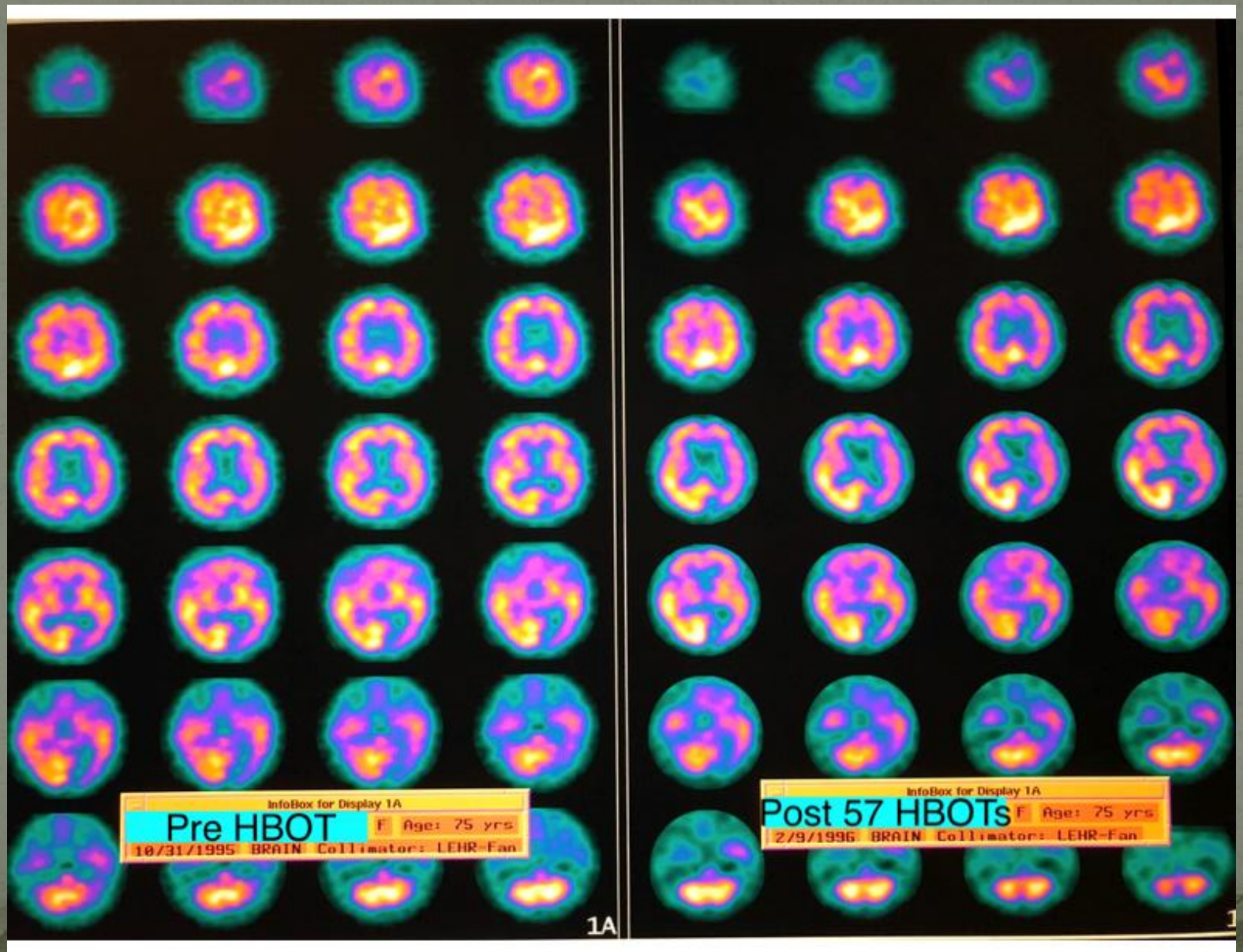
HBOT in Dementia-Case #1-Pre-HBOT



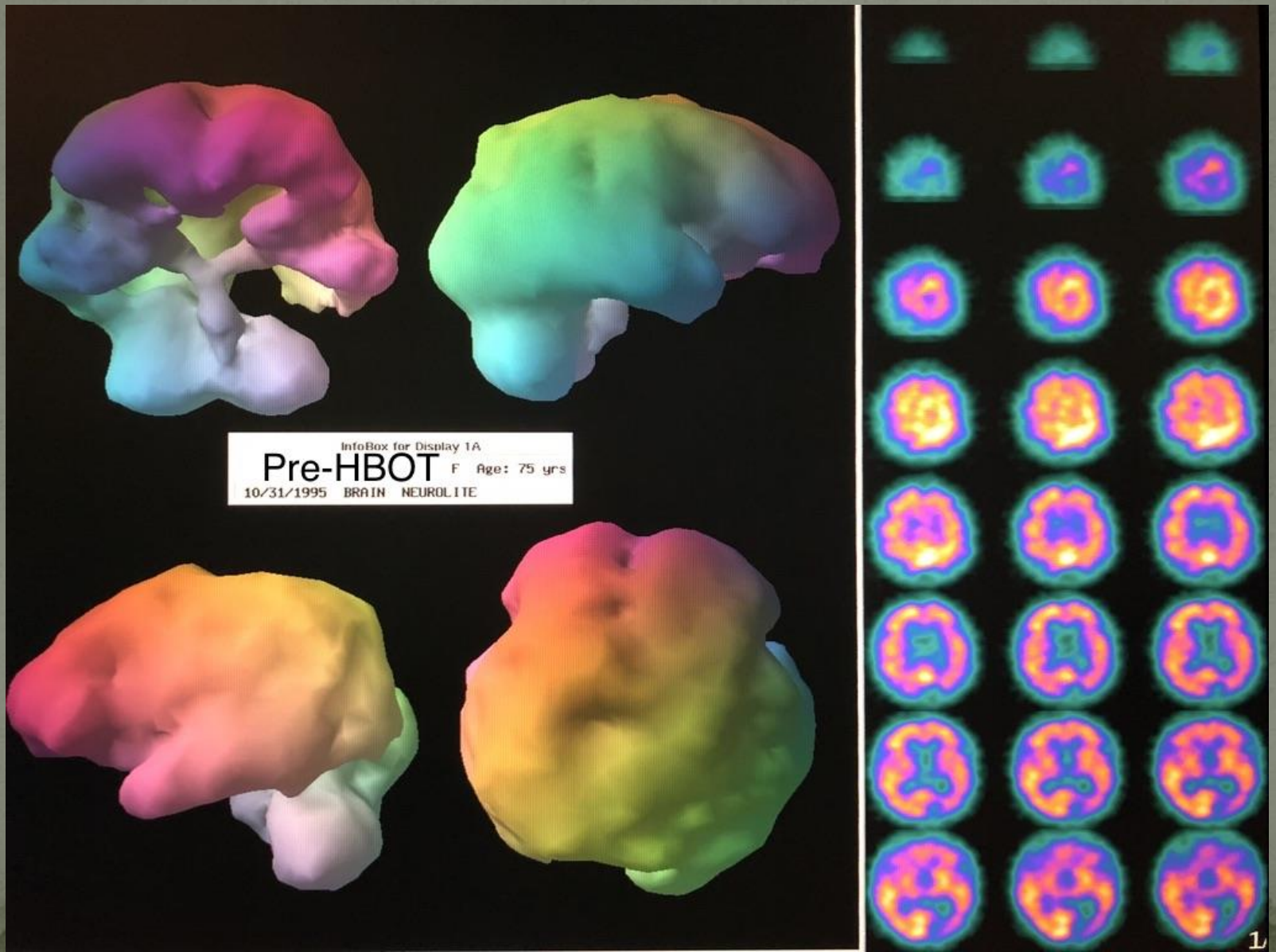
HBOT in Dementia-Case #1-Post 1-HBOT



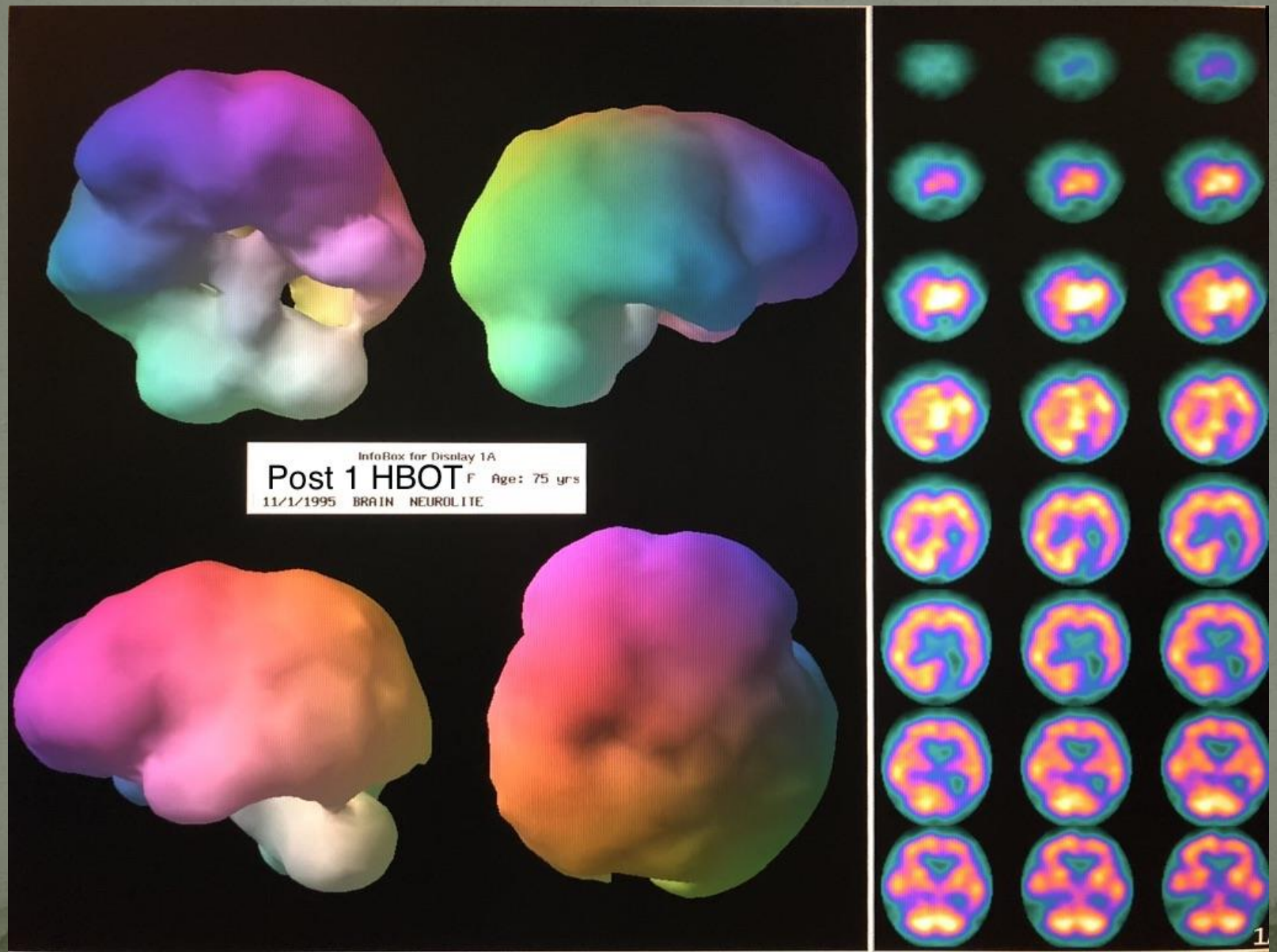
HBOT in Dementia-Case #1-Pre/Post 57 HBOTs



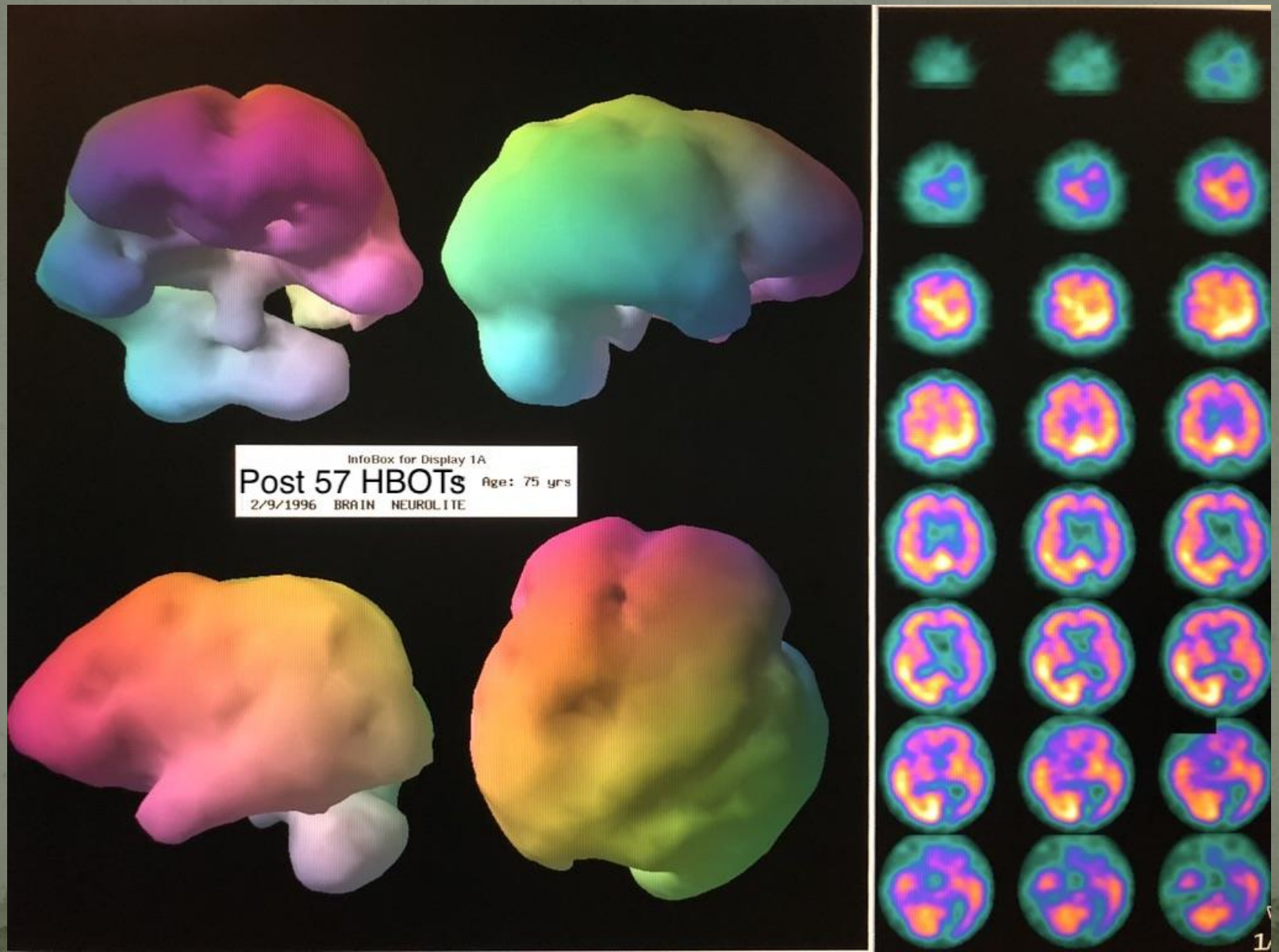
HBOT in Dementia-Case #1-Pre HBOT



HBOT in Dementia-Case #1-Post 1 HBOT

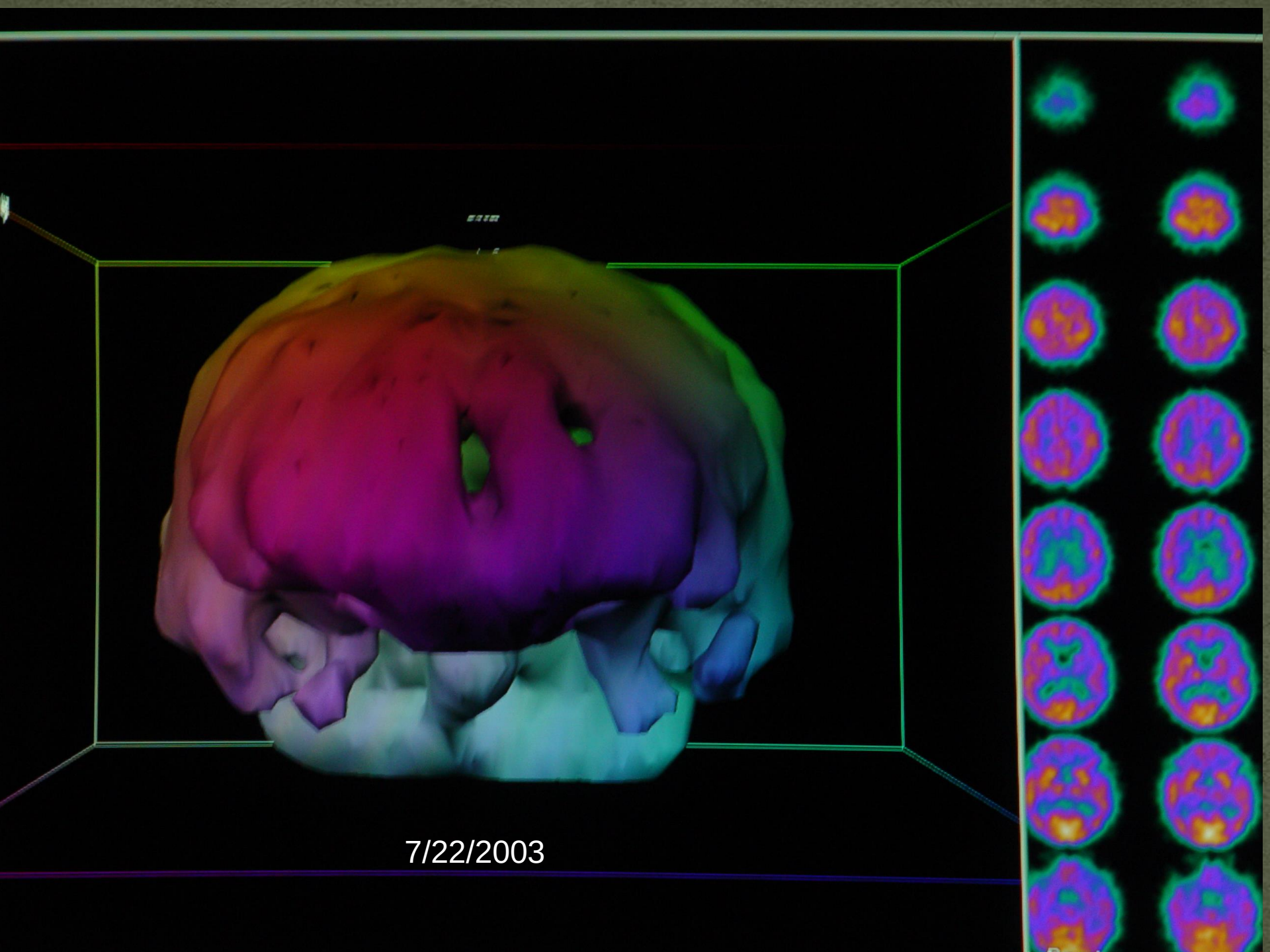


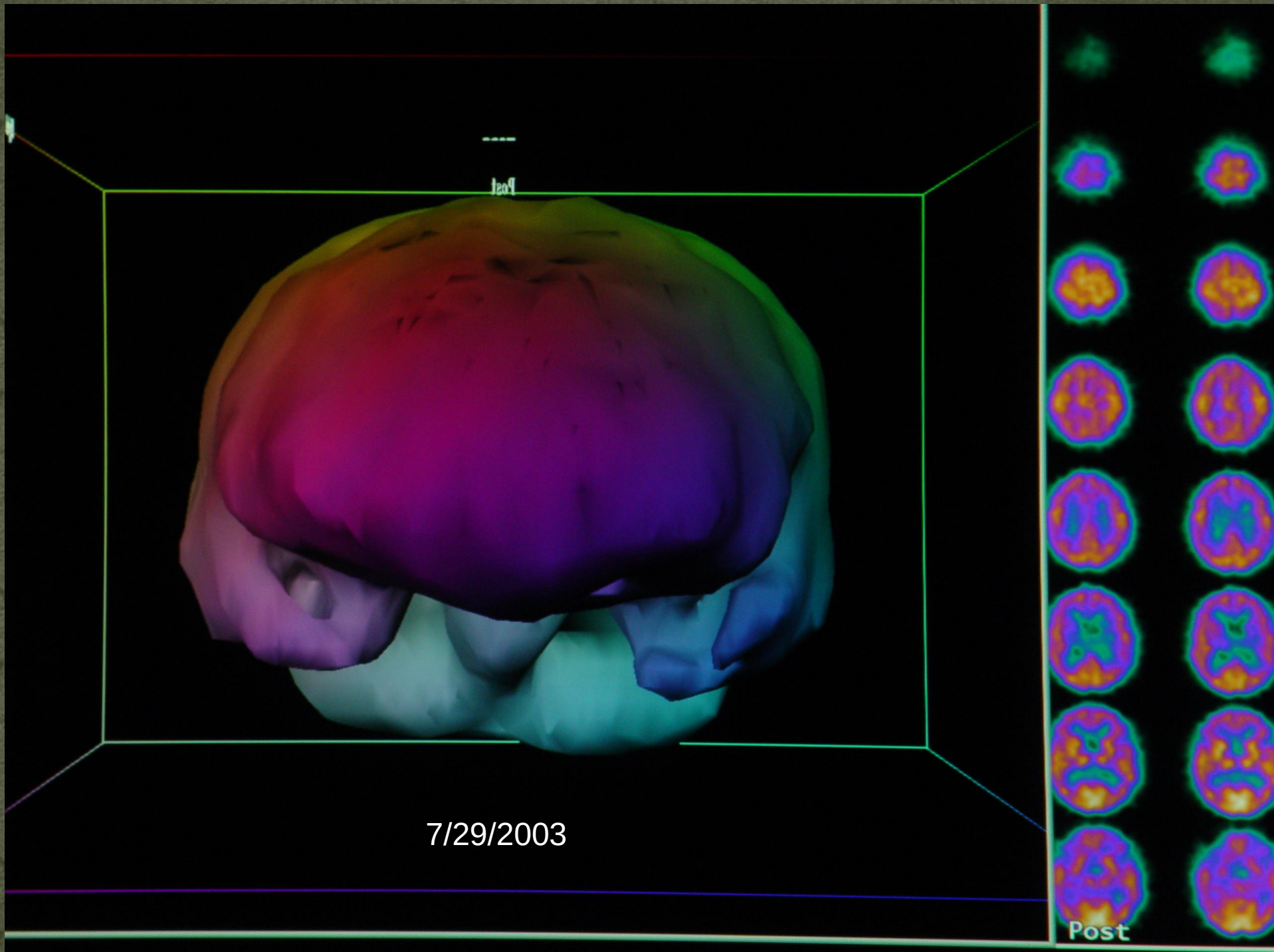
HBOT in Dementia-Case #1-Post 57 HBOTs

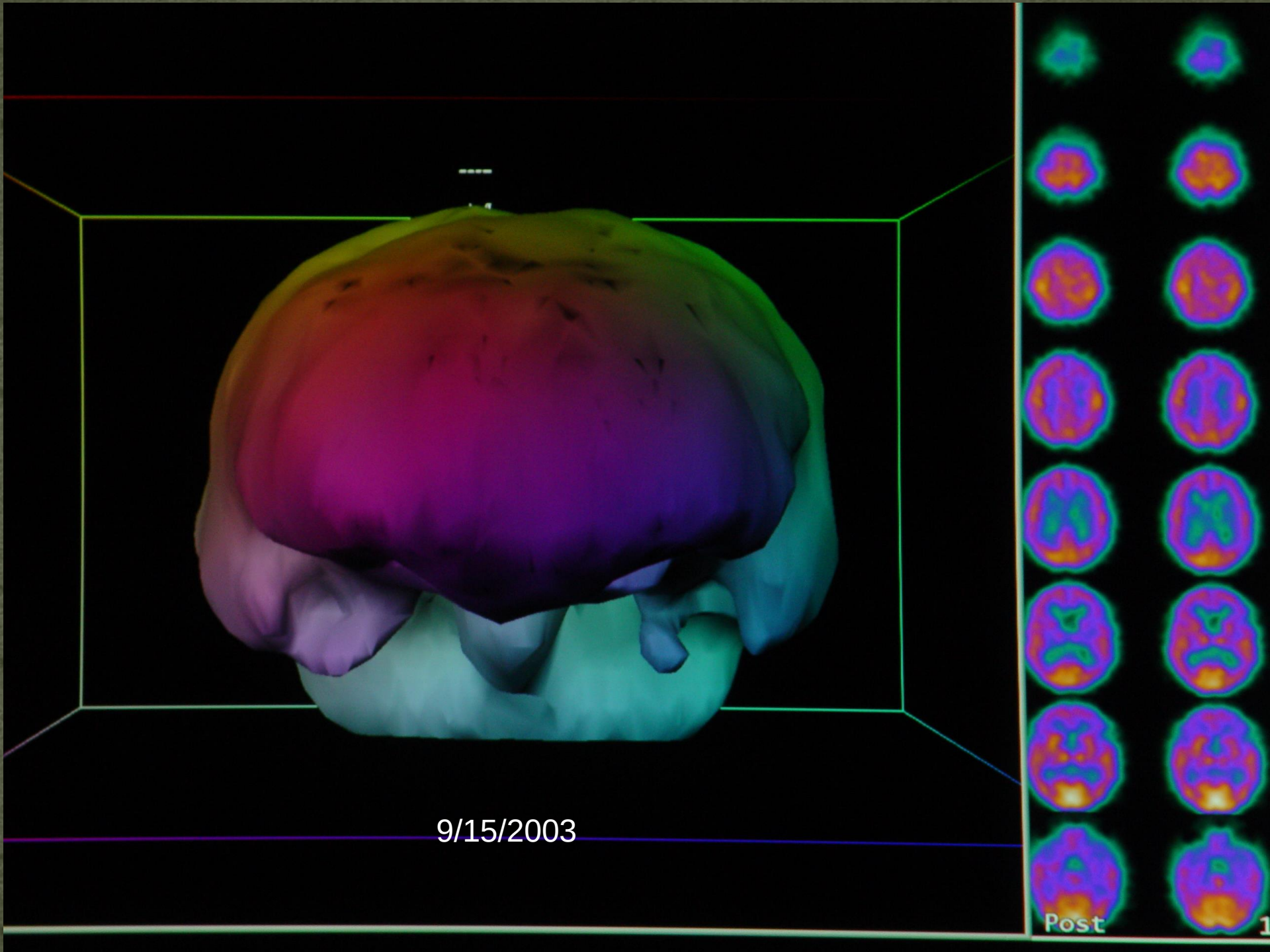


Case #3: 72 year old demented man facing institutionalization after death of wife

- Four months: nightly confusion, memory loss, paranoia, and inappropriate behavior. Removal from grandchildren's home.
- Three hospital admissions for GI bleed in three months.
- Emergency department visit for dementia and dehydration.
- Deterioration in flight to New Orleans with emergent hospital admission.
- 6th hospital admission: upon arrival inNew Orleans, Dx: dementia and SOB. PMH: Long history of alcohol and tobacco abuse with several TBI's and CO exposure (Normal aging?).
- PEx: Cachectic, SOB elderly man. Folstein: 15/30. 40 HBOT's:
  - Generalized cognitive improvement
  - Increased energy
  - Decreased SOB and confusion
  - Improved sleep, weight gain.
  - Followup: Semi-independent living. Some regression 3 months post HBOT.


7/22/2003


Post
7/29/2003


9/15/2003
Post

HBOT in Dementia

- Lecturer's personal experience:
  - Subsequent ~70+ cases of cognitive decline or dementia
    - All causes: small vessel ischemic disease, post-surgical/anesthesia, trauma, stroke, toxins, Alzheimer's, multiple cause/premature aging.
    - 1.15-1.5 ATA/60-90 minutes, qd, 40 treatments, or more.
    - Functional imaging (SPECT), MMSE, and clinical outcomes.
    - Best results in small vessel ischemic disease, TBI, post-anesthesia, post-chemo, Alzheimer's.
    - Least positive in cortico-basal ganglia degeneration, fronto-temporal dementia (Pick's), Parkinson's (motor findings), multiple systems atrophy.

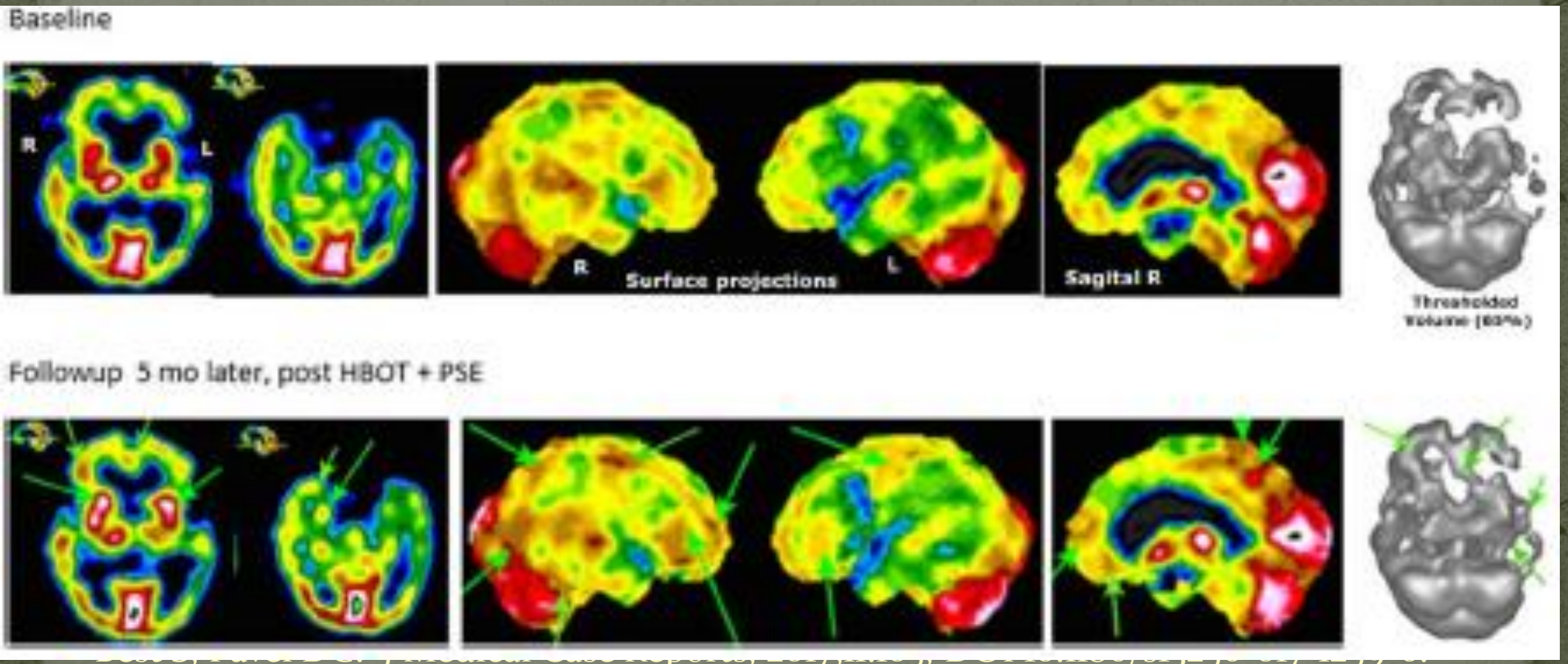
HBOT in Dementia: surgical/anesthesia etiology

- Case Report, Literature Review:
  - 77 y.o. male, 4.5 y post knee replacement.
  - Immediate deterioration post surgery.
  - Demented, unresponsive to pharmacotherapy.
  - HBOT, 1.75 ATA/60 minutes x 40. Post 11th HBOT weekly perispinal Enbrel (etanercept) for 5 months.
  - At the 5 month mark, patient was able to care for himself, go on walks by himself, had return of his personality, normal sleep cycle, interact with others.

Best S, Pavel DG. J Medical Case Reports, 2017;11:105, DOI 10.1186/s13256-017-1259-6.

HBOT in Dementia

- Case Report:
  - SPECT brain imaging at 5 month mark:



HBOT in Alzheimer's Disease

- Alzheimer's Disease Definition: An irreversible, progressive brain disorder that slowly destroys memory and thinking skills, and eventually the ability to carry out the simplest tasks…the most common cause of dementia.[1] Closely connected with deposition of amyloid beta plaques and neurofibrillary tangles in brain tissue.[2]

1. https://www.nia.nih.gov/health/alzheimers-disease-fact-sheet.
2. Miller E. Frontiers in Bioscience, Elite, 2017;9:214-234.

HBOT in Alzheimer's Disease

- Alzheimer's Disease Statistics:
  - Affects 30 million people worldwide,[1] 5.4 million in U.S.[2] Numbers double every 20 y.
  - Comprises 60-70% of all dementia.[3]
  - Costs: $818 billion/y worldwide (1% of global GDP),[1] $259 billion/y U.S.[2]
  - Treatment: largely pharmacotherapy.
  - Of 244 drugs tested from 2002-2012, only one with FDA approval (Onyango, 2018).[4]
  - No therapy has effectively halted disease progression.[4]

- https://www.alz.co.uk/research/statistics
- https://www.cdc.gov/chronicdisease/resources/publications/aag/alzheimers.htm
- http://www.who.int/mediacentre/factsheets/fs362/en/
- Frozza RL. Front Neurosci, 2018;12:37.

HBOT in Alzheimer's Disease

- Single case Report (See above: Harch, PG, congressional testimony 2002 and Townsend Letter 4/2018).
- Recent animal study:
  - Shapira:
    - Old mice: normal and transgenic Alzheimer's mice.
    - Behavioral, histological, and biochemical analyses pre and 24-48h post HBOT or the last behavioral task.
    - HBOT: 2 ATA/60 minutes qd x 14.
    - Results: HBOT reduced inflammation (decreased astrogliosis, microgliosis, IL-1Beta, TNF alpha, and increased scavenger receptor A, arginase 1, IL-4 and 10), reduced hypoxia,k amyloid burden, and tau phosphorylation. Ameliorated behavioral deficits.

1. Shapira R. Neurobiology of Aging, 2018;62:105-119.

HBOT in Alzheimer's Disease

- Lecturer's personal experience:
  - 11 cases since 2001
  - Diagnosis by various neurologists
  - Nearly all on dementia drugs
  - SPECT brain imaging pre/post HBOT on majority
  - HBOT at 1.15-1.5 ATA/60 minutes x 40 (most) or 80.
  - 8 of 11 with clinical and Mini Mental Status improvement.
  - PET imaging pre/post on most recent case:
    - Clinical symptomatic improvement
    - Improvement in FDG PET: average 17% global increase.
    - Subsequent intermittent treatment over 18 months with maintenance of Folstein Mini-Mental Status Score
    - Simultaneous use and disuse of Alzheimer's drugs.

Parkinson's Disease: Definition

- Parkinson's disease (PD) belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing brain cells in substantia nigra. The four primary symptoms of PD are tremor, or trembling in hands, arms, legs, jaw, and face; rigidity, or stiffness of the limbs and trunk; bradykinesia, or slowness of movement; and postural instability, or impaired balance and coordination.[1]

- Pathological characterized as intracellular deposition of alpha-synuclein (AS) in Lewy Bodies; a soluble protein w/ prion-like properties (spreading).[2]

- Essentially, is a multi-system disorder: CNS & PNS.[2]

1. http://www.ninds.nih.gov/disorders/parkinsons_disease/parkinsons_disease.htm
2. Borghammer P. Movement Disorders, 2017; Aug 26. doi: 10.1002/mds.27138. [Epub ahead of print]

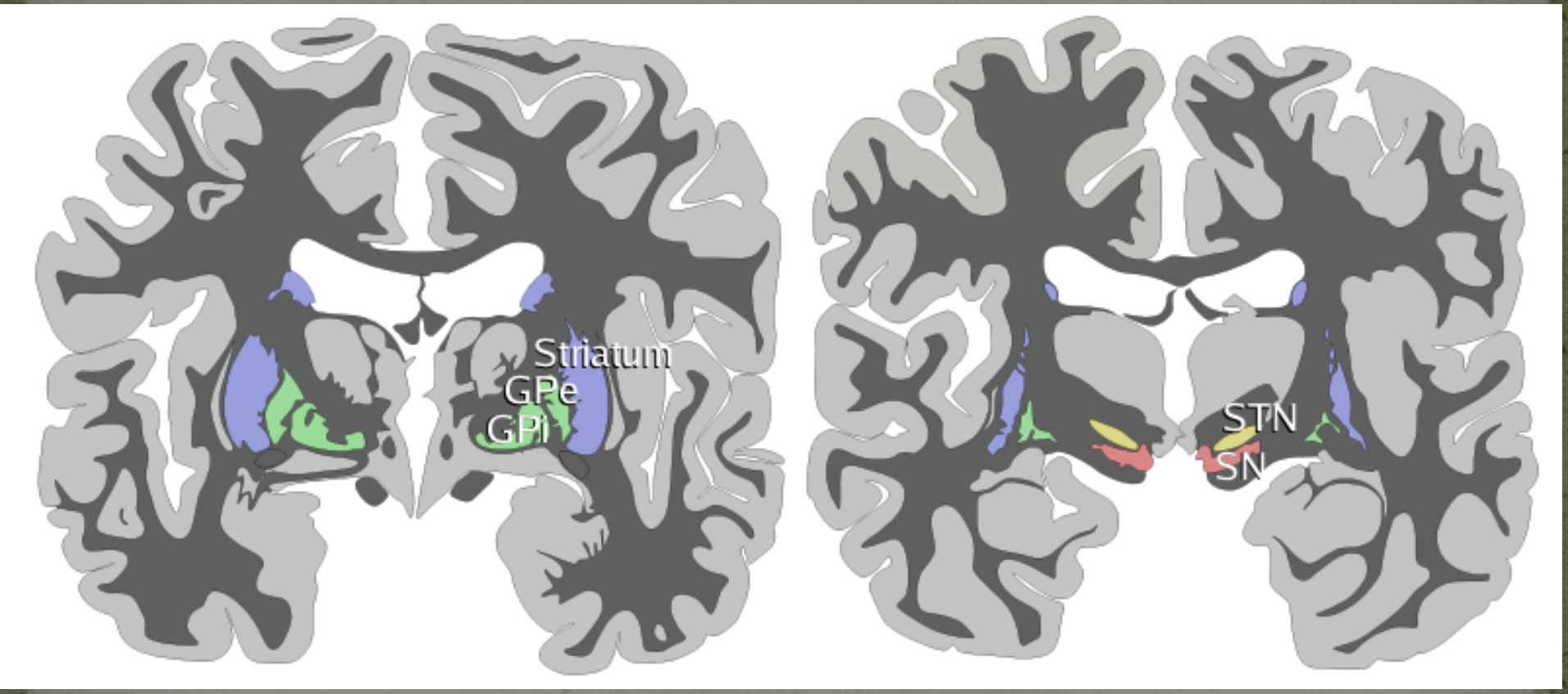
Parkinson's Disease-Pathogenesis

- However, AS affects an array of different neurons, including nigral, cortical, enteric, and cardiac neurons.[1]
- Alpha synuclein deposition in other areas of the brain outside the substantia nigra. may account for the diverse Sx in PD.[2]
- Release of AS from neurons and other evidence points to possible inflammation involvement in the pathogenesis of PD.[1]

1. Engelender S. Trends in Neurosciences, 2017;40(1):4-14.
2. Adler CH. Movement Disorders, 2016;31(8):1114-9.

https://en.wikipedia.org/wiki/Basal_ganglia

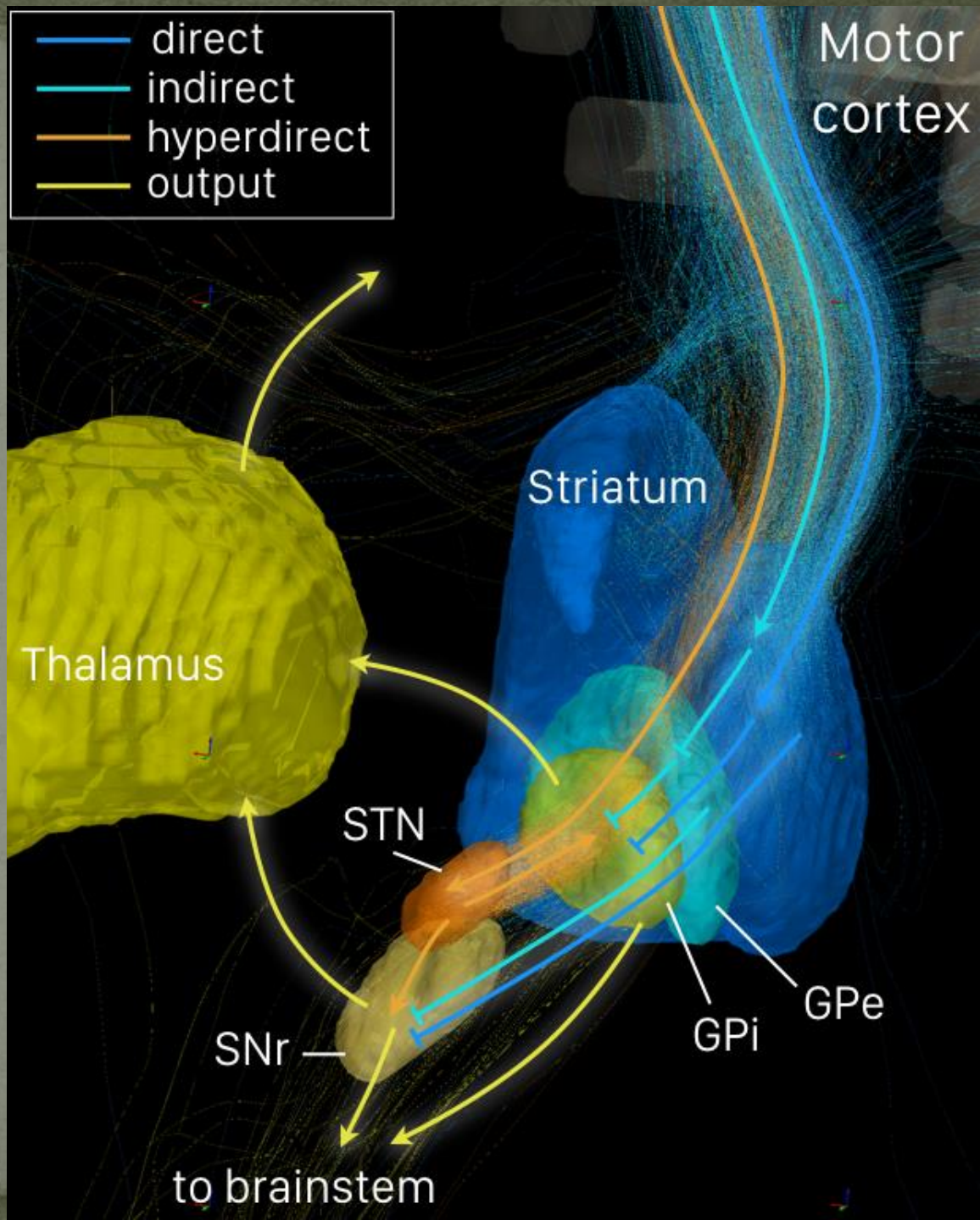
Anatomy of Parkinson's Disease



Coronal slices of human brain showing the basal ganglia. White matter is shown in dark gray, gray matter is shown in light gray.
Anterior: striatum, globus pallidus (GPe and GPi)
Posterior: subthalamic nucleus (STN), substantia nigra(SN)

Connectivity of the basal ganglia

https://en.wikipedia.org/wiki/Basal_ganglia

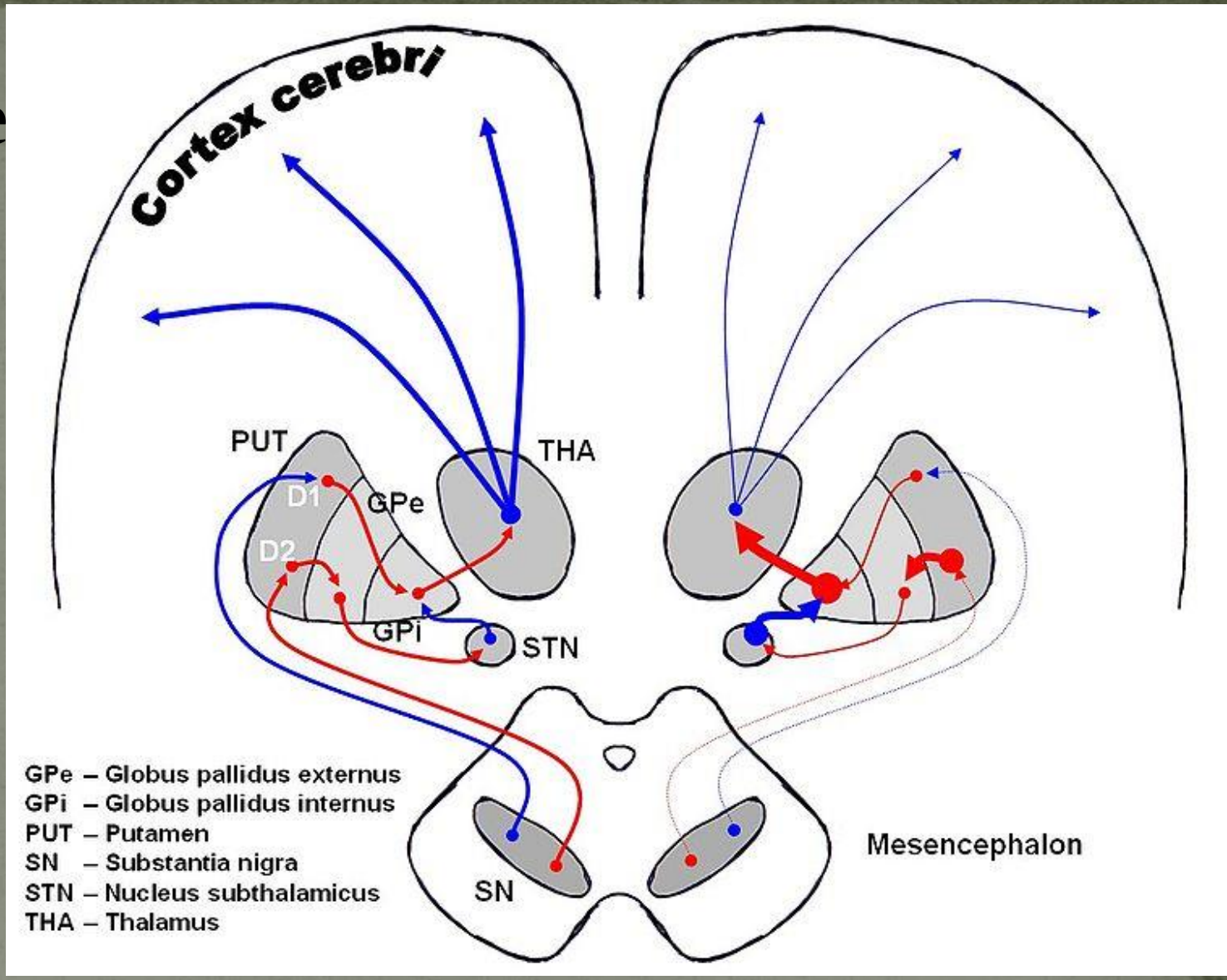


Connectivity of the basal ganglia as revealed by diffusion spectrum imaging based on thirty subjects from the Human Connectome Project. Direct, indirect and hyperdirect pathways are visualized in different colors (see legend). Subcortical structures are rendered based on the Harvard-Oxford subcortical thalamus as well as the Basal Ganglia atlas (other structures). Rendering was generated using TrackVis software.

Parkinson's Disease- Pathogenesis

- Different anatomical areas affected by Parkinson's are subserved by different neurotransmitter systems.
- The primary neurotransmitter is dopamine.
- However, there are multiple others.

Dopamine Pathways In the brain



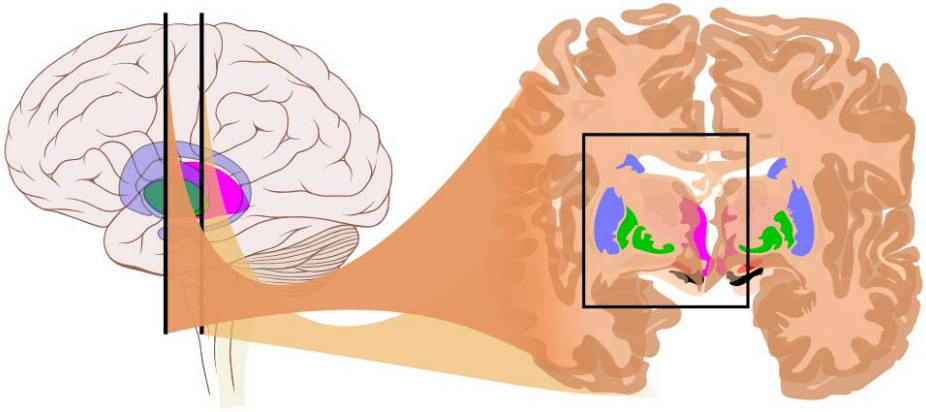
http://en.wikipedia.org/wiki/Ansa_lenticularis

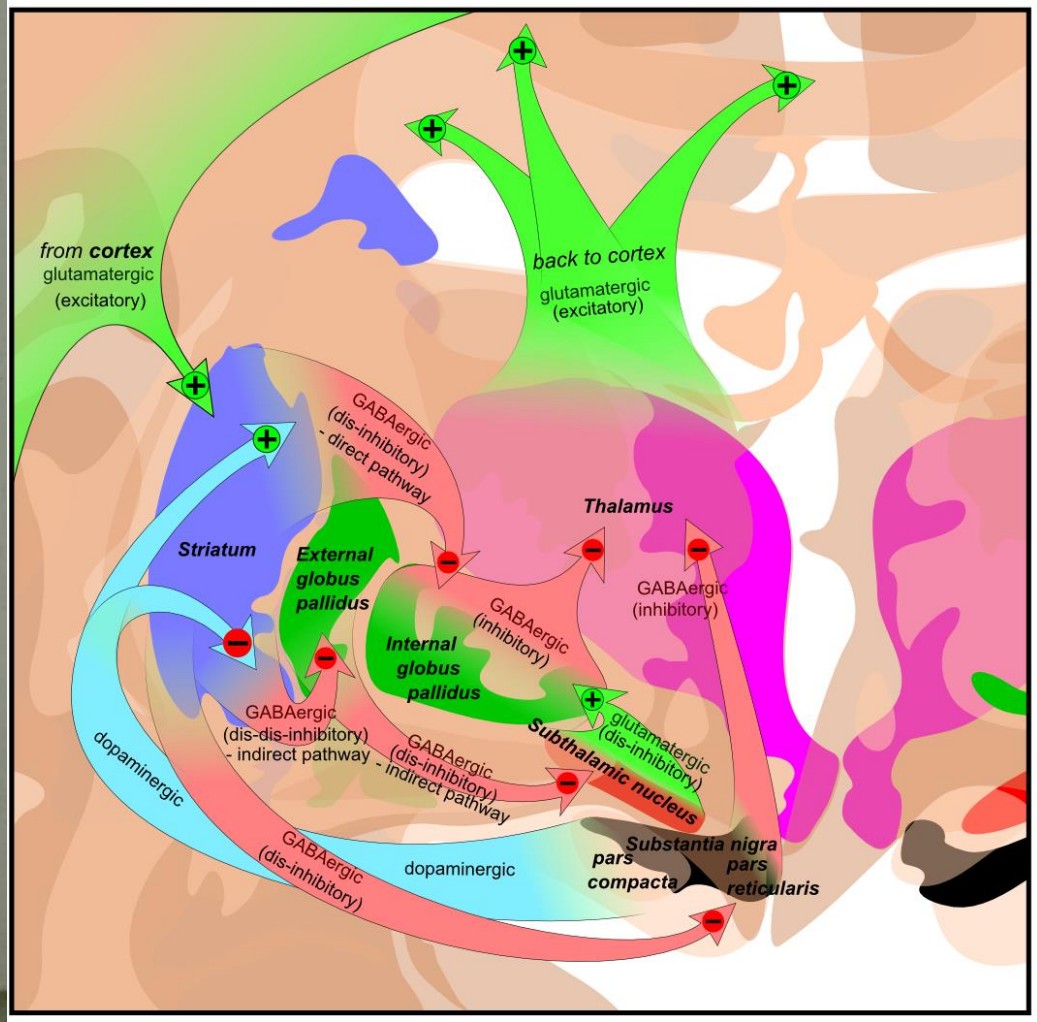
The image shows dopaminergic pathways of the human brain in normal condition (left) and Parkinsons Disease (right). Red Arrows indicate suppression of the target, blue arrows indicate stimulation of target structure. (Ansa lenticularis visible but not labeled, as red line from GPi to THA.)

Glutamine, GAB A, and Dopamine Path-ways in the basal ganglia

https://en.wikipedia.org/wiki/Basal_ganglia

Diagram shows two coronal slices that have been superimposed to include the involved basal ganglia structures. Green arrows (+) refer to excitatory glutamatergic pathways, red arrows (–) refer to inhibitory GABAergic pathways and turquoise arrows refer to dopaminergic pathways that are excitatory on the direct pathway and inhibitory on the indirect pathway.





Parkinson's Disease Causes: a combination of genetics and environment

- Heredity-10-15%, remaining 85% are sporadic, all causes:
- Drugs: MPTP (methyl phenyl tetrahydropyridine), designer drugs (Los Angeles outbreak in the 1980s).
- CNS infections
- Heavy metals (Manganese, others)
- Toxins: CO, pesticides, herbicides, Agent Orange, other
- Trauma (Muhammed Ali)
- Ischemia/hypoxia/vascular
- Rural living, well water contamination

Parkinson's Disease Foundation:http://www.pdf.org/causes#enviro

https://nwpf.org/stay-informed/news/2010/12/toxic-causes-of-parkinsons-disease/

HBOT in Parkinson's Disease- Review of Literature

- 64 patients, 37-78 years old, 29 men, 35 women
- Duration of illness: 1-15 years, at least 5 yrs. in most patients
- Causes:
  - Atherosclerosis: 49 patients
  - Atherosclerosis + high blood pressure: 6 patients
  - Encephalitis: 8 patients
  - Closed head injury: 1

Neretin VY, et al. Neuroscience and Behavioral Phys 1990;20(6):490-2

HBOT in Parkinson's Disease- Studies

- Treatment: HBOT @ 1.3-2.0 ATA/40-60 minutes for 8-12 Rxs.
- "Nootropic medications and preparations involving the microcirculation" in all. 37 continued their medications.
- Results:
  - 1 or two HBOTs caused improvement in general state of feeling in all patients.
  - Perceptible shifts in neurological status were identified (4-6 Rxs)
  - 1/3rd of patients: improvement in mood, cognition, decreased tone after 2-3 HBOTs.

Neretin VY, et al. Neuroscience and Behavioral Phys 1990;20(6):490-2

HBOT in Parkinson's Disease- Studies

- Results:
  - Akinetic-rigid had greater response than other forms (vascular etiology)
  - Good results: 18 patients, remission in 3 of these.
  - Satisfactory results: 26 patients.
  - Insignificant results: 11 patients.
  - Tremulous patients responded to higher dose

Neretin VY, et al. Neuroscience and Behavioral Phys 1990;20(6):490-2

HBOT in Parkinson's Disease- Studies

- Results:
  - No change: 5 patients, however, during HBO and for 1-3h afterwards, a decrease in the "frozen character and severity of tremor" were observed.
  - Discontinued treatment: 4 patients (claustrophobia and hypertensive crises)
  - Results better in vascular Parkinson's than in the encephalitic form
  - 36 patients maintained improvement for upto six months. The HBOT course was repeated two times/year to stabilize the condition.

Neretin VY, et al. Neuroscience and Behavioral Phys 1990;20(6):490-2

HBOT in Parkinson's Disease- Studies

- 15 patients, 46-85 years old (avg. 65.5), 8 men, 7 women
- Duration of illness: 6-25 years
- Causes:
  - Idiopathic: 7 patients
  - Vasculopathic: 4 patients
  - Encephalitis: 3 patients
  - Other: 1

Boromei A. Procs. of 12th Int. Congr. on Hyper. Med. Best Publishing Co 1998

HBOT in Parkinson's Disease- Studies

- HBOT: 2 protocols
  - Decompensated or complicated, non-vascular: 15 treatments + 5 treatments q 3 months: 1.9 ATA/80 w 10 mins./2mins. cycles of O_2/air.
  - Complicated, vascular causes: 25 treatments + 5 treatments q 3 months: 2.5 ATA/90 w 10 mins./2 mins. O_2/air.
- Outcomes measured with Webster Rating Scale (motor) and Crichton Geriatric Behavioural Scale (ADLs and behaviour).

Boromei A. Procs. of 12th Int. Congr. on Hyper. Med. Best Publishing Co 1998

HBOT in Parkinson's Disease- Studies

- Results:
  - Significant improvement on both scales
  - High correlation of the scores on the two scales after treatment
  - Improvements characterized by improvement in motor, mood, and overall function.
  - Average 9 month outcome.

Boromei A. Procs. of 12th Int. Congr. on Hyper. Med. Best Publishing Co 1998

HBOT in Parkinson's Disease-Literature: Case Report

- 45 y.o. man with 1.5 yrs. of progressive tremor, bradykinesia, accelerating in past 3 months with depression and anxiety.
- Prescribed anti-Parkinson's meds in past, ineffective, refused further meds.
- MRI brain and ultrasound head and neck negative.
- HBOT: 2.0 ATA/80 mins./10 min. air break qd x 30.
- Results:
  - After 4 HBOTs: improved sleep quality and duration (from 2-3h to 5h/nite). Improved mood.

Xu, Jin-Jin. Medicine, 2018;97:9(e0029)..

HBOT in Parkinson's Disease- Case Report

- At end of HBOT:
  - Normal sleep time (8-10h)
  - Weight increased by 10kg.
  - Tremor and bradykinesia improved significantly.
  - One month post: persistent gains, no need assistance with ADLs.

Table 1

Patient scores on clinical tests before and after hyperbaric oxygen treatment.

	UPDRS I	UPDRS II	HAM-D	HAM-A
Before treatment	38	15	31	32
After 1 month treatment	20	8	19	17

HAM-A = Hamilton Anxiety Rating Scale, HAM-D = Hamilton Depression Rating Scale, UPDRS = Unified Parkinson's Disease Rating Scale.

Xu, Jin-Jin. Medicine, 2018;97:9(e0029)..

HBOT in Parkinson's Disease- Studies

- Lecturer's Experience: crude recall
- ~10 cases
- HBOT at 1.25-1.5 ATA/60-90 minutes, qd, x 40
- Limited response:
  - Minor effect on motor symptoms
  - Some improvement on other symptoms of PD: cognition, affect.
  - ? Wrong dose or ineffective for this disease.

HBOT in ALS-Studies

- Amyotrophic Lateral Sclerosis: a rare group of neurological diseases that results from the gradual deterioration and death of upper and lower motor neurons that are responsible for controlling voluntary muscle movement.

- https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Amyotrophic-Lateral-Sclerosis-ALS-Fact-Sheet

HBOT in ALS-Studies

- Amyotrophic Lateral Sclerosis:
- Phase I study:
  - 5 patients
  - HBOT: 2 ATA/60 mins., daily, 5d/week, 4 weeks.
  - Measure neurological condition serially during 4 wks. of Rx and for 4 wks. post Rx.
  - Results:
    - 4/5 patients: decreased fatigue
    - Maximum isometric voluntary contraction of all muscle groups except right hand grip improved significantly by up to 97%.
    - Most improvement occurred during the 4 weeks after treatment.

Steele J. Amotroph Lateral Scler Other Motor Neuron Disord, 2004;5(4):250-4.

HBOT in ALS-Studies

- Amyotrophic Lateral Sclerosis:
- Phase II "single-blind (patients)" controlled study:
  - 10 patients divided into 2 groups, flip of coin, 1st group HBOT, 2nd group HBA.
  - HBOT: 2 ATA/60 mins., daily, 5d/week, 8weeks, by hood. HBA group: oscillating pressure to 1.3 ATA/60 mins. by mask.
  - Measure neurological condition and muscle strength serially every 4 wks. up to 20 weeks.

Steele J. Amotroph Lateral Sclerosis, 2007;8:274-275.

HBOT in ALS-Studies

- Phase II "single-blind (patients)" controlled study:
  - Results:
    - "Some patients in both groups did not complete all the treatments and evaluations due to disease-related problems. (1 dropout in HBOT due to non-related injury).
    - Data analysis of all HBOT patients and at the 12 week mark for the control group. No 20 week followup because HBOT group did not improve.
    - Progressive decline in function for HBOT group to 81.5% of baseline muscle function by week 20.
    - For Control Group decline to 89% of baseline by week 12.
    - Improvement in ~20% of muscle groups seen at 8 weeks in both groups.

Conclusion: Didn't work, don't recommend

Lecturer: Hard to reconcile these results with Phase I study. Overdose? (20 vs. 40 HBOTs).

Steele J. Amotroph Lateral Sclerosis, 2007;8:274-275.

HBOT in ALS-Studies

- Kim Cherry Case:
- 63 y.o. male diagnosed with bulbar ALS on 11/22/2011.
- Sx: problems swallowing, breathing, choking weakness, imbalance.
- Early response to NBO. Then gluten-free diet, supplements, ozone Rx, HBOT. Progressive improvement. 5/2017 stopped HBOT and started exercise on oxygen.
- Able to play golf, walk, talk, has good quality of life 6 years post-diagnosis.
- Keys to success: positive mental state, Higher Power, detox, diet, oxygen therapy.
- http://www.alswinners.com

HBOT and CTE

- What is CTE?
  - A progressive neuro- degeneration characterized by the widespread deposition of hyperphosphorylated tau (p-tau) as neurofibrillary tangles triggered by repetitive mild traumatic brain injury.[1]
  - Is a pathological diagnosis.
  - Originally described clinically in boxers ("punch drunk") as dementia pugulistica.
  - Clinically associated with symptoms of irritability, impulsivity, aggression, depression, short-term memory loss and heightened suicidality that begins 8-10 years after experiencing repetitive mTBI.[2]

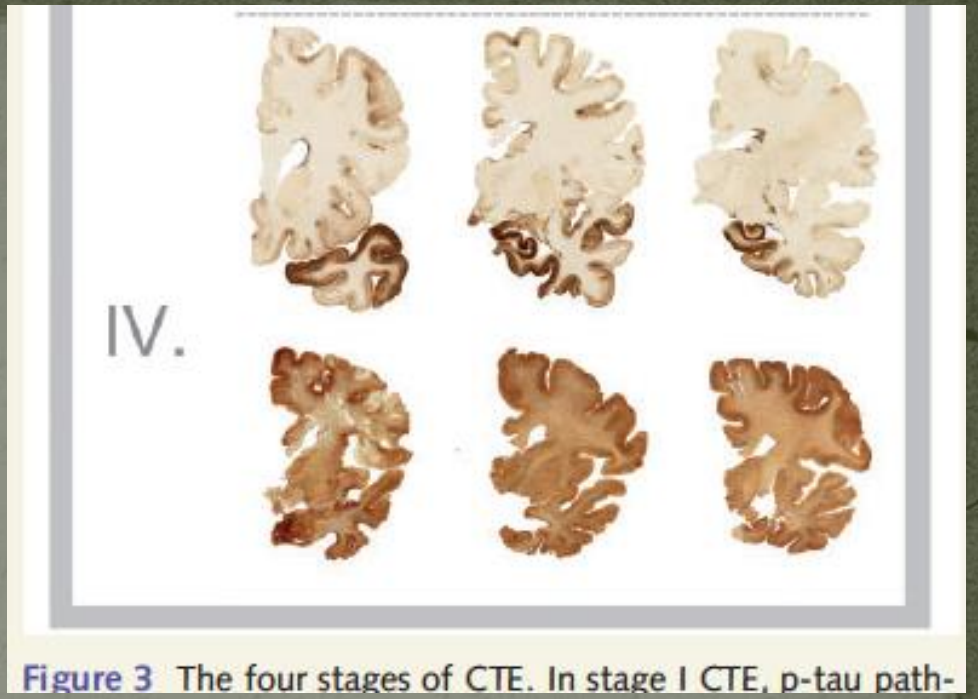
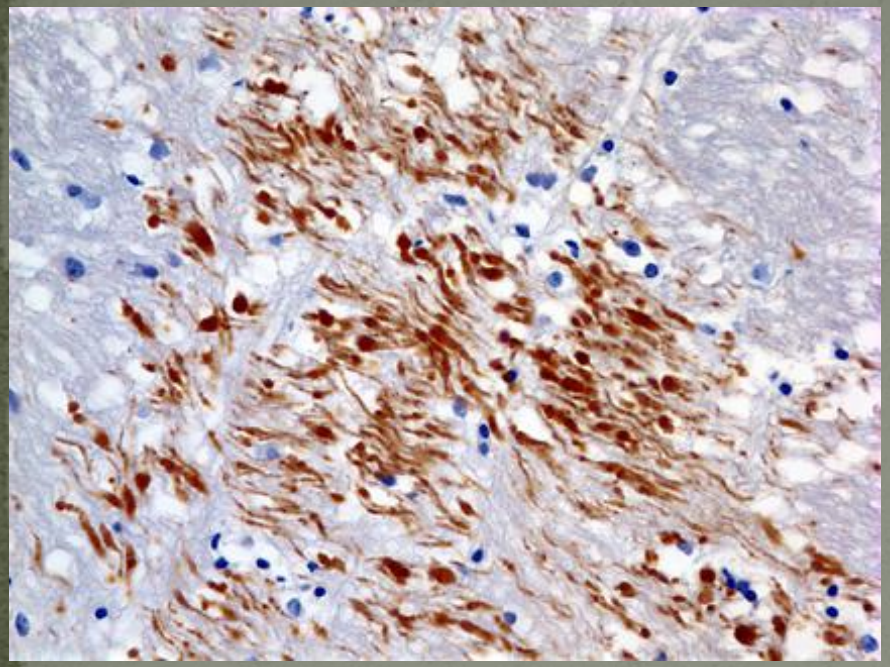


Figure 3 The four stages of CTE. In stage I CTE, p-tau path-

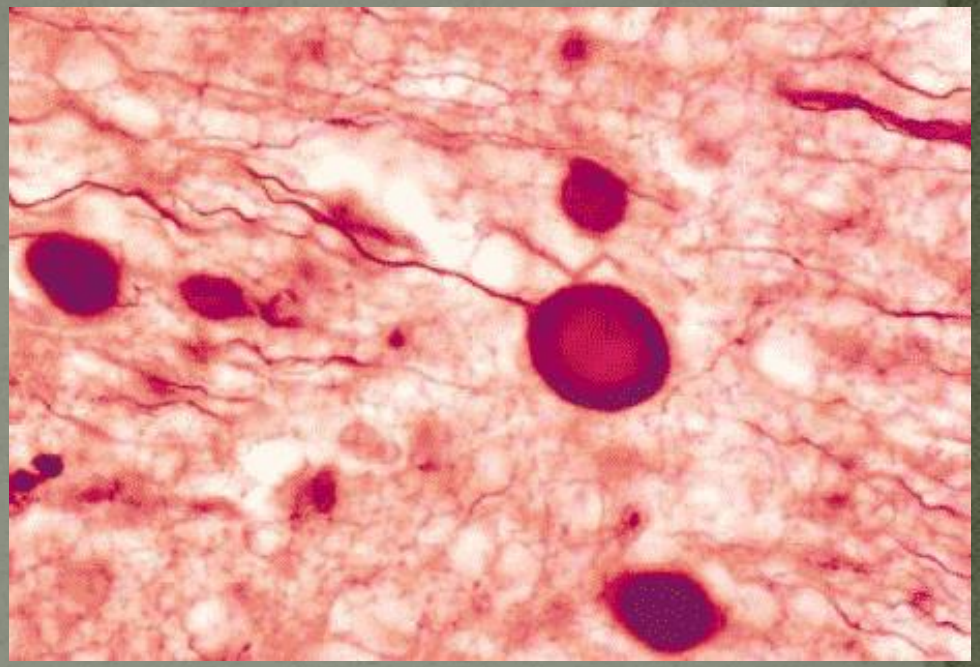
1. McKee AC. J Neuropathol Exp Neurol, 2009;68:709-35.
2. Mckee AC. Brain, 2013;136(Pt 1):43-64.

Diffuse Axonal Injury



Diffuse axonal swelling (brown)

http://neuropathology-web.org/chapter4/chapter4bContusions_dai_sbs.html

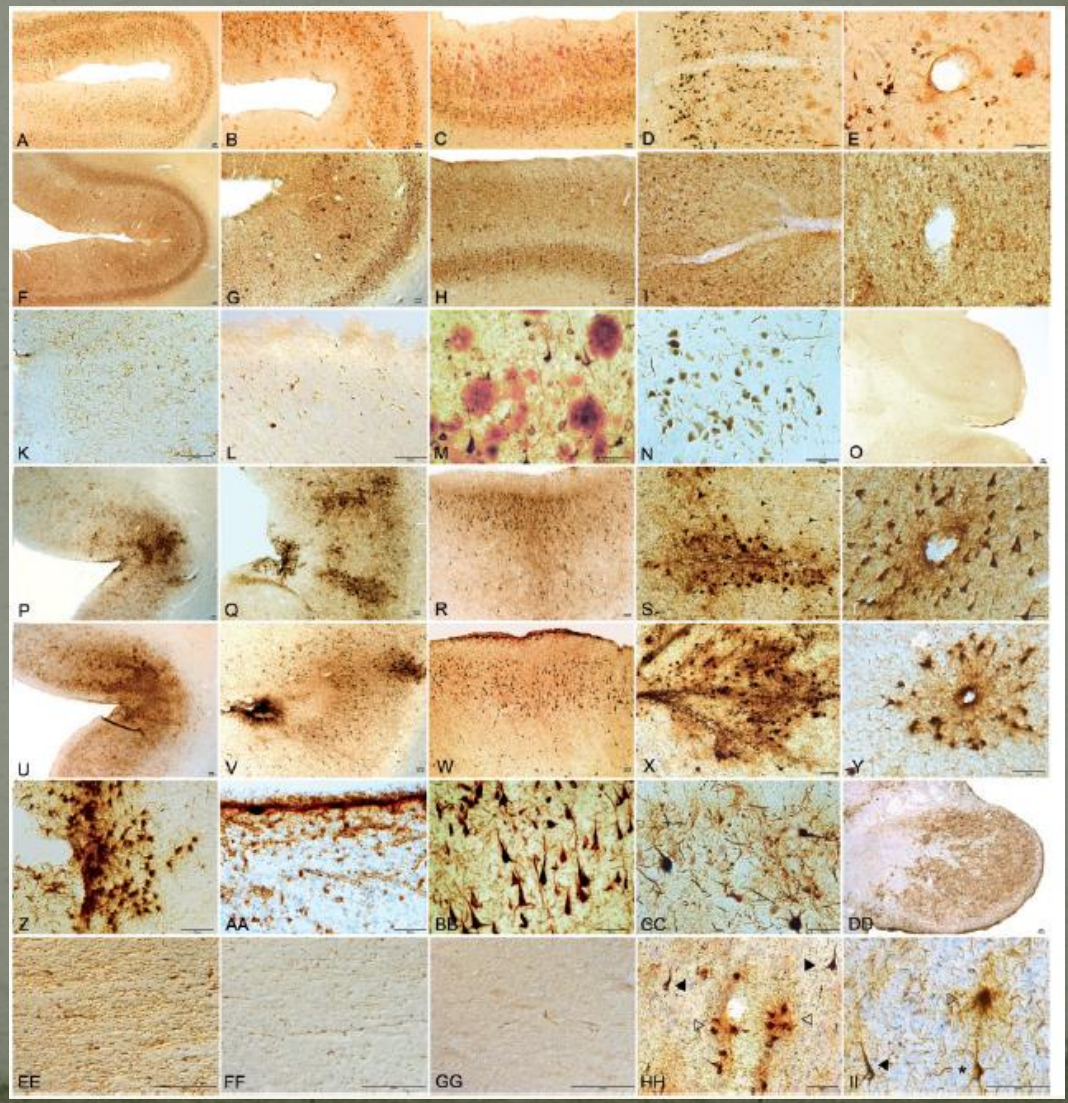


Axon contraction balls

http://moon.ouhsc.edu/kfung/JTY1/NeuroSim/Sim05-B-Diss-4-a.htm

CTE Neuropathology: Wounds in the Brain

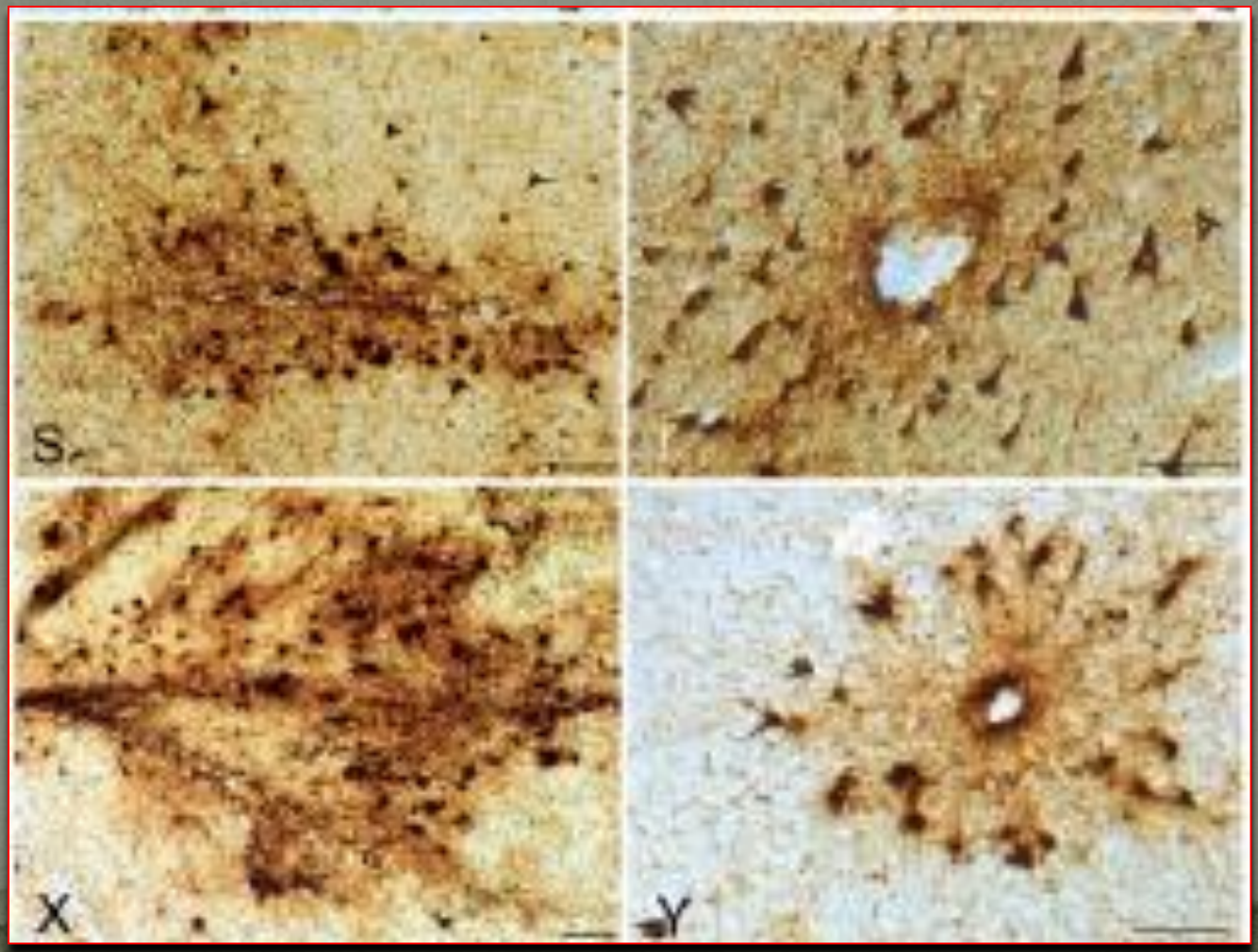
- Amyloid beta (red), Paired Helical Filaments of micro-tubule protein tau (brown).
- First 3 rows: Alzheimers
- Last 4 rows: CTE
- Lesions at depths of sulci and perivascular.



Mckee AC. Brain, 2013;136(Pt 1):43-64.

CTE Neuropathology: Wounds in the Brain

- Wounds in the Brain: Mckee AC. Brain, 2013;136(Pt 1):43-64.

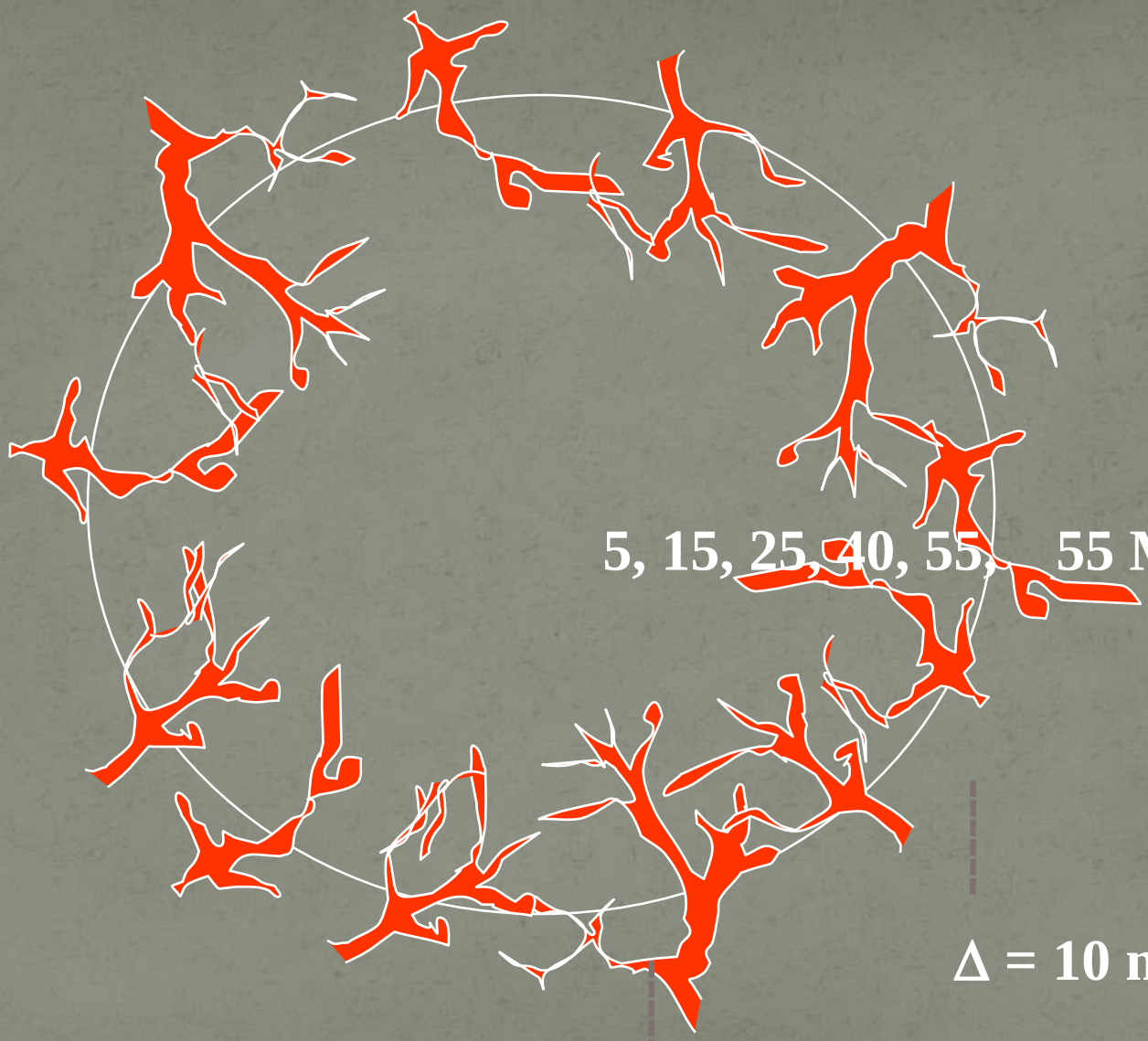


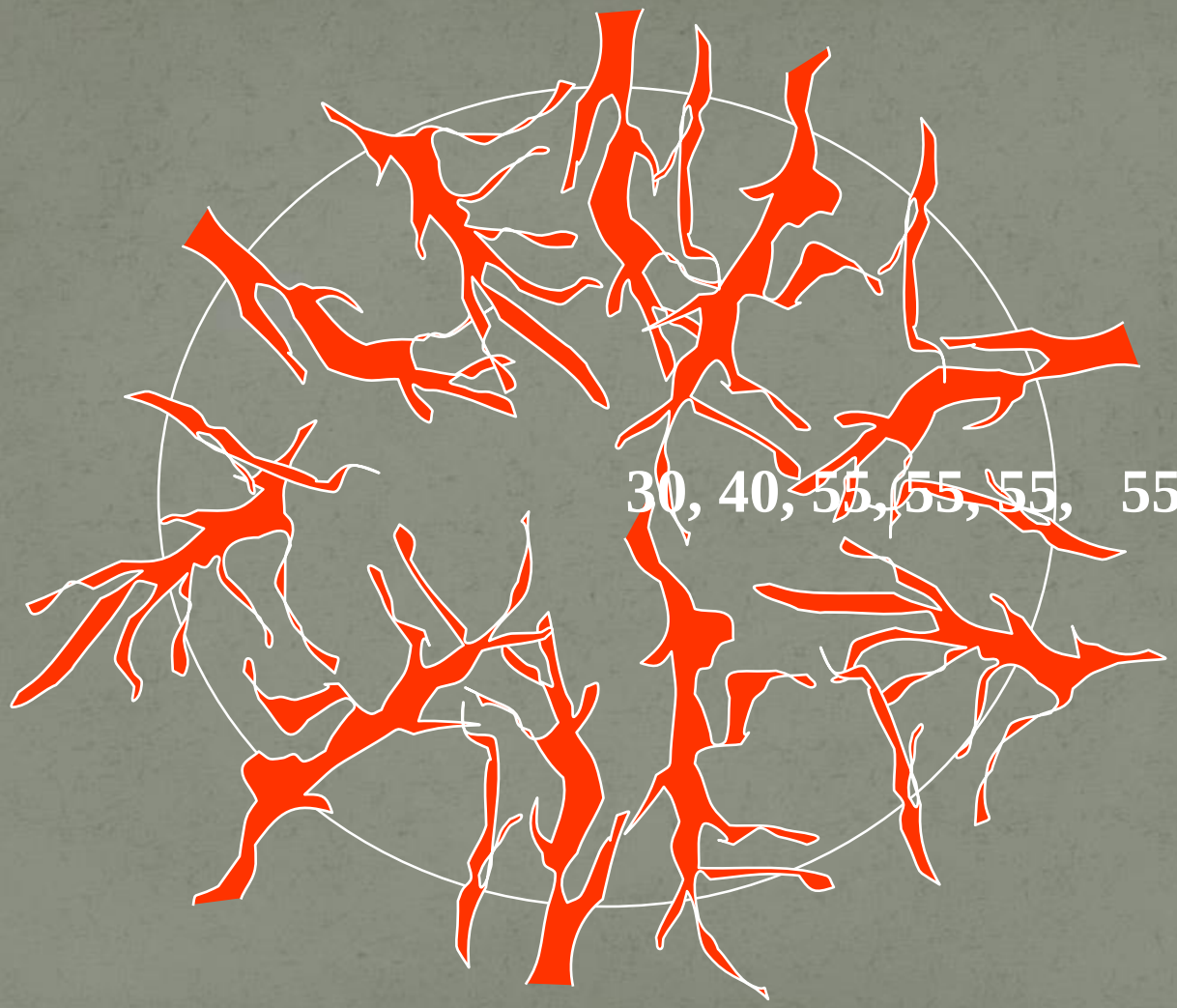
Marx Model of Perfusion Gradient Wound

During HBO at 2.4 ATA

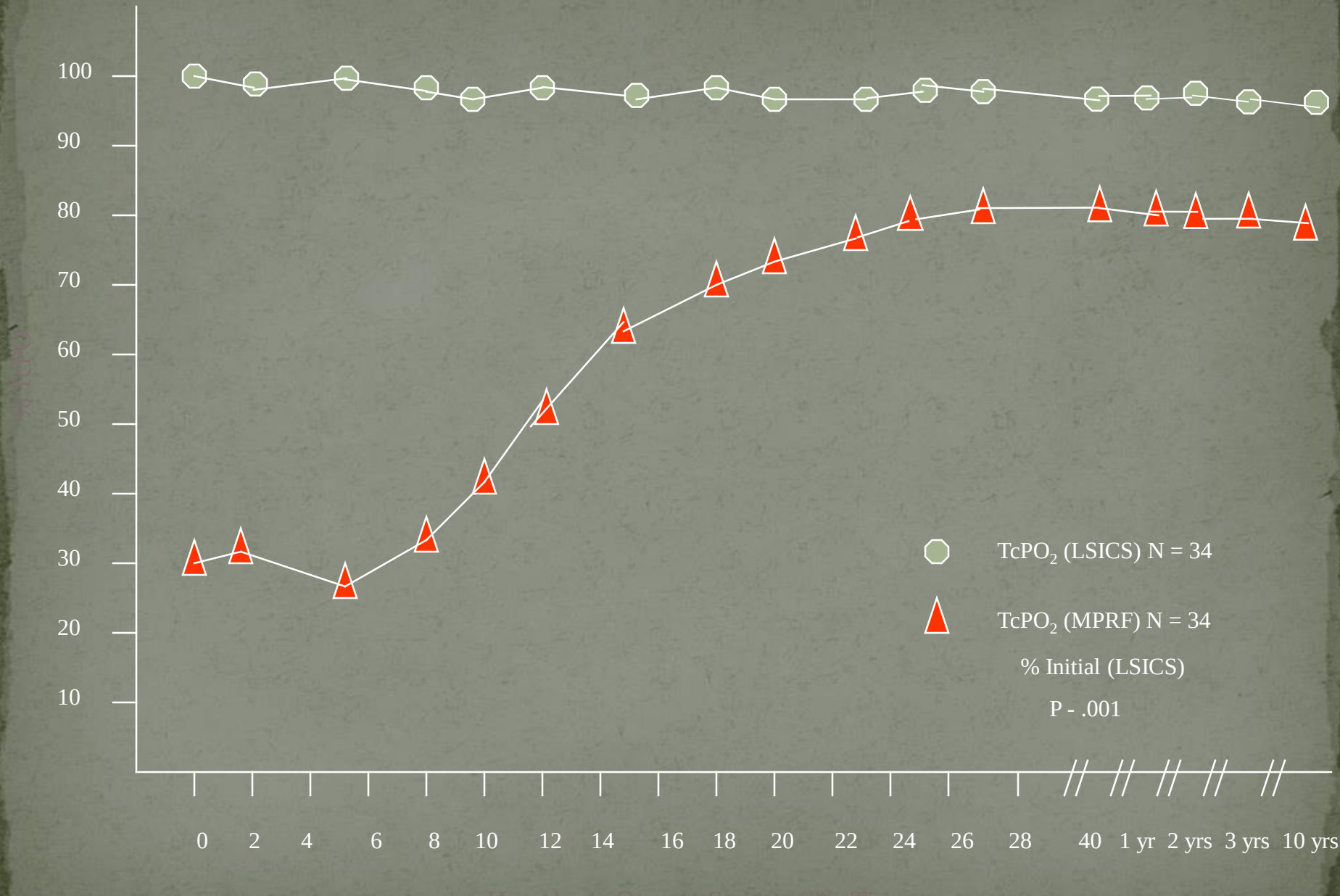
50, 50, 90, 15, 120 - 350 mm Hg

Δ = 230 mm Hg


5, 15, 25, 40, 55, 55 MM Hg
Δ = 10 mm Hg
Δ = 10 - 15 mm Hg



30, 40, 55, 55, 55, 55 mm Hg


100
90
80
70
60
50
40
30
20
10
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
40
1 yr
2 yrs
3 yrs
10 yrs
TcPO2 (LSICS) N = 34
TcPO2 (MPRF) N = 34
% Initial (LSICS)
P - .001
Hyperbaric Oxygen Session (#) - Time

HBOT

is a treatment for

WOUNDS

in the body in

ANY LOCATION

and of

ANY DURATION

HBOT and CTE

- **CTE: However!**
  - There is little doubt that *some* athletes may suffer from long-term adverse effects from multiple sport-related concussions (SRC).
  - A cause and effect relationship between concussions and/or contact sport participation and CTE (p-tau deposition, that causes the clinical syndrome) has not yet been demonstrated.
  - No compelling empirical evidence to indicate that SRC or subconcussive impacts are the sole and direct cause of psychiatric illness, suicide, MCI, or neurodegenerative disease/CTE.
  - Must account for genetic, medical, psychiatric, substance abuse, and biopsychosocial variables.

Solomon G. Develop Neuropsychol, 2018;43(4):279-311

HBOT IN CHRONIC BRAIN INJURY

Early case experience
(New Orleans and Slidell, LA)

1. **Gratuitous neurological improvement in extremity wound patients with chronic neurological diagnoses.**
2. **Divers with subacute cerebral decompression illness.**
3. **Louisiana boxers: Dementia Pugulistica Study:**
   a. **Community Hospital IRB**
   b. **Funded by The Hirsch Foundation ($20,000) to Keith Van Meter, M.D. and Sheldon Gottlieb, Ph.D. of the Baromedical Research Foundation of New Orleans.**
   c. **3 Boxers evaluated, two treated, one with dementia (1989).**

HBOT IN CTE

Dementia Pugulistica Study

Case Presentation

R.D.

55 y.o. male

Boxing 15-32 y.o., 15 years professionally

135 professional bouts, last one 23 years before HBOT

World champion

1 LOC in 1st 100 bouts, 4 LOCs in last 5 fights, last LOC x 3-5 mins.

HBOT IN CTE

Subsequent 10 years casino work with declining ability (Black Jack…roulette wheel… shuffle cards… fired)

Paranoia begins 2 years after last bout, eventual hallucinations.

Diagnosis: Paranoid schizophrenia, supervised care by family, able to dress and feed self.

Meds: Artane 2mg tid, Ativan 2 mg tid, Stelazine 2mg bid, occasional Percodan, Soma.

PEx: Conversant, suspicious, skulking panther like movements (basal ganglia injury?)

Slow speech, disoriented, abnormal balance and gait.

Slow speech. Poor short and long-term memory.

Neuropsychological testing: Marked global impairment with many tests in the 1-2% ile range.

HBOT IN CTE

SPECT, pre and post 1 HBOT (1.75 ATA/65):

Marked decrease in blood flow bilateral temporal lobes (R worse) and less so frontal lobes and right parietal lobe. Post HBOT marked increase in flow to the right TL, normalization of FLs and right PL.

MRI, brain: Moderate central and cortical atrophy, right occipital WM infarct and area of porencephaly.

HBOT IN CTE

HBOT:

10/1991-3/1992: 1.75 ATA/65 mins. x 1

1.5 ATA/65 mins. x 20

3 week break

1.75 ATA/70 mins. x21 (42 HBOTs)

3 week break

2.0 ATA/70 mins. x 21 (63 HBOTs)

Confusion, decreased memory, imbalance, shakiness during 1st 15 HBOTs.

HBOT IN CTE

HBOT:

Improved Symptoms: 16-20 HBOTs

21-42 HBOTs

43-63 HBOTs

Repeat SPECT hours post:

21st HBOT, at 1.5 ATA

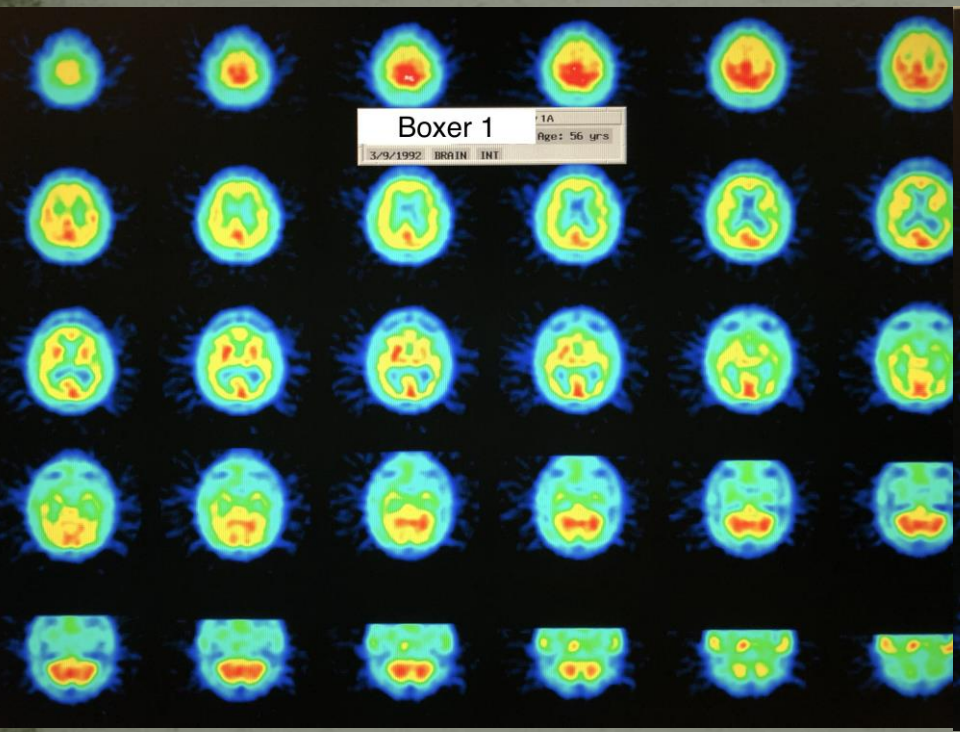
42nd HBOT, at 1.75 ATA

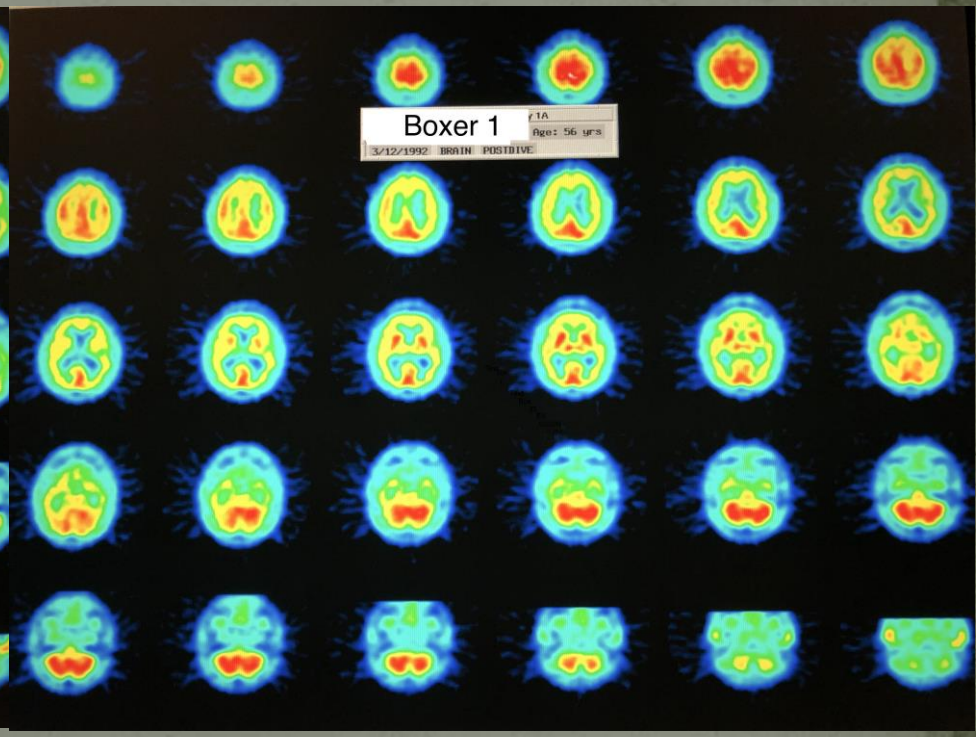
63rd HBOT, at 2.0 ATA

Results SPECT:

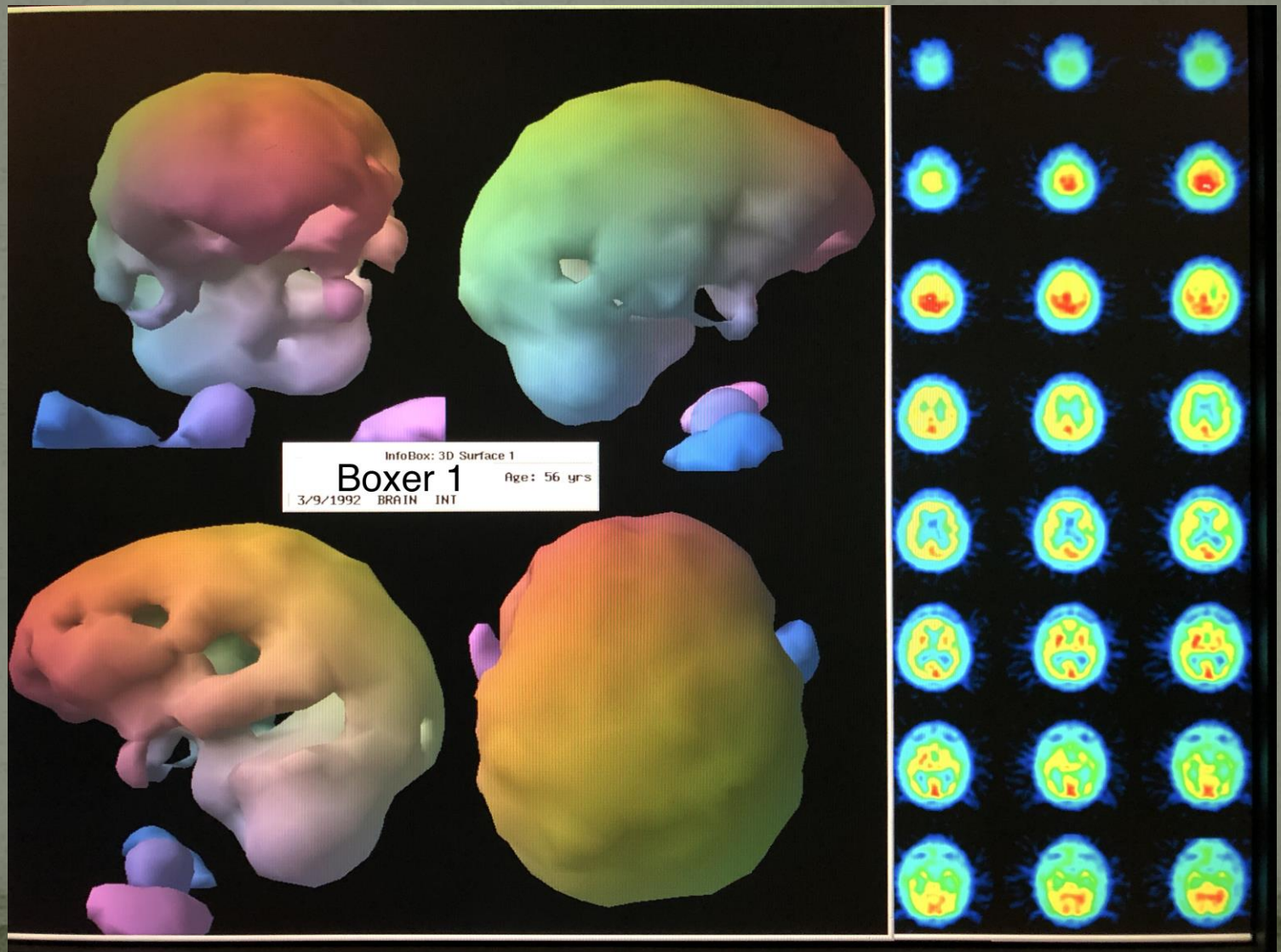
SPECT: 5d post 62nd HBOT and hours after 63rd HBOT @ 2.0 ATA

Transverse Slices

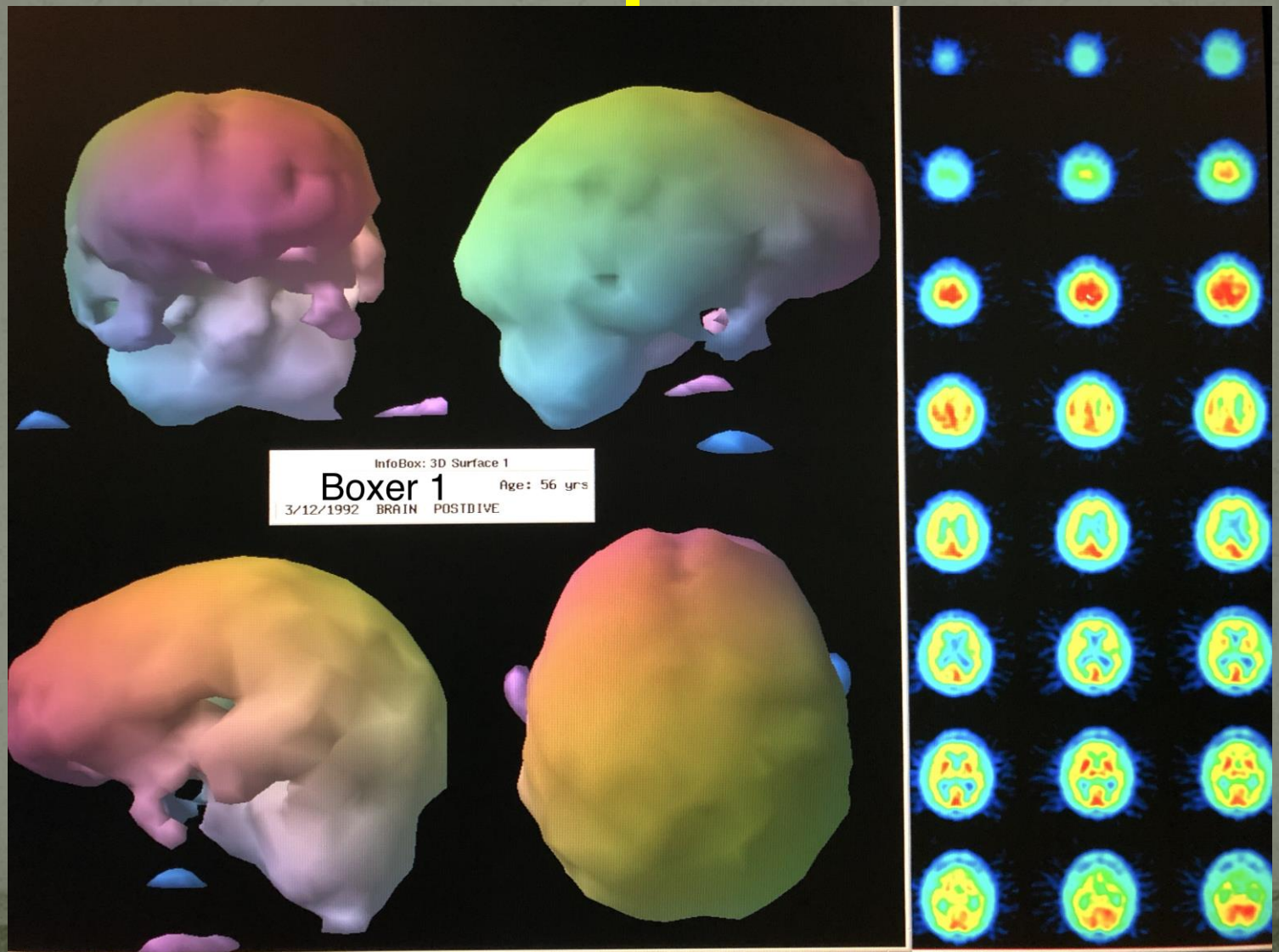




SPECT: 5d post 62nd HBOT-Surface Reconstruction 3-D



SPECT: after 63rd HBOT-Surface Reconstruction 3-D



HBOT IN CTE

Repeat PEx: Faster, more fluent speech, less paranoia, improved mood, energy, gait, balance. Family impressed with change in persona. Brother (former boxer) upset that he could not get treatment for his deficits.

Repeat NP testing: improvement in multiple domains, but only small improvement in %ile ranking. Patient was more oriented, knew for the first time on final testing why he was there, and the purpose of the testing.

HBOT IN CTE

Case Presentation #2

- Tom Dempsey, 64 y.o. retired NFL player (permissions granted).
- 6 concussions that he can count, but only remembers 3, none with LOC: 1969, 1971, and 1974.

https://www.detroitathletic.com/blog/wp-content/uploads/2012/12/tom-dempsey.png

https://en.wikipedia.org/wiki/Tom_Dempsey#/media/File:Tom_dempsey.jpg

- Each with confusion, HA, disorientation, played rest of game, symptoms lasted 1 week.
- Retired 1979. By 2008 developed irritability, mood disturbance with flashes of irrational anger. Significant alcohol intake, previous chewing tobacco, steroid use once. (Solomon article!)
- Entered study on brain imaging of NFL players in 2011 (Dr. Amen).

http://www.theadvocate.com/new_orleans/sports/saints/article_57cb7d51-2847-50a2-bf82-e6b6c1577d07.html

HBOT IN CTE

Case Presentation

- PMH: DM, Meds: supplements, Metformin, Glipizide, Lisinopril, Pravastatin.
- FH: dementia in two aunts manifest in their 50s.
- Neuro ROS: snoring (no evidence OSA pattern), dizzy in heat, poor enunciation, decreased balance, general cognitive decline, decreased energy level, mood swings, irritability.
- PEx: deformities of right hand and foot, positive glabella and snout, poor tandem gait, bradykinesia.
- SPECT: 3-D only—abnormal bilateral TLs, orbital FLs, and high parietal watershed areas.
- Folstein MMSE: 24

http://www.theadvocate.com/new_orleans/sports/saints/article_57cb7d51-2847-50a2-bf82-e6b6c1577d07.html

HBOT IN CTE

MicroCog Assessment 2011

EXAMINEE:	Tom Dempsey	REPORT DATE:	05/23/2011
TEST DATE:	5/23/2011	AGE:	64 years 4 months
DATE OF BIRTH:	1/12/1947	EDUCATION:	16 years
SEX:	Male	HANDEDNESS:	Not Specified
ETHNICITY:	White not Hispanic Origin	EXAMINER:	Kristen Willeumier
EXAMINEE ID:			

Test Form: Short

Summary Index Table

Age and Education Corrected Norms (Age: 55 - 64, Education: > High School)	**Sum**	**Scaled Score**	**%ile**	**95% Conf. Interval**	**Qualitative Description**
Level 3 - Indexes					
General Cognitive Functioning (GCF)	121	56	<1	50-63	Below Average
General Cognitive Proficiency (GCP)	30	66	1	59-73	Below Average
Level 2 - Indexes					
Information Processing Speed (IPS)	34	66	1	58-74	Below Average
Information Processing Accuracy (IPA)	33	55	<1	50-63	Below Average
Level 1 - Indexes					
Attention/Mental Control (Attn)	20	60	<1	50-72	Below Average
Reasoning/ Calculation (Reas)	18	50	<1	50-63	Below Average
Memory (Mem)	47	84	14	74-94	Low Average
Spatial Processing (Spat)	5	56	<1	50-67	Below Average
Reaction Time (RT)	19	78	7	70-86	Low Average
Reference Group Norms					
	Sum	**Scaled Score**	**%ile**	**95% Conf. Interval**	**Qualitative Description**
Level 3 - Indexes					
General Cognitive Functioning (GCF)	114	50	<1	50-58	Below Average
General Cognitive Proficiency (GCP)	29	67	1	59-75	Below Average
Level 2 - Indexes					
Information Processing Speed (IPS)	27	64	1	57-71	Below Average
Information Processing Accuracy (IPA)	33	50	<1	50-61	Below Average
Level 1 - Indexes					
Attention/Mental Control (Attn)	20	60	<1	50-75	Below Average
Reasoning/ Calculation (Reas)	14	50	<1	50-63	Below Average
Memory (Mem)	42	76	5	65-87	Low Average
Spatial Processing (Spat)	6	53	<1	50-68	Below Average
Reaction Time (RT)	10	56	<1	50-67	Below Average

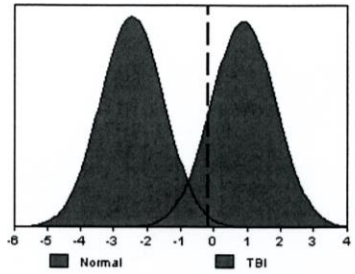
HBOT IN CTE

qEEG TBI Discriminant Analysis 2011

Traumatic Brain Injury Discriminant Analysis*

TBI DISCRIMINANT SCORE = -0.22 TBI PROBABILITY INDEX = 90.0%

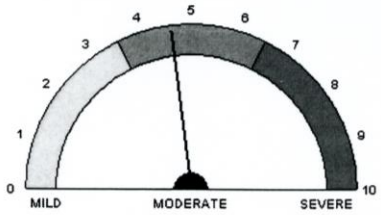
The TBI Probability Index is the subject's probability of membership in the mild traumatic brain injury population. (see Thatcher et al, EEG and Clin. Neurophysiol., 73: 93-106, 1989.)



			RAW	Z
FP1-F3	COH	Theta	84.75	0.34
T3-T5	COH	Beta	79.42	3.01
C3-P3	COH	Beta	73.30	-0.53
FP2-F4	PHA	Beta	-0.29	0.11
F3-F4	PHA	Beta	0.15	-0.53
F4-T6	AMP	Alpha	-0.56	0.34
F8-T6	AMP	Alpha	-74.89	-0.38
F4-T6	AMP	Beta	60.29	1.59
F8-T6	AMP	Beta	1.65	0.84
F3-O1	AMP	Alpha	-53.51	0.18
F4-O2	AMP	Alpha	-58.78	0.08
F7-O1	AMP	Alpha	-99.78	0.11
F4-O2	AMP	Beta	20.84	1.19
P3	RP	Alpha	41.80	-0.46
P4	RP	Alpha	43.02	-0.44
O1	RP	Alpha	48.38	-0.40
O2	RP	Alpha	48.79	-0.41
T4	RP	Alpha	28.56	-0.91
T5	RP	Alpha	48.68	-0.05
T6	RP	Alpha	41.23	-0.57

TBI SEVERITY INDEX = 4.59

This severity score places the patient in the MODERATE range of severity.



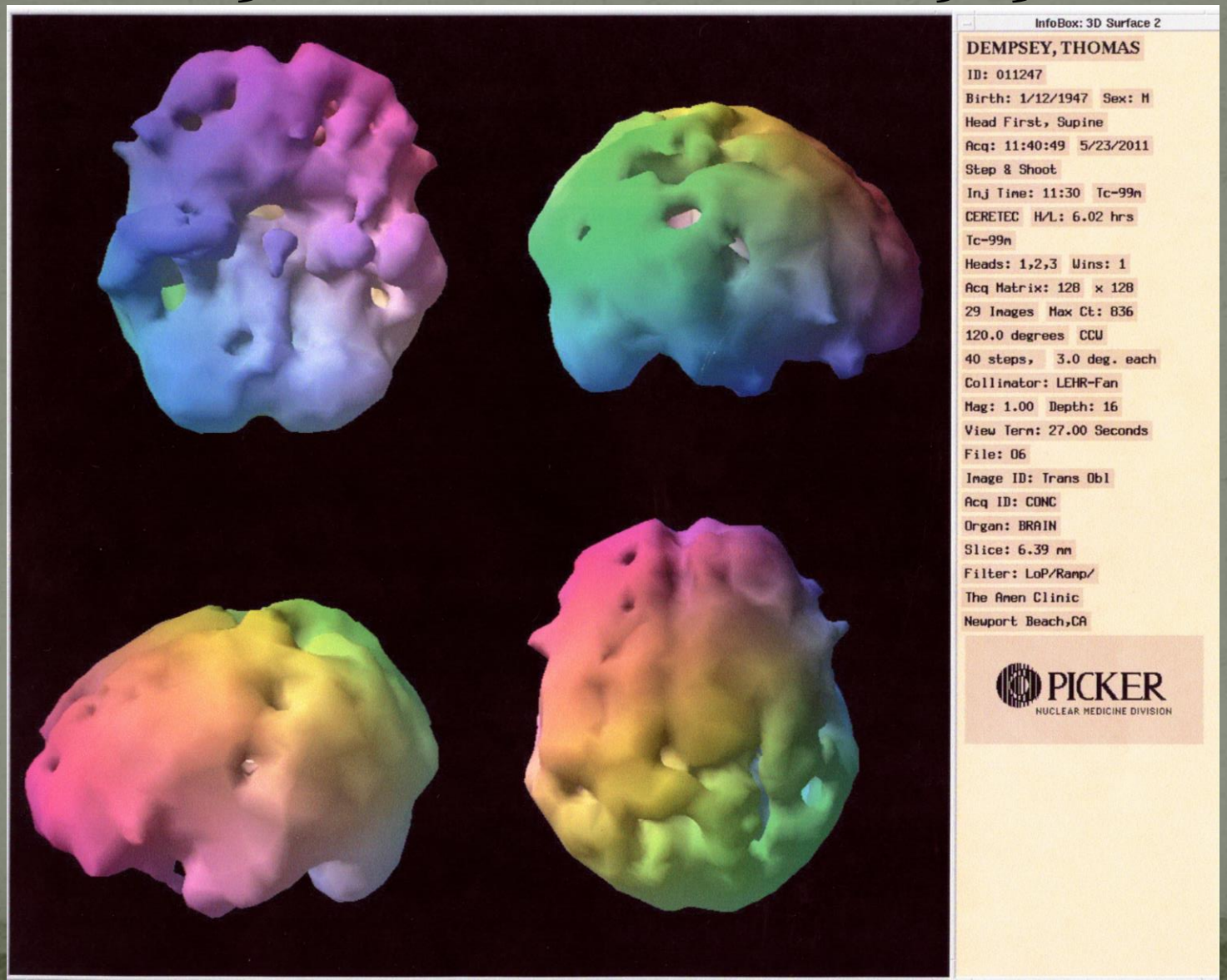
			RAW	Z
FP1-C3	COH	Delta	54.65	0.34
FP1-FP2	COH	Theta	90.30	1.09
O1-F7	COH	Alpha	27.93	0.24
O2-T6	COH	Alpha	89.90	1.25
P3-O1	COH	Beta	81.84	0.74
FP1-T3	PHA	Theta	-1.48	-0.82
T3-T4	PHA	Theta	-63.01	2.06
O1-F7	PHA	Alpha	5.86	-0.54
F7-F8	PHA	Alpha	-4.40	0.58
T5-T6	PHA	Beta	1.85	-0.32
C3-F7	AMP	Delta	47.46	3.81
FP2-F4	AMP	Delta	112.22	4.84
C4-F8	AMP	Delta	19.41	2.52
O1-O2	AMP	Theta	12.32	0.84
P3-F7	AMP	Alpha	-99.58	0.08
FP2-P4	AMP	Alpha	-36.82	1.14

The TBI Severity Index is an estimate of the neurological severity of injury. (see Thatcher et al, J. Neuropsychiatry and Clinical Neuroscience, 13(1): 77-87, 2001.)

*Statement of Indications of Use:
The Discriminant Analysis and Severity Index are to be used by experienced and qualified professionals for the post-hoc statistical evaluation of the human electroencephalogram (EEG). The Discriminant Analysis and Severity Index are to be viewed as an adjunct to the evaluation of the patient, and they do not serve as a primary basis for a diagnosis. Warning: Inclusion criteria of a history of traumatic brain injury and greater than 13 years of age must be adhered to.

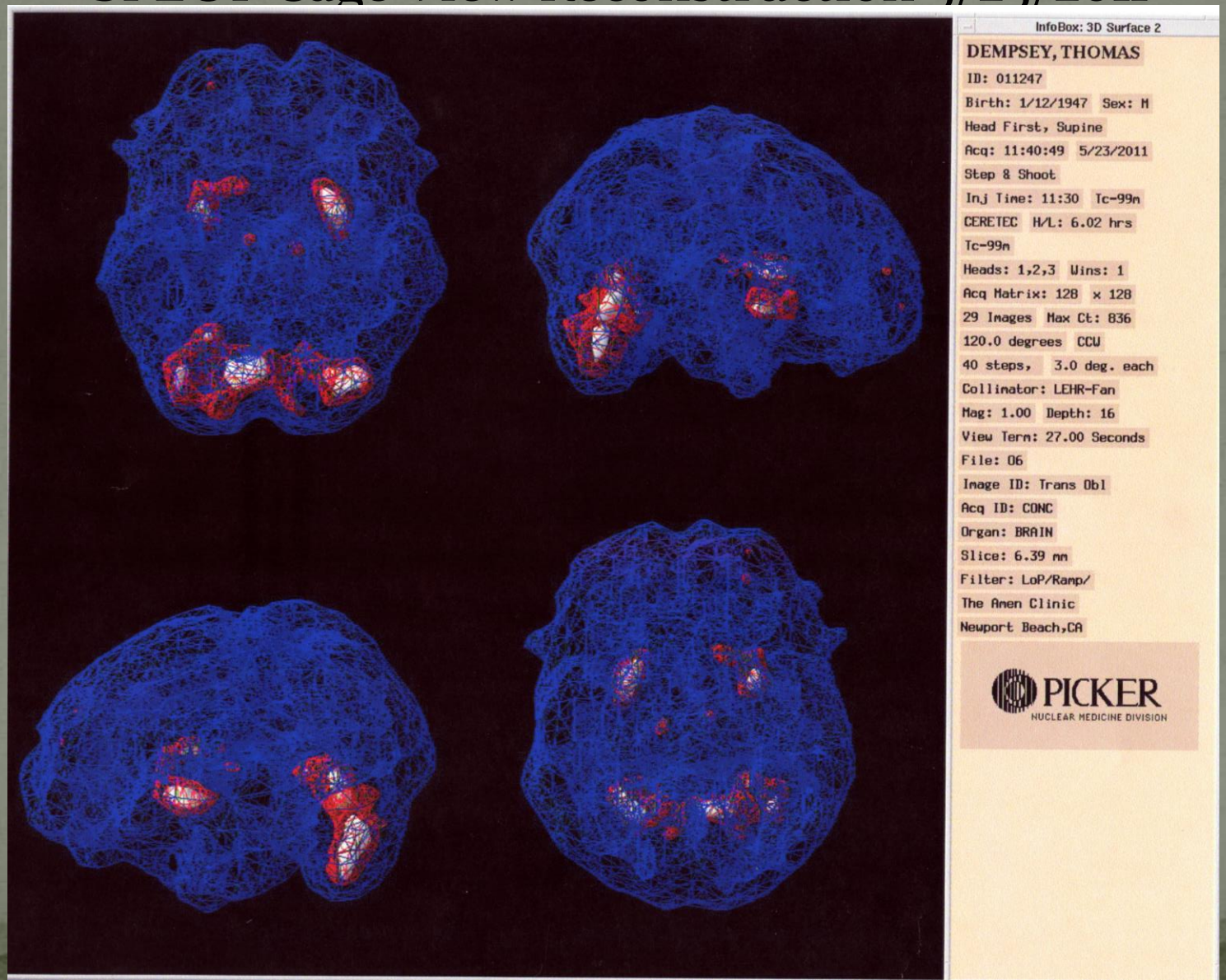
HBOT IN CTE

SPECT 3-D Surface Reconstruction 5/23/2011



HBOT IN CTE

SPECT Cage View Reconstruction 5/23/2011



HBOT IN CTE

Case Presentation: Tom Dempsey

- HBOT: 1.4 ATA/60, qd, x 40, 5-7/2011.
- Re-Eval:
  - Mixed result. Early symptomatic improvement. Disappointed later: pt. was hoping for big improvements.
  - Started driving again at times.
  - Mild improvement balance, memory at times, energy level
  - Could retell his stories better.
  - PEx: balance worse.
  - Folstein decreased to 21-22 (off by 1 day on date).

http://www.theadvocate.com/new_orleans/sports/saints/article_57cb7d51-2847-50a2-bf82-e6b6c1577d07.html

HBOT IN CTE

Case Presentation: Tom Dempsey

- In the months following HBOT, improvement.
- 1/2013, 18 months post HBOT: "clearcut improvement." Sustained driving. Getting after-care through Tulane Sports Medicine Program.
- Later 2013, 24 months post HBOT: "nosedived." Continued after-care. Wife unable to care for patient. Put in nursing home. Slow progressive decline.
- 5/5/2018: in nursing home, total dependence, can't feed self, "doesn't know how to walk." Jeri-chair. "Doesn't recognize anyone. " Physically healthy.

http://www.theadvocate.com/new_orleans/sports/saints/article_57cb7d51-2847-50a2-bf82-e6b6c1577d07.html

HBOT IN CTE

Case Presentation: Tom Dempsey

- Conclusion:
  - Initial response to HBOT with more noticeable improvement in months after treatment (Dose implications?).
  - No further HBOT.
  - Sustained benefit of HBOT, coupled with additional PT and stimulation.
  - Precipitous decline.
  - Alive, healthy, late stage dementia.

http://www.theadvocate.com/new_orleans/sports/saints/article_57cb7d51-2847-50a2-bf82-e6b6c1577d07.html

HBOT IN CTE

Case Presentation #3

- Retired NFL linebacker; 46 years old
- cc: Wants to preserve brain, scared of appearance of old friends, is tired, gets punchy after airplane flights.
- Played football from 10-37 y.o., professionally for 16 years. Tackled with head.
- 22 documented concussions, one with LOC. Remembers "seeing stars" at least once/game or practice for entire career.
- Steroid use throughout professional career, "always on some anabolic stimulant." Stimulants every year of professional football.
- Transient effects of concussions became permanent with simultaneous increasing fatigue.
- Contacts PGH, M.D. 2000-2001 football season: had been using HBOT (hardshell and portable) and was "exhausted," couldn't finish season.
- Recommendations to use HBOT for recovery and head injuries instead of performance enhancement.

HBOT IN CTE

Case Presentation

- Finished 2000-1 and 2001-2 seasons and was symptomatically improved.
- Traded to another team in 2002. No HBOT. Concussions accumulate, increasing toll, unable to play due to neuro Sx, confusion after away game in 2003. Couldn't travel home.
- Extensive workup: NP, MRI. ? Results. Sx improve over time.
- Repeat CT, MRI, EEG in 2006 @ U. of Pittsburgh-normal.
- Neuro ROS: STM problems, short-temper, irritable, avoids crowds, commotion, low energy level, decreased smell, taste, generalized cognitive decline
- PMH: testosterone, Arimedex (increases testosterone), vitamins, apnea in sleep, 500 mg caffeine/day
- FH: addiction, Alzheimer's in mother, two others with Alzheimer's, EtOH, depression. (Solomon article!)
- PEx: balance and coordination findings.

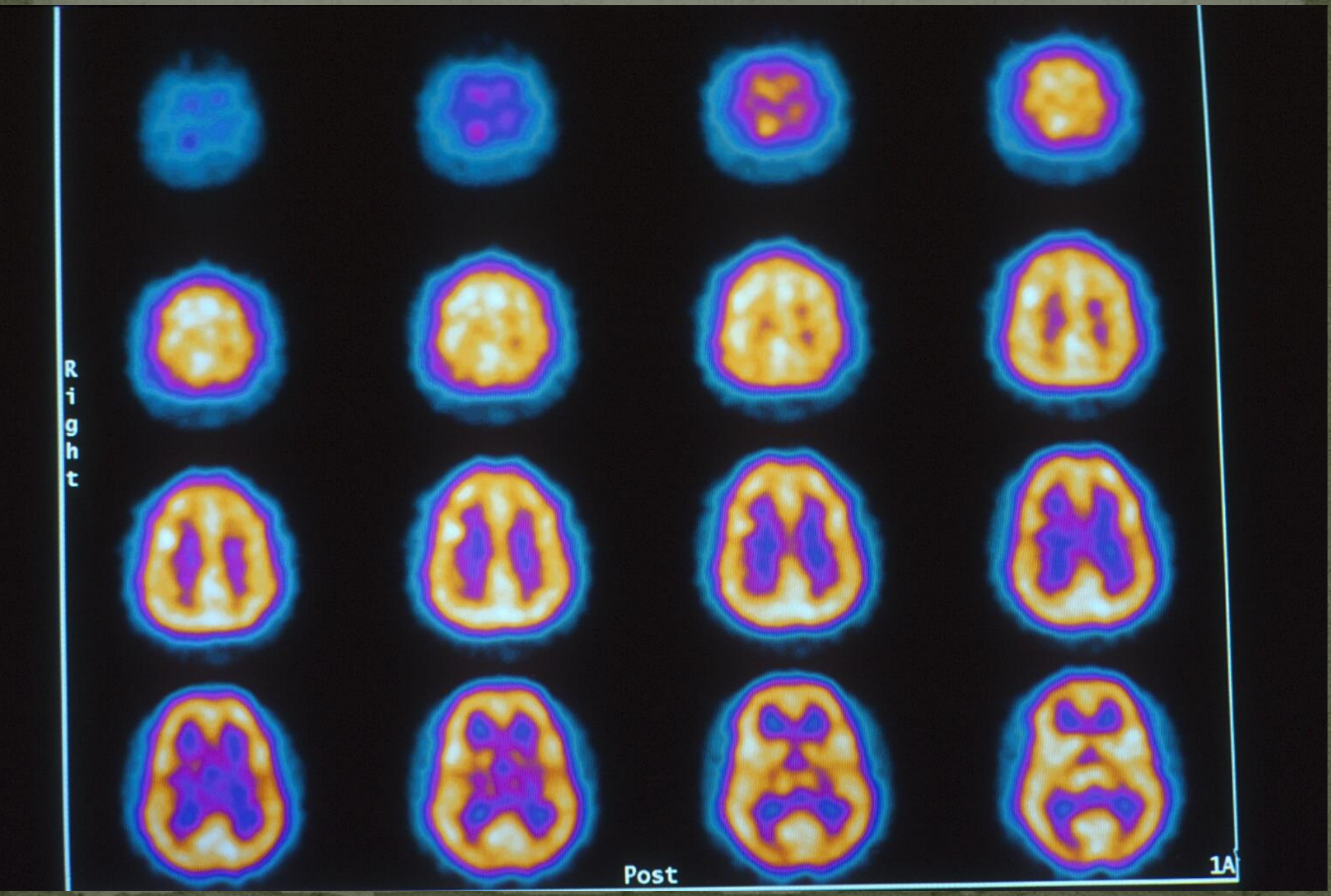
HBOT IN CTE

- SPECT, single HBOT at 1.4 ATA/50, repeat SPECT
- Improved vision, energy level, thinking clearer, feels better post single treatment.
- 35 additional HBOTs, 1.4/50, qd, 5d/week. IV glutathione and phosphatidyl choline, and NAC pre-HBOT, tiw.
- Re-Eval: improved on nearly all symptoms and PEx findings. Noted by wife and employees.
- Repeat SPECT, 4/2013: improved.
- One month later, Sx regression. Doing multiple therapies. No PCP F/U.
- One month later, 15 additional HBOTs. Improved. Continued treatment.....exhaustion, headaches. Stopped HBOT. Rebound.
- One month later, restart HBOT, additional 19 HBOTs, improved until last 10, deterioration.
- Evaluation 2 weeks later, overall improvement: focus, memory, reading, energy level, mood control. PEx: ~same as post 36 HBOTs.
- Repeat SPECT, 8/2013: slight deterioration compared to post 36 treatments.

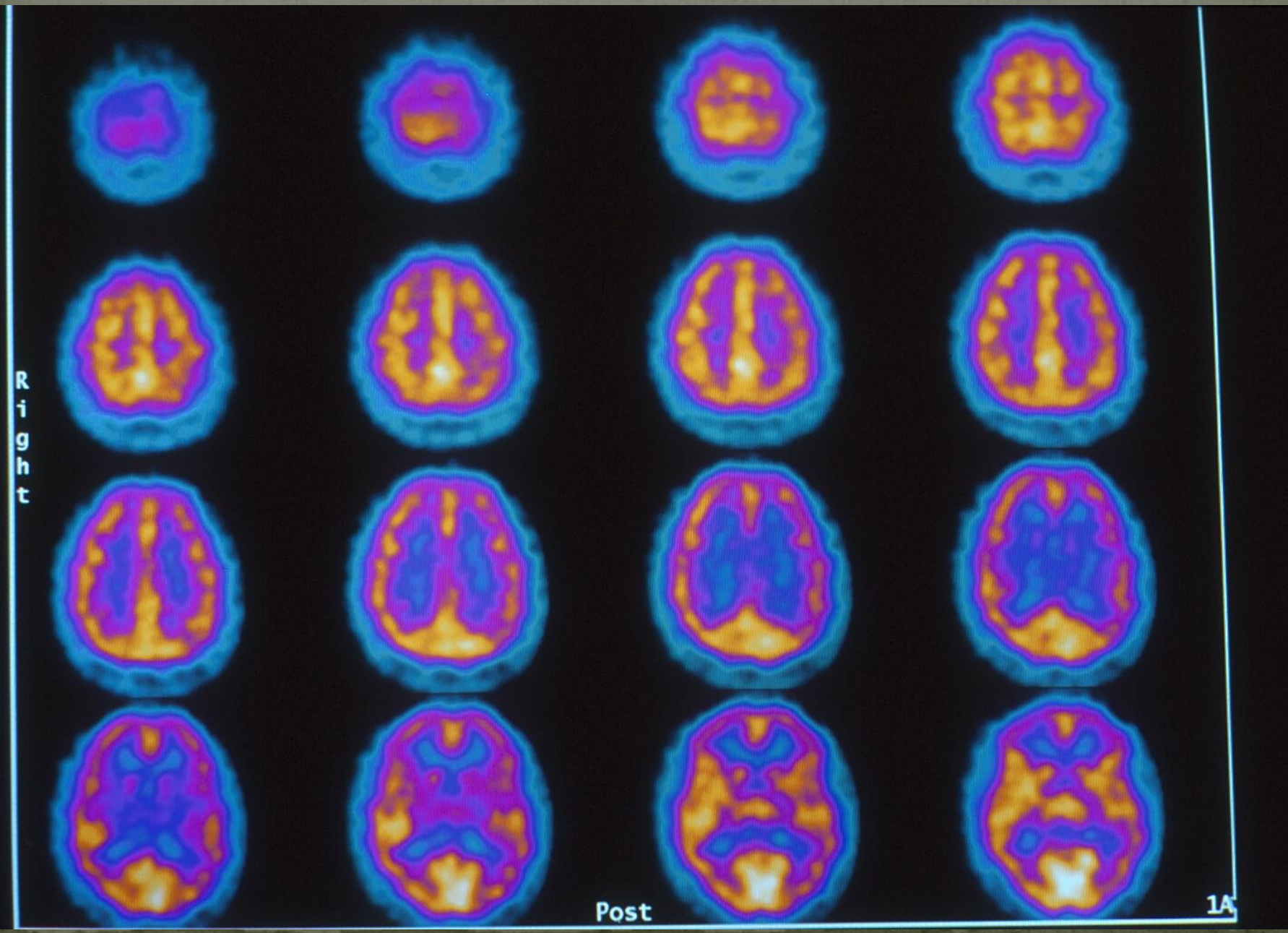
HBOT IN CTE

What does a normal person look like on brain blood flow scanning?

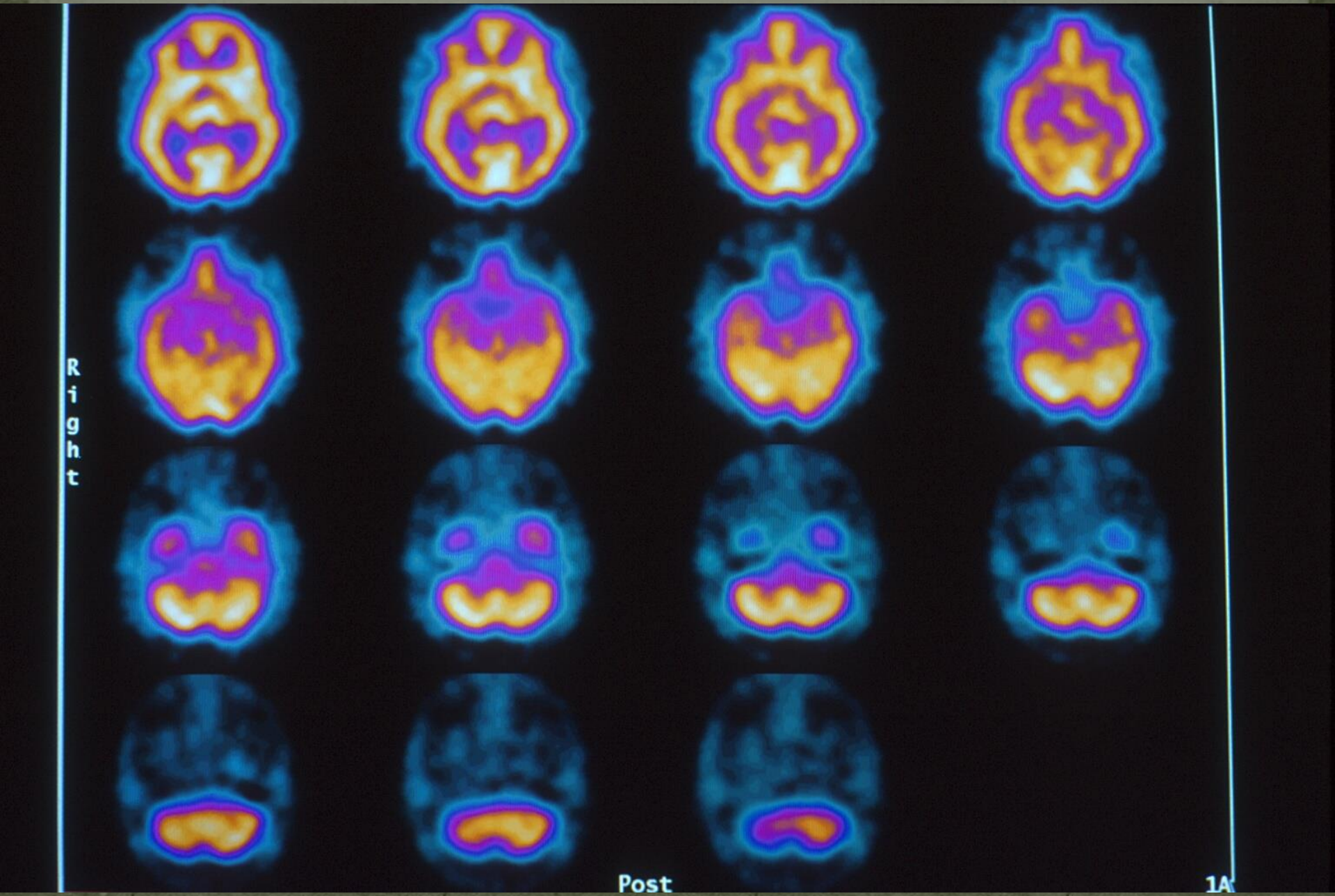
Normal 34 year old male: LSU IRB 1998-2001



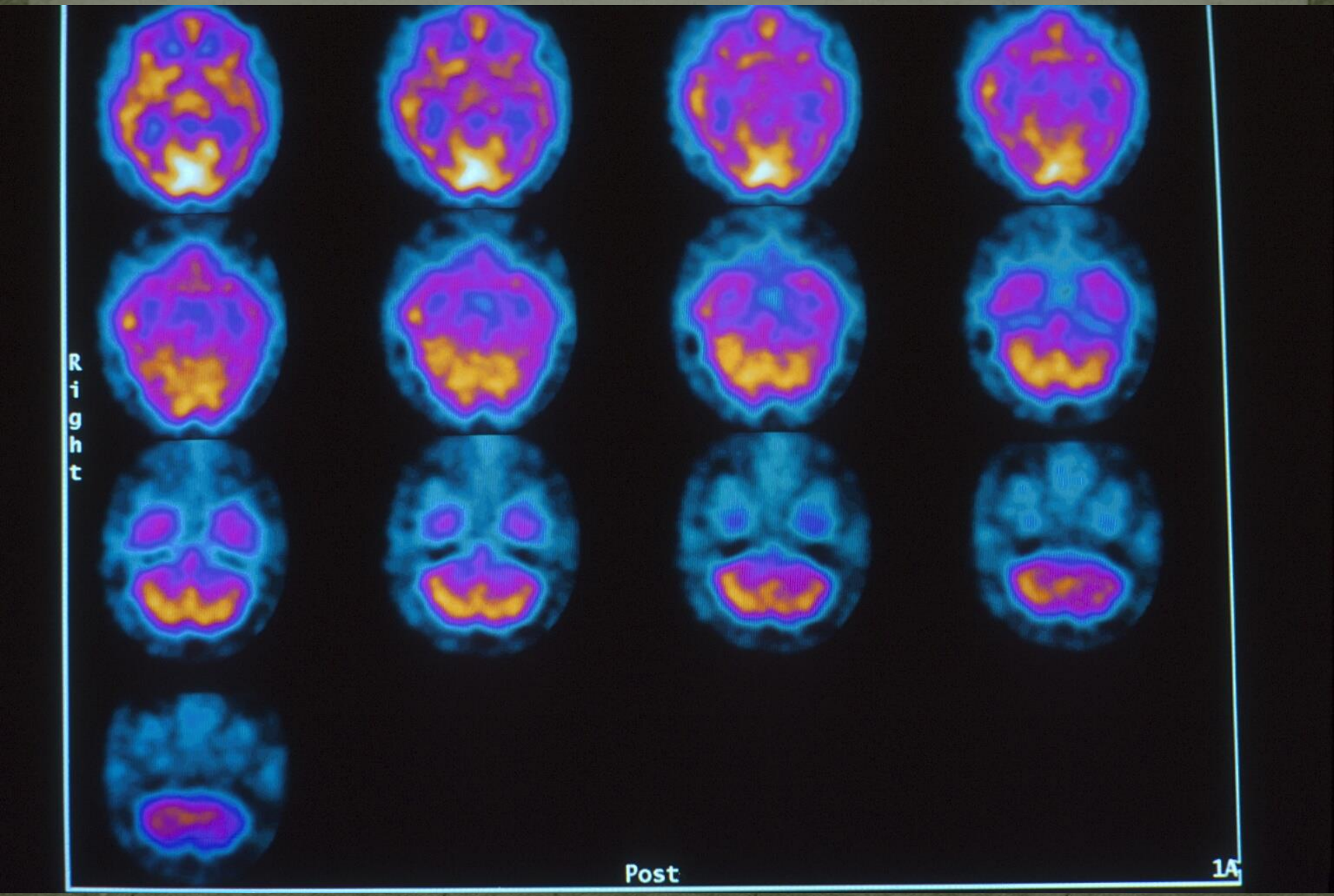
Purportedly Normal 34 year old male: LSU IRB 1998-2001



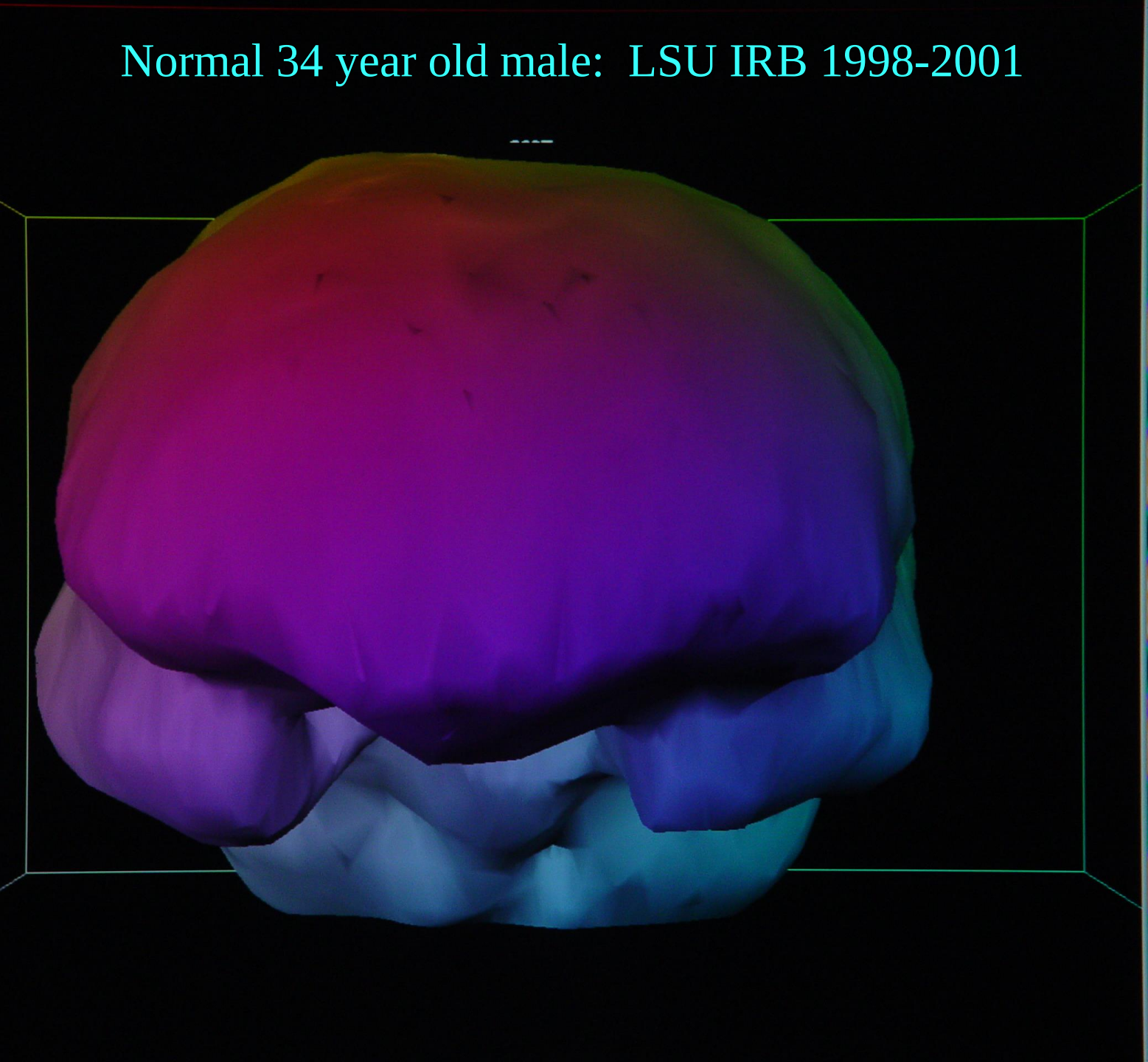
Normal 34 year old male: LSU IRB 1998-2001

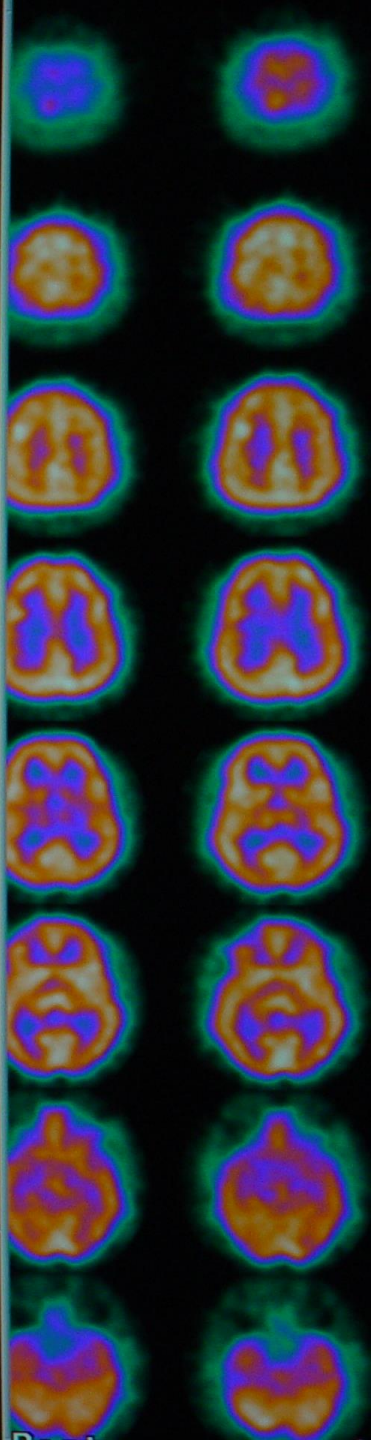


Purportedly Normal 34 year old male: LSU IRB 1998-2001

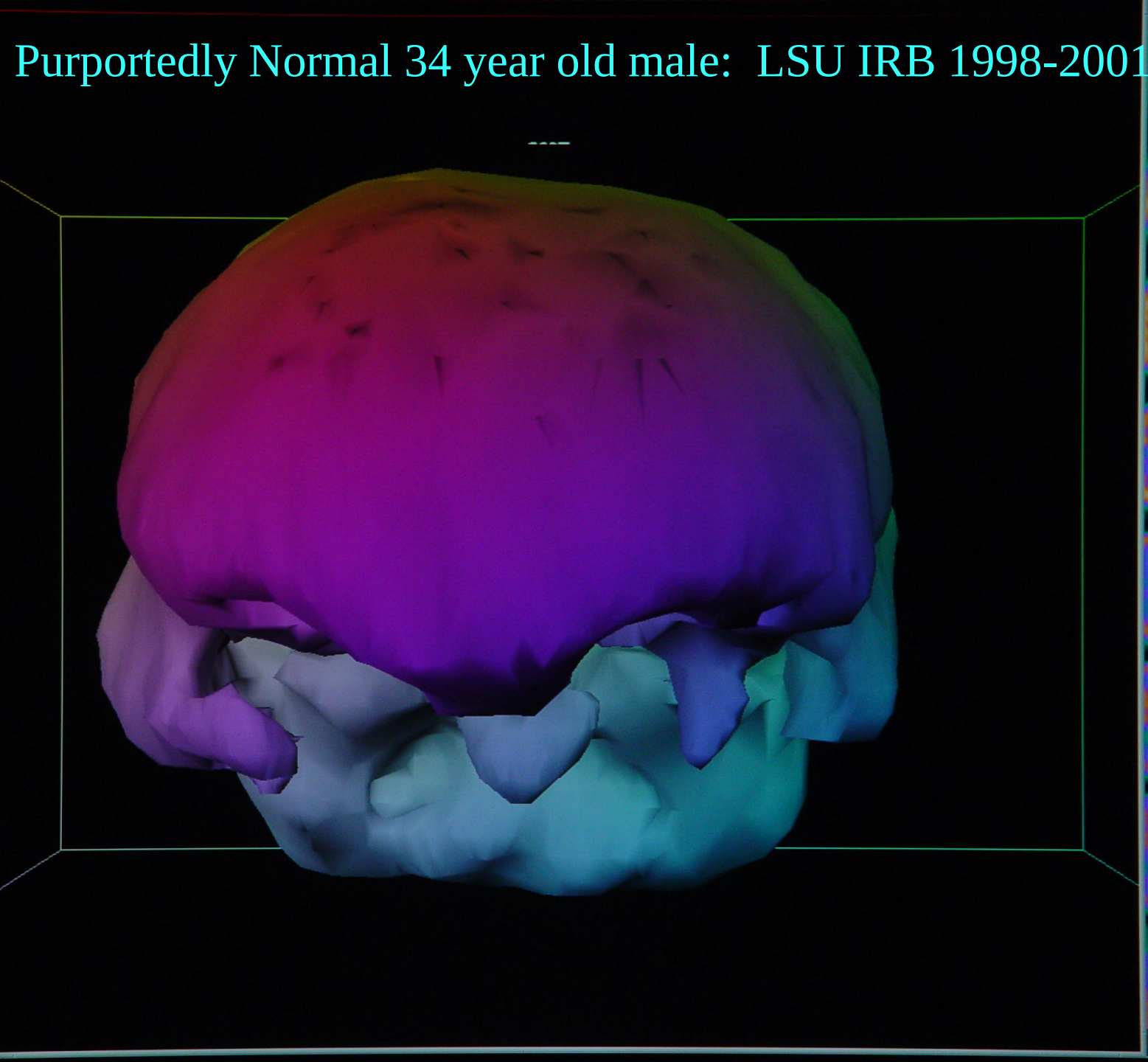


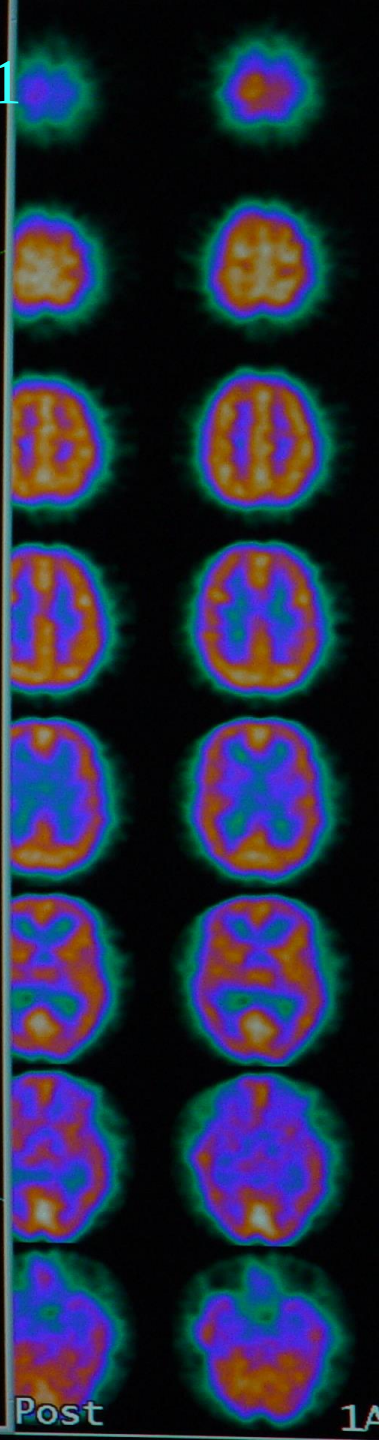
Normal 34 year old male: LSU IRB 1998-2001





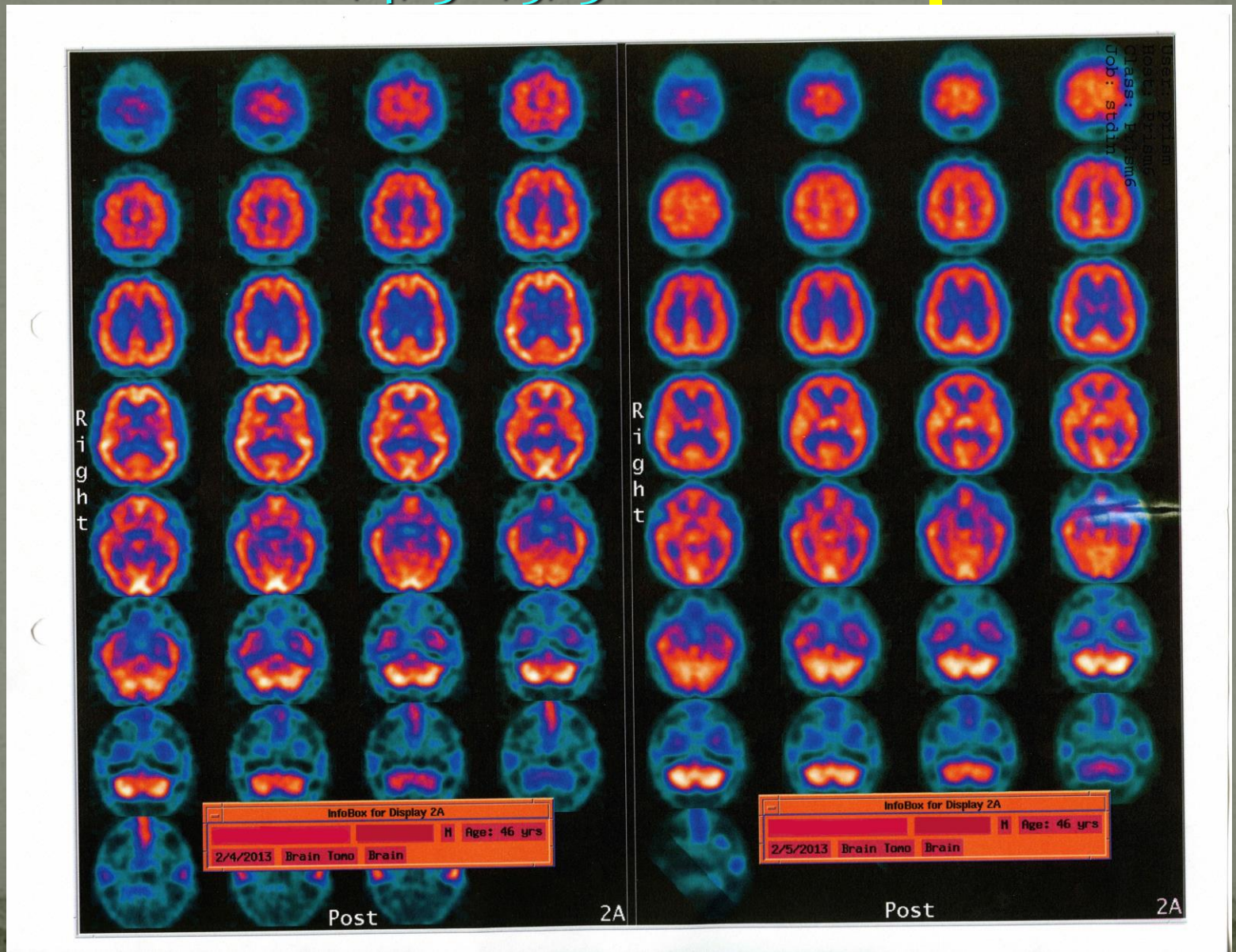
Purportedly Normal 34 year old male: LSU IRB 1998-2001





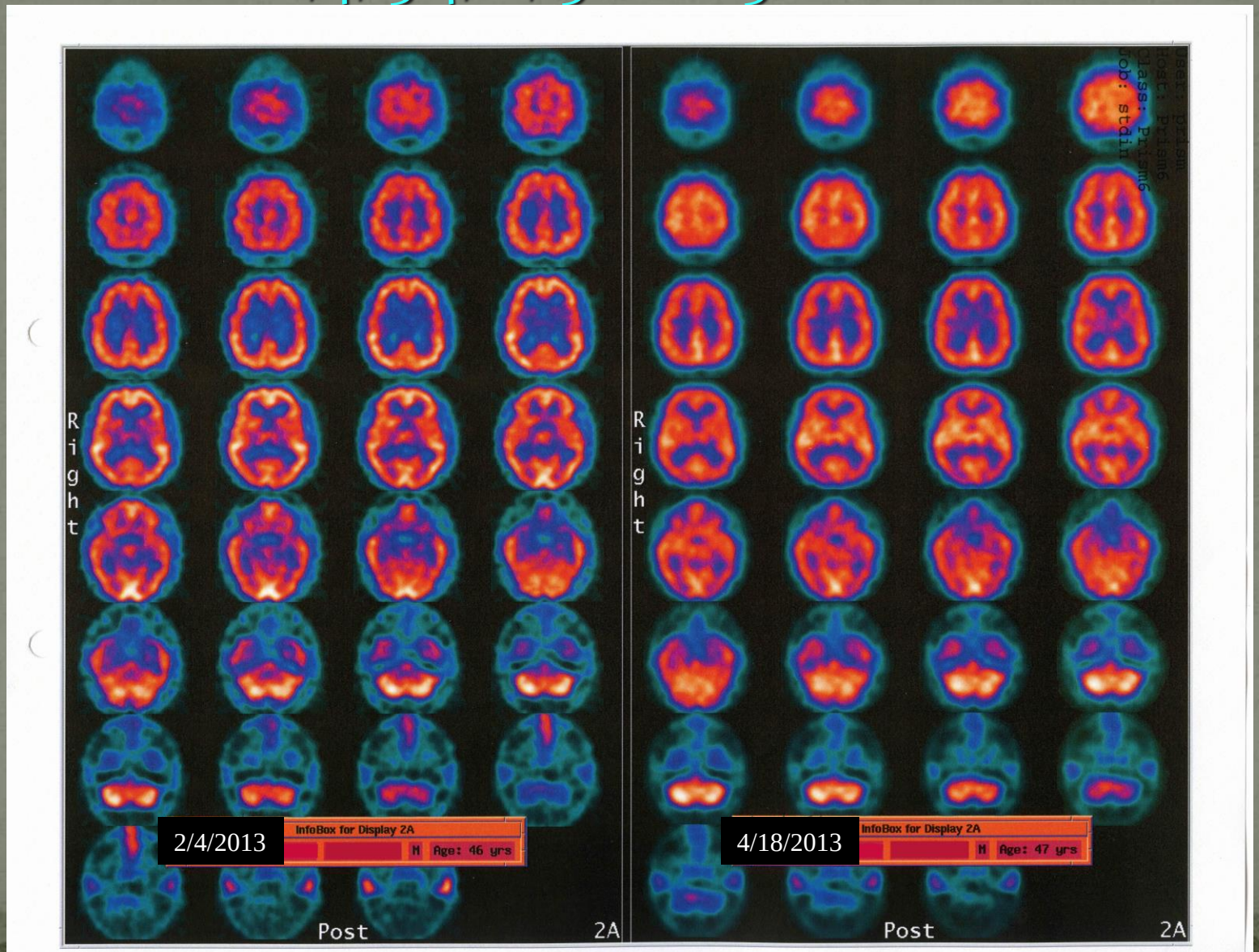
HBOT IN CTE

2/4/13-2/5/13—Post 1 HBOT



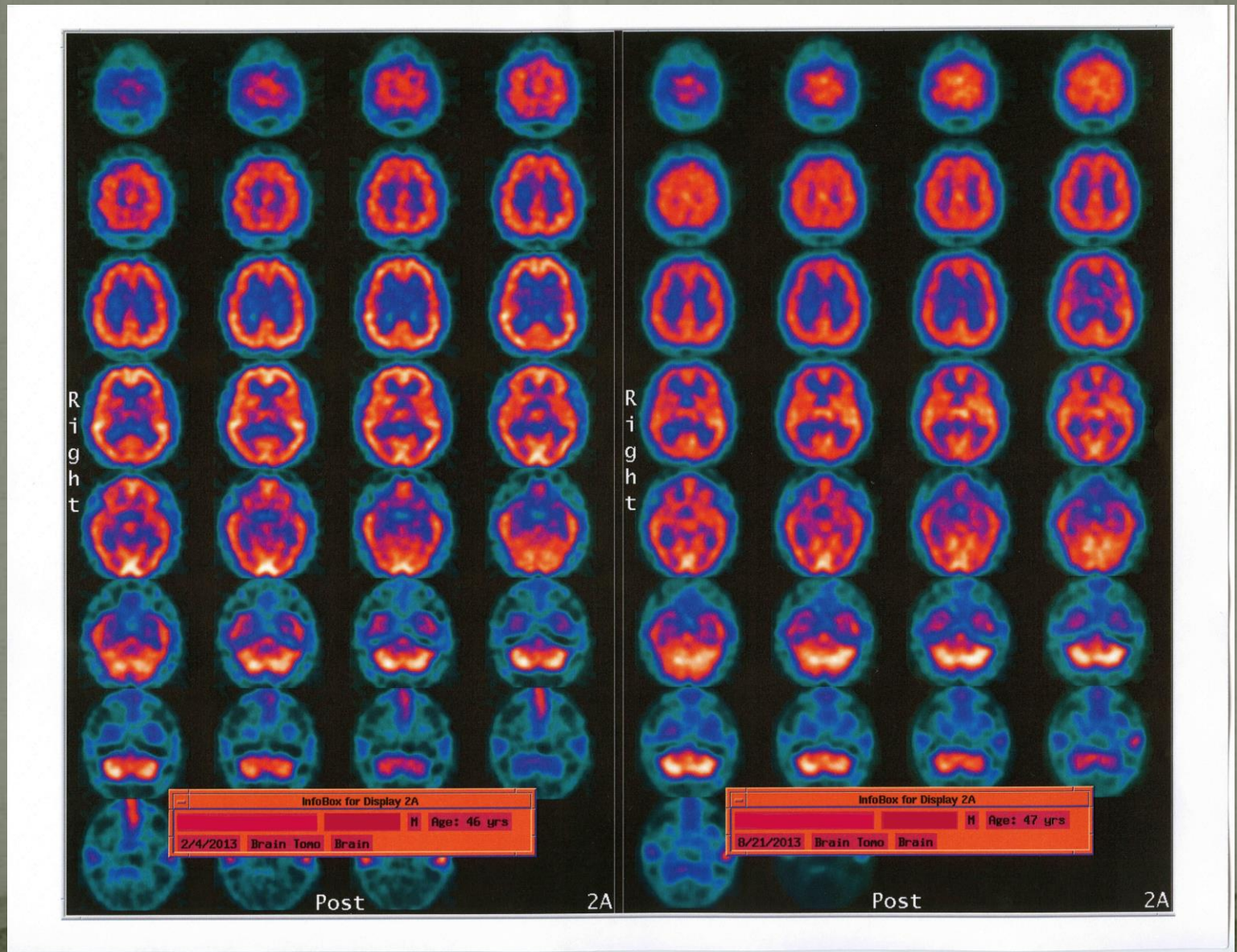
HBOT IN CTE

2/4/13-4/18/13—Post 36 HBOTs



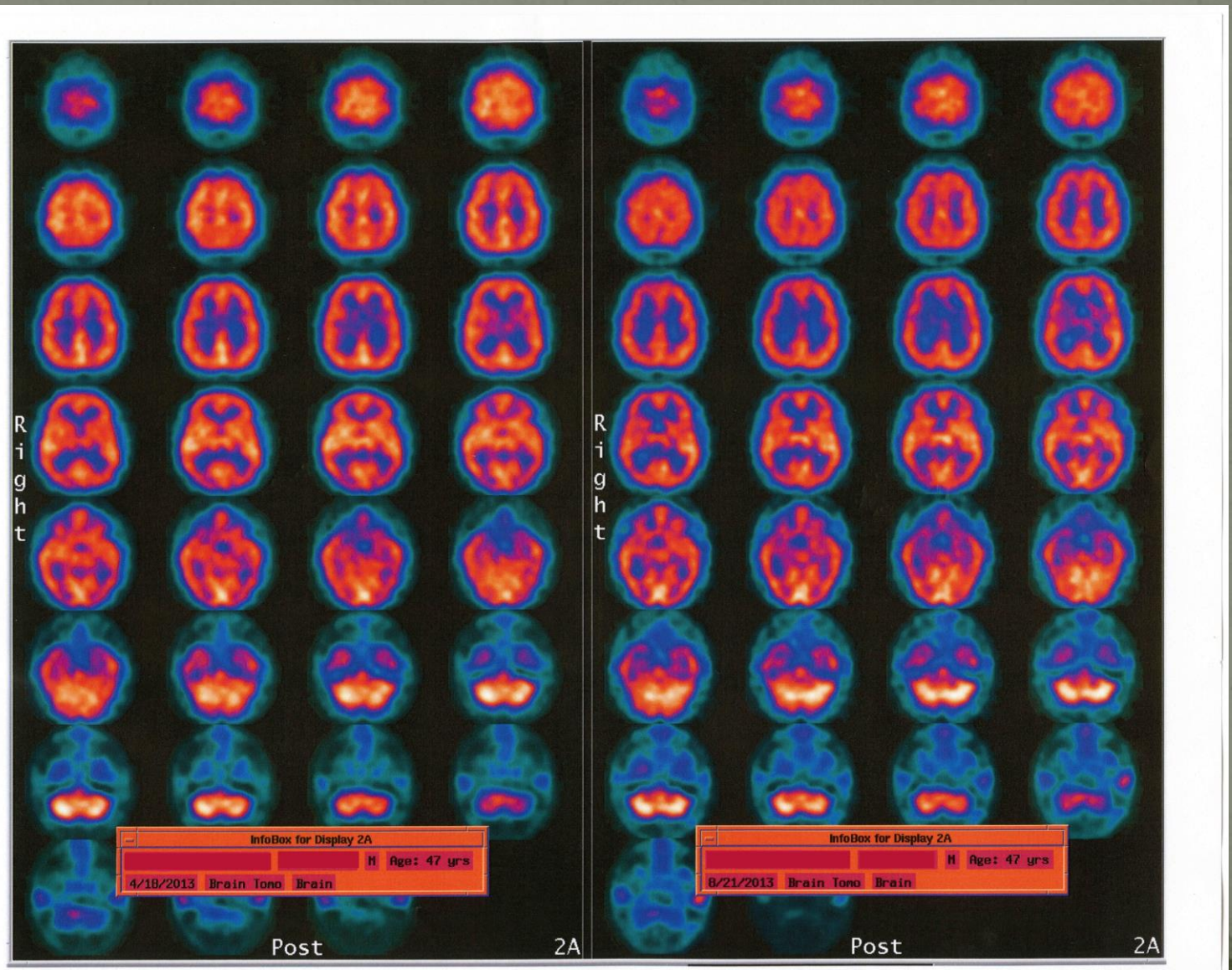
HBOT IN CTE

2/4/13-8/21/13—Post 70 HBOTs



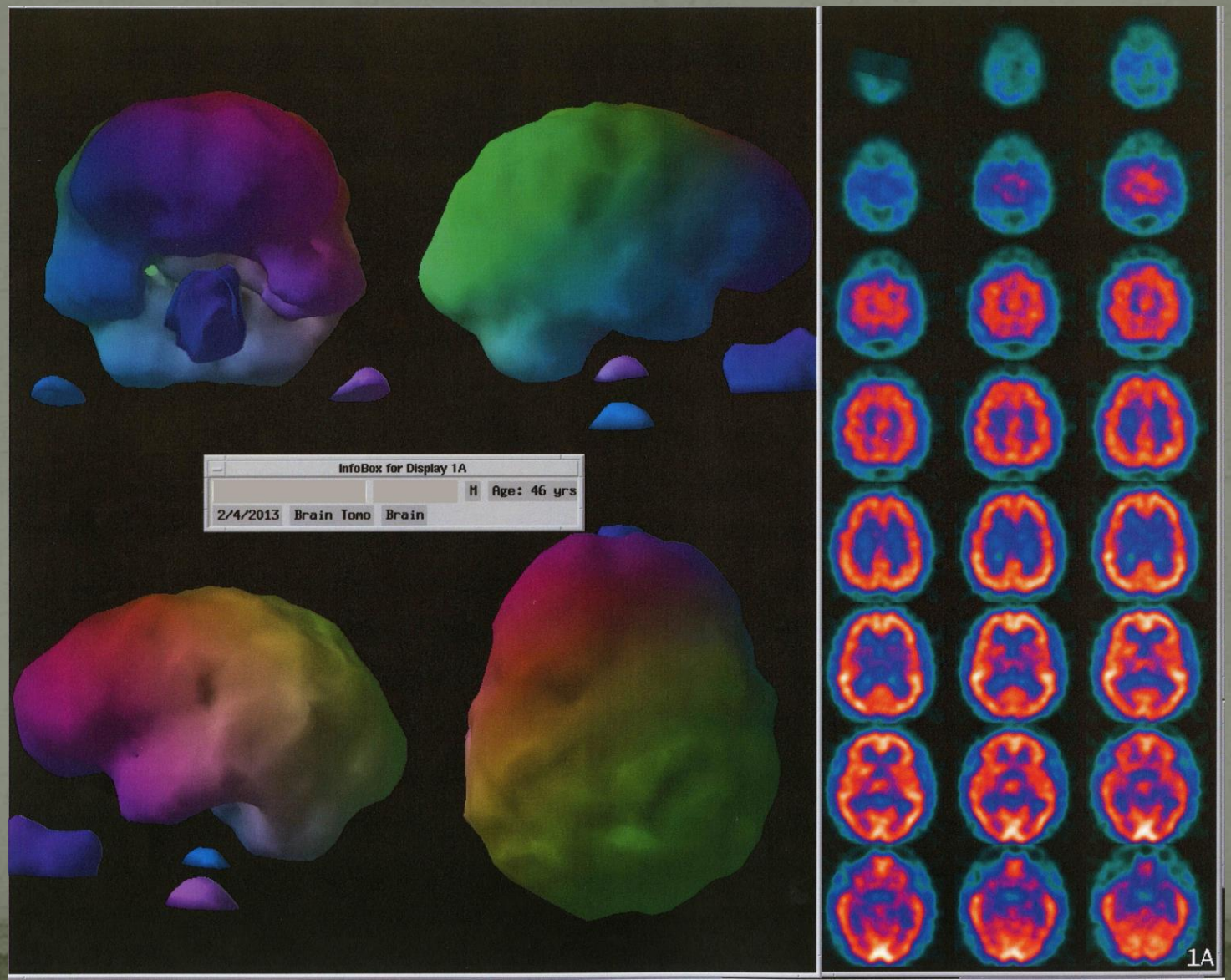
HBOT IN CTE

4/18/13-8/21/13—Post 36/70 HBOTs



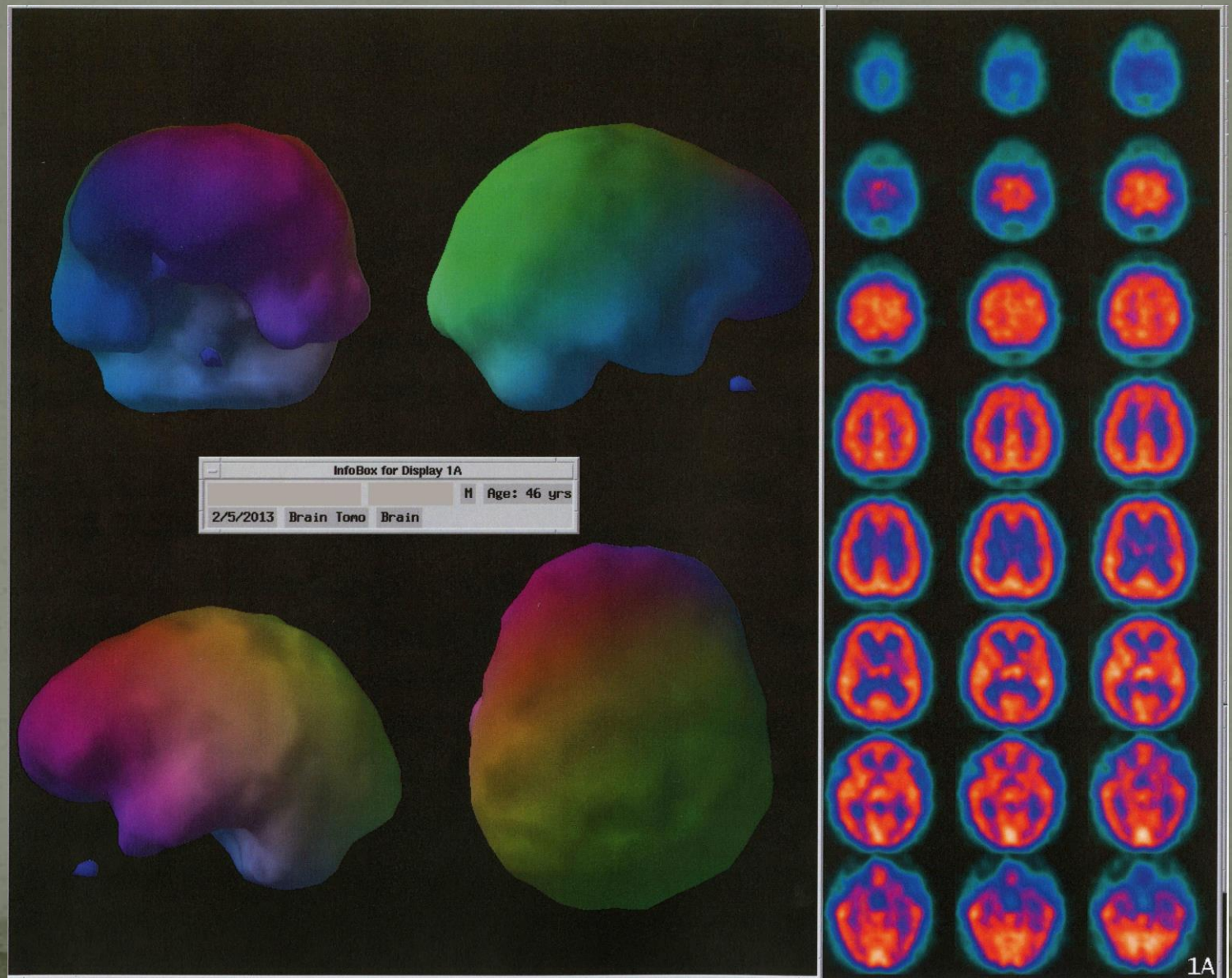
HBOT IN CTE

2/4/13—3-D Surface



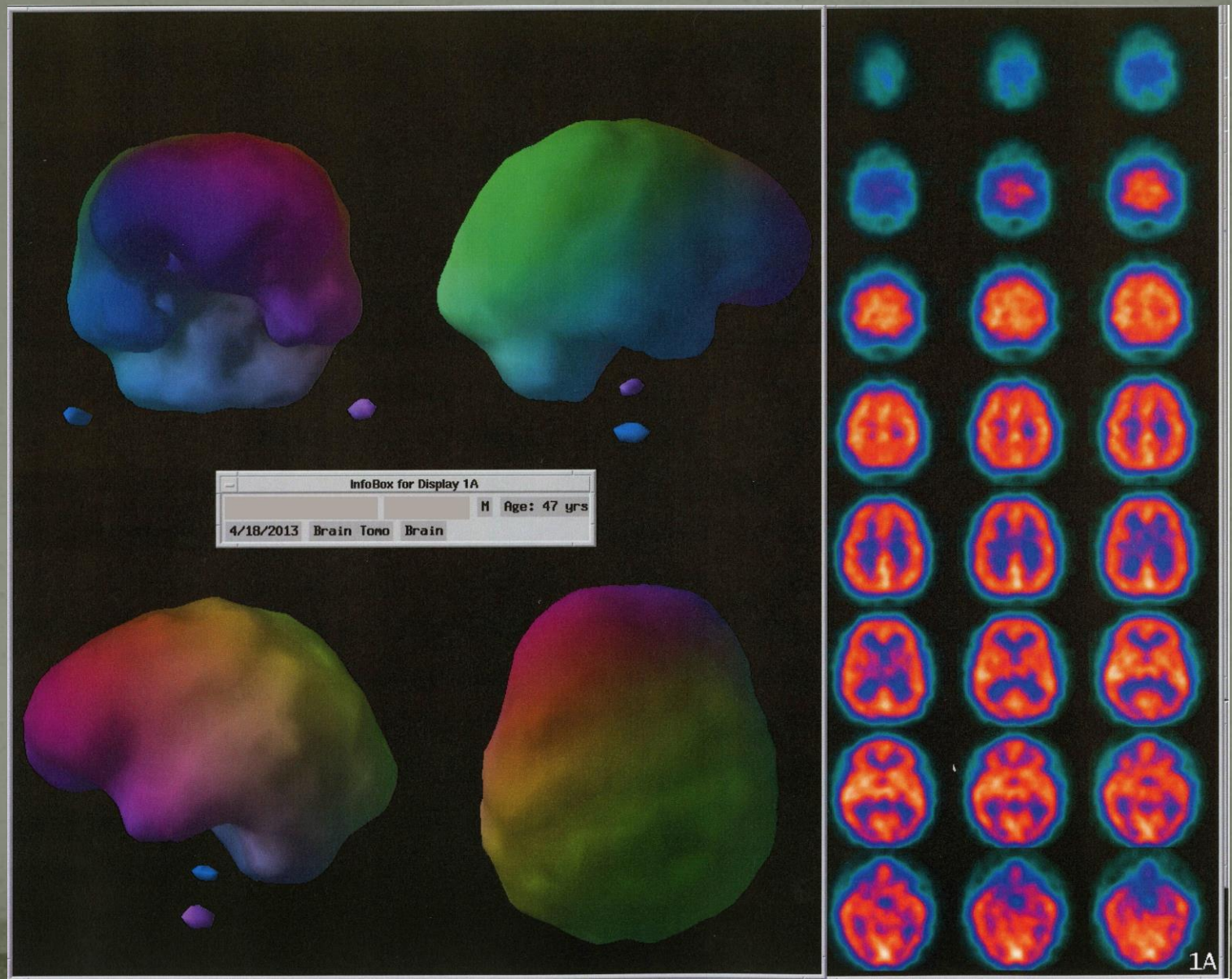
HBOT IN CTE

2/5/13—3-D Surface



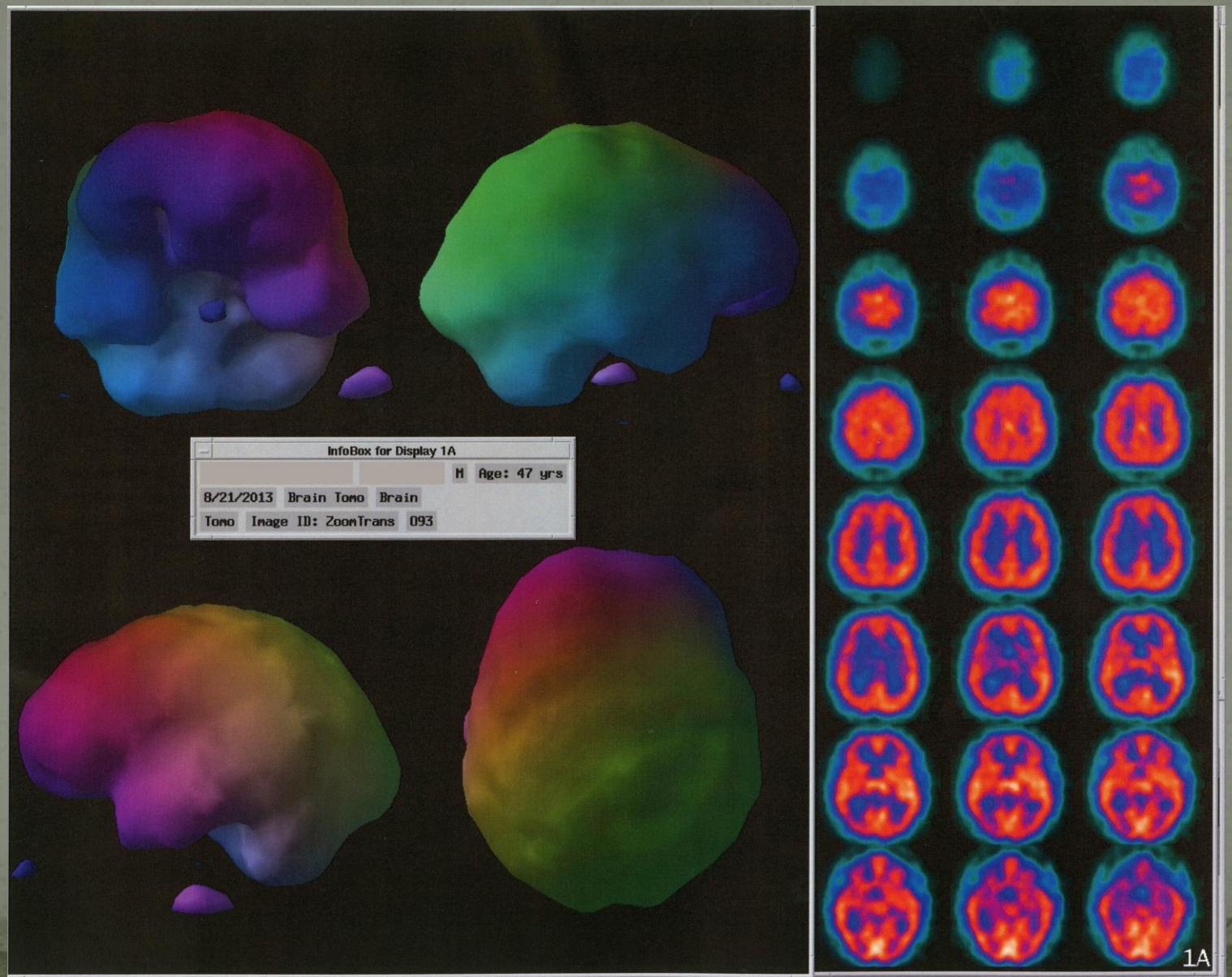
HBOT IN CTE

4/18/13—3-D Surface



HBOT IN CTE

8/21/13—3-D Surface



HBOT IN CTE

Followup:

5/12/2018: Patient remains active in his multiple businesses, has sponsorship by a national corporation, and hosts a radio show.

? Additional HBOT

HBOT and CTE

- Literature Review: Single publication
- Stoller, Medical Gas Research, 2011;1:17: 1 of 2 cases:
  - "In his early 50's", retired NFL player.
  - mTBI w/LOC Pop Warner football-youth
  - Numerous concussions through football career (high school, University of Colorado).
  - 2nd "major" concussion during 1st play in NFL, San Francisco 49ers.
    - 25-30 smelling salts to finish game.
  - 2nd season, concussion, headache, multiple evaluations by team trainer and physician. Pain pills.
    - Increasing headaches.

HBOT and CTE

- Stoller, Medical Gas Research, 2011;1:17
  - 2nd season,
    - Hydrocephalus.
    - Emergency VP shunt.
    - 11 subsequent shunt revisions over 9 years.
    - 19 years later (2009) undergoes 40 HBOTs at 1.5 ATA/60 minutes for ?Sx.
    - MicroCog assessment pre/post HBOT (improvement on 5/6 indices).
    - SPECT brain imaging pre/post HBOT (improved on surface 3-D reconstruction).

HBOT and CTE

- Stoller, Medical Gas Research, 2011;1:17

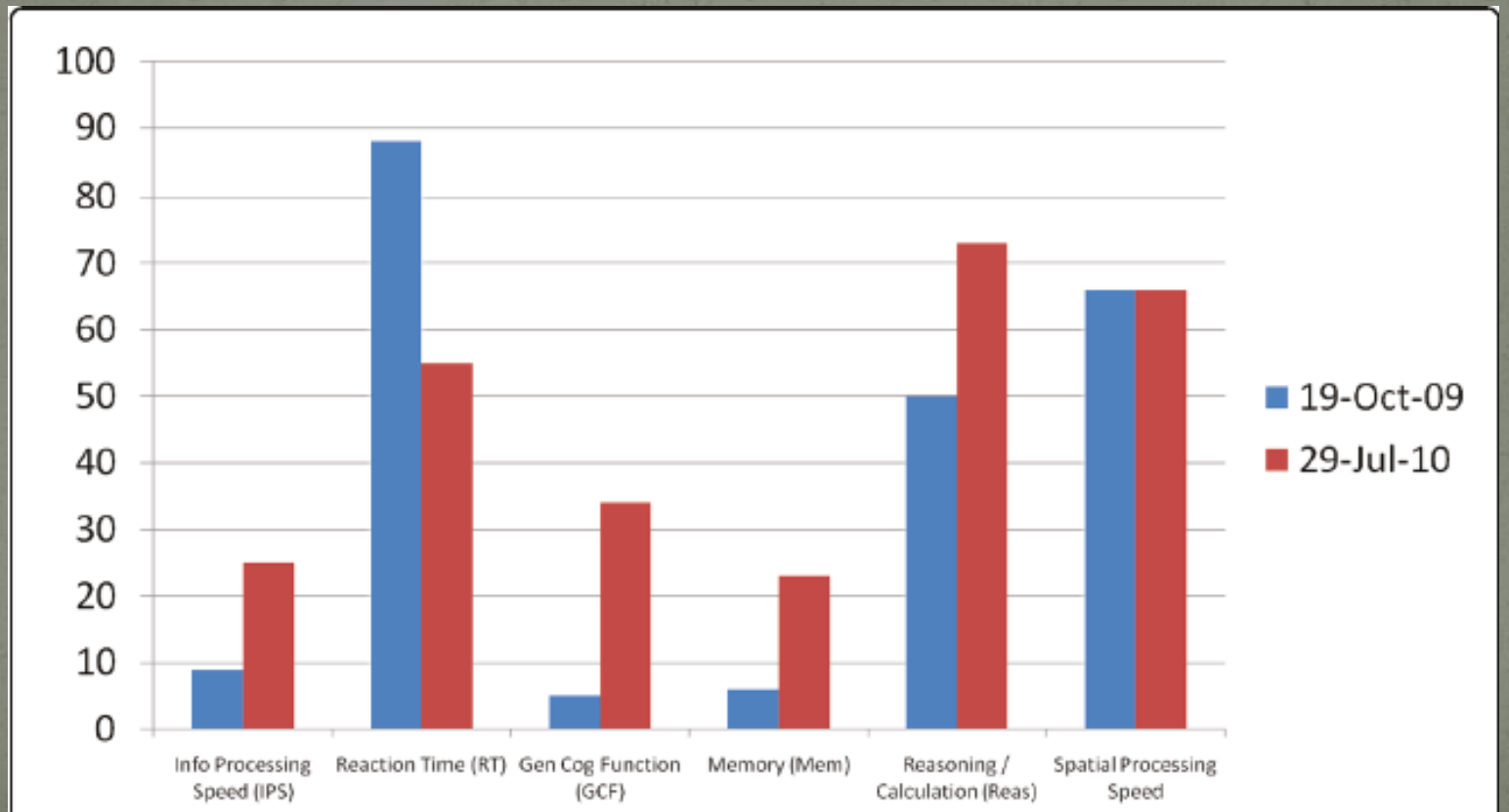
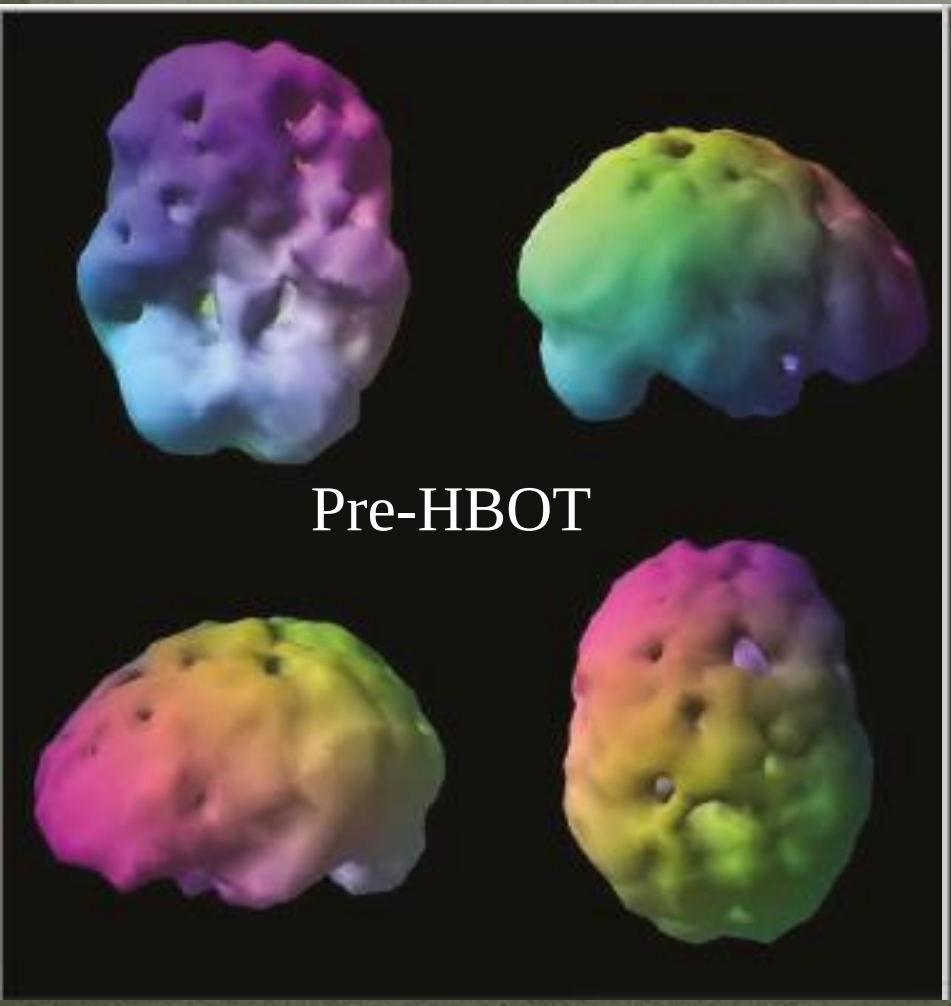
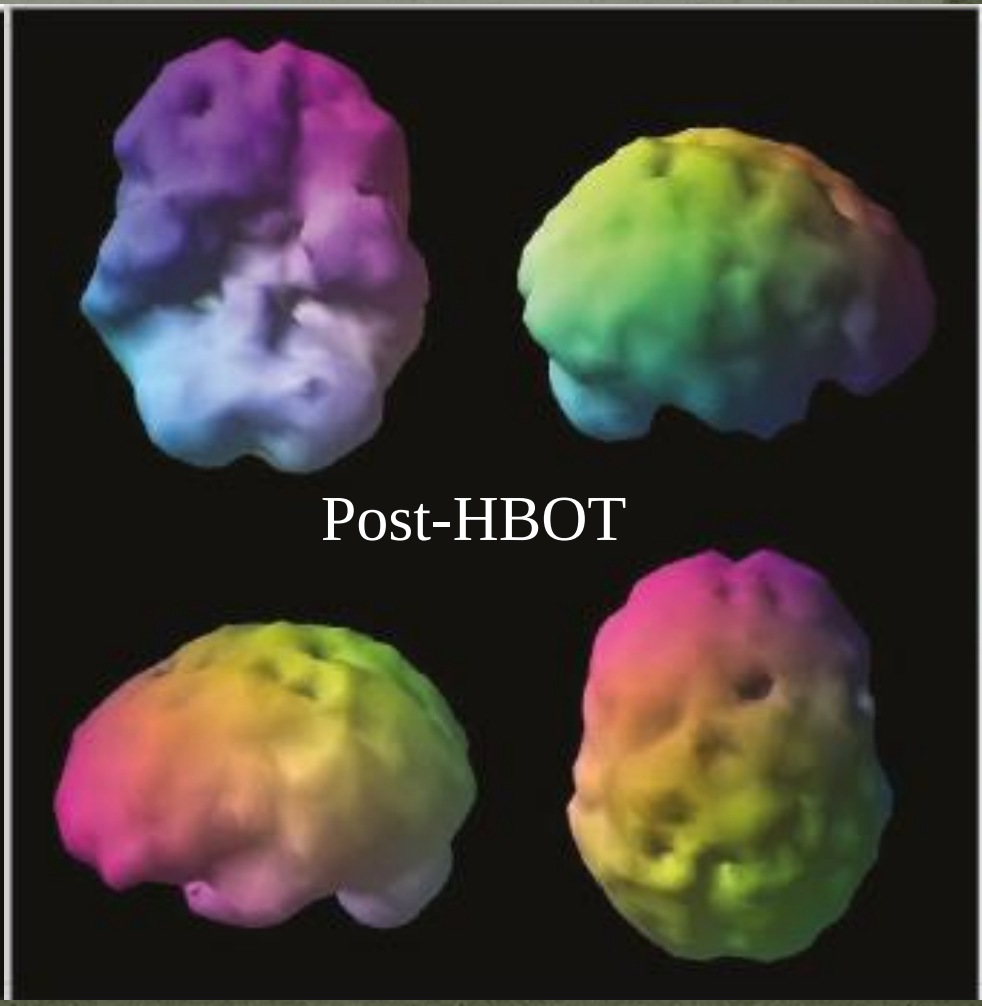


Figure 1 Source: MicroCog Assessment- Independent Evaluation by Amen Clinic. (The lower the score on reaction time the better the result).

HBOT and CTE

- SPECT surface 3-D pre/post HBOT:





HBOT and CTE

- Conclusions:
  - CTE is a pathological condition resulting from multiple traumatic wounds of the brain, possibly in combination with other insults, that is associated with a multi-domain clinical condition.
  - HBOT is a treatment for wounds in any location and of any duration
  - Limited case experience with HBOT in CTE.
  - Encouraging outcomes with HBOT in CTE consistent with HBOT treatment of other chronic cerebral wounding conditions, such as persistent post-concussion syndrome.

HBOT in Alzheimer's Disease: Case Presentation with PET

- 58 y.o. Caucasian female with cognitive decline over 8 months
- Extensive workup negative: blood work, MRI, MRA, bubble-contrast TTE, PVD study, abdominal ultrasound, 24h Holter monitor, carotid ultrasound.
- EEG: diffuse slowing.
- APOE: homozygous e3.
- Abnormal neuropsychological testing.
- Abnormal PET.
- PMH:
  - natural gas exposure/syncope 9 y.o.
  - Childhood exposure oil refineries, metallurgy plant.
  - 10 year work exposure to mold post Hurricane Katrina
  - Lifelong hypotension.

HBOT in Alzheimer's Disease: Case Presentation with PET

- FH: brother with dementia secondary to TBI (concussions, boxing), drug abuse, ECT.
- PEx: abnormal:
  - slight tremor, decreased pinprick bilateral face, instability on deep knee bend, decreased pinprick in distal 4 extremities, diffuse hyperreflexia, trouble following directions, tandem gait, disdiadokinesis, Romberg, finger-to-nose.
- Patient refused all medications except Lexapro, Biotin, Vitamins B12 and D three weeks pre-HBOT.
- HBOT: forty 1.5 ATA/50 minutes total treatment time, once/day, 5d/week HBOTs in 66d.
- After 21 HBOTS patient reported symptomatic improvement with increased energy/activity level, mood, ability to draw a correct clock face, perform activities of daily living, and work crossword puzzles.

HBOT in Alzheimer's Disease: Case Presentation with PET

- Neurologist started Exelon patch 9.5 mg for one week: discontinued by patient.
- At completion of 40 HBOTs patient reported
  - increased memory and concentration, not getting lost as frequently, resolution of anxiety, improved sleep, ability to use the computer, more good days (5/7) than bad days, better conversation, less frustration, increased appetite.
  - Tremor, deep knee bend, tandem gain, motor speed were improved.
- Repeat PET one month post HBOT showed global improvement in brain metabolism.
- Two months post-HBOT patient felt a regression in her symptoms. Exelon was begun at 9 mg, increased to 12, then decreased to 9 to GI intolerance.

HBOT in Alzheimer's Disease: Case Presentation with PET

- After 4 weeks Exelon was discontinued due to no improvement in symptoms.
- Four months post HBOT patient had repeat NP testing which showed improvement in some scores, no change in many, and worsening of many.
- Over the 18 months post NP testing patient has received 61 HBOTs.
- Folstein Mini-Mental status during this time is as follows:
  - 1/17/17: 22. Oxygen concentrator, 3x/wk x few weeks before this date. Restart Exelon patch 2/2017.
  - 5/12/17: 23. 70 HBOTs by this date.
  - 8/28/17: 23. Exelon, oxygen concentrator.
  - 2/7/18: 19. 88 HBOTs. Off Exelon x 2d. Start Donepezil, 5 mg/day.
  - 6/21/18: 22. 96 HBOTs.

HBOT in Alzheimer's Disease: Case Presentation with PET

- Conclusion:
  - HBOT generated a diffuse increase in brain metabolism, including the signature areas responsible for Alzheimer's Disease.
  - This implies an HBOT effect on more than just acetyl choline pathways.
  - Simultaneously, the patient experienced an improvement in symptoms and physical exam.
  - The HBOT effect was sustained with additional HBOT and medications.

HBOT in Neurodegenerative Disease (ND)-Take Home

- Neurodegenerative Disorders have many causes.
- Many of the causes of ND result in wounding of the brain.
- Persistent inflammation is crucial in the pathogenesis of ND.
- HBOT is a reparative treatment for wounds.
  HBOT is anti-inflammatory.
- HBOT dosing is a matter of matching the dose of pressure and oxygen to the pathological targets in the disease.
- The literature on HBOT in ND is not substantial, but sufficient enough to suggest that HBOT has a place in the treatment of ND, especially dementia.

Thank You