Modified Fractal Analysis of Brain PET and SPECT to Assess Grey and White Matter Function

Harold T. Pretorius, M.D., Ph.D.,^ Jerome J. Kelly, M.D.,^ Gwen Hubbell M.D.,^ Claire Hubbell M.D., M.B.A.,^ Ellen R. Hubbell, M.D., M.B.A.,^ Dennis Menke A.A.,^ Nichole M. Bodnar, B.S., CNMT,^ Betsy Budke, CNMT.

Objectives: Report new, modified fractal analysis of brain PET and SPECT.

Methods: Brain SPECT used a Siemens Ecam with IV Tc-99m-HMPAO or Tc-99m-ECD. Brain PET used a Siemens Ecat Exact 47 with MIE Scintron software and IV FDG or N-13 ammonia. Basal scans followed tracer uptake in a dimly lit, warm, quiet area. Perfusion stimulated scans used 0.8 mg nitroglycerin sl, or a quantitatively similar stimulus. Normalized peak activity was (1.6) (GW) where GW = mean of 3 axial slice average counts. Ln of isocontours, I, of peak counts, Pk, were plotted vs. Ln (Av/Pk), where Av is an average I count, to define Sb, a limiting positive slope extrapolated to (0,0), monitoring inhomogeneity in the area of most grey matter uptake. Similarly, a limiting negative slope, Sw, reflects inhomogeneity in the area of least white matter uptake from plots of Ln[(100+B)-I], where B is the I value at the brain outer border, vs Ln(Av/Mn), where Mn is minimum brain count. Basal cortical metabolic and perfusion-stimulated indices (CMi, CPi) were ratios of (the 60%(Pk) isocontour counts)/(total brain counts) in an axial slice 0.33 of the way from the most cephalad to most inferior axial slice, oriented with the longest frontal to occipital horizontal axis. Sb values were also calculated for other areas of grey matter. A white matter index WMi was calculated from the same axial slice as CMi, using numerator counts 0.33 of the way from the least brain count to the least grey matter count and denominator counts = total white matter counts; WMni = WMi/Sw. Statistical analysis used Excel 2013; results are +- Std Dev. The Montreal Cognitive Assessment (MoCA, normal > 25/30) monitored cognition.

Results: Sw 0.942+-0.089 for 8 near normal patients was similar to Sw 0.93 for a phantom with uniform activity. Sb for 18 near normal patients was normalized to Sbn = (AvC/CMi)(Sb) where AvC was the average near normal CMi (58.9+-5.2)%, yielding Sbn 0.407+-0.44. PET and SPECT values of Sbn were similar using CMi denominator counts in a 6% isocontour for the SPECT (without attenuation correction) instead of denominator counts in a 30% isocontour for attenuation and scatter corrected PET. For 5 near normals WMni -(53.4+-13.3)% was similar (p 0.41) to CMi (58.9+-5.2)%. Sbn 0.452+-0.016 for Insular cortex or putamen was similar to cerebellar grey matter Sbn 0.443+-0.052 in 7 near normals with MoCA 26.7+-1.6. For 104 patients with abnormal CMi and CPI (44.8+-7.3)%, Sbn was 1.089+-0.205 (p < 3 E-56) and MoCA 19.6+-2.9; among these 7 had WMni -(22+-10)% A patient with a midbrain lacunar infarct, despite normal CMi 57.0%, had midbrain Sbn 0.711 > putamen Sbn 0.574. Among 231 patients with CMi and CPI (52.1+-8.7)% and slightly low MoCA 24.1+-2.5, Sbn was 0.712+-0.102 (p < 1.0 E-22). Basal N-13 ammonia analysis was nearly equivalent to FDG or basal SPECT; perfusion-stimulated N-13 ammonia at < 6 min was similar to perfusion-stimulated SPECT.

Conclusions: Modified fractal analysis of basal and perfusion stimulated function in brain grey and white matter is sensitive, statistically robust and similarly applicable to pathophysiology elucidated by SPECT and PET. Analysis of white matter function also has potential to be very sensitive for abnormality not otherwise easily quantified.
1.

Fib 1: Near normal 15 year-old female high school basketball player post minor head injury has basal and perfusion, stimulated HMPAO SPECT at periventricular level showing visual stimulation of white matter (more green and less blue centrally, Sokoloff modified spectral scale) with CMi 65.3%, nml CMi 49.6-67.0% ; CPi 72.5%, nml (CPi 57.8-81.0)%,, WMi 60.7% ; WMni –56.5%,, Nml (60.0+-8.8)%,, Sw –1.074.

^ From Blue Ash Nuclear Medicine LLC, 4743 Cornell Rd, Cincinnati, OH, 45241 USA
Fig 2: HMPAO SPECT stimulated (omega 3 fish oil and coconut oil) over basal in a type 2 diabetic man with TYM 41/50 (corresponds to borderline abnormal MoCA 25/30). Above scan is in standard format 64 matrix with stimulated images shown in the top row of each set of axial, sagittal and coronal sections.
3.

Fig #: Same diabetic man, age 63 yrs as in Fig 2 but now post MI and CABG with LVEF 20% and Alzheimer’s pattern of parieto-occipital deficit (bottom images) which improves with perfusion stimulation with 0.8 mg nitroglycerin.
4.

Fig 24: Near normal appearing 67 year-old type 2 diabetic woman with similar ECD SPECT (above) and FDG PET (below) axial images showing sensitivity of the fractal analysis since CMi
Fig %: A 66 year-old man with advanced Parkinson’s disease also has evidence of Alzheimer’s disease with prominent mesial temporal abnormality. His insular cortex is preserved and even prominent, consistent with coexisting psychiatric depression.

Interestingly, analysis of his caudate by fractal methods showed a trend toward abnormality vs control patients with lower basal ganglia slopes. His DAT scan was markedly abnormal. Similar fractal analysis of DAT has shown promise, reported by others at SNMMI last summer.
Fig. 6 A Above, shows ECD perfusion on left and FDG PET on right in a mild depression in a near normal 68 y.o. man with MoCA 25/30; ECD SPECT CMi 51.9%, WMi 29.3%, WMni—28.6%, Sw –1.022 and FDG PET CMi 53.2%, WMi 30.9%, WMni –41.2% and Sw –.7489.

Fig 6B, Below shows ECD perfusion on left and FDG PET on right in severe depression with ECD SPECT CMi 40.7%, SPECT WMi 5.5%, WMni –4.3%, Sw –1.294 and FDG PET CMi 47.8%, WMi 24.3%, WMni –18.7%; Sw —1.405.
Fig 7: On left sagittal ECD SPECT shows focal decreased right frontal flow reserve deficit in a 74 y.o. man with proven stroke due to right carotid stenosis who had ECD SPECT CMi 47.6%, WMi 34.1%, WMni—19.8%, Sw –1.722 and FDG PET CMi 53.9%, WMi 22.5% and WMni –23.5%, Sw –.9575.

Below Right is an axial FDG PET with a more typical wedge-shaped deficit in a patient post aneurysm repair who had a left parieto-occipital stroke.
8.

Fig 8: A 66 y.o. woman has HMPAO SPECT on left with CMi 44.6%, WMi 26.4%, WMni – 26.9% and Sw –0.9826. Her CPI was 51.1% with WMi 17.1%, WMni—14.4%% and Sw -1.192. Values were similar with N-13 ammonia PET: CMi 49.9%, WMi 19.4%, WMni –21.8% and Sw –0.8906; & Nitrogly. Stim CPI 55.0%, WMi 15.2%, WMni –13.6% and Sw –1.1214.
Conclusion

1. Modified fractal analysis shows nearly fractal behavior (linear log-log plots) for near normal functional brain scans over the limited range of normal white and grey matter tracer intensities.

2. Deviations from normal are often most sensitively detected with analysis of white matter and its periventricular inhomogeneity, providing a quantitative but nonspecific measure of periventricular abnormality.

3. With appropriate standardization, similar results are obtained with technetium SPECT tracers of brain perfusion and metabolism as well as PET tracers including N-13 ammonia and FDG.

4. The method holds promise particularly for monitoring of therapy since it is relatively robust statistically and correlates well with patients clinical status.