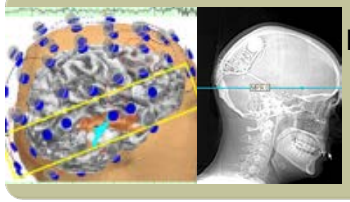

TIME-LAPSED TRANSIENT BRAIN BLOOD FLOW CHANGES DEMONSTRATED DURING DELIVERY OF DIRECT STIMULATION THERAPY THROUGH DEPTH LEADS IMPLANTED AT THE HIPPOCAMPAL GREY-WHITE MATTER JUNCTION

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AES 2011

1. SPECIFIC AIM

Novel dynamic SPECT technology using a 72-detector SPECT scanner system (NeuroLogica, Corp) demonstrated **time-lapsed** alterations in blood flow during hippocampal propagation of stimulation current delivered through a NeuroPace^{R} cortical stimulator depth lead. This dataset was compared with spatial imaging capturing the entirety of the activated circuit acquired with high-resolution static SPECT using the same scanner.

2. METHODS

A. Subjects

Three subjects (TS, SSp, SSm) with intractable independent temporal lobe epileptic sources were enrolled in the RUMC IRB-approved investigator-initiated study.

B. Technique

1. Testing was performed at 4.3 mo (TS), 27 mo (SSp) and 23 mo (SSm), respectively, following implantation of at least one hippocampal depth lead and skull-based stimulator. Prior to testing, 75 scalp electrodes were applied according to the 10-20 international system. The scalp positions were digitized using a Polhemus^{R} digitizer. The subjects were seizure-free for a duration of 24 hr prior to testing.

2. Stimulation current was delivered through two adjacent contacts of a 4-contact depth lead implanted longitudinally in the parahippocampal grey-white matter junction. Two adjacent left posterior depth electrode contacts (3-4) were stimulated in each subject using a bipolar configuration. An intravenous injection of Neurolite^{R} (Tc99m-ECD) was initiated as scalp data and concurrent depth electrode electrocorticography were acquired during continuous interrogation of the RNS generator. Stimulation settings during the session were as follows: stimulation current=4.0-5.0 mA, pulse width=160 usec, frequency=100 Hz, burst duration=60 sec, charge density=9.1 uC/cm^2. The duration of stimulation=60 sec. No after-discharge was recorded during the session. Transient blood flow changes were sequentially captured as 30 sec epochs.

3. Approximately 24 hours later, a baseline SPECT was obtained (when no stimulation was delivered, and no ictal activity recorded).

Subject TS

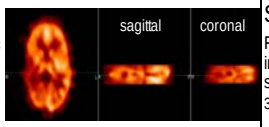

Figure 1. Average of 17 30-sec interval epochs (3-19) during scanning session.
3.6 cm thick slice through temporal lobe.

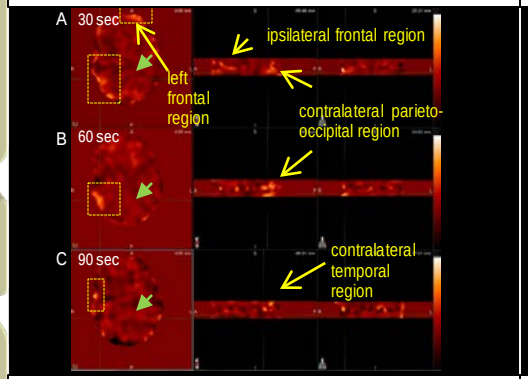

Figure 2. Dynamic SPECT. A slice is shown during each of 3-consecutive 30 sec epochs (30, 60, and 90 sec) *taken as a ratio* to the average of slices 3-19. Left depth electrode stimulation (green arrow; 30 sec duration) was initiated 60 sec after beginning the scan session. Hyper- (bright) and hypo-perfused (dark) regions demonstrate the activated neural circuit. Radiologically oriented.

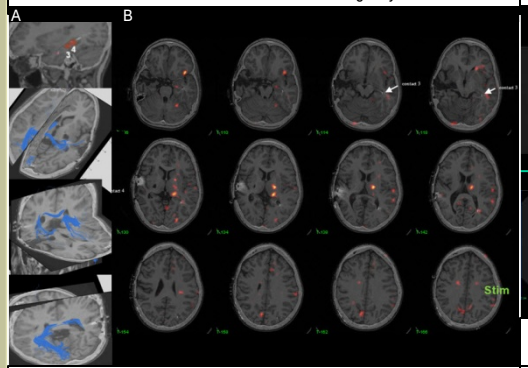

Figure 3. Static Activated SPECT. (A) Pre-implantation tractography model of 3.75mm radius 'seed volume of interest' surrounding depth electrode implant sites for contacts 3-4 on co-registered DTI-SPGR MRI.
(B) Post-implantation validation of tractography model using static subtracted activated SPECT co-registered to CT-MRI. Transient hyperperfusion-related changes are seen collapsed as a single snapshot while delivering a train of 12 brief pulses through depth contacts 3-4. The activated InSPira SPECT dataset was subtracted from a baseline study.

Subject SSp

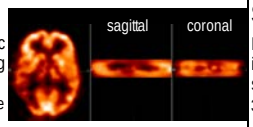

Figure 4. Average of 17 30- sec interval epochs (3-19) during scanning session.
3.6 cm thick slice through temporal lobe

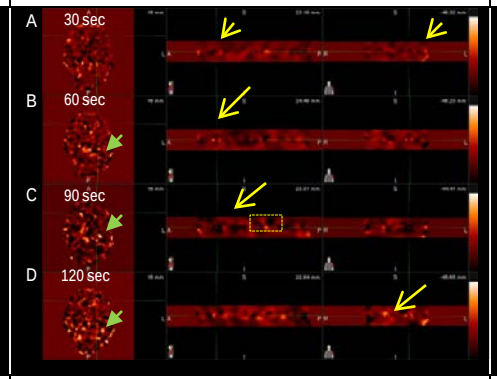

Figure 5. Dynamic SPECT. A slice is shown during each of 4 consecutive 30 sec epochs (A-D) *taken as a ratio* to the average of slices 3-19. Left depth lead stimulation (green arrow; 30 sec duration) was initiated 60 sec after beginning the scanning session. Increased blood flow is seen between hypoperfused regions of depth contacts (yellow dashed box).

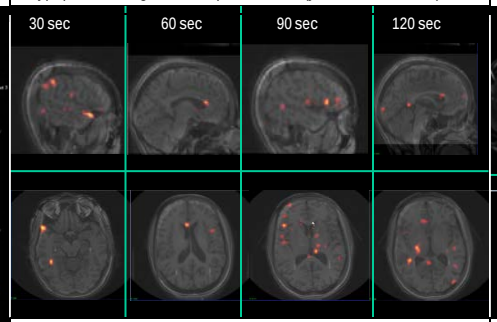

Figure 6. Dynamic ratio SPECT co-registered to MRI demonstrates transient hyper-perfused regions over 120 sec.

Subject SSm

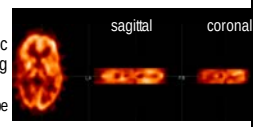

Figure 7. Average of 17 30-sec interval epochs (3-19) during scanning session.
3.6 cm thick slice through temporal lobe

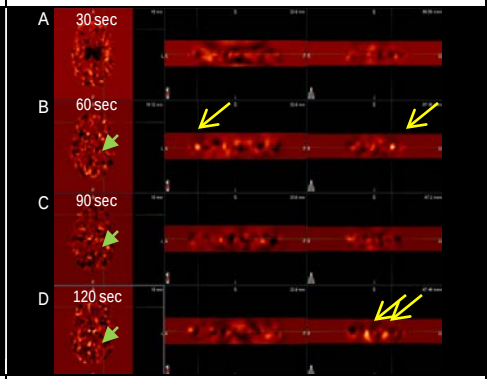

Figure 8. Dynamic SPECT. A slice is shown during each of 4 consecutive 30 sec epochs (A-D) *taken as a ratio* to the average of slices 3-19. Left depth electrode stimulation (green arrow; 30 sec duration) was initiated 60 sec after beginning the scanning session.

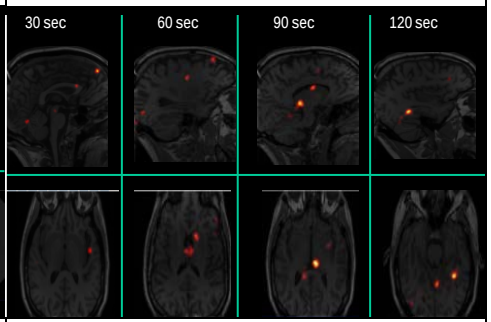

Figure 9. Dynamic ratio SPECT co-registered to MRI demonstrates transient hyper-perfused regions over 120 sec..

3. CONCLUSIONS

Dynamic SPECT complements static SPECT neuroimaging using a novel high-resolution SPECT scanner system. This technology and workflow offer a unique approach for validating depth lead implantation and delivery of stimulation therapy through the maximal extent of an epileptic circuit.

4. REFERENCES

Rossi et al (2010). Predicting White Matter Targets for Direct Neurostimulation. Epilepsy Res 91:176-186.

5. ACKNOWLEDGEMENTS

NeuroLogica Corp (Danvers, MA)
Institutional (RUMC)