Novel Microwave Pulser/Sampler ICs Enable Early Portable Functional Neuroimaging Prototype

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Summary

• Research Goal—low cost *real-time* medical microwave measurement using *non-ionizing* EM waves, no need for cryogenics or magnets, enabling portable *functional* imaging.

• Background – Have developed custom ICs for pulse-based radar and Communications, using these to show microwave pulse reflections from deep inside body and useful transmission through widest parts of body.

• Demonstrated preliminary feasibility for functional brain measurements using microwave pulses.

• Seeking collaboration and funds to develop and build a cranial functional microwave imager and potential neuroprosthesis.
The Team

- **Joel Libove** PhD, MSEE UC Berkeley, BSEE Cornell. Doctoral research in MRI flow imaging. 14 patents. Designed first VME bus and PCibus timing analyzers and protocol violation recognizers, and over 30 high speed data acquisition systems and four generations of high dynamic range variable aperture microwave pulse generation and sampling ICs in GaAs, GaN, InP, SiGe, and CMOS/SOI Si.

- **Mike Ingle** worked at UC Space Sciences Laboratory while studying Physics at UC Berkeley. 20 years experience designing nuclear instrumentation at UC Berkeley Nuclear Engineering Dept., SAIC, and Rapiscan Systems. Designed a variety of high channel count imaging systems, e.g. 256 channel simultaneous gamma ray time (TDC) (to tens of ps) and energy measuring system. This allowed the development of an over 100Mpps nuclear ADC

- **David Schriebman** BS in Applied Physics - Physical Electronics from UC Davis. Software modeling of physical processes and signal analysis of complex electronic systems, particularly statistical analysis.

- **Matthias Reinsch** Ph. D. in Theoretical Physics from UC Berkeley. Worked on Inverse Lithography Technology, electromagnetic vector diffraction problems and algorithm development. In recent years, his work at LBL has included extensive electrodynamics simulations and theoretical analysis.
WHAT ARE SAMPLERS AND PULSERS?

Function of an electrical sampler and electrical pulser

Sampler (top) acts like a switch that is turned on briefly and then turned off, storing the value of an input signal, usually in a capacitor.

Pulser (bottom) acts like a switch that is turned on briefly and then turned off, creating a brief electrical pulse that is fed to a load, such as an antenna.
Pulse trains generated by monolithic RACE pulser

Time Domain Waveform for 2GPPS pulse train.

- Pulse width approx. 10ps on chip
- Displayed pulse width 14ps, due to connector losses, convolution with scope response

Frequency spectrum for 1GPPS pulse train

- Comb tooth every 1GHz
- Declining output as frequency increases – due to finite pulse width, connector and cable losses

March 2015
Furaxa technology:
Rapid Automatic Cascode Exchange (RACE) Sampler/Pulser
PATENT 6,433,720 + auxiliary circuitry (not shown)

Works like a hose being rapidly swept along a brick wall with an opening.
100GHz Sampling and Pulse Generation on Single Monolithic IC

TDR/TDT/VNA Front-End IC

TDR/VNA front end using Indium Phosphide (InP) integrated sampler pulser IC
SEQUENTIAL EQUIVALENT SAMPLING, USING CONVENTIONAL HETERODYNING
Fast Monolithic Sampler/Pulser: 100 GHz BW, 110dB DR with 1s avg

500MHz freq. component

7ps pulses generated by IC, and sampled by sampler in same IC

1GHz… etc

Externally added 500MHz sinewave

Frequency spectrum to 140 GHz
L: Variable Width/Amplitude pulses generated by GaN 12V pulser
Right: Headband assembly. Pulser in center, samplers to sides.

Testing of group of 32 70GHz InP pulser/antenna/sampler assemblies
Our Picosecond Electrical Pulse Approach:

- **Portable** pulsed RADAR imaging
  - Pulser-sampler - low noise, high dynamic range
  - Tiny, low cost chips & boards
  - Usable signal detection through human body
  - Lightweight – use in ambulances, battlefield
  - Replacement for some MRI/MEG/CT/PET/EROS uses
  - Possible future new market for low cost imaging, Neuroprosthetics

- **MICROWAVES INTO MY HEAD? -- YIKES!!!?**

  Probably OK. Total average RF power absorbed by subject using this technology is approx. 10mW - comparable to that absorbed when using a cell phone and roughly 1/800 that absorbed during an fMRI image.
Single-chip containing pulse generator, proprietary diff-amp, antenna, sampler
And optional EEG electrodes and preamps
Present Functional Brain Imaging Methods

Functional brain imaging allows researchers and health care providers to spatially and temporally assess level of metabolism the brain, in response to neural activity.

- **Existing functional imaging solutions**
  - PET, SPECT – injection of radioactive tracers – Glucose uptake
  - fMRI – shows changes in blood flow – Response time 1-3 sec.
  - EEG, MEG, ECoG, NIR/EROS

- **Functional imaging difficult**
  - fMRI is slow, expensive, large unnatural environment
  - PET is slow, large, expensive, uses radioactive tracers
  - EEG is low resolution, low speed, requires scalp preparation
  - ECoG (electrocortigraphy) is invasive, covers surface of brain
  - MEG is large, expensive, non-portable
  - NIR/EROS is fast, portable, but shallow penetration, poor resolution \(\leftarrow\) Probably closest analog to our microwave method
Event Related Optical Signals (EROS)

Back-Scattering of NIR Photons under Conditions of rest and activity

Combination of underlying physical phenomena: Blood flow, cytochrome C oxidase, neural swelling


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Reflections from tissue boundaries, and other discontinuous regions
PAS (Pulser / Antenna / Sampler)

- Pulse Ampl.
- Pulser Clock
- Sampler Clock

Er = 50

Skin Er = 50 2mm
Skull Er = 20 6mm
CSF Er = 70 4mm
Cortex Er = 52 3mm
White Matter Er = 38

PCS (Pulser / Coaxial Probe / Sampler)

- Sampler Output
- Sampler Clock
- Pulse Ampl.
- Pulser Clock
- Coaxial Line
- Ground Flange

Er = 1

Skin Er = 50 2mm
Skull Er = 20 6mm
CSF Er = 70 4mm
Cortex Er = 52 3mm
White Matter Er = 38

Pulser/antenna/sampler radar (left) vs Pulser/coaxial-probe/sampler TDR/TDT (right).
EXTRACTION OF FUNCTIONAL COMPONENT (SIMPLIFIED ALGO.)
Right frontal lobe reflectivity plot obtained from antenna on forehead during 62-second TDR recording. Reflectivity changes from cerebral tissue are detected by same launch antenna, with those reflections from deeper tissue boundaries occurring later in time (2.4ns) vs 0.8ns for shallower tissues, representing depths consistent with cerebral tissue.
Offset-TDR Brain radar using GaN Pulser and SiGe sampler
R and L frontal lobe reflectivity plots obtained, in response to GaN pulser/antenna in center forehead during a 4-sec recording. Based on arrival time, we believe initial edge in each received waveform is due to a reflection from the interior surface of the skull (refl. from earlier tissue boundaries are less visible by offset TDR). Reflectivity changes from cerebral tissue begin approximately 0.6ns later consistent with the expected round-trip time to the surface of the cortex. Reflections from deeper tissue boundaries occurring later in time – over a 1.6ns round-trip range, represent depths consistent with those expected for cerebral tissue.
4-sec offset TDR plot with pulser placed at center back of head and samplers placed over the left and right occipital regions, taken while visual stimuli are delivered to the subject via a video. Waveshape of the signals in these occipital recordings differ from those of the frontal recording of prev. slide, and show more concurrent bilateral activity. Of note are several bursts of ~25-30Hz energy, superimposed on gradually ramping slow activity near the surface of the cortex, as well as evidence of deep brain activity at times.
Offset TDR experiment with massive motion artifacts on the left antenna, but just a minor/brief motion artifact and otherwise good data on the right antenna. Artifacts may also be caused by arterial pulsation and possible cerebrospinal fluid (CSF) pulsation. These, however have an obvious periodicity at the subject pulse rate, and have waveshapes that are recognizable as pulse-pressure-modulated waveforms.

**Question:**

**BUT IS IT REALLY NEURAL ACTIVITY?**
Pulsation from cerebral arteries at varying depths, measured noninvasively through skull. Note differences in pulse waveshape for likely-different vascular structures. Apparatus’ capability for charting, in real time, vascular bed motion, and possible CSF motion, on the same time axis as microwave functional activity and EEG. Drift from baseline in some traces, combined with broad antenna radiation pattern, make it difficult to ascertain exact depth and position with present algorithms.
POTENTIAL FUNCTIONAL IMAGING USES, IF SUCCESSFULLY DEVELOPED

Neuroprosthetics: Motor, Speech
Brain mapping – faster time response may allow new studies
Polygraphy - later, possible “thought identification”
New way to communicate at high speed.
Potential use in a non-invasive motor prosthesis
Futuristic Full-brain functional imager
POTENTIAL FOR USABLE SPATIAL IMAGING?

Considerable worldwide work, but limited results so far.

- Severe scattering, antenna density limitations, etc.

.... but some promising early results from many research groups.

Early use by several groups for breast cancer detection, differentiation of ischemic vs. hemorrhagic strokes.
Potential Structural Imaging Use
Hemispherical scanner prototype, and early 2-D depth images of forehead

February 2015
Early interferogram, shows narrow region of sharp tissue differentiation

March 2015
Work by various research groups

- Microwave imaging for breast cancer
  - Clinical trials: Dartmouth, University of Bristol, Chalmers University
  - Other universities: Duke, Calgary, Manitoba, Wisconsin, …
  - *Not able to image head or torso*
- Small spinoffs from universities
  - Medfield Diagnostics (Strokefinder) – A. Fhager from Chalmers University
  - EMTensor (Portable stroke diagnostics) – S. Semenov from Keele University
- Underlying technology from competitors
  - Network analyzers (NA) and existing circuits limited to <140 dB
    - Cost of NA $25K-100K, not portable, expensive switching, cabling
  - Furaxa can replace NA for this limited purpose, for $100 for 4 antennas, 4 chip, & AD converter.
Development plan toward commercialization

- **Design of new chips**
  - GaN with pulser and sampler on same chip  SEEKING COLLABORATION
  - Fab, assembly and testing
- **Build helmet / mechanical prototypes**
  - Digital simulations for antenna design
  - Data acquisition HW for large number of channels
  - Prototype using physical phantoms
- **Imaging algorithms**
  - Simulate realistic digital phantom, use for testing algorithms
  - **Full waveform inverse scattering**  SEEKING COLLABORATION
    - Forward simulation FDTD
    - Inverse problem – nonlinear optimization
    - Regularization algorithms
SAFETY

Transmitted RF Power Measurements and Patient/Subject Safety Analysis for Proposed Novel Non-Invasive, Portable Electrical Pulse-based Structural and Functional Brain Imaging Modality
Safety of Proposed Imaging method vs Conventional Functional Brain Imaging Methods

Existing RF-based functional imaging solution

FMRI – Subjects patient/subject to 1-3T magnetic fields, and several watts of absorbed RF power, with SAR of up to 3.2W/KG of body tissue, and 0.6 degree temp. rise:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2705217/
https://www.biac.duke.edu/research/safety/tutorial.asp

I had an fMRI on 5/24/15 in a 3T 60cm dia. long-bore magnet and had trouble staying still enough to do good 10-minute retinotopic experiments.

Proposed Imaging Method:
No static field, no magnetic gradient field. Uses RF pulse train having approximately 6mW total average power, radiated over approximately a 2 square cm area. Time domain and frequency domain power measurements of emitted pulse train are on next two slides. Apparatus would move with head – movement OK.
Frequency Domain Power Measurement.

Comb teeth in 100MHz increments, with ~-1.2dBm (630 microwatts) in each tooth into 50 ohm half-antenna load. For 100 ohm differential antenna feed, total power is 1260 microwatts in each tooth. For comb teeth with significant power (>~30dBm), total average power = 50 x 1260 microwatts = 63 milliwatts. Measured with Rohde & Schwarz FSP38 spectrum analyzer.
Time Domain Power Measurement

Each complementary pulse half reaches peak amplitude of 6V into 50 ohm half-antenna load, as shown in the oscilloscope measurement below. For 100 ohm differential antenna feed, total voltage is 12V peak. Width used in experiments will not exceed 400pS FWHM. For 100 million pulse per second repetition rate used, total average power is given by:

\[ P = \frac{V^2}{R} \times \text{duty cycle} = \left( \frac{12 \times 12}{100} \right) \times \frac{0.4\text{ns}}{10\text{ns}} = 1.44 \times 0.04 = 57.6\text{mW} \]
Other Clinical Research Apparatus Utilizing Microwave Energy Similar to that Proposed for New Imaging Modality

Microwave Head Imaging for Stroke
http://www.jpier.org/PIERM/pierm21/12.11082907.pdf
http://emtensor.com/publications-list/
http://www.nhs.uk/news/2014/06June/Pages/can-a-microwave-helmet-really-detect-strokes.aspx

Microwave Diathermy Machines
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1478902/?page=1

Microwave Breast Imaging Research Prototypes
Brain and other Nervous System Cancer: New Cases, Deaths
Location of Gliomas in Relation to Mobile Telephone Use: A Case-Case and Case-Specular Analysis

“These results do not suggest that gliomas in mobile phone users are preferentially located in the parts of the brain with the highest radio-frequency fields from mobile phones.”

http://aje.oxfordjournals.org/content/174/1/2.long
Environmental Health Perspectives

Epidemiology of Health Effects of Radiofrequency Exposure
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1253668/

This paper reviews long term studies of occupational exposure (eg Navy veterans) with regards to cancer:

“In conclusion, there is no cancer site for which there is consistent evidence, or even an individual study providing strong evidence, that occupational exposure to RFs affects risk. “
Conclusion

- Ultra high-speed, low-noise, low-cost IC technology, proven in other applications
- Promising new imaging modality - portable, early screening, low cost, new insights from new modality,
  ... Difficult path ahead - Seeking collaboration.
- Large potential market, new functional imaging category

CHALLENGES:

- Severe degree of scattering, attenuation at high f
- Prone to motion artifacts – Can be mitigated (TDR)
- Requires new GaN combined Pulser/Sampler ICs
THANK YOU.

Short video to follow
Background

- Furaxa formed in 2001 – proprietary IC & boards for ultrafast electronic sampling and pulse generation
  - 2 patents granted – 6,433,720 and 6,642,878
  - Additional patents in progress for circuit and imaging techniques and apparatus
  - Complete RADAR on single chip, integrated with antenna
- Company history
  - DoD funding has resulted in 15 IC runs to validate and refine pulse generation and sampling technology
    - SiGe, InP, GaN, GaAs, CMOS/SOI
  - Customers include:
    - Ground penetrating radar (GPR) manufacturer
    - Endoscope manufacturer
    - University and national research labs
Pre-existing types of microwave pulsers and samplers*:

Pulser: Step recovery diode (high jitter, requires high voltages)
Sampler: Step recovery diode driving Schottky Diode bridge
Pulser: Avalanche Transistor (high jitter, requires high voltages)
Pulser or Sampler: Pulsed picosecond laser striking Photoconductive semiconductor (fast, expensive, large)
Slower current steering pulsers and samplers
Pulser: Nonlinear Transmission Line (Expensive, large IC size)
Sampler: “ “ “ driving Schottky

*Overview: M. Kahrs, 50 Years of RF and Microwave Sampling. IEEE Transactions on Microwave Theory and Techniques, VOL. 51, NO. 6, JUNE 2003
Quick Background – IF (bandpass) Sampling and Frequency Comb Generation

Samplers/pulsers with high analog BW and moderate sampling rate can capture or generate very high frequencies

Requires Analog BW >> Sampling rate
BP Filtering for desired band of interest (centered around nth comb tooth)

Sampler Analog bandwidth
Highest Frequency governed by the width of the sampling aperture.

Typical sample/pulse widths with “R.A.C.E.” technology (Pat 6,433,720)
- 7ps 30GSPS in production InP ICs
- 10ps 20GSPS in production SiGe ICs
- 50ps FWHM 2GPPS 20V differential pulser ICs in production GaN ICs

Sampling (repetition) rate
Higher sampling rate results in stronger (but sparser) frequency harmonics.

Does not affect analog bandwidth. Too high sampling rate can muddy measurement, due to reflected response including residual signals from earlier pulses.

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Exp 29
Coarse grid for display purposes only
Based on exp 28

Two antennas, in same plane, one in the original location.

Place an object in the brain in order to study reflections.

The object (a sphere) and one side of the head are visible in the image at right.

Look at signal with and without the object.
Differences in reflected echo due to functional change is *tiny*. 