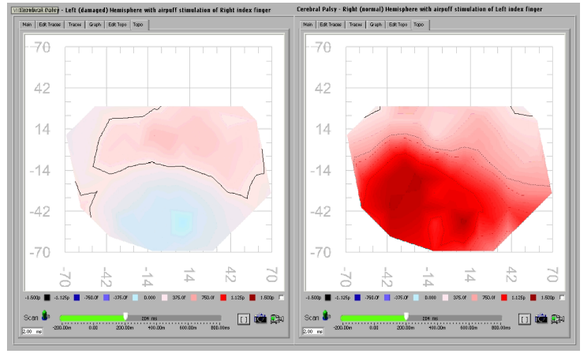
Current Studies

The babySQUID® is also being used to study cerebral palsy and epilepsy in a clinical setting. Representative data taken on a 9 year old cerebral palsy patient is shown below:



The left side shows the haptic stimulus response (at +205 msec) of the patient's abnormal left hemisphere, when the right index finger is stimulated with a repetitive air-puff. The right side shows the response of the patient's normal right brain hemisphere to air-puffs on the left index finger. Red indicates +1 picoTesla, light blue indicates -0.1 picoTesla.

Clearly, there is a lack of response on the left side, which normally should be similar to the right side. The existing response of the right side can be accurately modeled using the BESA or EMSE add-on software packages, and superimposed on MRI data if desired.

Detection of the early stages of cerebral palsy and epilepsy, *before* they have progressed to behavioral symptoms, is critical for intervention to treat later stages of motor impairment and retardation.

Developmental Processes

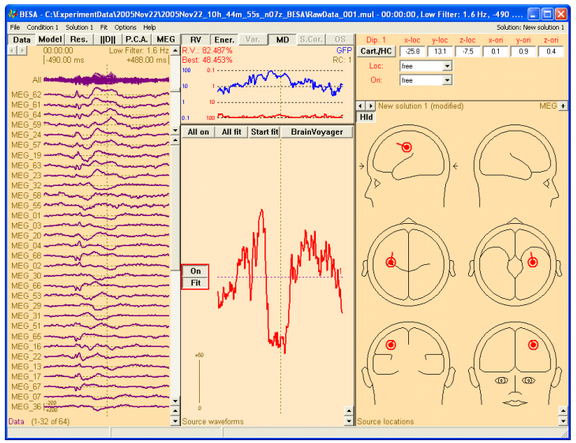
The system should also useful for developmental studies of infants and children. Because this instrument is the first of its kind, there are nascent research opportunities to study developmental processes, such as language learning or motor coordination. Instead of relying solely upon behavioral studies, a researcher could acquire highly precise measurements of actual brain activity.

The physical openness of the cart design means that a researcher is not limited with stimuli, and the parents can clearly see and be with their baby at all times.

The inherent safety of MEG measurements means that it is uncomplicated to obtain parental approval. Unlike other brain-monitoring techniques, there are no injections, no radioisotopes, no sedatives, no applied magnetic field, no attaching of leads or helmet of EEG wires, no confining or claustrophobic deep enclosure, and no expensive shielded room. Simply lay the infant on the bed, map the head and begin acquiring data.

Source Localization

The babySQUID® system data is fully compatible with the BESA and EMSE source localization packages. These are well-known third-party software tools for identifying from where in the brain the electrical sources are emanating.



BESA: http://www.megis.com/index_home.htm

EMSE: http://www.sourcesignal.com

Both of these packages can import MRI data and superimpose it with MEG and EEG data, so that the user can see where in the brain activity is occurring, and follow its movement.

Power and Physical Requirements

- Power: 1.5 kW filtered circuit
- Patient bed: 1 m x 2 m x 1.1m (40" x 79" x 42")
- Patient bed weight: 200 kg (440 lbs)
- Instrument cart size: 19" electronics rack
- Instrument cart weight: 150 kg (330 lbs)

Larger coverage areas, higher channel counts, and/or different coil dimensions and configurations are available on request. Contact Tristan for additional information.

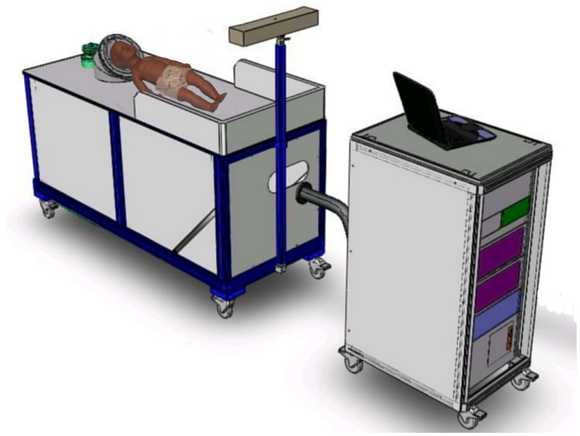
All Tristan products are covered by a 1-year warranty. Service contracts may be purchased to provide post warranty coverage.

TRISTAN TECHNOLOGIES
6185 Cornerstone Court East, Suite 106
San Diego, CA 92121
(858) 550-2700 [fax] 550-2799
http://www.tristantech.com

TRISTAN TECHNOLOGIES

babySQUID® *Neonatal Biomagnetometer*

A new, noninvasive investigational tool for pre- and full-term infants



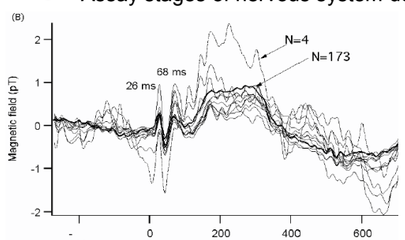
Mapping brain function and detection of neurological abnormalities in infants

Detection of cortical function in newborns is needed for clinical intervention in the early stages of neurological disorders, before external signs appear and the conditions develop and worsen. Areas where babySQUID® could be used for neonatal neurological assessment include:

- Epilepsy
- Cerebral palsy
- Perinatal asphyxia
- Hypoxemic-ischemic encephalopathy
- Periventricular white matter injury
- Monitoring recovery from trauma

Identifying how infants learn is of interest to many sectors of society, but such studies rely heavily on behavioral analyses. Having a direct measure of cortical activity would provide precise information on the dynamic response in the brain during learning processes. Potential uses of babySQUID® for developmental studies include:

- Mapping of sites and dynamics of sensory functions - auditory, somatosensory, and visual modalities
- Assay stages of nervous system development



Somatic evoked magnetic field (SEF) obtained from a 7-month old infant. The waveforms are the differences of the SEF at two field extrema.

This shows that only a small number of averages are needed to acquire SEF data

Unique Features of babySQUID®

Superior spatial resolution and sensitivity

- babySQUID® is significantly more sensitive to neuronal sources than conventional whole-head MEG systems
- Spatial resolution is four times better than existing whole-head MEG sensors
- Better spatial resolution than EEG (EEG signals are distorted by skull defects (fontanels and sutures), making it difficult localize epileptiform tissue
- No need for gluing and attaching any EEG leads
- Rapid scanning: A typical clinical scan can be completed within thirty minutes
- Anti-vibration construction; infant motion will not cause vibrational artifacts
- Sensor noise < 20 fT/√Hz

- A dense array of closely-spaced sensors is located just below the outer surface of a headrest.
- Allows measurement of the occipital area (infant in nose-up position), and parietal and temporal areas (infant lying on its side)
- Includes position tracking device and software. No need to immobilize the head. This permits measurements during sleep or relatively quiescent wakefulness

Unshielded Operation

- babySQUID® is designed to operate outside the large and expensive magnetically shielded rooms needed for adult MEG measurements
- The measurement cradle and its companion electronics cart are portable and can be wheeled in and out of elevators, obstetric suites and neonate ICUs

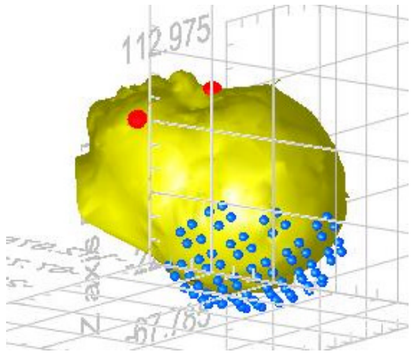
BabySQUID® System Description

Principles of Operation

Like adult Magnetoencephalography (MEG), babySQUID® uses superconducting sensors to non-invasively detect and map magnetic fields generated by cortical neural activity. However, babySQUID® takes advantage of the fact that the infant's scalp and skull are very thin. Tristan's fabrication methods put the sensing coils very close to the infant brain's sources of activity, even though SQUIDs must operate in an ultra-cold liquid helium environment. The net result is a significant increase in amplitude of neonate MEG signals. Also, the high density of detectors results in higher spatial resolution as compared to adult whole-head MEG. The large improvement of signal to noise means a capacity to operate in clinical environments without the usual magnetically shielded room.

System Components

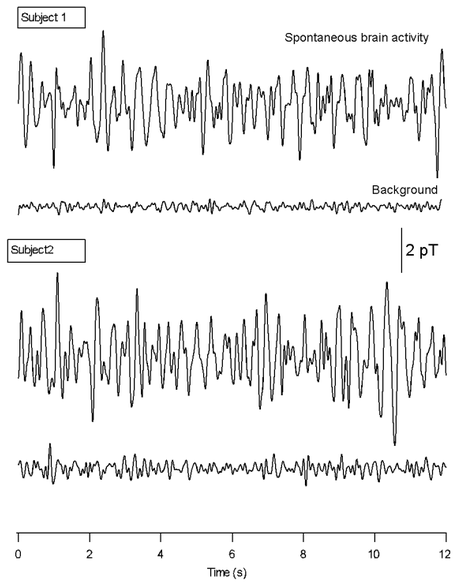
- Sensor/Cradle/Bed on mobile cart – easily accessed height
- Power supplies and computer on companion mobile cart to minimize noise
- Subject Tracking - optical tracking system updates movement at 30 Hz with ½ mm accuracy
- Part-wise mapping or optional optical one-click 3D imaging system



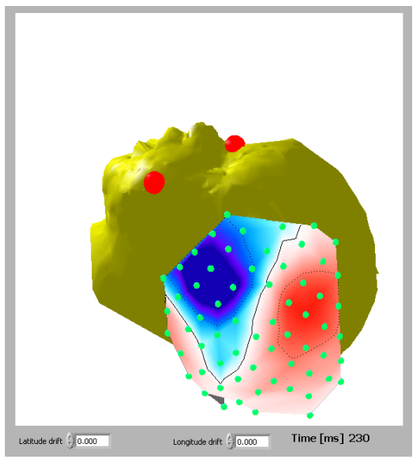
SQUID Sensor Array

- 300 cm^2 sensor coverage area
- 76 detection coils
- Coil type: 6 mm-diameter first order gradiometers. Adjacent coils can be electronically combined to form planar (dB_z/dx and dB_z/dy) gradiometers
- Coil gap: < 5 mm from sensor to outer surface
- Coil sensitivity: better than 20 fT/√Hz
- Reference channels: 8-element tensor array for noise reduction by subtraction of common mode noise

Patient Data



Spontaneous activity obtained from two 6-month old infants in an unshielded hospital room.



Evoked Response of an 8 month old infant Left hemisphere MEG slow wave response 230 msec after right index finger somatosensory stimulus Red indicates +1 picoTesla, and blue represents -1 picoTesla, resulting from a flow of neural current between the two regions. The separation of the regions gives a measure of the current source depth.

Data Acquisition and Display

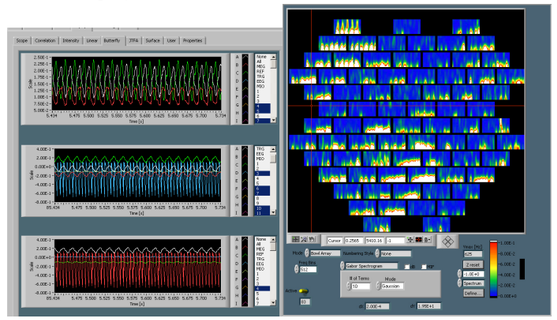
The award-winning[1] babySQUID® acquisition and display software is LabVIEW® making it easy to use and expand.

Data Acquisition

- Data acquisition at 10 kSamples/sec. Faster rates (up to 100 kSamples/sec) are available on request
- 24 bit data acquisition hardware, operating under MS Windows® (other operating systems available on request)
- Output ports for triggering sensory stimuli
- Data export utilities to BESA and EMSE software packages for mapping sources onto cortical locations
- Expandable for EEG and other sensors

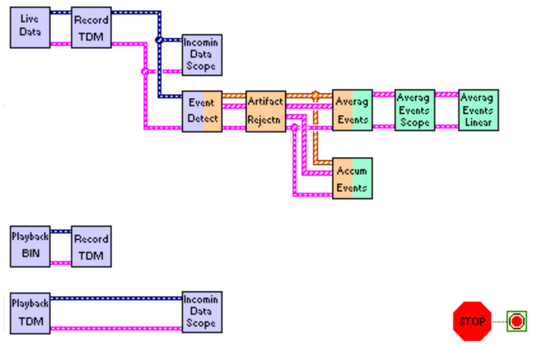
Display Software

- Raw data and averaged data side by side
- Scrolling vertical or overlapped channel display
- Real time, playback, and simulation modes
- Signal analysis features include IIR, FIR, wavelet, and spatial filtering, and filter editors
- Foreign language support available
- Display modes include: grouped channels (below left) and time-frequency spectrograms (below right)



Expandable Software Base

Tristan recognizes both the need for research flexibility *and* the need for clinical simplicity. Thus, Tristan provides much more than a pre-packaged software application. The user also has access to the architecture of the software through a very simple data-stream wiring diagram. The software is designed as distinct modules that the user can simply wire together to build a system that presents data in the way the user wants it. The user can select modules from a library to assemble a data-stream that performs steps such as data acquisition, data file playback, stimulus event detection, averaging of stimulus events, and graphing. The user can branch the data stream through more modules, and recombine them; it's even possible to have independent parallel data streams, as shown in the example below.



Source Code Example

The simplicity of this means that, within 60 seconds, the user can assemble their own software to exactly what is needed for an experiment. The software *is* the modules that have been assembled, which can then be used and set aside. Tristan supplies a set of applications for typical MEG measurements, ready to use. They are composed of these assemblies, and can be used as examples that can be modified by the user.

For even more flexibility, this open design means that the user can write their own modules, in any language such as C, C++, C#, or Visual Basic, add it to the library, and use it accordingly. Furthermore, the modules can be dynamically loaded, so that code can be edited while data is actively streaming through the system. For the advanced researcher, tools are available for distributed processing among CPUs, DSPs, and FPGAs.

Each module has its own User Interface that can be displayed as independent windows, or organized into a coherent panel, or however the user wishes to configure the displays. The user can make them complex for research studies, or simple for clinical usage. This allows the user to seamlessly transition from a research system to a clinical system. Any configuration can be locked into a new fixed stand-alone application.

The same software can be used on a desktop computer anywhere, for post-processing analysis away from the lab. This avoids the need to learn a separate post-processing software package.

A record of data provenance is automatically maintained within the data-stream itself, so that the user will *always* have a record of how the data was processed. There is also a separate system log that maintains a record of user operations. Encryption is available upon request.

---

[1] Tristan's babySQUID® software was named the 2005 Best Application of Virtual Instrumentation by National Instruments: http://www.ni.com/niweek/best.htm. LabVIEW® is a registered Trademark of National Instruments.