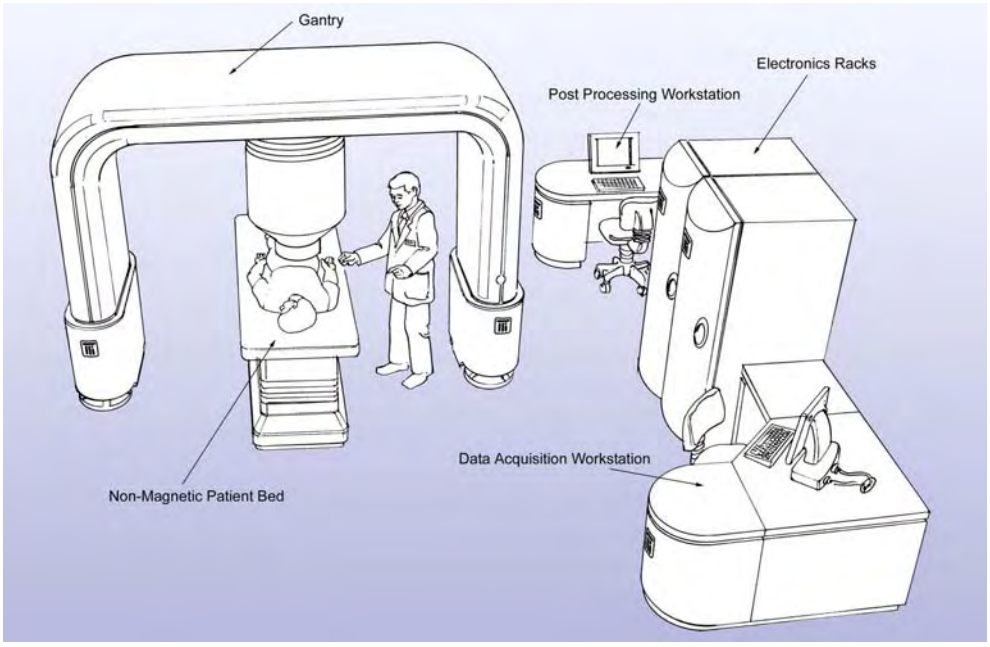
10.3. TRISTAN PRODUCTS

SQUID instruments and Systems

from

Tristan Technologies



System layout of Model 663 Spinal Cord Measurement System (see page 6 for actual photos)

SMM-770 magnetic microscope

model 607 MicroSQUID™ system

Tristan and its key personnel have produced a number of measurement systems for a variety of applications. Additional information on Tristan's commercial product line can be found at our website: http://www.tristantech.com. Some of them are listed here:

- Multiple single- and multi-channel SQUID magnetometers for NDE and paleoarcheology use. These are state-of-the-art systems, some with spatial resolutions approaching 1 μm.
- Multiple single- and multi-channel SQUID magnetometers for biomedical applications for animals and humans. The Ferritometer® is routinely used for clinical assessment of iron overload diseases. This system is a turnkey operation including patient scanning bed, computer control, along with complete data acquisition and analysis software.
- Tristan's magnetometer systems are based on its iMAG® line of commercial SQUID electronics, which have been supplied worldwide to both end users and OEMs.
- Tristan's model DRM-300 geophysical rock magnetometer uses closed cycle refrigeration to eliminate the need for liquid helium and reduce operating costs. This technology is available for use on many of Tristan's products.

Systems built by Tristan's present personnel during the time period of 1991-1996 include:

- A DC and AC susceptibility variable temperature and field platform. Twelve systems were made. These systems integrated SQUID magnetometers, sample motion control, sub-mK thermal control from 2 – 350 K, variable applied fields to 17 T and truly user-friendly automated control software. This product demonstrated Tristan's ability to produce state-of-the-art complex analysis equipment with minimal user requirements.
- A six-channel system for Vanderbilt University for general-purpose NDE studies. Comprised of a magnetometer, dewar, electronics, software and multiple magnets, this system has extremely high sensitivity (10^{-14} tesla) and sub-mm resolution.
- A three-channel Superconducting (SQUID) NDE system for use by a large Japanese steel company, comprising magnetometer probe, dewar, superconducting magnets, custom electronics, and custom software. Using a welding robot, this compact system is scanned over samples.
- A dual-channel magnetometer system for use by a private company to study materials for nuclear-fuel rod integrity. The package includes a magnetometer probe, dewar, computer controlled sample scanner, electronics and software.
- A compact (12") six-channel high sensitivity susceptometer capable of generating tesla fields and operating in both vertical and horizontal orientations. The ultra-compact system, when attached to the end of a robot arm, is used by a large Japanese nuclear reactor inspection company for scanning the interior of nuclear pressure vessels.
- The first commercial scanning magnetic microscope (SMM-1000) to study small electronic circuits and material samples. This comprised a dewar, cryogenic sample handling stage, magnetometer, custom software, vacuum system, and custom electronics. It is comparable to a SEM in complexity. Nine detection coils were fabricated in a linear array with 100 μm coil separation. Spatial resolution was at the μm level.
- A mixed stage (Gifford-McMahon/Joule-Thomson) cryocooler that routinely achieved 2 K.

There are many applications for SQUIDs. General areas where SQUIDs are used include:

Laboratory Applications include measurements of current, voltage, resistance, magnetization, etc. along with exotic (General Relativity, magnetic monopole) applications.

Current:	10^{-12} ampere/√Hz	dc Resistance:	10^{-12} Ω
Magnetic Fields:	10^{-17} tesla/√Hz	Mutual/Self Inductance:	10^{-12} Henry
dc Voltage:	10^{-14} volt	Magnetic Moment:	10^{-10} emu

Geophysical Applications include oil and mineral exploration, pollutant monitoring, magma flow measurements, rock magnetometry and paleoarcheology, etc.

Tristan HTS SQUID gradiometer in flight

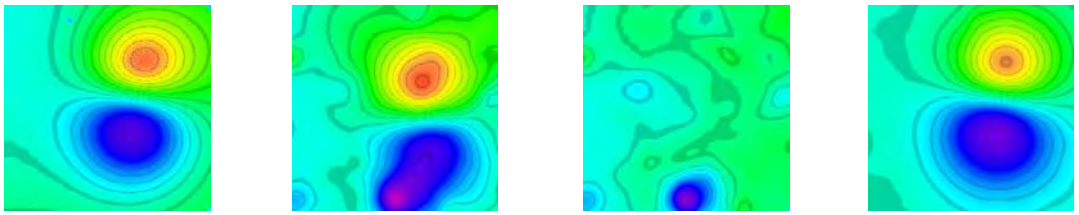
DRM-300 3-axis cryocooled rock magnetometer

Non-Destructive Test & Evaluation (NDE) scanning systems are used for defect detection, corrosion measurement, magnetic microscopy, etc. Some examples of SQUID NDE include:

Intrinsic currents measurements, such as:
- Remnant magnetization
  - Embedded magnetic sensors *(see figure below)*
- Flaw-induced perturbations
- Johnson noise in metals
- Eddy currents in an applied ac field (flaws)

Hysteretic magnetization due to:
- cyclic stress (strain)
- simultaneous dc & ac magnetic fields

Magnetization of paramagnetic, diamagnetic and ferromagnetic materials in dc fields.



A B C D

SMM-701 magnetic field scans of an embedded strain sensor under a 4 cm thick concrete overcoating. **A** - bare sensor showing dipole characteristics, **B** - sensor under concrete, **C** - bare concrete. Image **D = B** – **C** is a digital subtraction of B and C showing that it is possible to image objects deep underneath magnetically complex coverings. The scans cover a 6 cm x 6 cm area.

Medical Applications include:

Studies of the Brain—Neuromagnetism
- Epilepsy
- Neonatal and prenatal Brain Disorders
- Presurgical Cortical Function Mapping
- Peripheral nerve and spinal cord studies
- Drug Development and Testing
- Stroke
- Alzheimer's
- Neuromuscular Disorders
- Performance Evaluation

Animal Systems
- Pharmaceutical drug development

Studies of the Heart—Magnetocardiography
- Arrhythmia
- Heart Muscle Damage
- Fetal Cardiography

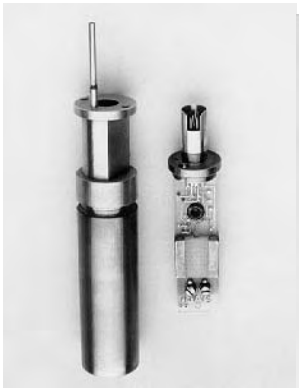
Other Medical Applications
- Non-invasive *in-vivo* Magnetic Liver Biopsies (Ferritometry)
- Studies of the Stomach—Gastroenterology
  - Intestinal and Mesenteric Ischemia
- Lung Function and Clearance Studies
- Peripheral and Single Nerve Studies
- Organ Transplant Rejection Risk
- Blood Flow Disorder

Tristan non-magnetic dewars

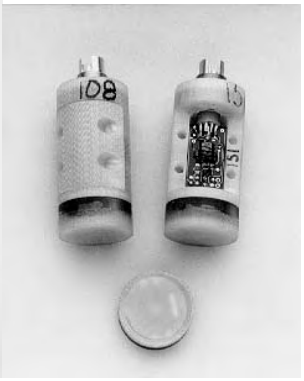
Model 607 biomagnetometer

Probe and dewar assembly

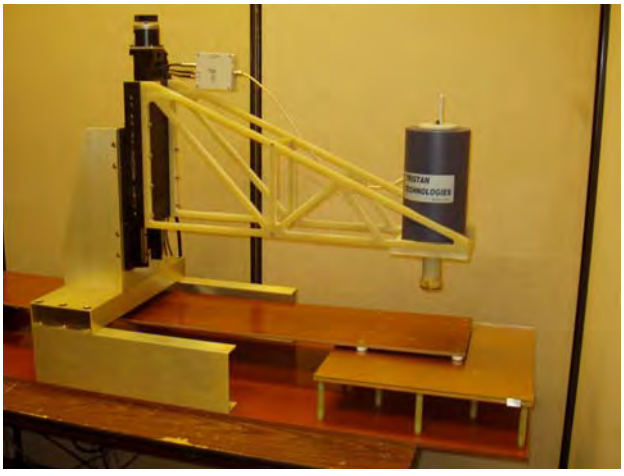
iMAG® electronics and laboratory probes



LTS SQUID sensor



HTS SQUID sensor



SMM-701 NDE scanning system

Model SMM-770 Scanning SQUID Microscope

The following Tristan systems illustrate just some of Tristan's capability to design and manufacture a broad range of sophisticated measurement systems. In particular, we have made a wide variety of high density, high number count, and close gap measurement systems. We also have extensive experience in refrigeration systems and cryocoolers extending over 20 years. Our biological and medical systems can be supplied with *fully* integrated with electronics, source localization software, gantries, and patient beds, each component designed to the specifications required for the application.

Model 663 Spinal Cord Measurement System

Designed to non-invasively measure spinal cord activity and localize the source of the activity. The system is adaptable for humans or animals. The system acquires data at the rate of 108,000 samples per second on each of its 71 channels, more than 10 times faster than conventional MEG devices. The system includes 8 tensor reference channels for noise reduction; signal acquisition, processing and display workstations; a sensor positioning gantry; a patient bed; patient/sensor position indicator.

(Left) Installed model 663 spine system dewar , showing pneumatically assisted x-y, and z- orientation control. (Center) Dewar insert, with array of 71 channels plus reference channels. (Right) Control electronics rack for 108 kSample/sec data acquisition and RAID arrays for simultaneous monitoring, storage, and data upload.

Ferritometer®

Tristan's Ferritometer® is a clinical instrument to quantitatively measure liver iron stores in patients suffering from Hemochromatosis, Thalassemia and Sickle-Cell Anemia. The Ferritometer® uses biomagnetic liver susceptometry (BLS) to quantitatively and accurately measure iron stores in the liver and spleen for adults and children. Tristan has delivered this system to hospitals in Europe and the United States, Unlike needle biopsies, the BLS method is rapid, non-invasive and provides more accurate data. The Ferritometer® operates in an unshielded environment (no MSR).

microSQUID™ (animal study) Systems

Animal experiments require that the detection coils be much closer (a few mm) than human MEG systems (typically 20 mm). Tristan's microSQUID™ technology permits small diameter detection coils to be placed within a few mm from the dewar bottom. This combines high spatial sensitivity along with the unsurpassed sensitivity of SQUID magnetometers. MicroSQUID™ systems feature small diameter (typically < 5 mm) detection coils and very close (< 4 mm) spacing between the detection coils and room temperature.

babySQUID®

Tristan's babySQUID® Neonatal Biomagnetometer is a MEG system specifically designed for detecting cortical function in newborns. The magnetometer is located in the infant bed with the detection coils pointing upward towards the infant. The rectangular device at the end of the infant bed is the projector for the optical positioning system. It is designed to operate without the need for a MSR. The measurement cradle and its companion electronics cart are portable and can be wheeled in and out of elevators, obstetric suites and neonate ICUs. It has 76 detection coils with a sensor coverage area of 300 cm^2. Using 6 mm detection coils with 17 $fT/\sqrt{Hz}$ sensitivity, its spatial resolution is four times greater than existing whole-head MEG sensors. An optical one-click 3D imaging system is used to track patient movements. Its award winning open architecture software is LabVIEW® based, making it easy to use and expand.

monkeySQUID™

The monkeySQUID™ is a research tool made to meet the specific requirements of research on mapping functional neurophysiology in primates. It is used to non-invasively measure weak magnetic fields produced by electrical activity within the cortex and to characterize and locate the source of the activity.

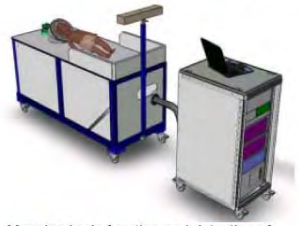
OTHER BIOMAGNETIC MEASUREMENT SYSTEMS

The Model 637 Biomagnetometer (gutSQUID®) is used for measurement of the Basic Electric Rhythm (BER) associated with intestinal activity. The specific application is detection of Mesenteric Ischemia, a life threatening condition with no conventional reliable method of diagnosis. Pre-clinical trials are underway. Tristan's personnel fabricated the first commercial system for HTS cardiac measurements in unshielded environments. Tristan has also built systems for peripheral nerve studies, adult magnetoencephalography and magnetopneumography.

TRISTAN TECHNOLOGIES

babySQUID® Neonatal Biomagnetome

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



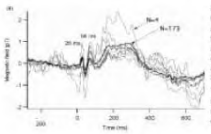
Mapping brain function and detection of neurological abnormalities in infants

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 as a function of number of averages from N=4 to 173 epochs. The waveforms are the differences of the SEF at two field extrema.

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

Unique Features of babySQUI

Superior spatial resolution and sensitivity

- babySQUID® is significantly more se neuronal sources than conventional w MEG systems
- Spatial resolution is four times better tha whole-head MEG sensors
- Better spatial resolution than EEG (EEG s distorted by skull defects (fontanels anc making it difficult localize epileptiform tissu
- No need for gluing and attaching any EEG
- Rapid scanning: A typical clinical scar completed within thirty minutes
- Anti-vibration construction; infant motio cause vibrational artifacts
- Sensor noise < 20 fT/√Hz

- A dense array of closely-spaced sensors just below the outer surface of a headrest.
- Allows measurement of the occipital area nose-up position), and parietal and temp (infant lying on its side)
- Includes position tracking device and sof need to immobilize the head. This measurements during sleep or relatively wakefulness

Unshielded Operation

- babySQUID® is designed to operate o large and expensive magnetically shield needed for adult MEG measurements
- The measurement cradle and its c electronics cart are portable and can be v and out of elevators, obstetric suites an ICUs

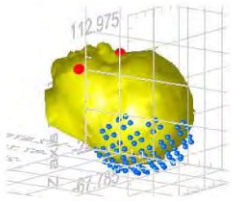
BabySQUID® System Description

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

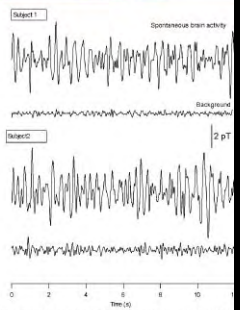
- Sensor/Cradle/Bed on mobile cart – easily accessed height
- Power supplies and computer on companion mobile cart to minimize noise
- Subject Tracking - optical tracking system updates movement at 30 Hz with ½ mm accuracy
- Part-wise mapping or optional optical one-click 3D imaging system



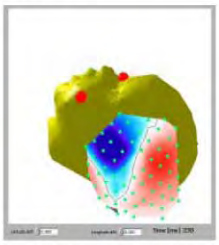
SQUID Sensor Array

- 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 unshielded hospital room.



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

Data Acquisition and Display

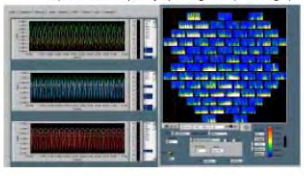
The award-winning[1] babySQUID® acquisition and display software is LabVIEW® making it easy to use and expand.

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

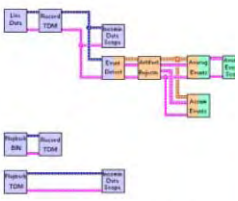
Display Software

- 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 seco can assemble their own software to exactly wh for an experiment. The software *is* the modul been assembled, which can then be used ar Tristan supplies a set of applications for measurements, ready to use. They are compo assemblies, and can be used as examples modified by the user.

For even more flexibility, this open design me user can write their own modules, in any langu C, C++, C#, or Visual Basic, add it to the libra accordingly. Furthermore, the modules can be loaded, so that code can be edited while da streaming through the system. For the advance tools are available for distributed processing a DSPs, and FPGAs.

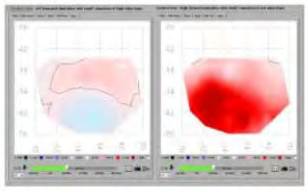
Each module has its own User Interface displayed as independent windows, or orga coherent panel, or however the user wishes to displays. The user can make them complex studies, or simple for clinical usage. This allow seamlessly transition from a research system system. Any configuration can be locked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

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

A record of data provenance is automatically within the data-stream itself, so that the use have a record of how the data was processed. a separate system log that maintains a re operations. Encryption is available upon request

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

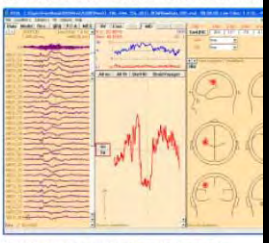
The system should also useful for developmental studies of infants and children. Because this instrument is the first of its kind, there are nascent research opportunities to study developmental processes, such as language learning or motor coordination. Instead of relying solely upon behavioral studies, 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 v BESA and EMSE source localization packages. Th well-known third-party software tools for identifyin where in the brain the electrical sources are emanatin



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

EMSE: http://www.sourcesignal.com

Both of these packages can import MRI da superimpose it with MEG and EEG data, so that t can see where in the brain activity is occurring, and f 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, different coil dimensions and configurations are availa request. Contact Tristan for additional information.

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

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

[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.

The Tristan babySQUID® (patents issued and pending) is classified as an investigational device and is currently offered for research use only. Tristan is in the process of seekin (European) medical device directive and FDA (U.S.) certification for clinical use. Specifications subject to change without notice.