Protocol Title: Comprehensive Imaging of Perforator Vessels and Subcutaneous Vascular Network with No-Exogenous Contrast and Non-Ionizing-Radiation Magnetic Resonance Angiography

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OBJECTIVE

The perforator flap is a new improvement in reconstructive microsurgery that is increasingly gaining popularity in many different reconstructive applications to breast, torso, and extremities [Saint-Cyr 2009; Geddes 2003]. Because there is considerable inter-patient variation in the number, size, and position of perforator vessels, success of perforator flap surgery relies on state-of-the-art preoperative planning based on detailed understanding of the three-dimensional (3D) structure of the associated vasculature. Currently, computed tomography angiography (CTA) is the method-of-choice for preoperative vascular imaging in breast reconstruction surgeries. While CTA is capable of generating excellent anatomical details of perforator vessels, patients are also exposed to additional risks associated with the use of ionizing radiation and iodinated contrast agents. Magnetic resonance angiography (MRA) using intrinsic contrast mechanisms (without the use of any external contrast medium), such as velocity-encoded phase contrast, can generate accurate, high-resolution 3D vasculature maps without the risks associated with CTA. Therefore, non-contrast MRA is a more desirable alternative to CTA in preoperative planning of flap surgeries.

The *overall objective* of this pilot study is to develop and optimize preoperative MRA imaging protocols for various perforators commonly used in flap surgery with phantom and healthy volunteers, and to obtain clinical validation of the optimized protocols with a group of patients receiving flap surgery at the OSU Wexner Medical Center. Data obtained in this study may also serve as the basis for statistical planning of future clinical trials.

Based on our previous experience with other magnetic resonance imaging (MRI) techniques, we hypothesize that optimal MRA images can only be obtained with a carefully selected combination of imaging hardware, acquisition, and postprocessing factors. The *main objective* of this pilot study is to

determine this optimal combination through the comparison of image quality between different combinations.

The *secondary objective* of this pilot study is to evaluate, both qualitatively and quantitatively (for details see below), the quality of the optimized MRA images and compare them with clinical CTA images. Our hypothesis is that the quality of the optimized MRA images is at least comparable to that of the CTA images. The quantitative measurements obtained from this pilot population will also serve as the preliminary data for future studies and be used in statistical calculations that determine their study population.

BACKGROUND AND RATIONALE

Perforator Flap Surgery

Although the history of flap surgery – transplantation of tissue carrying its own blood supply – can be traced back to around 600 B.C. according to record in *Sushruta Samita*, the importance of adequate blood supply to flap survival is not fully demonstrated until Milton's work in 1970 [Milton 1970]. With this understanding, musculocutaneous flap surgery became popular in late 1970s due to the reliable blood supply of muscles [Ger 1966; Orticochea 1972]. However, removal of bulk muscular tissue from the donor site may have a negative impact on its structural and functional integrity. In an evaluation of the long-term abdominal consequences of Transverse Rectus Abdominis Musculocutaneous (TRAM) flap surgery, Mizgala et al. reported decreased abdominal strength and exercise ability in 46% and 25% of 150 patients, respectively. Other undesirable side-effects include asymptomatic diffuse bulges through the fascial harvest site, abdominal laxity, and increased back pain [Mizgala 1994].

In 1989, the musculocutaneous perforator flap was introduced by Koshima and Soeda [Koshima 1989]. In this procedure, the major perforator arteries feeding the donor site are carefully dissected from bulk muscle and transplanted to the recipient site with the attached skin and subcutaneous fat. By preserving the passive muscle carriers at the donor site, the plastic surgeons get more versatility in surgery design, and the patient experiences less donor site morbidity than in a musculocutaneous flap procedure. A number of studies have been conducted to compare the outcomes of perforator and musculocutaneous flap procedures, predominantly between the Deep Inferior Epigastric Perforator (DIEP) flap and TRAM flap used in post-mastectomy breast reconstruction. These studies demonstrated that TRAM flap patients have statistically significant weakness of abdominal and back muscles compared with patients receiving DIEP flap surgery [Blondeel 1997; Futter 2000]. DIEP flap patients were also reported to have slightly shorter hospital stay and lower risk for abdominal wall hernia than pedicled TRAM flap patients [Garvey 2006]. Recently, Man and colleagues conducted a meta-analysis of DIEP and free TRAM data published in English-language journals up to April, 2007. The results of this meta-analysis confirmed that donor-site morbidity is generally lower in DIEP patients [Man 2009].

Commonly Used Perforator Flaps

The perforator flap method was quickly applied to various branches of plastic surgery soon after its introduction [Saint-Cyr 2009; Geddes 2003]. Currently, the most commonly used perforator flaps include:

- Deep Inferior Epigastric Perforator (DIEP) flap: This is the original perforator flap described by Koshima and Soeda. The perforators used in this procedure are branched from the deep inferior epigastric artery, and harvested from the rectus abdominis muscle. The primary application of DIEP flap is in post-mastectomy breast reconstruction. It has also been used in reconstruction of defects in lower limbs and head and neck.
- Thoracodorsal Artery Perforator (TDAP) flap: The perforators used in this procedure are branched from the thoracodorsal artery, and harvested from the latissimus dorsi muscle. The TAP flap is a highly versatile procedure because of the long pedicle and large cutaneous area in this region. It has been used for the reconstruction of defects in head and neck, torso, and extremities. Application in breast reconstruction has also been reported.
- Superior/Inferior Gluteal Artery Perforator (SGAP/IGAP) flap: The perforators used in these procedures are branched from the superior/inferior gluteal artery, and harvested from the gluteus maximus muscle. The gluteal artery perforator flaps are used as an alternative to abdominal flaps in breast reconstruction when abdominal flaps are considered unsuitable for the patient.
- AnteroLateral Thigh (ALT) flap: The perforators used in this procedure are branched from the descending branch of the lateral circumflex femoral artery, and harvested from the vastus lateralis muscle. The ALT flap is a popular procedure for head and neck reconstructive surgery in the Asian population.

Preoperative Planning for Perforator Flaps

Because there is a large inter-patient variation in the number, size, and position of perforator vessels [Hallock 2001], careful, personalized preoperative planning for every patient is of essential importance to the success of perforator flap surgery. Initially, this was done with acoustic Doppler ultrasound sonography and color duplex sonography [Hallock 1994; Giunta 2000]. In this examination, a Doppler probe is scanned over the skin of the donor site. Pulsating Doppler signals mark out the presence of flow in blood vessels. The point with the loudest signal is identified as the position of the perforator. A major problem of the Doppler ultrasound technique is that its signal strength is only dependent on one component of the relative motion speed along the direction of the ultrasound beam. Therefore, a small vessel along the ultrasound beam direction may generate stronger signals than a large perforator running along an oblique direction. This technique thus tends to detect many small vessels that are not suitable for perforator flap surgery and yield a high proportion of false positive results. Giunta and colleagues reported that 47.6% of 271 “perforators” detected with acoustic Doppler ultrasound sonography were actually not dissected intraoperatively in DIEP and SGAP flap surgeries [Giunta 2000]. Yu et al. had similar findings for the ALT flap procedure, and observed that the accuracy of Doppler examination decreases with increasing body mass index [Yu 2006]. Other minor disadvantages of

Doppler ultrasound sonography include suboptimal presentation of images to the surgeons and the lack of the capability to reconstruct a 3D tomographic volume.

Several other non-invasive imaging modalities, including near-infrared fluorescence angiography [Matsui 2010], CTA [Karunanithy 2011; Rozen 2008a], and contrast enhanced MRA (CE-MRA) [Greenspun 2010; Neil-Dwyer 2009], have been evaluated in efforts of finding a better planning tool for perforator flap surgeries. Currently, the plastic surgery community considers CTA as the method-of-choice for preoperative planning in breast reconstruction surgeries using DIEP or SGAP/IGAP. Despite some recent critics on inaccuracy in perforator caliber measurement [Cina 2010], CTA has substantial advantages in several aspects compared with the traditional Doppler techniques: It generates less false positive results and is more sensitive than Doppler ultrasound in detecting perforators [Rozen 2008b]. It is also superior in visualizing the intramuscular course of the perforators and the superficial subcutaneous vascular network [Cina 2010]. CTA images can be rendered as a 3D volume for comprehensive preoperative planning, and saved for intraoperative display. This helps to substantially improve planning quality and reduce operative time. Acosta and colleagues reported that incorporating CTA into their workflow has led to a mean reduction of 90 minutes to the operative time of DIEP flap breast reconstruction [Acosta 2011].

However, all these advantages come with a price of additional health risk to patients: The ionizing radiation used in Computed Tomography is known to have carcinogenic, teratogenic and mutagenic effects [Bushberg 2001]. Although the radiation dose of a single abdominal CTA is moderate (Phillips et al. estimated the average effective dose to be 6 mSv [Phillips 2008]), a large proportion of the patient population are also subject to repetitive scans and/or radiotherapy due to their medical conditions that raise the need for a perforator flap surgery. For those patients, it is important to reduce any unnecessary exposure to ionizing radiation to minimize the accumulative dose they receive. Moreover, in order to get high quality CT images of small perforators, intravenous injection of iodinated contrast agents is required. Iodinated contrast agents can induce anaphylactic reactions in a dose-independent and unpredictable way. The overall adverse reaction rate (including the anaphylactic reactions and chemotoxicity of the contrast agents) is estimated to be 4% to 12% for ionic contrast agents and 1% to 3% to nonionic contrast agents [Cochran 2005]. All of these adverse effects sum up to a non-negligible health risk to patients using CTA in their perforator flap surgery planning. Therefore, we propose this pilot study to investigate the use of non-contrast, non-ionizing-radiation MRA techniques as a better alternative to CTA in preoperative planning for perforator flap surgeries.

Non-contrast MRA for Perforator Imaging

Various non-contrast MRA methods have been developed using different intrinsic contrast mechanisms [Bernstein 2004]. After careful review of the basic physical principles behind these methods, we decided that the following portfolio is the most suitable for visualizing perforators and subcutaneous vascular network:

- Phase contrast MRA uses flow-encoding gradients to create image contrast between moving and stationary magnetizations [Moran 1982]. The flow-encoding gradients can be applied in

three orthogonal directions so that blood flows in all directions can be simultaneously visualized in the same image. This feature is particularly important in imaging DIEP and TAP because blood in these vessels flows in opposite direction to aorta blood that supplies them, which makes flow direction sensitive techniques like time-of-flight (TOF) MRA unsuitable. Moreover, phase contrast MRA can be acquired as a 3D volume for better SNR to support the high spatial resolution needed for the visualization of small perforators. This technique will be used to obtain an overview of the perforators and their connections to their feeding vessels and subcutaneous vascular network.

- Sometimes a plastic surgeon also wants to know the anatomy of the subcutaneous vascular network. This information can be used to help him make surgical decisions that minimize the impact to the donor site. Images of the subcutaneous vascular network can be obtained with superb spatial resolution (300-500 μm) using the fat-water differences in their resonance frequencies (i.e. chemical shift contrast) [Wang 1998] or spin-lattice relaxation rates (i.e. T1 contrast) [Delfaut 1999].
- The capability of differentiating arteries and veins is a major advantage of color Doppler ultrasound over CTA. We would like to explore if non-contrast MRA techniques can provide a comprehensive preoperative imaging solution that combines the advantages of CTA and color Doppler ultrasound. Therefore, we also plan to acquire an MR venogram with a susceptibility weighted imaging (SWI) sequence, which is particularly sensitive to the paramagnetic deoxyhemoglobin rich in venous blood [Haacke 2010].

According to the result of a simulated phantom experiment on the MR scanner that will be used in this pilot study, it takes 20-30 minutes to acquire this protocol, along with a short localizer and a typical abdominal anatomical sequence. This is substantially shorter than a typical clinical MRI scan, which takes up to 60 minutes.

RESEARCH DESIGN AND METHODS

Design Overview

In this study, we plans to enroll 25 evaluable volunteers for the development and optimization of perforator imaging protocols, and 50 evaluable clinical patients receiving flap procedures at OSUMC for the clinical validation of the optimized protocol. Both genders will be included. Pediatric patients will be excluded. All subjects will be non-invasively imaged with a set of angiographic and anatomical MRI techniques. No extrinsic MR contrast agent will be injected. Clinical patients' MRI images will be evaluated independently by radiologists and plastic surgeons, and compared to clinical CTA images. The protocol will be performed in accordance with the Ohio State University Institutional Review Board regulations.

Recruitment

Clinical patients will be recruited from the investigators' clinical practices. Once a potential study subject is identified by a recruiting physician, the study PI will be notified for the determination of eligibility.

Volunteers will be recruited through electronic advertisements posted on OSU websites, paper advertisement posted in OSU campus (see the attached brochure), and word of mouth.

All participants will be screened prior to entering the MRI environment.

Subject Selection Criteria

Study subjects will be recruited for the MRI exam according to the following inclusion criteria:

- Greater than or equal to 18 years at time of enrollment.
- Able to provide informed consent.
- Able to lie in both prone and supine positions for at least 30 minutes.
- The clinical patients need to have a flap procedure scheduled at the Ohio State University Medical Center within the next 24 months.

If any of the following are applicable to a volunteer subject then he/she will be excluded from this study for the sake of their own safety:

- Use of an IUD (intrauterine device) or medicine patch
- Subjects with any type of activatible implants (e.g. cardiac pacemakers, deep brain stimulators, spinal cord stimulators, cochlear implants, electronic infusion pumps, etc.).
- Subjects with any type of metallic implants or foreign objects in torso region (e.g. cardiac stents, surgical clips, shrapnel fragments from war wounds, etc.).
- Metal works and machinists (who may have metallic fragments in the near eyes).
- Severe auto accident victims.
- Subjects with permanent tattoos that may contain metallic coloring.
- Subjects with previous history of perforator flap surgery.
- Subjects who cannot communicate with the researcher for any reason.
- Claustrophobia.

General Magnetic Resonance Imaging Procedure

The study subjects will be scanned with a 3.0 Tesla Philips Ingenia CX whole body clinical MRI system located at the Wright Center of Innovation of The Ohio State University Medical Center. The built-in body volume coil will be used for radio frequency (RF) transmission, and a phased array coil will be used to pick up the MRI signal. Anatomical and angiographic MR images will be acquired for one of the most commonly used flap surgery donor perforators including but not limited to:

- The deep inferior epigastric perforators (DIEP);
- The superior gluteal artery perforators (SGAP);
- The inferior gluteal artery perforators (IGAP);
- The thoracodorsal artery perforators (TDAP);

- The anterolateral thigh (ALT) perforators.

Upon the investigator's decision, all or part of the following imaging sequences will be acquired:

- Fast, low-resolution localizer.
- Reference scan for phased-array coil signal intensity inhomogeneity correction with the CLEAR technique.
- B1 calibration sequence for the RF field inhomogeneity correction with the Multi-Transmit technique.
- Typical anatomical imaging sequences (e.g., T2-weighted).
- Phase-contrast angiography.
- Susceptibility-weighted venography.
- Subcutaneous vascular imaging sequences using intrinsic contrast (e.g. T1 contrast and chemical shift contrasts).

The angiographic sequences may be repeated multiple times with different combinations of scanning parameters and acquisition hardware for the purpose of protocol optimization (for details see below). The scan time for each visit will be no greater than 60 minutes for the subject's comfort. If all planned sequences cannot be acquired within the first visit, an investigator or study key personnel will contact the subject after the scan and arrange additional visits upon the subject's willingness for continuous participation.

In MRI examinations,

- Volunteers may experience a metallic taste while entering or leaving the MRI system.

- Metallic objects can be accelerated by the magnetic field and become projectiles. Volunteers will be evaluated prior to entering the MRI system to exclude metal objects. Metal objects are excluded from the MR suite.

- If volunteers have a metal implant or foreign object in your body, the object could be displaced by the magnetic field. There can be increased heating near metal structures. If volunteers have any implants in their body, they will inform the researcher conducting this study, and they will not be eligible to participate in this study.

- Volunteers will be placed in the long tube of the MRI system. Some volunteers may have a claustrophobic reaction (uneasiness at being in a confined space). If this happens, volunteers will be asked if they wish to continue, or if they would like to terminate the study.

- Volunteers will hear loud thumping sounds that may be annoying. Volunteers will be supplied with earplugs that you should wear while they are in the MRI system.

- Exposure to the rapidly changing electrical fields could cause twitching of your muscles. This effect is usually temporary.

- When volunteers close their eyes, they might see tiny light flashes similar to those that occur when they rub their eyes in the dark. This has no known harmful effects.

- All these listed effects are transient, that is, seeing light flashes, metallic taste and muscle twitching will end once exposure to the MRI fields is ended. Based on this, effects of repeated MRI studies are not expected, however, long-term effects are not known at this time.

Imaging Protocol Optimization

Development and optimization of perforator imaging protocols will be conducted with phantoms and volunteers.

The quality of MR images is determined by a large number of hardware, acquisition, and postprocessing factors. According to our previous experience, we identified the following factors as the most critical for this study:

1. Spatial resolution: While a higher spatial resolution is generally required to detect smaller objects (such as small blood vessel branches) in an image, the SNR of MR image is also proportional to the voxel volume. When the spatial resolution is decreased to some threshold level, stochastic noise will dominate in the image and mask important anatomical structures of interest.
2. Physiologic gating: Respiratory and cardiac motions can generate ghosting artifact and image blurring in MR images, especially in thoracic and abdominal regions. Because perforators are small vessels (whose diameters are typically between 500 μm to over 1 mm), the influence of physiologic motion needs to be carefully controlled to allow effective visualization of perforators.
3. Parallel imaging: The use of parallel imaging techniques, such as Sensitivity Encoding (SENSE), can substantially reduce image acquisition time, thus minimizing image blurring and ghosting artifacts caused by subject motion. However, it also decreases the image SNR, and may cause reconstruction artifacts if the SENSE factor is set outside the optimal range.
4. Maximum phase-contrast velocity: In phase-contrast angiography, the maximum phase-contrast velocity specifies the maximum blood flow velocity that can be accurately encoded as brightness in the MR image. If this parameter is set too low, higher blood flow velocities will be phase-wrapped and the corresponding vessels may be invisible in the angiography image; if this parameter is set too high, the image contrast will be compressed. The vessel-of-interest may not have enough signal to be recognized from background noise.

Therefore, we plan to optimize our imaging protocols by testing various combinations of the four parameters mentioned above.

Other acquisition parameters, such as the repetition time (TR), echo time (TE), and flip angle (FA), will be determined by the investigator for each individual sequences based on our previous experience with those sequences and computer simulation of magnetization evolution at 3.0 Tesla.

The MR images will be reviewed by the research team after acquisition. The investigator will grade the overall image quality on a semi-quantitative scale. The protocol with the highest image quality score will be identified as the optimal protocol, which will be used in the clinical patient group.

Clinical CTA Data Extraction

For patient subjects who had at least one pre-operative CTA performed at OSUMC within the past 48 months, or will have at least one pre-operative CTA performed at OSUMC prior to a scheduled flap procedure, an investigator will review their CTA cases available on OSUMC PACS and select the most recent one for further comparison and evaluation.

For patient subjects who do not have any pre-operative CTA on OSUMC PACS and are not expected to get one within the next 24 months, a radiologist will review previously acquired CTA cases saved on OSUMC PACS that were obtained in the past 48 months, and select an age- and gender-matched case with clear depiction of the relevant perforator(s) for further comparison and evaluation.

Comparison with clinical CTA is not necessary for volunteer data acquired for protocol development and optimization purposes.

The selected CTA data set will be retrieved from the Ohio State University Wexner Medical Center Picture Archiving and Communication System (OSUWMC PACS) and downloaded to a research data server protected by secure password and firewall. The downloaded data will be immediately de-identified with validated software and verified by imaging Corelab staff.

On investigational images, any incidental findings will be shared with the participant and his/her primary care physician who was identified during the consent process. However, the investigational images are not diagnostic and do not replace usual care.

Medical Record Review

The medical record of all clinical patients will be reviewed by the investigators after the completion of their flap procedure to identify intra- and post-operative findings that may be correlated to pre-operative imaging data. Patient (age, obesity, radiation, chemotherapy, smoking, and other medical comorbidities) and surgical factors (flap type, laterality, and surgical time) that are known to affect free flap procedure outcomes will be collected.

Data Analysis

Standard postprocessing techniques including but not limited to noise filtering, co-registration to anatomical images, and 3D rendering will be applied to the optimal MRA images before the data are presented to the investigators for further analysis. The clinical CTA data will only be postprocessed with a 3D rendering algorithm because they already contain basic anatomical information.

De-identified optimal MRA and CTA data will be presented, in a randomized order, to the investigators for their independent assessment.

The radiologists will assess the imaging data on the following aspects:

- Imaging artifacts;
- Noise Level;

- Any other findings that may affect clinical interpretation of the images.

The plastic surgeons will assess the imaging data on the following aspects:

- The overall image quality;
- Anatomy accuracy;
- Vascular network continuity;
- Perforator branching pattern;
- Clinical applicability;
- Any other findings that may affect the planning, or the execution, or the follow up strategy of the flap procedure.

The plastic surgeons will also identify target perforators that are suitable to build a flap upon. An investigator will make the following quantitative measurements on each target perforator using a commercial workstation or custom-built software:

- Signal-to-noise ratio (SNR);
- Contrast-to-noise ratio (CNR) to muscle and fat;
- Perforator size;
- Length of the Perforator Intramuscular Course;

- Any other quantitative metrics that may support clinical decision-making.

Statistical Analysis

Statistical comparison between the optimal MRA and CTA data sets will be performed with appropriate testing methods and multi-comparison correction using standard statistical software packages. Summary statistics will also be calculated for the quantitative measurements obtained from the MRA data set. These summary statistics will serve as the pilot data for sample size calculation in future clinical trials.

Consent Procedures

A printed copy of the Consent Form will be provided to the subjects for review at their initial visit to the MRI facility, or prior to this visit if requested by the volunteer. An investigator or study key personnel will review the Consent Form with each subject, and answer any question regarding the nature of the study, study procedures, risks and alternatives. Subjects will be informed that participation is voluntary and that they can withdraw from the study at any time. Subjects will then be asked to complete a written MRI Safety Screening Form under the guidance of an investigator or key personnel. The investigator/key personnel will collect signed Consent Form and MRI Safety Screen Form from the subjects, and determine whether the subject is eligible to participate in the study according to the inclusion/exclusion criteria specified above. A copy of the signed Consent Form will be provided to the subject for their records. The documents will be stored in a locked cabinet upon completion at the Wright Center of Innovation.

Compensation

All patient subjects will be compensated with a $40 gift card at the Wright Center of Innovation for each research MRI scan they participate. Those who come to the Wright Center but are not able to complete the research MRI scan (due to unforeseen medical reasons or equipment breakdown) will be still compensated. All patient subjects will be asked to sign a form as proof of receiving payment. By law, payments to subjects are considered taxable income.

Volunteer subjects will not be compensated for their participation.

Data Confidentiality

Personally identifiable information in Consent Forms, HIPAA Forms, and MRI Safety Screening Forms will be kept in a locked cabinet in the research area in the Department of Radiology. Only authorized members of the research team will have access to these identifiable records.

The raw image data will be coded at the time of acquisition through the use of subject ID codes instead of subject names. The coded data will be saved on a password-protected data server behind a firewall. The data server is located in a locked server room with limited access to authorized personnel only. The research team may share coded data with collaborating investigators, MRI scanner and coil vendors, or the FDA.

Adverse Events

No invasive procedure or extrinsic agent will be applied or delivered to the subjects participating in this study. All MRI sequences used in this study will be identical to those used in daily clinical standard of care practices. Therefore, the health risk to the participants will not be greater than that of patients receiving a standard care diagnostic MRI examination.

The United States Food and Drug Administration (FDA) classified MRI up to 8.0 Tesla as non-significant risk. Potential risks include:

1) Excessive heat deposition in tissue due to high specific absorption rate (SAR);
2) Undesired neural stimulation due to fast switching of magnetic field gradients;
3) Malfunction of functional implants whose operation can be interfered by the RF field or the magnetic field gradients;
4) Temporary or permanent hear losses due to loud acoustic noises.

In this study, these potential risks are minimized:

1) The Philips 3.0 Tesla MRI system has both hardware and software limits on the maximum SAR level to less than or equal to 4.0 W/kg. This is the FDA approved limit. Excessive heat deposition may happen on the surface or near the tip of metallic objects embedded in body. However, these subjects will be excluded from participating this study by the use of the MRI Safety Screening Form;

2) The Philips 3.0 Tesla MRI system operates within the FDA guidelines regarding time varying magnetic field gradients;
3) All MRI sequence to be used are included in the FDA released clinical system sequence packages;
4) According to our exclusion criteria, all subjects with any type of activatible implants will be excluded from participating this study;
5) Dual ear protections (i.e. ear plugs and headphones) will be provided to all subjects participating in this study. With these protections in place, the scanner noise level will be under the FDA limit for sound (140 dB peak or 99 dB average).

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