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An MR Safe Algometer to Study Phantom and Residual Limb Pain*

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***Abstract*—Researchers are interested in understanding phantom limb pain (PLP) and residual limb pain (RLP) in amputees and the neural mechanisms leading to it. fMRI can provide information on the intensity and the location of activated centers in the brain that control PLP and RLP. MR safe algometers are important to this work. This paper described the new pneumatically actuated algometer and the evaluation methods for MR safety. Our results indicate that the custom device is an improved MR safe algometer capable of autonomously producing reproducible pressure profiles.**

I. Introduction

Currently, approximately 185,000 amputations are performed each year in America, with an estimated 1.2 million Americans living with an amputated limb [1]. Phantom limb pain (PLP) is defined as painful sensations coming from the absent limb, whereas residual limb pain (RLP) is defined as pain at the site of amputation in the "stump" [2]. The prevalence of phantom limb and residual limb pain has been estimated to be 80% and 67.7% respectively, with 38.9% reporting severe pain (7-10 on the visual analog pain scale) in the case of phantom limb pain, and 29.9% reporting severe pain in the case of residual limb pain. [1] Currently, the mechanism of phantom limb and residual limb pain is poorly understood.

Researchers are interested in understanding amputee pain and the neural mechanisms leading to it. The method of assessing PLP and RLP clinically is through the application of pressure either with or without an algometer to a tender spot and evaluating the pain through the subjective ordinal Visual Analog Scale (VAS) or Numerical Rating Scale (NRS) [1,2]. While useful clinically, the VAS scale combined with palpating the tender spot with the algometer does not provide information on the underlying cause of the stump pain experienced. Functional magnetic resonance imaging (fMRI) can shed insight on the neural mechanisms underlying the stump pain and how treatment to reduce the pain with drugs such as lidocaine and Botolinum Toxin A (Botox) work. fMRI can provide information on the intensity and the location of activated centers in the brain that control amputee' stump pain. MR safe algometers are important to this work.

Two previous fMRI studies conducted in Japan by Uematsu et al. [3] and Maeda et al. [4] on normal healthy subjects help to provide data on where increased activation levels in the brain are expected in response to a painful stimulus. Both experiments used a hand held digital algometer (Pressure Algometer NPA-1, Shinko, Japan) with a 10mm diameter hemispherical probe. A 1.5 Tesla MRI scanner (Signa EXCITE X1 11.0, GE Healthcare, Milwaukee, WI) was used. The use of a handheld algometer lacks accurate reproducibility of pressure profiles and is operator dependant. Another example of an MR compatible algometer is described by Gracely et al. in which the algometer used weights in conjunction with hydraulic pistons [5, 6]. However, such a design has limited flexibility in the pressure profiles it can create and lacks the ability to monitor and record the pressure applied.

Our goal is to develop an improved MR safe algometer capable of autonomously producing reproducible pressure profiles as needed. This paper describes a new pneumatically actuated algometer and our evaluation of whether it was MR safe. This algometer can be operated from the fMRI control room and is capable of autonomously producing a reproducible adjustable pressure profile. To assess safety, we investigated whether the device when placed in the scanning room of the 3.0Tesla GE Scanner would distort the image capture by the scanner and whether the magnetic environment would affect the device itself.

II. Method

A. Algometer Device Description

A major concern when designing a device for use in an MR environment is to ensure the device will not cause injury to any person or other equipment, is not affected by the strong magnetic field, and will not affect the MR image quality. The MR environment is defined as the area inside of the 5 Gauss line [7]. The algometer device was designed to meet the following key requirements. It had to be portable with two main parts: a) a manipulandum portion that is compact to fit in scanner bore (60cm), made of MR safe materials (non-ferrous), mountable on the scanner bed, comfortable and easily applied over the amputee stump with a stump clamp (the human machine interface (HMI)), that contains a probe that can be triggered remotely and can apply 0 to 7lbf with a resolution of 0.25lbf. b) a controller portion that controls the force probe remotely (30 ft), failsafe operation to ensure that during normal operation the algometer would be limited in its ability to apply forces that could harm a subject, accessible e-stop buttons, and custom software control.

Figure 1a-c (page 4) shows images of the algometer with controller case and manipulandum (HMI). Fig 1b shows how the manipulandum stump clamp can attach to the amputee stump and Fig 1c shows the system attached to a scanner bed. The final design consists of a Pelican Case which houses the pneumatic power plant, control valves, data acquisition, and

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control circuitry. This controller portion of the algometer remains outside of the MR environment and stays in the MRI control room. A second MR safe portion of the algometer, the manipulandum or HMI, also connects to the Pelican Case. The HMI consists of a supporting armature to which a stump clamp is attached. The stump clamp consists of two large padded clamps and a pneumatically actuated probe.

A pneumatically actuated cylinder was used to apply forces to control the probe. A rolling diaphragm cylinder type was selected for its near frictionless operation and precise force application characteristics. The single acting class of cylinders was chosen to reduce the required number of control valves down to one for the sake of simplicity and cost. A custom built controller system was used. A laptop running the algometer's control software (developed in LabVIEW) connects to the system's hard case via a USB cable. The main portion of the software (Fig. 2) is utilized when the system is running in the MR environment.

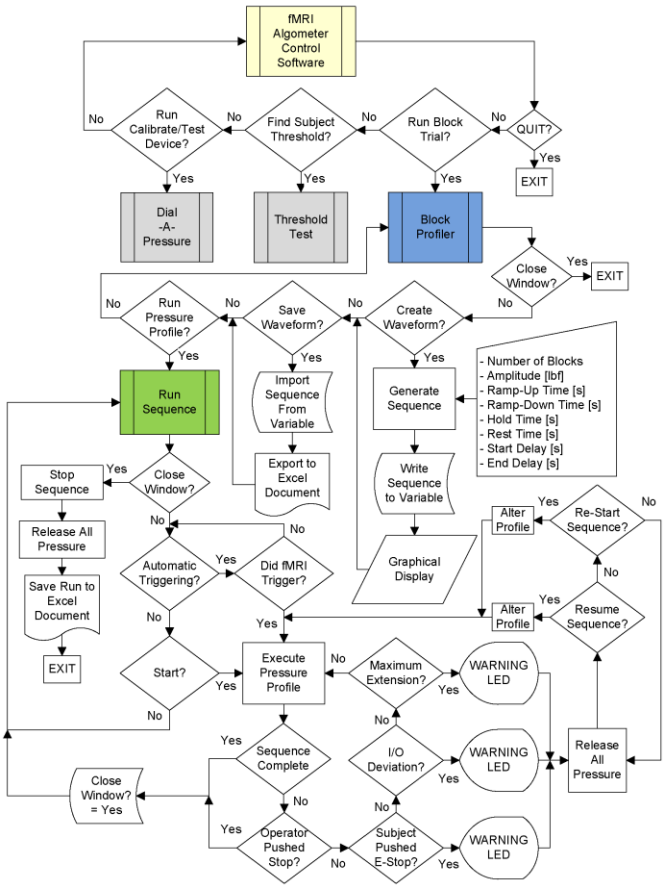

Figure 2: Software flow for algometer control

This module of the software (*Block Profiler*) initializes with a window that allows the user to enter a series of parameters that will define the block style pressure stimulus profile that the system will automatically execute during a scan (Fig. 3). Once the sequence is generated and displayed in graphical form for the user to review, the user has the ability to save and run the profile (*Run Sequence*). Once started, the sequence can be stopped by either of the emergency stops or by the operator clicking the stop button on the screen. Once the sequence is started, the software indirectly reads in, displays out, and controls the applied pressure of the probe by sensing the pressure in the actuating cylinder. This is done in a twofold manner. First, the value read in from the pressure sensor is converted into applied force using a series of experimentally determined system calibration parameters. Second, a potentiometer engaged to the push rod of the pressure probe is used to sense the extension of the probe. This compression distance is then used in a feedback loop calculation to continuously adjust for the amount of return force being generated by the return spring in the actuated cylinder such that the resultant force experienced by the subject is what the operator specified in their generated sequence ±0.25 lbf.

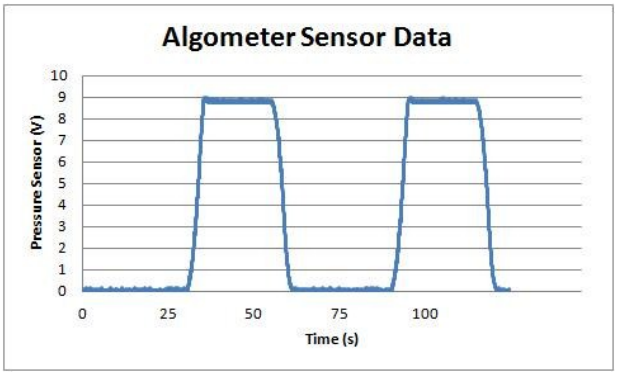

Figure 3: External pressure sensor data profile.

B. Experimental Set-up and Analysis

Compatibility was determined from two perspectives. MR compatibility was determined to ensure the device and any of its operations does not affect the quality of the MRI data collected by the scanner. Device compatibility was determined to ensure the echo planar imaging does not affect any device operations or the data collected by the device's sensors.

1) MR Compatibility

MR compatibility was determined using a testing procedure developed by Suminiski et al [8]. The MR compatibility was tested by scanning a phantom (3.0T General Electric (GE) spherical head phantom) placed inside a split transmit/receive quadrature head coil. The selected gradient echo planar pulse sequence is as follows: 48 continuous axial slices, TE=15.7ms, TR=2500ms, flip angle=80, FOV=200mm, 64*64 matrix and 3.75*3.75*4 mm spatial resolution. MRI data was collected on a phantom (spherical ball filled with water) with the algometer in the MRI control room (phantom only) to be used as a control. Following this run, the MR compatible portion of the algometer was then placed at the foot of the patient bed of the MRI scanner, and fMRI data was collected on the phantom while the algometer was off, performing a pressure profile with maximal pressure, zero pressure, as well as pressing the emergency stop (Estop) button in the middle of a maximal pressure profile run. Each of these conditions was done twice. The maximal pressure profile consisted of a 30 second off followed by a 5 second

ramp up, a 20 second on, and a 5 second off. There were two cycles of this in one run resulting in a 2 minute run.

The MRI data of the phantom was analyzed by first obtaining a time series average of each voxel. Then, seven equal volume 10x10x10 voxel regions of interest (ROI) within the spherical phantom to be used as signal and one 10x10x10 voxel ROI outside of the phantom to be used as noise were taken. The mean of each signal ROI and the standard deviation of the noise ROI were taken and the signal-to-noise ratio (SNR) was calculated for each ROI as follows:

$$SNR_{ROI} = \frac{\mu_{ROI}}{0.665\,\sigma_{noise}} \quad (1)$$

A scaling factor of 0.665 was used as a correction for changes to the statistical distribution of σ_{noise} caused by calculating the magnitude image from the original complex MRI data [8]. The SNR for each ROI of each condition was then normalized to the corresponding SNR of each ROI of the phantom only condition. A general linear mixed model was used for analyzing the normalized MRI data of the SNR of the seven ROIs. There were three group variables being: 1) Device off (no pressure controlled), 2) Maximum pressure profile (8.8 psi), Maximum pressure profile with Estop, and 3) Zero Pressure. There were also eight regions (ROIs) analyzed. Seven regions were inside the phantom head with 1 region outside. The details for these regions can be found in [8]. The SNR for seven regions inside were calculated using Eqn 1 with the region outside providing the standard deviation of the noise. We hypothesize there is no correlation between the different variables and regions.

1) Device Compatibility

Device compatibility was determined using the data obtained from the pressure sensor in the MR compatible portion of the algometer. Data from this sensor was collected with the algometer in the MR control room while performing a maximal pressure profile, as well as pressing the emergency stop button in the middle of a maximal pressure profile run to be used as a control. The MR compatible portion of the algometer was then placed at the foot of the bed of the MRI scanner and data was collected from the sensors on the algometer while fMRI data was being collected. The same two conditions were run twice. The SNR of each of the runs was calculated using the formula as follows:

$$SNR = 20\log_{10}\left(\frac{RMS_{Signal} - RMS_{Noise}}{RMS_{Noise}}\right) \quad (2)$$

Root mean squared values of the signal (RMS_{Signal}) were taken to be the pressure sensor values during the two on phases of the pressure profiles during which the pressure would be at a maximum. RMS_{Noise} values were taken to be the pressure sensor values during the two off phases of the pressure profiles during which pressure would be at a minimum. Each SNR was then normalized to the control SNR of the corresponding condition. One sample t-test was used for analyzing the normalized SNR data from the algometer's external pressure sensor. We hypothesize there is no difference to the SNR of when the algometer is inside or outside of the scanning room.

III. Results

Comparisons of the phantom MRI data were done using AFNI and MATLAB to detect any gross differences between the control (phantom only) run and the other various conditions. An example of a comparison between run 3 (maximal pressure) and run 9 (control) at a section halfway through the phantom sphere is shown in Fig. 4. An example of the data obtained from the external pressure sensor performing a maximal pressure profile is shown in Fig. 3.

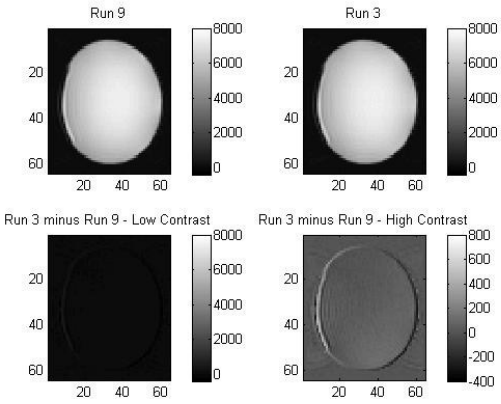

Figure 4: Comparison between maximal pressure and control at slice 24.

A. MRI Compatibility Results

"Group" and "region" were used as two fixed effects and "observation" was included as a repeated effect. Our result showed that the "group" (3 levels) and "region" (8 levels) variables don't show a significant association with MRI reading. Also, we found that there was no correlation between regions. Table I and II shows the statistical results.

TABLE I. Type 3 tests of fixed effects for MRI SNR data.

Type 3 Tests of Fixed Effects				
Effect	Num DF	Den DF	F Value	Pr > F
GROUP	2	47	1.43	0.2490
REGION	6	47	1.50	0.1984

B. Device Compatibility

One sample t-test was used for analyzing normalized SNR data. The null hypothesis, E(SNR)=1 (Mean of SNR equals to 1), states there is no difference with algometer inside or outside of the scanning room. The four normalized SNR observations have mean 0.9935 (SD 0.0689, 95% CI (0.8838, 1.1031), p-value 0.8617). Thus, we failed to show that the algometer significantly changes the SNR signal.

TABLE III. T-TEST THE ALGOMETER EXTERNAL PRESSURE SENSOR DATA .

Mean	95% CL Mean		SD	DF	t Value	Pr > |t|
0.994	0.884	1.103	0.07	3	-0.19	0.862

IV. DISCUSSION AND CONCLUSION

In order to determine MR compatibility, the algometer must not affect the MR data, and the magnetic field must not affect the algometer's function as well as its sensors. As seen in Tables I-III there is no correlation between the different experimental conditions and the regions of interest on the SNR for the MRI data. Thus, it is shown that the algometer and its various functions do not affect the MR image quality. As seen in Table I, the results show that the null hypothesis can't be rejected. Thus, the magnetic field is shown to have no significant affect on the algometer's external pressure sensor. It is shown that this device is fMRI safe. One possible source of error is the limited number of experimental runs. However, the results of the statistical analysis are considered to be statistically sound. Although the device was collected using the static non-perfused phantom, the device should not interfere with magnetic imaging during dynamic scanning. This will be confirmed when the system is tested with patients.

In summary, the development and testing of a pneumatically actuated algometer which can be operated from the fMRI control room and is capable of autonomously producing a reproducible and adjustable pressure profile was described. The algometer was shown to be MR compatible, neither affecting the MR image quality nor being affected by the magnetic field in the MR environment. We plan to use this algometer in studying the neural mechanisms of phantom limb and residual limb pain,and the effect lidocaine and botox may have on phantom limb and residual limb pain on amputees.

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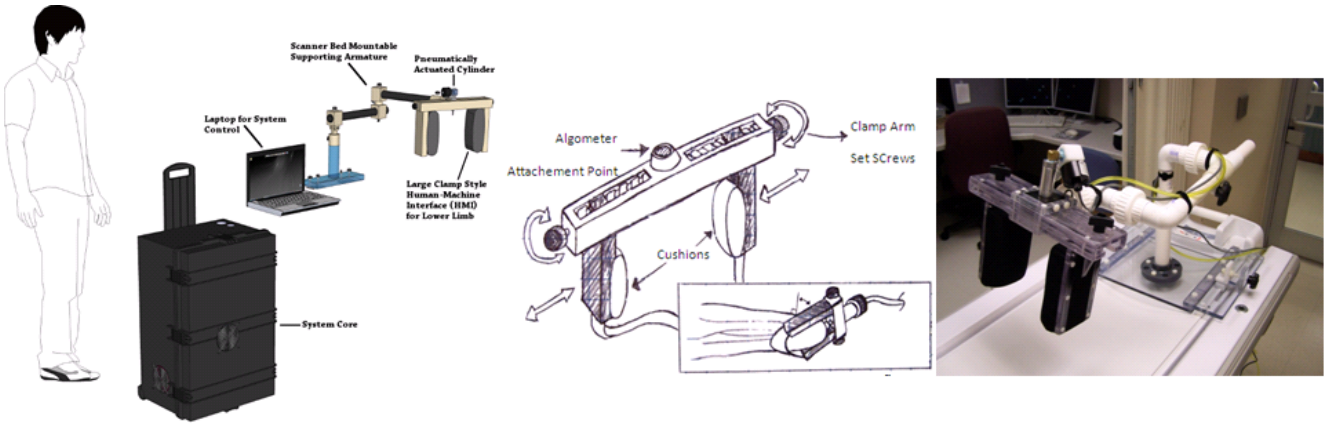

Figure 1: (a) Algometer case in control box. (b) Clamping mechanism on stump. (c) Algometer attached to scanner bed. The manipulandum for use inside the scanner was made from standard low-cost PVC circular tubes (links), acrylic (screws and base plate), and non-ferrous parts.

TABLE II. NORMALIZED MRI DATA FOR MRI COMPATIBILITY RESULTS

Regions of Interest							Group Variable
1: Right	2: Center	3: Left	4: Anterior	5: Posterior	6:Rostral	7:Caudal	
1.007	1.005	1.008	1.007	1.010	1.009	1.010	Device off
1.009	1.004	1.007	1.002	1.010	1.007	1.007	Zero pressure
1.006	1.003	1.006	0.9994	1.009	1.005	1.005	Max pressure /E-Stop