3-Tesla MRI in patients with fully implanted deep brain stimulation devices: a preliminary study in 10 patients

Francesco Sammartino, MD,1 Vibhor Krishna, MD,1 Tejas Sankar, MDCM,3 Jason Fisico, MMedRadSc(MRI), MRT(N)(MR),2 Suneil K. Kalia, MD, PhD,1 Mojgan Hodaie, MD, MSc,1 Walter Kucharczyk, MD,2 David J. Mikulis, MD,2 Adrian Crawley, MD, PhD,2 and Andres M. Lozano, MD, PhD1

1Division of Neurosurgery, Department of Surgery, and 2Department of Medical Imaging, University of Toronto, Ontario; and 3Division of Neurosurgery, University of Alberta, Edmonton, Alberta, Canada

OBJECTIVE The aim of this study was to evaluate the safety of 3-T MRI in patients with implanted deep brain stimulation (DBS) systems.

METHODS This study was performed in 2 phases. In an initial phantom study, a Lucite phantom filled with tissue-mimicking gel was assembled. The system was equipped with a single DBS electrode connected to an internal pulse generator. The tip of the electrode was coupled to a fiber optic thermometer with a temperature resolution of 0.1°C. Both anatomical (T1- and T2-weighted) and functional MRI sequences were tested. A temperature change within 2°C from baseline was considered safe. After findings from the phantom study suggested safety, 10 patients with implanted DBS systems targeting various brain areas provided informed consent and underwent 3-T MRI using the same imaging sequences. Detailed neurological evaluations and internal pulse generator interrogations were performed before and after imaging.

RESULTS During phantom testing, the maximum temperature increase was registered using the T2-weighted sequence. The maximal temperature changes at the tip of the DBS electrode were < 1°C for all sequences tested. In all patients, adequate images were obtained with structural imaging, although a significant artifact from lead connectors interfered with functional imaging quality. No heating, warmth, or adverse neurological effects were observed.

CONCLUSIONS To the authors’ knowledge, this was the first study to assess the clinical safety of 3-T MRI in patients with a fully implanted DBS system (electrodes, extensions, and pulse generator). It provided preliminary data that will allow further examination and assessment of the safety of 3-T imaging studies in patients with implanted DBS systems. The authors cannot advocate widespread use of this type of imaging in patients with DBS implants until more safety data are obtained.

https://thejns.org/doi/abs/10.3171/2016.9.JNS16908

KEY WORDS magnetic resonance imaging; safety; implants; deep brain stimulation; neurostimulator; specific absorption rate; Activa; electrodes; functional neurosurgery

Deep brain stimulation (DBS) is an established treatment for advanced Parkinson’s disease, medically refractory tremor, dystonia, and obsessive compulsive disorder.17,22 Several hypothesis-driven DBS trials are underway to study the potential therapeutic effect of neuromodulation in dysfunctional circuits in other neurological and psychiatric disorders such as epilepsy, Alzheimer’s disease, and depression.8 It is becoming apparent that DBS has profound effects on the anatomy and function of distant but interconnected brain regions (that is, networks).1,16,18 For example, stimulation of the subthalamic nucleus (STN) results in activation of cortical motor regions. More recent data suggest that DBS may also induce structural changes in brain networks; e.g., in a cohort of patients with Alzheimer’s disease treated with DBS of the fornix, the progression of hippocampal atrophy may have been delayed.27 These effects may involve mechanisms including brain-derived neurotrophic factor release and hippocampal neurogenesis.10,30

MRI can accurately demonstrate brain structure at high

ABBREVIATIONS DBS = deep brain stimulation; fMRI = functional MRI; FRFSE = fast recovery fast spin echo; FSPGR = fast spoiled gradient–recalled; GRE-EPI = gradient-echo echo-planar imaging; IPG = internal pulse generator; PROBE-SV = point-resolved single-voxel spectroscopy; PVE = periventricular gray; RF = radiofrequency; SAR = specific absorption rate; STN = subthalamic nucleus; VIM = ventral intermediate.

SUBMITTED April 11, 2016. ACCEPTED September 1, 2016.

INCLUDE WHEN CITING Published online December 23, 2016, DOI: 10.3171/2016.9.JNS16908.
resolution and assess functional changes in the brain related to variations in the blood oxygen level–dependent signal. Thus, at first glance, MRI is an ideal technique for studying the effects of DBS on the overall structure and function of the brain in human patients. Unfortunately, there are barriers to the use of MRI in the post-DBS setting.

Current manufacturer guidelines restrict patients with DBS systems from being scanned at field strengths that are > 1.5 T. One of the more important reasons for this is the potential risk of heating the implanted electrodes due to induced voltages in the DBS system from interactions with the applied radiofrequency (RF) field. This could theoretically result in thermal lesions in the tissue adjacent to the electrodes and serious physical harm to the patient.9,29

For optimal structural imaging, high-field MRI at 3 T is desirable because of its superior signal-to-noise ratio.7 Indeed, in animal research applications, 3-T MRI imaging has shown the ability to reveal DBS-mediated modulation of brain activity, in particular its relationship with specific cognitive and affective processes.20,21 Another potential concern with MRI is the possibility of changing the settings of the implantable internal pulse generator (IPG) during scanning (switching it between the on and off states) or damaging its components.

In this study, we aimed to investigate the safety of imaging patients with fully implanted DBS systems (IPGs, extensions, intracranial electrodes) using 3-T MRI with specific sequences that are common in the clinical setting. This was accomplished in 2 steps. The temperature changes associated with different imaging sequences were first assessed by scanning a phantom containing an implanted DBS electrode, IPG, and lead extensions, to ensure that the maximum temperature increases were within safe margins for each sequence. A prospective cohort study was then performed to assess both clinical safety and image quality of 3-T MRI scanning—under theoretically safe acquisition configurations and parameters—in patients with an implanted DBS system at a variety of brain targets.

**Methods**

This study was approved by the Research Ethics Board of the University Health Network.

**Phantom Study**

A phantom was assembled using an intracranial DBS lead (Model 3387; Medtronic, Inc.), an extension wire (Model 7482; Medtronic, Inc.), and an IPG (Soletra, Medtronic, Inc.). The system was configured in a Lucite phantom, as shown in Fig. 1. The phantom was filled with a polyacrylic acid salt (Aldrich Chemical) (8 g/L distilled H2O) dissolved in sodium chloride (0.7 g NaCl/L distilled H2O) to create a semisolid gel that has been used in previous phantom studies to simulate human tissue.3,6 The electrode tip was positioned in the head portion of the phantom and passed through a bur hole in a straight line parallel to the z-axis. The configuration of the intracranial lead, the extension wire, and the IPG resembled the surgical placement of these devices in patients. The excess lead wiring was secured in a random configuration to the top of the phantom with clear plastic tape. The IPG was programmed to the off configuration for the duration of the study.

A fiber optic temperature probe was then connected to a fiber optic thermometer (Model 790; Luxtron) with a temperature resolution of approximately 0.1°C. The tip of the thermometer probe was positioned in proximity to the DBS electrode tip (4 mm) and submerged in the gel. For the transmit-receive head coil setup (see below), an additional probe tip was placed 7 mm beyond the electrode tip. The distance between the electrode tip and the thermometer probe was measured on axial T2-weighted fast recovery fast spin echo (FRFSE) images of the phantom. After recording a stable baseline temperature, temperature data were recorded manually at 30-second intervals during the pulse sequences.

The phantom was scanned on a 3.0T GE Signa MRI scanner (software level HDx version 16.0_V02_1131; GE Healthcare) in a supine, head-first position. Two different head coils were tested on the head portion of the phantom to simulate a brain scan of a patient with a DBS system: 1) a circular polarized transmit-receive head coil; and 2) a transmit body-receive only head coil. Scan parameters and sequences are listed in Table 1, and the temperature increases registered are shown in Table 2. Sequences were deemed safe if the observed increase in temperature from baseline was within 2°C.3,13

**Patient Cohort**

A total of 10 patients were scanned on the 3-T MRI (GE Signa Excite) machine at Toronto Western Hospital between February 2015 and January 2016. The patients agreed to participate in the study and signed an informed consent. The patient cohort included 1 subject with chronic pain and 2 DBS electrodes in 1 hemisphere, 1 subject with essential tremor, and 8 subjects with a diagnosis of Parkinson’s disease and bilateral DBS electrodes. The targets used were the ventrocaudal thalamus, the periventricular gray (PVG) matter, the ventral intermediate (VIM) thalamus, and the bilateral STN (Table 3).

**Surgical Procedure and Experimental Design**

All patients underwent stereotactic implantation of quadripolar DBS electrodes (Model 3387; Medtronic, Inc.) at the target (guided by microelectrode recording and stimulation following a technique previously described). The electrodes were secured to the skull using a plastic bur hole ring and cap system and were then tunneled in the subgaleal plane above the ear. In a second-stage procedure, the electrodes were connected to a set of extension leads to reach a pocket in the chest wall below the clavicle. The lead extensions were then connected to the IPG (Model Activa; Medtronic, Inc.) and excess extension wiring was coiled behind the IPG body. The Activa Patient Programmer (Model 37642; Medtronic, Inc.) was used at this stage to check for any open circuits.

All participants underwent MRI on an in-patient basis to allow for delayed observation after the scan.

All medications that could potentially interfere with a
patient’s level of consciousness were stopped before imaging. The IPG was programmed to OFF and the voltage set to 0. The patients were supine on the MRI table. A circular polarized receive-only head coil was positioned, and the head was immobilized using specific padding materials. Patients were instructed to relax, keep their eyes closed, and try not to move throughout the procedure. During the scan, the specific absorption rate (SAR) estimated values and a pulse oximeter trace were monitored continuously.

The specific scan parameters are reported in Table 1. Briefly, for each participant, a 3-plane localizer, an axial T2-weighted FRFSE centered on the thalamus and basal ganglia, a volumetric 3D fast spoiled gradient-recalled (FSPGR) echo, and an axial resting-state gradient-echo echo-planar imaging (GRE-EPI) sequence were acquired (Fig. 2). A neurosurgeon with expertise in DBS surgery was present for the entire duration of the scan. After each pulse sequence, patients were evaluated for any side effects (paresthesias, motor deficits, cranial nerve deficits, pain, any neurological changes from the baseline, and any discomfort or heating at the IPG site). After imaging, the IPG was interrogated using the N’Vision programmer (Medtronic, Inc.) to check for any changes.

**Results**

**Phantom Study**

No significant temperature changes were observed during the 3-plane localizer sequence. The highest recorded temperature change from baseline, measured at 4 mm from the DBS electrode, was observed with the T2-weighted FRFSE sequence (Fig. 2). The temperature increase was 0.6°C at the tip measured for the transmit body-receive only head coil. The 3D FSPGR echo, GRE-EPI, and point-resolved single-voxel spectroscopy (PROBE-SV) sequences did not produce temperature changes > 1°C.
The temperature measurements with individual sequences are shown in Table 2. The DBS configuration remained consistent for each experimental setup (Fig. 1).

**Patient Cohort**

The features of the patients in this study are described in Table 3. We studied 10 patients with a mean age of 64 years, 3 different diagnoses among them, and a total of 19 implanted DBS electrodes. All patients except for 1 had 2 DBS electrodes. Each participant was able to complete the scan. The scan took approximately 20 minutes. Adequate structural images were obtained for both T1- and T2-weighted sequences (see Fig. 2). For the EPI sequence, a significant artifact was observed close to the vertex, probably related to the connection site between the distal end of the DBS electrode and the lead extensions.

There were no patient reports of warmth or heating along the DBS system during imaging. No adverse neurological effects were reported nor detected on examination of the patients. The interrogation of the IPG at the end of the pulse sequences showed no change from the OFF state. The participants reported no transcranial movements at the level of the IPG or the connectors during the imaging sequences.

We measured the apparent size of the cross-sectional diameter of the electrodes with the various imaging sequences used in this study as a measure of the image distortion that occurred with these sequences related to the metal artifact. The known diameter of the Model 3387 DBS electrodes is 1.27 mm. In the T1-weighted FSPGR and T2-weighted FRFSE sequences, the mean lead artifact diameters were 3.5 ± 0.2 mm and 2.5 ± 0.2 mm, respectively.

**Discussion**

In this study, we report on the safety of specific 3-T MRI sequences in patients with implanted DBS systems. Specifically, the changes in temperature associated with these sequences were within safety limits reported in the literature. None of the patients in the prospective cohort experienced any adverse effects due to 3-T imaging. Our findings suggest that 3-T MRI, acquired under certain conditions, is suitable in patients with implanted DBS systems. In addition, our results pave the way for future MRI studies that may advance our understanding of the mechanisms underlying DBS, and eventually improve patient care. For example, a better understanding of DBS-mediated modulation of network dysfunction can potentially aid stimulation parameter optimization or help in the identification of novel stimulation targets. Finally, the use of noninvasive neuroimaging modalities would allow researchers to explore the metabolic and electrophysiologic mechanisms that support motor, sensory, emotional, and cognitive processes.

Performing MRI in patients with DBS implants has long represented a potential challenge, largely due to the restrictive guidelines of manufacturers and to previous reports of scanner-related injuries to patients with these implanted devices. In some institutions, patients with electronically activated implants are strictly prohibited from undergoing MRI. The major concern in scanning patients with implanted DBS systems is that RF-induced current in the wires (that is, the leads and lead extensions) cannot be dissipated through the IPG body and could potentially induce a lesion at the tip of the electrodes. Furthermore, the IPG itself could be switched on and off intermittently during the scan.

The MRI-related safety of exposures of different implants in vitro and in vivo in various configurations has been assessed by previous authors. Unfortunately, these safety results have limited generalizability due to the association of temperature changes with the specific imaging platform and the type of pulse sequences used, in addition to the implanted hardware. For example, phantom experiments have shown that heating at DBS electrodes varies considerably depending on the manufacturer and software platform of the MRI system, the source of the

---

**TABLE 1. MRI sequences and parameters used in the study**

<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR (msec)</th>
<th>TE (msec)</th>
<th>TI (msec)</th>
<th>BW (kHz)</th>
<th>FOV (mm)</th>
<th>FA (°)</th>
<th>ST (mm)</th>
<th>Gap (mm)</th>
<th>ETL</th>
<th>Matrix</th>
<th>Frequency Direction</th>
<th>NEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axial T2-weighted FRFSE</td>
<td>Var</td>
<td>85.0</td>
<td>NA</td>
<td>62.5</td>
<td>220 × 220</td>
<td>90</td>
<td>2.0</td>
<td>0</td>
<td>Var</td>
<td>512 × 512</td>
<td>A/P</td>
<td>3</td>
</tr>
<tr>
<td>Axial 3D FSPGR</td>
<td>7.9</td>
<td>3.1</td>
<td>450</td>
<td>31.3</td>
<td>220 × 220</td>
<td>12</td>
<td>1.0</td>
<td>0</td>
<td>1</td>
<td>256 × 256</td>
<td>A/P</td>
<td>1</td>
</tr>
<tr>
<td>GRE-EPI multiphase (fMRI)</td>
<td>2000</td>
<td>30</td>
<td>NA</td>
<td>62.5</td>
<td>240 × 240</td>
<td>85</td>
<td>5.0</td>
<td>0</td>
<td>1</td>
<td>64 × 64</td>
<td>S/I</td>
<td>1</td>
</tr>
<tr>
<td>Axial 2D MRS (single-voxel PRESS)</td>
<td>1500</td>
<td>144</td>
<td>NA</td>
<td>NA</td>
<td>200 × 200</td>
<td>180</td>
<td>20.0</td>
<td>NA</td>
<td>1</td>
<td>1 × 1</td>
<td>A/P</td>
<td>8</td>
</tr>
</tbody>
</table>

A/P = anterior/posterior; BW = bandwidth; ETL = echo train length; FA = flip angle; FOV = field of view; MRS = MR spectroscopy; NA = not available; NEX = number of excitations; PRESS = point-resolved spectroscopy; S/I = superior/inferior; ST = slice thickness; TE = echo time; TI = inversion time; TR = repetition time; Var = variable.

**TABLE 2. SAR and temperature values corresponding to MRI sequences used in the study (transmit body-receive head coil only)**

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Time, Hr/Mins</th>
<th>Estimated Body SAR, W/kg</th>
<th>Peak Body SAR, W/kg</th>
<th>Max Temperature Increase, °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axial T2-weighted FRFSE</td>
<td>4:06</td>
<td>1.15</td>
<td>2.30</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Axial 3D FSPGR</td>
<td>9:17</td>
<td>0.18</td>
<td>0.37</td>
<td>&lt;1</td>
</tr>
<tr>
<td>GRE-EPI 120</td>
<td>4:00</td>
<td>0.23</td>
<td>0.45</td>
<td>&lt;1</td>
</tr>
<tr>
<td>PROBE-SV 144</td>
<td>3:48</td>
<td>0.53</td>
<td>1.06</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
transmitted RF field (transmit head coil vs transmit body coil), variations in positioning of DBS electrode leads and extensions, and the SAR of the scanning.4
Carmichael et al.6 demonstrated heating levels ≤ 2.2°C using a transmit-receive head coil on a 3-T MRI scanner. This issue of changes in stimulation parameters is partially resolved with shielding and insulation during the IPG manufacturing. For example, Kahan et al.13 showed that an Activa PC IPG (Medtronic, Inc.) in a phantom did not change DBS frequency, pulse width or amplitude, or general function during their functional MRI (fMRI) sequence. With the increasing interest in using MRI for improving the care and postoperative management of patients, different research groups have performed experiments to determine the real safety profile associated with specific sequences and implant configurations.

Currently, it is considered safe to scan patients with implanted DBS systems only if specific guidelines are observed.14,33 Recommended exposures for RF energy include SAR < 4.0 W/kg whole body for 15 minutes, 3.0 W/kg averaged over the head for 10 minutes, 8.0 W/kg in any gram of tissue in the head or torso for 15 minutes, or 12.0 W/kg in any gram of tissue in the extremities for 15 minutes. In December 2015, the Activa portfolio (Medtronic, Inc.) of DBS neurostimulators received Food and Drug Administration approval for full-body MRI under specific conditions of use.19

At our institution, we routinely scan patients with implanted DBS systems at 1.5 T (GE Signa Excite) under the condition that the IPG is deactivated (switched off and voltage set to 0). In 1999, our group showed that it was safe to do fMRI in patients with externalized transcutaneous leads at 1.5 T.26 To evaluate the safety of implanted DBS systems in the 3-T environment, we first conducted a phantom study. The concentration of the gel in our study was similar to that used in previous phantom studies.6

In addition, the composition of the gel we used has been shown to be a valid model of temperature dispersion comparable to human tissue. During this preclinical phantom study, we found that the transmit-receive head coil generated temperature increases at the tip of the DBS electrode, especially during the T2-weighted FRFSE sequence. However, in all cases, the rise in temperature was < 1°C. This is consistent with the fact that these sequences had the highest SAR values for the head, meaning more RF energy would be absorbed in this part of the phantom as heat. Conversely, the T2-weighted FRFSE sequences acquired using the transmit body-receive only head coil produced far lower temperature changes of 0.6°C at the electrode tip.

The FSPGR, EPI-GRE (that is, fMRI), and PROBE-SV sequences all produced temperature changes within acceptable limits of patient safety. This is in agreement with a previous report by Phillips et al.,21 showing similar temperature changes in a phantom study with externalized DBS electrodes and IPG in the MRI control room. Similarly, for the clinical study, none of the patients reported any side effects during or after the scan. With the exception of 1 patient, all participants were implanted with 2 electrodes connected to an Activa PC IPG implanted in the subclavicular area. The IPG remained in the OFF state during and after the scan.

Local tissue-related changes have been reported by several authors following the insertion of DBS electrodes.2,12,15 Indeed, it is certainly possible that postoperative, chronic, stimulation-related changes in characteristics of tissue surrounding DBS electrodes may influence tissue heating. Furthermore, it is difficult to account for such changes in the setting of a phantom study. Consequently, the phantom findings in our study apply predominantly to the perioperative setting, and may not necessarily be generalizable to MR images obtained in patients with long-standing DBS implants.5

We also observed that the size of the leads artifact in the T2-weighted sequence using a 3-T magnet was smaller when compared to the values previously reported by our group under similar conditions using 1.5 T.26 Furthermore, the use of FSE imaging has been reported as a way to reduce electrode-related artifact.28

Limitations of this study include not having tested the phantom in the DBS on state. Furthermore, we did not test different combinations of IPGs and electrodes from other manufacturers. The data we present here are specific to Medtronic DBS hardware and to the MRI scanner make and model mentioned in Methods. The authors acknowledge that further testing is required for other configurations of DBS systems or MRI scanner make/models. In addition, we used a fiber optic thermometer to monitor the temperature increases, but we did not correlate the findings with real-time MR-thermometry estimation.

Finally, our sample size of 10 patients is small. We cannot rule out adverse events that could occur at a low frequency and would only be seen in a larger patient sample. For this reason, we cannot advocate the general use of 3-T imaging for patients with implanted DBS systems before more extensive studies are performed in a larger number of subjects.

Conclusions
We have demonstrated that under specific conditions, a fully implanted DBS system can be safely scanned with

<table>
<thead>
<tr>
<th>Pt No.</th>
<th>Age at Op (yrs)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Target</th>
<th>Electrodes</th>
<th>Days From Imaging to Op</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>83</td>
<td>M</td>
<td>ET</td>
<td>Lt VIM</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>M</td>
<td>PD</td>
<td>Bilat STN</td>
<td>2</td>
<td>420</td>
</tr>
<tr>
<td>3</td>
<td>65</td>
<td>M</td>
<td>Central pain</td>
<td>Rt ventrocaudal/PVG</td>
<td>2 (rt hemisphere)</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>M</td>
<td>PD</td>
<td>Bilat STN</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>65</td>
<td>F</td>
<td>PD</td>
<td>Bilat STN</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>59</td>
<td>M</td>
<td>PD</td>
<td>Bilat STN</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>M</td>
<td>PD</td>
<td>Bilat STN</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>54</td>
<td>M</td>
<td>PD</td>
<td>Bilat STN</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>56</td>
<td>F</td>
<td>PD</td>
<td>Bilat STN</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>67</td>
<td>M</td>
<td>PD</td>
<td>Bilat STN</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

ET = essential tremor; PD = Parkinson’s disease; Pt = patient.
3-T MRI. This is a crucial, preliminary safety study because 3-T MRI has several advantages, including higher signal-to-noise ratio and higher sensitivity to detect blood oxygen level–dependent signal for fMRI studies. In parallel with the expanding indications for DBS, the results of this study provide a foundation to allow for more complex imaging studies with 3-T MRI. These studies will help advance our understanding of the mechanisms of action of DBS and the fundamental pathophysiological mechanisms of DBS-induced network modulation in different neurological and psychiatric disorders.

Acknowledgments
We thank Eugen Hlasny for help in organizing and supervising the scans.

References
F. Sammartino et al.


Disclosures

Dr. Hodaie has received grant support from Medtronic for efforts not related to this study. Dr. Lozano is the owner of Functional Neuromodulation and has served as a consultant for St. Jude, Boston Scientific, and Medtronic.

Author Contributions

Conception and design: Sammartino. Acquisition of data: Sammartino, Krishna. Analysis and interpretation of data: Sammartino, Krishna. Drafting the article: Sammartino, Krishna, Lozano. Critically revising the article: Krishna, Sankar, Fisico, Crawley, Lozano. Study supervision: Sammartino, Krishna, Fisico, Crawford, Lozano. Study supervision: Sammartino, Krishna, Fisico, Crawford, Lozano.