Animal Experiment

Evaluation of Interaction between a Spinal Cord Stimulator and Implanted Cardioverter-Defibrillator in a Swine Model

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Background: Spinal cord stimulators (SCS) have been used for many years to treat a myriad of chronic pain conditions using electrical signals to diminish the perception of a painful stimulus. Because of the electrical nature of the devices, there is a concern about the potential for electromagnetic interaction between the device and lifesaving cardiac implantable cardioverters-defibrillators (ICVD).

Objective: The purpose of this study was to use a swine model to evaluate the potential for interaction between an implanted SCS and ICVD using the closest possible proximity, highest stimulation settings, and most sensitive ICVD settings.

Methods: A pig was anesthetized and subsequently an ICVD and ICVD lead (Cogni 100-D and Endotak Reliance®, Boston Scientific, Natick, MA) were placed into the right prepectoral region and the right ventricle, respectively. An SCS (50 cm linear ST Precision Plu octad electrode lead [Boston Scientific, Valencia, CA] with 3 mm wide contacts spaced one mm apart) was implanted using fluoroscopic guidance into the posterior epidural space. Remote interrogation and programming of the ICVD were performed while the SCS lead was placed in as close proximity as possible, using fluoroscopy to guide the final position of the SCS electrode. After confirming that both systems were working, appropriately 9 stimulating configurations of varying current, pulse width, and frequency, including maximal settings, were delivered through the SCS. The effects on the ICVD were recorded at 2 sensitivity settings.

Results: None of the tested SCS configurations caused interference with the proper functioning of the ICVD.

Limitations: The anatomical proximity of the posterior epidural space and right ventricle of the swine is different from humans. While the entire pacer, including generator, was imbedded in a subcutaneous pocket, an implantable pulse generator for the SCS was not implanted, which did not allow us to study if any damage or a resetting of settings had occurred to the generator. Only one manufacturer was used in this study. Also, this study was performed in an anesthetized pig and the anatomical positions remained static. Realistically, changes in position of the devices would occur in patients who perform activities of daily living, and this can potentially shorten the distance between the 2 leads causing adverse interaction.

Conclusion: This study clearly demonstrated the feasibility of the 2 devices coexisting and functioning appropriately in an animal model using an ICVD and SCS donated by Boston Scientific. Further studies are needed to elucidate restrictions, optimal settings and parameters in a human setting.

Key words: Spinal cord stimulator, interaction, implantable cardioverter defibrillator, pacemaker, swine model, cross-talk.

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Spinal cord stimulators (SCS) were initially introduced for the treatment of chronic pain based on the "gate control" theory with the first unipolar SCS implanted in 1967 (1). They function by transmitting electrical impulses generated from an implanted battery to electrode contacts placed at different locations within the epidural space depending on the painful area to be treated. SCS implantation has been successfully used to treat patients with complex regional pain syndrome, neuropathic pain in the extremities, nonsurgical severe peripheral vascular disease, diabetic neuropathy, failed back surgery syndrome, and chronic angina secondary to ischemic heart disease.

Implanted cardioverter-defibrillators (ICVD) are used to electronically detect and treat potentially life-threatening cardiac arrhythmias. As the population of patients we treat ages, the incidence of patients with both chronic pain and cardiac disease will increase. Because of the electrical nature of SCS and ICVD, there has been concern that electromagnetic interference or cross-talk between the 2 devices implanted in the same patient may lead to failure of one or both of the systems or inappropriate shocks from the ICVD in response to stimulation from the SCS. The purpose of this study was to demonstrate the possible effects of SCS on ICVD sensing and triggering utilizing a swine animal model.

Methods

Animal Preparation

An animal use protocol form was submitted and approved by our institution's Animal Care and Use Committee. All of investigators involved in the study underwent training provided by the Division of Laboratory Animal Resources. The laboratory staff provided an approximately 57 kg male Yorkshire pig which was acclimated and cared for prior to the procedure in accordance with the standard care and use of laboratory animals protocol at our institution. Prior to the start of the procedure the animal was prepared as follows: ketamine (11-33 mg/kg intramuscular) was administered after which vital signs were obtained. The animal was bathed, an IV line established in the ear, and necessary shaving conducted. The animal was intubated with an appropriately sized endotracheal tube and mechanically ventilated with oxygen; isoflurane was administered for anesthetic maintenance. Buprenorphine (0.005-0.01 mg/kg intramuscular) was given during this procedure for analgesia. The anesthetic depth was continuously monitored and assessed by laboratory personnel. They determined the depth of the anesthesia by monitoring jaw tone and eye reflexes, and by hoof and skin pinch.

Placement of the ICVD

A right internal jugular cutdown was performed and a splittable 9 French sheath was advanced into the vein. Through this sheath, an Endotak Reliance® integrated bipolar dual coil defibrillator lead (Boston Scientific, Natick, MA) was advanced. Using fluoroscopic guidance, the lead was advanced into the right ventricle and affixed to an apical position. Impedance, capture, and sensing thresholds were tested and found to be excellent. The sheath was removed and the lead was affixed to the fascial tissue using 2 silk sutures. Then a pre-pectoral pocket was created on the right ventral surface of the swine similar to the location in humans. Once the pocket was created, the lead was then tunneled to the pocket and plugged into a Cognis 100-D internal cardiac defibrillator (Boston Scientific, Natick, MA) and the set screws were tightened (Fig. 1). The device was placed in the pocket and the wound was closed. Baseline measurements through the device demonstrated R wave sensing of 17.1 mV impedance of 530 ohms, and capture threshold of 0.1 V at 0.5 milliseconds.

Placement of the SCS

With the pig placed in the left decubitus position, a 14-gauge modified Tuohy needle was percutaneously advanced from the dorsal surface into the epidural space using fluoroscopic guidance in both anteroposterior and lateral views, and by using the loss of resistance to air technique using a glass syringe. Once the epidural space was reached, a single 50 cm linear ST Precision Plus octad electrode lead with 3mm wide contacts spaced 1mm apart (Boston Scientific, Valencia, CA) was advanced under fluoroscopic guidance in the posterior epidural space to the area overlying the heart closest in physical proximity to the intracardiac defibrillator lead (Figs. 2,3). The lead was then connected to an external generator provided by Boston Scientific. The stimulation was programmed using a patient programmer via infrared technology. There were 9 different settings programmed into the stimulator electrode with varying currents, pulse widths, and frequencies up to the maximum allowable settings (Table 1).

Stimulation and detection of interference

For this study, sensing of the ICVD was programmed
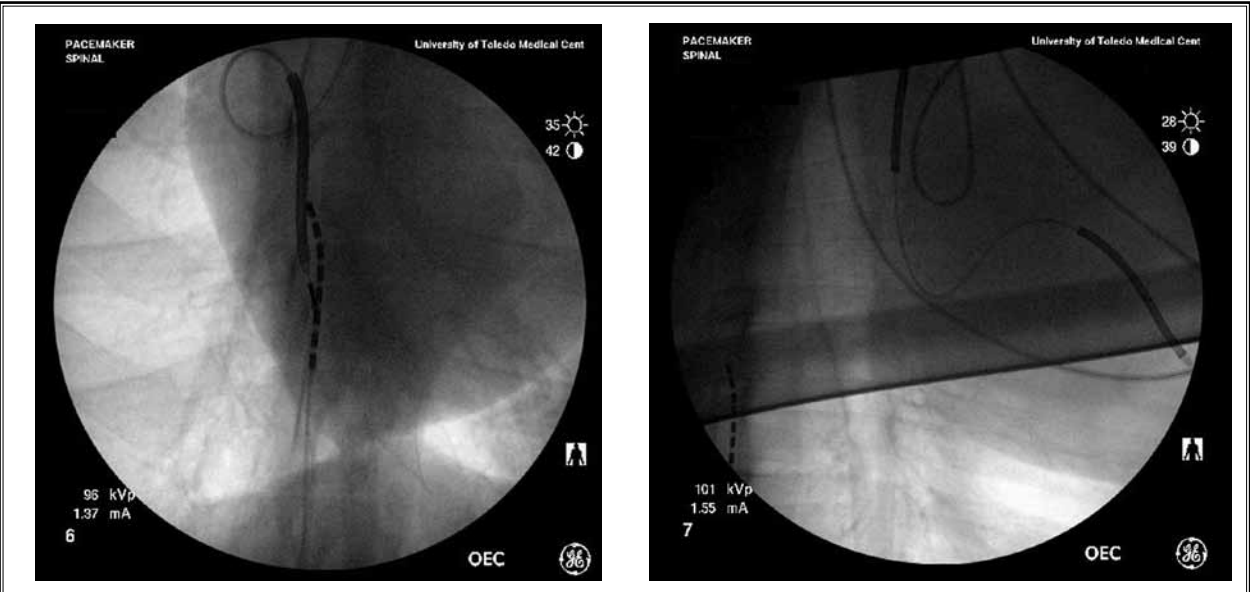
Fig. 1. *ICD embedded in pocket prior to closing skin.*

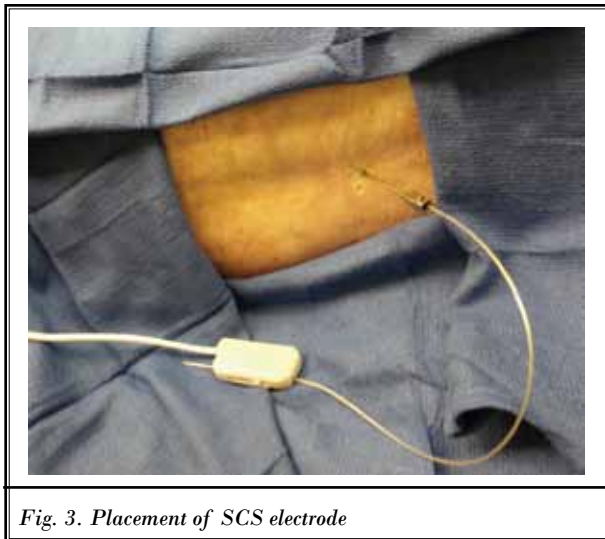Fig. 2. *AP view and Lateral view of final lead position.*

Fig. 3. *Placement of SCS electrode*

Table 1. *Settings, currents, frequencies of SCS.*

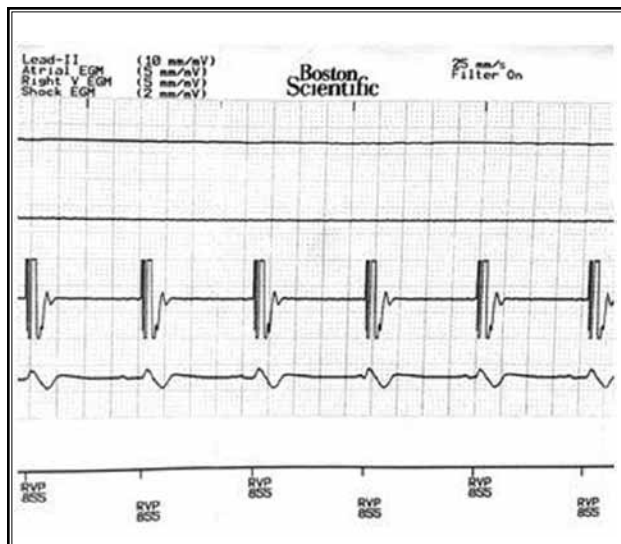| Setting	Current (mA)	Pulse Width (ms)	Frequency (Hz)	Interference (Yes/No)
1	1	210	40	No
2	4	210	40	No
3	4	500	40	No
4	6.5	800	40	No
5	10	1000	40	No
6	12.7	1000	100	No
7	12.7	1000	130	No

Fig. 4. *No noise detection.*

and evaluated at 2 different sensitivity settings during 9 different spinal stimulator settings. The first setting was a sensitivity of 0.6 mV which is what the device would be programmed at in vivo based on implant measurements. The second setting of 0.15mV was the most sensitive setting available on our model ICVD. The duration of stimulation was approximately one minute for each setting, which allowed time for recording of the electrocardiogram, and printing of a copy for further evaluation.

Remote wireless interrogation of the device was done continuously. During each of the 9 stimulator settings a strip was recorded showing the rate-sensing bipolar sensing channel and the marker channel to show if any cross stimulator "noise" was recorded and/or inappropriately detected by the ICVD at 0.6 mV and 0.15 mV sensitivity.

Results

There was no noise visually seen or detected by the device at any of the above settings. Figure 4 demonstrates appropriate pacing with no oversensing, inhibition or noise detection through the ICVD set at its most sensitive level (0.15 mV) during spinal stimulation at a pulse width of 180 microseconds, frequency of 1100 Hz and current of 2.2 mA. Additionally, while undergoing spinal stimulation the swine spontaneously developed ventricular fibrillation during which the device appropriately detected and shocked into a ventricular paced rhythm. This demonstrated appropriate sensing of ventricular fibrillation by the device at the most sensitive setting while undergoing significantly high spinal stimulation settings. The stimulating electrode was not adversely affected by the ICVD discharge. The impedance readings remained in normal range, and stimulation continued uninterrupted.

Discussion

Implantable electrical devices are becoming increasingly common treatment modalities for a variety of conditions. These devices include cardiac and gastric pacemakers, ICVDs, insulin pumps, deep brain stimulators (DBS), intrathecal drug delivery pumps and pain neuromodulators. As the utility of these devices continues to expand, it becomes more likely that as our average lifespan lengthens multiple devices will be implanted within the same patient. There has been extensive work reported in the literature regarding external electromagnetic interference (EMI) on these devices, and EMI between multiple devices in the same

patient (2-7). While there have been many case reports describing the successful use of multiple devices in the same patient, there are some reports of EMI causing disruption of the normal functioning of a device which keeps us questioning not only whether it really is safe to place multiple devices in the same patient, but if you do, what is the safest way to do it?

One of the first publications to report a case series of 10 patients implanted with a permananent Pacemenr (PPM) and SCS was by Romano M et al (4). They discussed one case that revealed intermittent inhibition of a pacemaker with increasing stimulation amplitudes from a spinal cord stimulator, while the other 9 patients had no problems. Based on that study the use of multiple devices in the same patient could not be recommended (8). A review of the simultaneous use of neurostimulators with cardiovascular implanted electronic devices by Ooi et al (1) suggested that PPMs and neurostimulation (NS) can be safely used together. They reviewed 17 studies which revealed 57 uniquely published cases, 41 in which SCS and PPM were used simultaneously. There was only the single case from Romano et al (4) which showed any evidence of interaction (1). In contrast to the use of PPM and SCS simultaneously, there are fewer case reports on the coexistence of SCS and ICVDs.

Our MEDLINE search revealed 13 studies which included 22 unique cases of patients who have an ICVD and either SCS or DBS (1,5,7,9-17) (Table 2). Two of the cases had adverse outcomes. There is a case report by Tavernier et al (5) of a total reset of the electrode polarities and resetting of the output state to off in 2 pectorally implanted pulse generators of a DBS. This occurred after an appropriately sensed arrhythmia and discharge from an abdominally placed ICVD. In this case the functioning of the ICVD was not affected by the presence of the stimulators, but the electrical discharge from the internal defibrillation had a significant effect on the programming of the DBS pulse generators (5). In the case series presented by Molon et al (13) one patient experienced SCS power reset due to multiple ICVD shocks caused by T-wave oversensing. None of the other cases reported ICVD discharge during testing. The functioning of both systems was evaluated and no cross-talk between the devices was described despite having used maximum stimulation settings and maximum sensitivities on the ICVDs (13).

Our study used both an ICVD and SCS provided by Boston Scientific. In our literature review none of the cases that we found included both an ICVD and SCS manufactured by Boston Scientific. The cases that we found were predominantly devices manufactured by Medtronic.

The Web sites of the 3 major neurostimulator manufacturers (Boston Scientific, Medtronic, and St. Jude) have warnings about using ICVDs and SCS simultaneously. Medtronic's Web site warns, "Sources of strong electromagnetic interference (e.g., defibrillation, diathermy, electrocautery, [magnetic resonance imaging] MRI, [radiofrequency] RF ablation, and therapeutic ultrasound) can interact with the neurostimulation system, resulting in serious patient injury or death. These and other sources of EMI can also result in system damage, operational changes to the neurostimulator or unexpected changes in stimulation" (7). It also mentions the presence of ICVDs stating, "An implanted cardiac device (e.g., pacemaker, defibrillator) may damage a neurostimulator, and the electrical pulses from the neurostimulator may result in an inappropriate response of the cardiac device" (7). The Boston Scientific Web site states, "Spinal cord stimulators may interfere with the operation of implanted sensing stimulators such as pacemakers or cardioverter defibrillators. The effects of implanted stimulation devices on neurostimulators are unknown" (18). For their neurostimulators, the St. Jude Web site states, "The system is contraindicated for patients with demand-type cardiac pacemakers." It also provides the warning that, "neurostimulation systems may adversely affect the programming of implanted cardioverter defibrillators" (19).

Based on our literature search, there have not been any published prospective trials that studied the interaction between an ICVD and SCS implanted in the same patient. An animal model can closely approximate the anatomical locations in a state that is physiologically equivalent to a human model. In this study we actively attempted to cause interference between the 2 devices by placing the leads of both devices in as close an anatomical relationship as possible. We increased the settings of the stimulating electrode to generate as much current as possible, and set the ICVD to be as sensitive as possible to maximize vulnerability for interference between the 2 devices. We observed for signs of over- or under-sensing and the possibility of leading to inappropriate shocks. None of the settings that were programmed into the SCS caused interference or inappropriate shocks from the ICVD, indicating that both may be safely used in the same body. Additionally, the ICVD appropriately detected ventricular fibrillation which it successfully defibrillated with 36 joules when the anesthetized swine spontaneously developed ven-

Table 2. Cases and studies relevant to SCS research.

Author, year published	# of cases reported	neuro stimulation type	Level of SCS leads	Stimulator make and model	AICD make and model	Interference
A.Katwal 2009	1	SCS	C7	ITREL 3, 7425 Medtronic	Medtronic, Vertuoso D154AWG	No
R.Schimpf 2003	1	SCS	T11	ITREL 3, 7425 Medtronic	GEM 3, AT 7276 Medtronic	No
K.Monahan 1998	1	SCS	T10	ITREL 3, 7425 Medtronic	Medtronic 7221gx active can	No
J.Rosenow 2003	1	DPS	BSTN	Medtronic, Model 6947	Isoletra ,Medtronic	No
A.Obwegeser 2001	1	DPS	UVIN	Medtronic, model 3387	GEM DR 7271 model	No
R Tavernier 2000	1	DPS	BSTN	ITREL 3 7425,7221D Medtronic	Medtronic 6945	Reset of the DBS after ICD shock
A.Sharan 2010	2	SCS	T10-11	ITREL 2, Medtronic	Medtronic, Virtuoso	No
		DBS	BSTN	Kinetra, Medtronic	Medtronic, Concerto	No
H.Dorman 2011	1	SCS		Synergy, versitrel Medtronic	Consulta D234TRK medtronic	No
T.Enggaard 2009	5	SCS	C7-T1	ITREL 3, Medtronic	Guidant/ Medtronic	No
		SCS	C7-T1	ITREL 3, Medtronic	Guidant/ Medtronic	No
		SCS	C7-T1	ITREL 3, Medtronic	Guidant	No
		SCS	C7-T1	ITREL 3, Medtronic	Medtronic	No
		SCS	C7-T1	Synergy, Medtronic	Medtronic	No
G. Molon 2011	3	SCS		ITREL 3, 7425 Medtronic	Intrinsic ,Model 7288	Temporary damage to SCS after multiple ICD discharges at 35 J
		Sacral neurostimulator	3rd sacral foramen	InterStim, Model 3023 Medtronic	Consulta, Medtronic	No
		SCS		ITREL 3, 7425 Medtronic	Consulta, Medtronic	No
S.Eckert 2009 (abstract)	5					No

AICD:Automated implantable cardioverters-defibrillators. SCS: Spinal cord stimulator. C: Cervical. T: Thoracic. BSTN: Bilateral subthalamic nucleus. UVIN: Unilateral ventral intermediate nucleus. DBS: Deep brain stimulators.

tricular arrhythmias while the stimulator was actively being used.

The limitations of this study include that the anatomical proximity of the posterior epidural space and right ventricle of the swine are different from humans. While the entire pacer, including generator, was imbedded in a subcutaneous pocket, an implantable pulse generator for the SCS was not implanted, but remained outside the body. This did not allow us to study if any damage or a resetting of settings would occur to the generator as had happened in the 2 cases

mentioned previously. We only used one manufacturer in this study to ensure that the ICVD and stimulator were from the same company. In practice, this is not always the case. There are multiple manufacturers of ICVDs, pacemakers, and stimulators, and the possibility of interactions between different device companies or different models of devices was not addressed in this study. This may be an area to study in the future. The duration of time that we performed stimulation at each of the settings was brief (approximately one minute); this limitation does not help address the question of

duration of stimulation. In the future the possibility of a longitudinal study where the effects of placement of multiple devices is evaluated after several months or a year after implantation should be considered. Finally, this study was performed in an anesthetized pig and the anatomical positions remained static. Realistically, changes in position of the devices will occur in patients who perform activities of daily living, and this can potentially shorten the distance between the 2 leads, causing adverse interaction. Case reports have tested the compatibility between an ICVD and SCS during position changes by the patient as part of their algorithm for determining compatibility (9). In our study we positioned the electrodes of the SCS as close as anatomically possible to the sensing portion of the defibrillator lead. We do not know if placing the leads in closer proximity to the ICVD generator would have caused interference. This may become a concern in cases where peripheral nerve field stimulation occurs as in the treatment for occipital neuralgia, when the generator for the ICVD and the stimulating electrodes may both be embedded in the subcutaneous tissue in close proximity to each other (20). The stimulation settings were also incrementally increased in our study, whereas in use, patients randomly switch between settings that can be drastically different. They can also turn their stimulator on and off at will.

There have been many case reports which describe the safe implementation of both PPM and SCS in patients. Only the St. Jude Web site had a specific contraindication to the placement of a demand pacemaker and neurostimulator (19). The other 2 companies did not list specific contraindications on the use of both simultaneously, but general caution and frequent assessment has been advocated in the literature to ensure proper functioning of both systems (1,21). The same appears to hold true for the placement of an ICVD and SCS, where none of the case reports indicated any interference with the functioning of the lifesaving ICVD, even though there are 2 reports of ICVD discharge resetting the stimulators. In our opinion, previously proposed recommendations to avoid potential interaction should continue to be followed. These include putting the 2 devices in op-

posite sides of the body, programming both systems to be in bipolar configurations, and ventricular fibrillation testing of the ICVD should be immediately performed (1). Studies have provided recommendations for programming the SCS to bipolar configuration with a pulse width as low as possible and a frequency higher than 60 Hz, to reduce the risk of interaction (13). Intraoperative and immediate postoperative tests combining different configurations, even if it raises the parameters of the stimulator to an uncomfortable level for the patient, can be done just to confirm whether some values might give rise to interference (13).

Close followup and frequent testing of both systems should continue to occur after placement. Schimpf et al (9) postulated that during the life of an electrode, possible complications might occur such as fracture, migration, or insulation failure that could generate leakage of current which could be detected and inappropriately treated by the ICVD. This would continue to necessitate that patients with 2 or more implanted electrical devices be carefully assessed to detect any potential interactions early on during implantation. Also, after the implantation of SCS, fibrosis around the electrode can cause the impedance to change by up to 26% by 3 months after implantation (22). This can require changing the settings and direction of current in order to successfully continue capture of all painful areas. This mandates short follow-up time intervals after implantation with the suggested evaluation of all implanted systems once per month for the first 3 months, followed by every 3 months for the first year, and then every 6 months thereafter. Additionally, if any changes are required to the devices, they should be rechecked for the possibility of interaction.

Conclusion

In conclusion, this study clearly demonstrated the feasibility of the 2 devices coexisting and functioning appropriately in an animal model using an ICVD and SCS provided by Boston Scientific. Further studies are needed to elucidate restrictions, optimal settings, and parameters in a human setting.

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