Implanted Medical Devices in the Radiation Environment of Commercial Spaceflight

David P. Reyes, Steven S. McClure,
Jeffery C. Chancellor, Rebecca S. Blue,
Tarah L. Castleberry, and James M. Vanderploeg

Reyes DP, McClure SS, Chancellor JC, Blue RS, Castleberry TL, Vanderploeg JM. ***Implanted medical devices in the radiation environment of commercial spaceflight.*** **Aviat Space Environ Med 2014; 85:1106–13.**

Introduction: Some commercial spaceflight participants (SFPs) may have medical conditions that require implanted medical devices (IMDs), such as cardiac pacemakers, defibrillators, insulin pumps, or similar electronic devices. The effect of space radiation on the function of IMDs is unknown. This review will identify known effects of terrestrial and aviation electromagnetic interference (EMI) and radiation on IMDs in order to provide insight into the potential effects of radiation exposures in the space environment. ***Methods:*** A systematic literature review was conducted on available literature on human studies involving the effects of EMI as well as diagnostic and therapeutic radiation on IMDs. ***Results:*** The literature review identified potential transient effects from EMI and diagnostic radiation levels as low as 10 mGy on IMDs. High-energy, therapeutic, ionizing radiation can cause more permanent device malfunctions at doses as low as 40 mGy. Radiation doses from suborbital flight altitudes and durations are anticipated to be less than those experienced during an average round-trip, cross-country airline flight and are unlikely to result in significant detriment, though longer, orbital flights may expose SFPs to doses potentially harmful to IMD function. ***Discussion:*** Individuals with IMDs should experience few, if any, radiation-related device malfunctions during suborbital flight, but could have problems with radiation exposures associated with longer, orbital flights.

Keywords: ionizing radiation, commercial spaceflight participant, defibrillator, pacemaker, electromagnetic interference, neurostimulator.

THE ADVENT OF commercial space operations opens spaceflight to broad participation. Historically, career astronauts have been healthy and well trained; however, commercial spaceflight participants (SFPs) may be older and in less than perfect health. Concern about certain medical conditions causing potential hazards to the nascent field of commercial spaceflight led to research studies conducted under the FAA's Center of Excellence for Commercial Space Transportation to evaluate the impact of the space environment on the health of SFPs. One such issue is the viability of implanted medical devices (IMDs) in the space radiation environment.

IMDs include cardiac pacemakers or defibrillators, insulin pumps, neurostimulators (including vagal, sacral, phrenic, laryngeal, or gastric nerve stimulators), deep brain stimulators, medication pumps, bone growth stimulators, and similar devices. IMDs are placed surgically, with varying lead lengths, and at different locations on or in the body. The devices generally consist of a pulse generator, battery, electrodes, and leads, with circuitry that allows for programming, memory, and even wireless accessibility (12). In the United States, around 3 million pacemakers and 1 million defibrillators were implanted between 1993 and 2008, while in 2009 alone over 1 million pacemakers and 300,000 defibrillators were implanted worldwide (20).

Ionizing radiation affects electronic circuits by several mechanisms that can lead to device malfunction or failure. Varying sources of radiation form a continuum of energy and effects on electronic devices. Two common effects of radiation on electronic circuits are single event upsets (SEU) and single event latch-ups (SEL) (27). SEUs, simply known as "bit flips," are caused by a single ionizing radiation particle that changes, nearly instantaneously, the state of a memory register. SEL constitutes a state of induced and prolonged current flow caused by the interaction of ionizing radiation with the circuit substrate, which can potentially lead to circuitry failures. If SEL occurs, reset of the device may be required to end the latch-up state, provided that no permanent damage has occurred (27).

Cardiac implanted devices (CIDs), such as pacemakers or defibrillators, contain circuitry "gates" that pass current when a cardiac electrical impulse is detected (13). These gate circuits control the direction of current flow by the composition of the substrate material and the number of permeable "holes" in the silicon dioxide substrate. Ionizing radiation causes increased permeability in the silicon dioxide and thereby alters the flow pattern of electrons (1,13). These changes result in aberrant electrical paths that cause temporary or permanent defects, such as premature indication for replacement, inhibited or inappropriate pacing or shock delivery due to over-sensing (interpretation of a cardiac signal when none is present), reversion to reset or safe mode, loss of telemetry, and device failure (3).

From the University of Texas Medical Branch, Galveston, TX.

This manuscript was received for review in July 2014. It was accepted for publication in August 2014.

Address correspondence and reprint requests to: Tarah L. Castleberry, D.O., M.P.H., Department of Preventive Medicine and Community Health, University of Texas Medical Branch, 301 University Blvd, Galveston, TX 77555-1110; tlcastle@utmb.edu.

DOI: 10.3357/ASEM.4104.2014

Five major sources of radiation in the space environment can potentially affect IMDs. The first four are intrinsic to the space environment. First, solar particle events (SPEs) are high-energy solar ejections occurring throughout the 11-yr solar cycle, with the frequency of events increasing during solar maximum. SPEs are generally unpredictable in timing, composition, and energy (24). SPEs consist mostly of ionized hydrogen nuclei (protons) and a very small amount of helium and heavier particles (24). The magnetic field and atmosphere of the Earth provide some protection from SPEs, with increasing protection at lower latitudes and altitudes; therefore, higher latitudes and altitudes correspond with increasing radiation dosage. A suborbital flight during a large SPE may result in higher exposure (24). In contrast, the second source of space radiation, trapped charged particles located within the Van Allen radiation belts, are mostly attenuated by geomagnetic and typical spacecraft shielding and are unlikely to be of significant concern for suborbital and short-duration low-Earth orbital spaceflight (25,33). In some geographical areas, such as in the South Atlantic Anomaly, the offset and tilt of the geomagnetic field dipole axis from the Earth's rotational axis brings these trapped radiation belts closer to the Earth, with decreased geomagnetic shielding from radiation than in other regions. Longer-duration orbital spaceflights that pass through the Anomaly would, therefore, result in SFP exposure to higher levels of radiation (2). Again, this is unlikely in short-duration commercial and suborbital spaceflight operations.

The third source, galactic cosmic radiation (GCR), generally consists primarily of ionized, energetic hydrogen (87%) and alpha particles (12%) with a small contribution ($<$ 1%) from heavier, high charge and energy (HZE) particles (23–25). HZE particles are rare relative to the hydrogen and helium nuclei, but have a greater ability to penetrate and damage electronics. The flux of GCR particles varies inversely with the solar cycle by approximately a factor of two and is much greater during solar minimum. The fourth source of space radiation occurs when HZE particles impact solid material, such as the wall of a spacecraft, human skin, IMD casing, or any other medium. The impact generates a shower of secondary particles, which can carry sufficient energy to cause damage to electronic circuits (25). Finally, though not intrinsic to the space environment, electromagnetic interference (EMI) from the normal operation of spacecraft electronics can affect IMD function.

Due to similarities between terrestrial and space environment radiation in both exposure level and character, terrestrial reports of the effects of radiation exposure upon IMDs can provide insight into the potential effects of similar exposures in the space environment. This report will review those effects and use terrestrial data to extrapolate the impact of radiation in the space environment. This extrapolation can then be used to provide recommendations regarding mitigation of adverse effects on IMDs in the commercial spaceflight arena.

METHODS

A systematic review was conducted in PubMed, Web of Science, the Defense Technical Information Center, and Google Scholar for all available literature on human studies involving radiation and IMDs. The search terms included "radiation," "implanted medical device," "pacemaker," "defibrillator," "spinal stimulator," "deep brain stimulator," "neurostimulator," "insulin pump," "electromagnetic interference," "diagnostic radiation," "computed tomography," "magnetic resonance," and "radiation therapy." All titles obtained from these criteria were reviewed. Studies published in a language other than English without available translation and articles regarding IMDs that did not specifically address EMI or radiation were discarded. All other articles were reviewed in their entirety. Data characterizing the space radiation environment were obtained from the National Aeronautics and Space Administration and the National Academy of Sciences technical documentation and publications archives, while background information concerning the effects of radiation on electronics was provided by the Space Radiation Analysis Group at NASA's Jet Propulsion Laboratory and Johnson Space Center.

Using these methods, 45 references were identified that met search criteria and addressed the topics of interest. Of these, five were published in languages other than English, without available translations, and six addressed spaceflight concerns outside the scope of this article, such as long-duration orbital or interplanetary flights. The remaining 34 studies were included in the review. Literature obtained includes in vitro and in vivo studies, case studies, technical reports, white papers, device operating manuals, and review articles. Most of the relevant literature was for CIDs, such as pacemakers and defibrillators; however, as CIDs are generally the most common and most critical applications of therapeutic device implantation technology, literature regarding CIDs was considered a useful proxy for other IMDs.

Radiation doses are often given in Grays (Gy) or Sieverts (Sv). Gy are a measure of absorbed dose and are commonly used in the medical literature reviewed. Sv are used to quantify biological exposure and vary depending on the type of radiation and tissue exposed. A tissue-weighting factor is applied to the absorbed dose to yield an equivalent biologic dose in Sv (7). In this document, each unit is used where appropriate; readers should note that, while relative dosages are often close to 1:1, these units are not interchangeable and depend upon the type of radiation and the relative susceptibility of the tissue in question.

RESULTS

The literature review revealed a number of papers addressing the effects of radiation on IMDs, particularly CIDs, and the potential for levels of radiation seen within the space environment to affect IMD function. Much of the literature addressed terrestrial sources of

radiation exposure; where possible, such data have been extrapolated for relevance to the space environment.

Effects of Electromagnetic Interference

EMI exposure can result in transient effects on CIDs, which resolve when the EMI ends or when the CID is moved away from the source of EMI emission (14,20). CID manufacturers include countermeasures against EMI, such as specialized casings, signal filters, interference rejection circuits, feed-through capacitors to block environmental EMI (such as cellular phone interference), and bandpass filters to filter out unwanted cardiac and other muscle electrical signals (1,31,38). Despite these countermeasures, EMI may still cause device malfunction, especially with intermittent exposure from high-output devices at frequencies that overlap the cardiac signal range (0-60 Hz) (1,38). Device algorithms monitor signals that occur over a set period of time. If the filter period is exceeded, spurious signals are interpreted as noise. However, intermittent EMI that falls within the filter period may be interpreted as cardiac activity (20). If EMI is interpreted as cardiac activity in a pacemaker-dependent patient, this could theoretically result in withheld pacing and subsequent dysrhythmia or even induce unsynchronized defibrillation from an implanted defibrillator. Additionally, EMI may reset the pacemaker into a default pacing mode or interfere with data recording (1,20).

Despite theoretical risks, there are few cases of environmental EMI actually leading to CID malfunction in the literature. Studies have examined the effects of environmental technologies with EMI output in normal work environments and their effect on CIDs, and most demonstrate that even EMI-outputting devices in close proximity to CIDs have little to no effect on CID function (1,29,31). Avionics in normal flight environments, including general aviation and commercial airline flights, demonstrate no significant interference leading to CID malfunction from EMI output from onboard equipment (8,28). Improvements in shielding techniques, including nanomagnetic insulation in lead design and hermetically sealed cases, have provided improved protection for CIDs exposed to EMI (1). High-output devices designed to emit high-frequency electric current for treatment purposes, such as electrosurgical devices or nerve stimulators, can cause significant, directed EMI and transient effects on CIDs in the direct EMI field; however, the use of such devices is generally limited to hospital environments (1,16,38). In general, most literature sources suggest that environmental and industrial sources of EMI are likely safe, but recommend limited exposure time and maximal distance between the source and the CID (1).

Neurostimulators are currently used for treating seizure, depression, incontinence, tremor, and pain. Unlike CIDs, they generally perform a continuous or timed function, without sensing (26). Because they have no sensing capability they are less sensitive to EMI (26). Studies have demonstrated that shorter leads are less susceptible to EMI and that devices must be located very near to the emitting source in order to be affected (27). Finally, effects of EMI on neurostimulators are transient and cease when emissions are stopped (26). One review of Federal Drug Administration adverse event data for deep brain neurostimulators noted that there were a total of 76 adverse events associated with EMI reported from 1999 to 2005, including 9 events involving deep brain stimulators and 67 events involving spinal stimulators (9). Adverse events included altered settings, devices that were inappropriately turned off, abnormal shocks, increased stimulation, and device failure (9). However, the vast majority of these events were transient malfunctions causing pain or irritation from spinal stimulation after the patient had passed through strong magnetic fields such as highly magnetized metal detectors (9). Adverse effects from more common electronics in every day environments have not been reported.

Effects of Diagnostic and Therapeutic Radiation Exposure

Like EMI, diagnostic radiation effects are transient and usually end when the IMD is removed from the radiation field or radiation is stopped. Diagnostic radiation levels (most commonly 10-65 mGy, with maximal dosages of as high as 100 mGy) have been demonstrated to cause device malfunctions, particularly in CIDs (18). The most common malfunctions observed are over-sensing errors, occasionally accompanied by device inhibition with failure to pace or defibrillate (18). At maximal dosages, malfunctions such as device reset are occasionally observed (18). The liberation of free electrons by diagnostic radiation may create small current flows (photocurrent) that are interpreted as cardiac activity, leading to over-sensing; again, these effects are only seen while CIDs remain directly in the radiation path (18).

Higher levels of ionizing radiation are often used as treatment modalities. Many studies demonstrate significant effects of therapeutic radiation doses, including IMD failure. It has been consistently demonstrated that defibrillators are generally more sensitive to radiation than pacemakers (15,17,22). Pacemakers have been demonstrated to malfunction with as low as 10 Gy of irradiation, with failures occurring at doses ranging from 20–130 Gy (15,17,36). One study demonstrated pacemaker tolerance of up to 60 Gy prior to failure; however, this study was a demonstration of radiation mitigation protocol for CIDs, with maximal precautions taken (36). The most common device failure identified is loss of device output, though premature battery replacement warnings are also commonly reported (14). In contrast, defibrillators have demonstrated malfunctions with irradiation of as low as 0.4 Gy, with common malfunctions including low shock energy and ineffective defibrillation, partial reset, and loss of historical data (15,17). Devices outside of the direct radiation beam path exposed to high levels of only indirect radiation have malfunctioned; however, no failures have been

reported without direct irradiation (17). Defibrillator failure has been identified at as low as 0.5 Gy of direct exposure, again demonstrating lower tolerance to irradiation than pacemakers (15). Defibrillator device instructions are stored in rewritable random access memory, which is more easily corrupted and could account for the increased sensitivity to radiation (30). Comparative effects of varying levels of radiation exposure on CIDs are provided in **Table I**.

Cardiac device manufacturers have variable dose limit and shielding recommendations for their devices (3,30). All manufacturers suggest placing the device outside of an expected radiation field whenever possible, and most recommend a cardiology consult before and after treatment (21,30). Specific manufacturer guidelines for therapeutic radiation range from 5-30 Gy for pacemakers to 1-5 Gy for defibrillators (3,21,30). Finally, technical guidelines generally include a disclaimer that no level of radiation can be considered "safe" for CID exposure, and proper device function following irradiation cannot be guaranteed (3).

Aerospace Radiation Exposure and Device Malfunction

The SEU rate in any electronic device is proportional to the particle flux in a given environment, which increases with altitude, and to the susceptibility of a given circuit. As integrated circuits steadily get smaller and operate at lower voltages, ionizing particles can more easily change the memory state of a device (19,30). Integrated circuits contain several types of gate technologies, including antifuse, flash, and static random access memory (SRAM). Antifuse and flash gates require high voltage to change and are thus less susceptible to SEU. In contrast, SRAMs are low-energy, reprogrammable circuits that are often used to store device operating parameters and, due to their low-power state, they are susceptible to ionizing radiation (19). While memory errors can be corrected by subroutines that perform periodic rewrites of the SRAM, these areas of SRAM that hold the device configuration data are also subject to SEU (3,19). An SEU in this particular block of memory would result in a "hard" error or device failure. In one study that specifically addressed the aviation environment, estimates of SEUs in the configuration memory of some SRAMs resulted in mean time between failures of 1.23 to 2.61 mo at altitudes of 40,000 ft (12,192 m) (19,37). Other studies have demonstrated software errors directly attributable to the effect of GCR on CIDs (5,10). Radiation exposure during cross-country and international airline flights has been sufficient to cause SEUs; while no reported incidents have resulted in significant clinical manifestations, such cases have resulted in the patient's loss of confidence in their device (10). However, with a relatively low number of reported errors, it is difficult to extrapolate the malfunction or failure rates for potential exposures during suborbital or orbital flight.

At sea level, background radiation from various sources delivers 3.6 mSv per year to the average person (25). About half of this terrestrial exposure is from radon gas, with the remainder from GCR (0.26 mSv/yr) and other natural and artificial sources (25). Occupational exposures to radiation workers and astronauts can be higher. At 25,000 to 40,000 ft (8000 to 12,000 m) of altitude, where most commercial airliners fly, the dose rate is 3-7 μSv/h, for an average of about 0.025 mSv for a 5-h cross-country flight, or 0.05 mSv for a round trip (24,32). In comparison, the dose for a chest x-ray is about 0.05 to 0.2 mSv (11,24,32). A high-altitude (> 40,000 ft/12,192 m) dose rate is about 0.02 mSv/h and an orbital dose would be approximately 0.2-1.0 mSv per day (11,32). Comparative radiation doses are provided in **Fig. 1**.

A suborbital flight from a mid-latitude launch site, with only about 5 min at maximum altitude (~100 km /62 mi), would expose occupants up to an estimated radiation dose of 0.0026 mSv, significantly less than the 0.05 mSv dose for a typical round-trip, cross-country airline flight (32,33). If such a suborbital flight were to take

TABLE I. EFFECTS OF THERAPEUTIC RADIATION ON IMDs. RADIATION TRIAL EFFECTS FOR SELECTED STUDIES ARE COMPARED TO DOSES AT TIME OF MALFUNCTION AND FAILURE.

Study	Device (*N*)	Type of Study	Exposure Source	Exposure Dose	Dose at Malfunction	Type of Malfunction	Dose at Failure	Notes
Hurkmans et al. (14)	Pacemaker (19)	In vitro	6 MV photon beam	120 Gy in fractions	10-120 Gy	Loss of telemetry	20-130 Gy	Direct irradiation through "bolus" material
Hurkmans et al. (15)	Defibrillator (11)	In vitro	6 MV photon beam	120 Gy in fractions	0.5-120 Gy	Low shock energy	0.5-120 Gy	Direct irradiation through "bolus" material
Mouton et al. (22)	Pacemaker (96)	In vitro	18 MV photon beam	200 Gy in varying fractions	0.15 Gy	Loss of signal > 10 s	0.5 Gy	Largest in vitro study
Makkar et al. (17)	Pacemaker (50), Defibrillator (19)	In vivo	6-16 MV photon beam ± 6-16 MeV electron beam	0.009-5.0 Gy, pacemaker 0.04 -1.69 Gy, defibrillator	0.04 Gy, defibrillator	Partial reset of two defibrillators	No failures	CIDs offset from beam path
Wadasadawala et al. (35)	Pacemaker (8)	In vivo	6 or 15 MV photon beam or Cobalt 60 – gamma	0.14-60 Gy in fractions	No malfunction	None	No failures	CID offset from beam, CID shielded

MV = million volts; MeV = million electron volts; Gy = Gray; CID = cardiac implanted device.

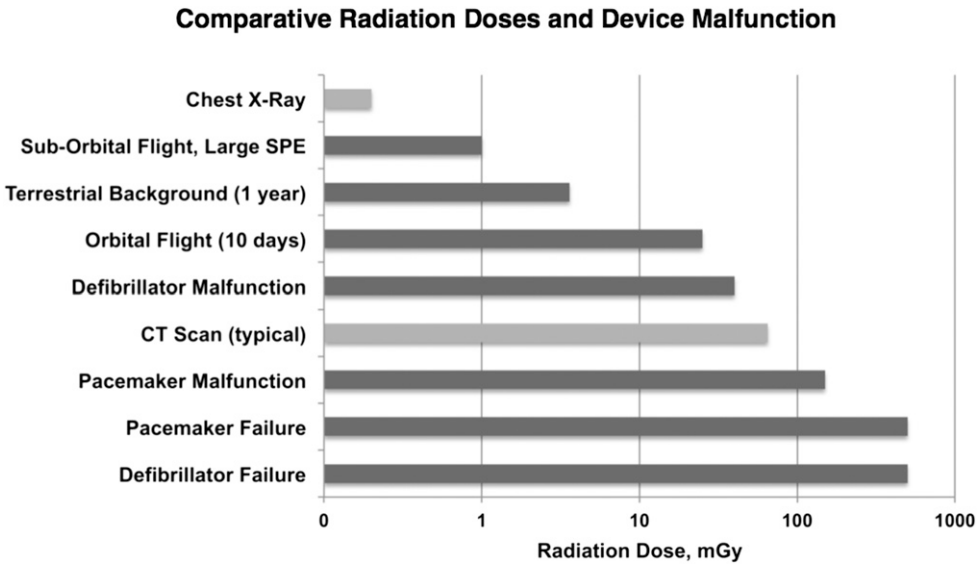

Fig. 1. Comparison of potential radiation doses and the radiation doses at first malfunction and failure for cardiac implanted devices. Lighter bars indicate nonionizing radiation that causes transient effects, where darker bars indicate the potential for more detrimental and longer-lasting effects. SPE = solar particle event, CT = computed tomography, mGy = milliGray.

place during a typical SPE, estimated dosage ranges from 0.1-1.0 mSv (32,33). Assuming an approximate 1:1 conversion to mGy, these doses are much less than those associated with CID malfunction (≥ 40 mGy) and failure (≥ 500 mGy) (14,15,17). Anticipated radiation exposures by flight profiles are provided in **Table II**.

Radiation exposure for orbital flight can also be extrapolated from modeled and historical exposure data. Orbits can be divided into low-altitude and low-inclination, such as early Space Shuttle flights, or high-altitude with high-inclination, as with the International Space Station. According to one model, 10 d on orbit during a solar minimum behind 10 $g \cdot cm^{-13}$ of aluminum shielding would limit exposure to approximately 3–5 mSv at low-latitude and 12–25 mSv during high-latitude orbital flights (32). The dosages predicted by this model compare favorably with actual mission data from Mercury through NASA-MIR missions, where exposure rates of 0.18 to 21 mSv were seen (7,32). A 10-d dose maximum of 25 mGy corresponds to levels that approach potential CID malfunction, where malfunction has been observed at ≥ 40 mGy (14,15,17). With these predicted levels, it would take 200 d of accumulated radiation exposure to approach the 500-mGy radiation level where CID (defibrillator) failure is first observed (14,15,17). Actual effects could vary significantly depending on the type and amount of shielding, the type of IMD, the orbital parameters, and the type of radiation.

TABLE II. RADIATION EXPOSURE AND EFFECTS BY MISSION PROFILE.

Mission Type (Altitude)	Radiation Relative to Earth Surface	Possible Dose	IMD Effects
Round Trip, Cross-Country Flight (12 km)	Radiation Belts—not encountered SPE—slight increase, latitude dependent GCR—minimal additional from ground levels	0.05 mGy (23)	Very low rate of SEU
Suborbital (100 km)	Radiation Belts—not encountered	0.00034-0.0026 mGy if no SPE (6,30)	Very low rate of SEU due to very short exposure time
	SPE—slight increase, latitude dependent GCR—minimal additional from ground levels	0.2-1.0 mGy if large SPE (32)	
Orbital (~400 km)	Radiation Belts—orbit dependent	3-25 mGy in 10 d (7,32)	Rate of SEU or other effects dependent on duration of exposure
	SPE—significant increase GCR—increased	250 mGy in 100 d (7)	Malfunction likely if > 10 d Eventual failure possible for long-duration flights

Extrapolated dosages of radiation according to mission profile and anticipated effects on IMDs exposed to the flight profile indicated. SPE = solar particle event; GCR = galactic cosmic radiation; mGy = milliGray; SEU = single event upset.

DISCUSSION

While literature on these topics is scarce, the case reports and manuscripts cited give insight into the likely effects of radiation that might be expected in the commercial space environment. Literature correlates suggest that SFPs with IMDs should have no greater impact from a suborbital flight than during a cross-country airline flight during normal levels of SPE activity, and may not be significantly more affected by suborbital flight during a major SPE. Further, even short-duration orbital flight appears to fall within radiation dosages commonly seen with treatment radiation modalities. Finally, onboard sources of EMI are unlikely to cause significant interaction or disruption of IMD function based on terrestrial industrial and environmental correlates. Based on these literature findings, some conclusions and recommendations can be made regarding the use of IMDs in the space environment.

Existing guidelines for the management of IMD during radiation therapy are conservative and can be easily adapted to commercial spaceflight applications. Guidelines based on the literature for the management of IMDs during radiation therapy (9,35) are adapted for SFPs and shown below:

Preflight
- Identify all persons with IMDs
- Obtain manufacturer specific data, date of implantation, complications
- Obtain last device check results and current function
- Assess degree of device dependence and severity of symptoms without device
- Determine if the device can be turned off or put in "safe mode"?
- Brief SFP about the space radiation environment
- Brief SFP about device management during spaceflight
- Determine potential radiation dose to the device
- Perform preflight physical exam and device interrogation (if no recent data)
- Perform ECG for persons with CID
- Consult with appropriate device specialist as needed
- Brief flight crew or on-orbit physician/medical personnel about potential IMD issues
- Provide for relevant on-call specialist

In Flight
- Use an appropriately placed dosimeter
- Monitor SFP vitals during spaceflight, if possible
- Instruct SFP to self-monitor for device malfunction
- Instruct SFP to turn off or place device in "safe mode" if applicable
- Provide SFP with back-up device or treatment, if possible
- Ensure an AED with pacer function is available for CID-dependent SFPs on orbital flights
- Brief on-orbit physician/medical personnel on IMD management

Postflight
- Perform physical exam of patient, including ECG for persons with CID
- Perform full interrogation of device if any in-flight anomalies occurred
- Follow-up with specialist as needed
- Obtain weekly vital signs measurements and symptom checks for at least 6 wk
- Interrogate device periodically for SFPs with cardiac or other critical IMDs
- Perform IMD reprogramming or replacement as needed

IMD management for SFPs should include preflight evaluation, in-flight monitoring, and postflight follow-up. Preflight evaluation should consist of a physical exam, device interrogation, and expert consultation as needed to ensure device stability. The primary preventable risk factor is the mere identification of persons with IMDs and confirmation that they are outside of the initial postsurgical period following device placement (13). While not directly related to radiation concerns, ensuring that SFPs with IMDs have had at least 1 yr of normal device function from the time of placement may prevent other IMD-related issues, such as lead displacement (6). Finally, the potential effects of space radiation on an IMD should be made clear to SFPs for appropriate informed consent for participation.

Accurate space weather forecasting is a basic requirement of normal spaceflight operations and may be essential for predicting IMD radiation exposure (25). Mission holds may be appropriate for extreme SPE for commercial launches. IMDs should be evaluated to determine whether they pose a risk of EMI with spacecraft systems or vice versa and, whenever possible, SFPs with an IMD should be positioned away from any EMI source or strong magnetic field (14,20). In-flight monitoring of SFPs with IMDs may be limited as onboard medical monitors may not be available. Remote monitoring of the SFP by periodic vital sign assessment may be helpful; similarly, wireless interrogation of an IMD may be useful in some scenarios, though this capability would be dependent upon available telemetry options in a given spacecraft. If possible, the SFP could be briefed before flight to monitor their IMD and potentially place the device in safe mode as appropriate. Alternatives to IMD therapy, such as medication control, could be explored to limit IMD dependence for the duration of the flight. Postflight care should involve a postflight exam and follow-up on any anomalies.

Interestingly, the literature reports relatively low dosages of radiation, particularly diagnostic radiation, resulting in electronic failure of devices (18). However, most electronic device failures are secondary to cumulative radiation exposure, with total ionizing doses of 10 s of Gy. For failures occurring at dosages as low as reported here, in the 10–100 mGy range, failures are likely photocurrent (dose rate) induced due to the high sensitivity of the devices examined. As these results are consistent throughout the literature, implanted cardiac devices in particular do seem to be quite sensitive to radiation in comparison to other electronics, perhaps due to the rhythm-sensing functions.

In the space environment, SEUs and SELs may be caused by proton or heavy ion exposure, which would be quite rare and limited in the altitudes expected for short-duration suborbital spaceflight. None of the devices discussed here have been characterized for proton or heavy ion-induced SEUs or SELs; as such, this remains an unknown risk. While unlikely to be of consequence in low-altitude suborbital flights, this may pose a significant problem for future orbital or interplanetary travel. Further study and device testing is warranted to evaluate this risk.

Due to the unique aspect of this work there are other limitations as well. CIDs dominate the relevant studies addressing IMDs, with few studies addressing other types of devices. While CIDs make an excellent proxy due to their critical function and higher sensitivity, the impacts on other types of IMDs are less well known, and the total number of studies and actual devices examined is low compared to the number and types of devices in use. The electronics contained in IMDs are constantly evolving and may become more or less susceptible to radiation as technology changes, and the space radiation environment may be relatively quiescent or more active than reported in the historical record (25). Further, as onboard electrical equipment may generate greater EMI emissions than terrestrial and aviation correlates, preflight testing for EMI interference with IMD function may be warranted to ensure that no significant interference occurs. Additionally, the references used in this paper report radiation in Sv, Gy or both. Sv is a biologic dose that is tissue dependent and derived by application of tissue factor; therefore Sv and Gy are not strictly equivalent. However, this may lend a degree of conservatism to this work, as a numerically equivalent dose in Sv often represents slightly more radiation than in Gy (4,34). Finally, it is worth noting that the IMD-related medical literature reviewed usually report total doses administered; however, many of the detrimental effects on IMDs can be caused by a single ionizing radiation particle, leading to SEUs. Therefore even low total doses, in some circumstances, can cause device malfunction; it is for this reason that even conservative estimates of radiation susceptibility must be considered as estimates of risk, not predictions of outcome.

Although no dose of ionizing radiation can be declared "safe" for IMDs according to some device manufacturers, literature suggests that SFPs with IMDs should incur no more risk from space environment radiation than a cross-country airline flight, and may thus participate in suborbital flight as long as sensible precautions are taken. SFPs that are device-dependent should be limited to suborbital and short orbital flights ($\leq$ 10 d) to limit potential malfunctions, at least until IMD electronics are more robust or shielding is improved. Future work in this area could involve documentation of IMD performance data during actual flight, as well as collection of radiation exposure data with in-flight dosimetry monitoring. These data should be thoroughly evaluated before estimations of risk are extrapolated for longer orbital or interplanetary missions. Ultimately, the decision to participate in spaceflight despite known medical conditions will be dependent upon a mutual agreement by the SFP, flight surgeons, and commercial entities to accept potential risk in an effort to help these individuals achieve their dreams of spaceflight.

ACKNOWLEDGMENTS

The authors wish to thank Nicholas Stoffle of the Space Radiation Analysis Group at NASA Johnson Space Center for critical review and additional radiation references. The authors further acknowledge the contributions of the FAA Center of Excellence grant for Commercial Space Transportation as well as additional support from the National Space Biomedical Research Institute (NSBRI) through NASA NCC 9-58. While the FAA and NSBRI sponsored this project, neither endorsed or rejected the findings of this research. The presentation of this information is in the interest of invoking technical community comments on the results and conclusions of the work.

Authors and affiliations: David P. Reyes, M.D., M.P.H., Rebecca S. Blue, M.D., M.P.H., Tarah L. Castelberry, D.O., M.P.H., and James M. Vanderploeg, M.D., M.P.H., Department of Preventive Medicine and Community Health, University of Texas Medical Branch, Galveston, TX; Steven S. McClure, Space Radiation Analysis Group, NASA Jet Propulsion Laboratory, Pasadena, CA; and Jeffrey C. Chancellor, M.Sc., Department of Materials Science & Engineering, Texas A&M University, College Station, TX.

REFERENCES

1. Beinart R, Nazarian S. Effects of external electrical and magnetic fields on pacemakers and defibrillators: from engineering principles to clinical practice. Circulation 2013; 128:2799–809.
2. Benton ER, Benton EV. Space radiation dosimetry in low-Earth orbit and beyond. Nucl Instrum Methods Phys Res B 2001; 184:255–94.
3. Boston Scientific. Therapeutic radiation and implantable pacemakers and defibrillators. Marlborough, MA: Boston Scientific Corporation; 2012. Retrieved 29 May 2014 from http://www.bostonscientific.com/templatedata/imports/HTML/CRM/A_Closer_Look/pdfs/ACL_Therapeutic_Radiation_20120925.pdf.
4. Bottollier-Depois JF, Chau Q, Buisset P, Kerlau G, Plawinski L, Lebaron-Jacobs L. Assessing exposure to cosmic radiation during long-haul flights. Radiat Res 2000; 153:526–32.
5. Bradley PD, Normand E. Single event upsets in implantable cardioverter defibrillators. IEEE Trans Nucl Sci 1998; 45:2929–40.
6. Bulava A, Lukl J. Single-centre experience with coronary sinus lead stability and long-term pacing parameters. Europace 2007; 9:523–7.
7. Cucinotta F, Schimmerling W, Wilson J, Peterson L, Badhwar G, et al. Space radiation cancer risk projections for exploration missions: uncertainty reduction and mitigation. Houston, TX: National Aeronautics and Space Administration; 2001. Report No: NASA TR JSC-29295.
8. De Rotte AA, Van Der Kamp P. Electromagnetic interference in pacemakers in single-engine fixed-wing aircraft: a European perspective. Aviat Space Environ Med 2002; 73:179–83.
9. Dustin K. Evaluation of electromagnetic incompatibility concerns for deep brain stimulators. J Neurosci Nurs 2008; 40:299–303.
10. Ferrick AM, Bernstein N, Aizer A, Chinitz L. Cosmic radiation induced software electrical resets in ICDs during air travel. Heart Rhythm 2008; 5:1201–3.
11. Friedberg W, Copeland K, Duke FE, O'Brien K, Darden EB. Radiation exposure during air travel: guidance provided by the Federal Aviation Administration for air carrier crews. Health Phys 2000; 79:591–5.
12. Halperin D, Kohno T, Heydt-Benjamin TS, Fu K, Maisel W. Security and privacy for implantable medical devices. Pervasive Computing 2008; 7:30–9.
13. Hudson F, Coulshed D, D'Souza E, Baker C. Effect of radiation therapy on the latest generation of pacemakers and implantable cardioverter defibrillators: a systematic review. J Med Imaging Radiat Oncol 2010; 54:53–61.
14. Hurkmans CW, Scheepers E, Springorum BG, Uiterwaal H. Influence of radiotherapy on the latest generation of pacemakers. Radiother Oncol 2005; 76:93–8.
15. Hurkmans CW, Scheepers E, Springorum BG, Uiterwaal H. Influence of radiotherapy on the latest generation of implantable cardioverter-defibrillators. Int J Radiat Oncol Biol Phys 2005; 63:282–9.
16. Idzahi K, de Cock CC, Shemesh H, Brand HS. Interference of electronic apex locators with implantable cardioverter defibrillators. J Endod 2014; 40:277–80.
17. Makkar A, Prisciandaro J, Agarwal S, Lusk M, Horwood L, et al. Effect of radiation therapy on permanent pacemaker and implantable cardioverter-defibrillator function. Heart Rhythm 2012; 9:1964–8.
18. McCollough CH, Zhang J, Primak AN, Clement WJ, Buysman JR. Effects of CT irradiation on implanted cardiac rhythm management devices. Radiology 2007; 243:766–74.

19. Microsemi Corporation. Single-event upsets (SEUs) and medical devices. Irvine, CA: Microsemi Corp.; 2010. Retrieved 29 May 2014 from http://www.eejournal.com/files/5913/0219/5116/SEU_Medical_WP.pdf.
20. Misiri J, Kustumoto F, Goldschlager N. Electromagnetic interference and implanted cardiac devices: the non-medical environment (part 1). Clin Cardiol 2012; 35:276–80.
21. Misiri J, Kustumoto F, Goldschlager N. Electromagnetic interference and implanted cardiac devices: the medical environment (part 2). Clin Cardiol 2012; 35:321–8.
22. Mouton J, Haug R, Bridier A, Dodinot B, Eschwege F. Influence of high-energy photon beam irradiation on packemaker operation. Phys Med Biol 2002; 47:2879–93.
23. National Council on Radiation Protection. Information needed to make radiation protection recommendations for space missions beyond low-Earth orbit. Bethesda, MD: NCRP; 2006. Report No. 153.
24. National Research Council. Managing space radiation risk in the new era of space exploration, Committee on the Evaluation of Radiation Shielding for Space Exploration. Washington, DC: National Academies Press; 2008.
25. National Research Council. Space Radiation Hazards and the Vision for Space Exploration: Report of a Workshop, Ad Hoc Committee on the Solar System Radiation Environment and NASA's Vision for Space Exploration. Washington, DC: National Academies Press; 2006.
26. Pantchenko OS, Seidman SJ, Guag JW, Witters DM Jr, Sponberg CL. Electromagnetic compatibility of implantable neurostimulators to RFID emitters. Biomed Eng Online 2011; 10:50.
27. Petkov MP. The effects of space environments on electronic components. Pasadena, CA: California Institute of Technology, NASA Jet Propulsion Laboratory; 2003. Report No: 03-0863. Retrieved 29 May 2014 from http://trs-new.jpl.nasa.gov/dspace/bitstream/2014/7193/1/03-0863.pdf.
28. Pristas JM, Lee J, Wheeldon DR, Portner PM. Flight experience with the Novacor LVAS. ASAIO J 2001; 47:266–71.
29. Seidman SJ, Brockman R, Lewis BM, Guag J, Shein MJ, et al. In vitro tests reveal sample radiofrequency identification readers inducing clinically significant electromagnetic interference to implantable pacemakers and implantable cardioverter-difibrillators. Heart Rhythm 2010; 7:99–107.
30. Solan AN, Solan MJ, Bednarz G, Goodkin MB. Treatment of patients with cardiac pacemakers and implantable cardioverter-defibrillators during radiotherapy. Int J Radiat Oncol Biol Phys 2004; 59:897–904.
31. Sweesy MW, Holland JL, Smith KW. Electromagnetic interference in cardiac rhythm management devices. AACN Clin Issues 2004; 15:391–403.
32. Turner R. Radiation health risks to commercial space flight (suborbital and orbital). Proceedings of the Fifteenth Annual Commercial Space Transportation Conference; 2012 February 15-16; Washington, DC. Reston, VA: AIAA; 2012.
33. Turner R, Farrier T, Mazur J, Waltersheid R, Seibold R. Space weather biological and system effects for suborbital flights. Cambridge, MA: The Aerospace Corporation; 2008. Report No: ATR-2009(5390)-1.
34. United States Nuclear Regulatory Commission. Measuring radiation. 2013; Retrieved 3 June 2014 from www.nrc.gov/about-nrc/radiation/health-effects/measuring-radiation.html.
35. Venkatraghavan L, Chinnapa V, Peng P, Brull R. Non-cardiac implantable electrical devices: brief review and implications for anesthesiologists. Can J Anaesth 2009; 56:320–6.
36. Wadasadawala T, Pandey A, Agarwal JP, Jalali R, Laskar SG, et al. Radiation therapy with implanted cardiac pacemaker devices: a clinical and dosimetric analysis of patients and proposed precautions. Clin Oncol (R Coll Radiol) 2011; 23:79–85.
37. Xilinix Application note, XAPP1073, NSEU Mitigation in Avionics Applications. 2010; Retrieved 29 May 2014 from http://www.xilinx.com/support/documentation/application_notes/xapp1073_NSEU_Mitigation_Avionics.pdf.
38. Yerra L, Pratap R. Effects of electromagnetic interference on implanted cardiac devices and their management. Cardiol Rev 2007; 15:304–9.