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Electrode fracture rates and occurrences of infection and granuloma associated with percutaneous intramuscular electrodes in upper-limb functional electrical stimulation applications

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Abstract—This study was performed to assess the rate of electrode fracture and to provide an account of the occurrences of infection and granuloma associated with percutaneous intramuscular electrodes implanted in upper-limb muscles. Data were reviewed on 858 electrodes implanted in 62 research participants between October 1978 and July 1998. Survival analyses showed that the probability of an electrode remaining intact within the body at 6 months after implantation is 95%, and at 1 year is 91%. The probability of the electrode surviving both the in situ period and extraction after 6 months is 78%, and after 1 year is 57%. Ten participants (16%) experienced at least one occurrence of infection or granuloma associated with indwelling electrodes. Five of the twenty-three total adverse medical incidents were associated with electrode fragments retained in the body; the others were associated with intact electrodes. All incidents were localized nonsystematic occurrences and were resolved by administering antibiotics, cleaning the implant site, removing electrodes, cauterizing with silver nitrate, or excising electrodes or granulomas.

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Key words: *adverse effect, electrode fracture, functional electrical stimulation, granuloma, infection, percutaneous intramuscular electrode, survival.*

INTRODUCTION

Central nervous system injury generally results in paralysis of the limbs and alteration of normal muscle tone. Electrical stimulation of paralyzed muscles that remain innervated is a technique that is being used to restore lost muscle function [1]. Functional electrical stimulation (FES) systems use low levels of electrical current to stimulate the peripheral nerve fibers near the neuromuscular junctions of key muscles, thereby eliciting muscle contractions. Electrodes conduct electrical pulses generated by a stimulator to the targeted motor points. Percutaneous intramuscular electrodes are often used in FES studies. Several variations in design exist [2–6], but in general, percutaneous intramuscular electrodes are fine wires with deinsulated electrical conducting tips anchored inside the target muscles, with leads exiting through the skin for connection to external stimulation hardware [7].

Percutaneous intramuscular electrodes are a valuable tool in FES research and clinical practice. They have been used in the development of fully implantable neuroprosthetic

systems designed to restore hand function in tetraplegia and ambulation in paraplegia [8–15]. The use of percutaneous FES systems, as a model for implantable systems, provides a minimally invasive technique in investigating the feasibility of restoring functional movement without prematurely subjecting research participants to implantable systems surgery. Percutaneous intramuscular electrodes also may be used in therapeutic treatments that employ electrical stimulation, such as promoting motor relearning after stroke or preventing the development of decubitus ulcers [16–18].

Previous studies have reported on the in situ durability of various designs of percutaneous electrodes used in a number of applications, but not one has provided data either on electrode fracture rates at extraction or on the incidence and severity of adverse physiological reactions [6,7,15,19–21]. Our previous work on the reliability of percutaneous electrodes in the upper limb reported the probability of an electrode remaining functional over time. The work reported that an electrode was rendered nonfunctional by the occurrence of one or more of three failure mechanisms: electrode fracture, altered response to stimulation, or adverse sensation [19]. This paper provides a more detailed analysis of one of those failure mechanisms—electrode fracture in the upper limb. An analysis of fracture that occurs while the electrode is in the body and an analysis of fracture that occurs during extraction are used to calculate probabilities of fragment retention, an assessment that has not been made before now. Also included in this paper is an account of the incidents of infection and foreign body granuloma that occurred in association with both intact electrodes and electrode fragments while the subjects were enrolled in the FES program.

The electrode design, implantation, use, and maintenance are among the numerous factors that are likely to affect the probability of electrode fracture and adverse physiological reaction. An ideal electrode lead would be adequately strong and flexible to withstand the stresses and strains to which it will be subjected during the study. Its conducting tip would adequately anchor in the muscle so that it does not move relative to the peripheral nerve branch over time, which would cause inconsistent muscle contraction characteristics. Ideally, the electrode size and configuration would not cause irritation or trigger a chronic immune response either at the skin surface or at deeper levels. The materials from which the electrode is fabricated would elicit negligible tissue reaction and be resistant to corrosive reactions. The electrodes would be implanted so that exit sites of lead wires are at a position on the body that the recipient, or his or her caregiver, can keep clean and dry, while at the same time, the leads are routed so that they are exposed to minimal strain and protected from trauma at the skin interface. While it may be impossible to optimize each of these factors simultaneously, they all were considered in the design and implementation of the electrodes described in this paper. Besides these design and implementation factors, subject-specific physiological and behavioral factors are also expected to affect the likelihood of electrode fracture and adverse reaction.

Despite appropriate design and implementation of the electrode, fracture of the electrode lead and adverse physiological reaction can occur. An indwelling electrode lead may fracture sometime during the course of the study or when it is being extracted. In either case, a portion of the electrode lead remains in the body. Adverse physiological reactions, such as infection or foreign body granuloma, can occur in association with indwelling functional electrodes or retained electrode fragments.

This paper reports on the fracture rate and occurrences of infection and granuloma associated with percutaneous intramuscular electrodes used in four upper-limb FES protocols conducted at the Cleveland Department of Veterans Affairs (VA) Medical Center and MetroHealth Medical Center. Specifically, we address the following two questions: (1) What is the incidence of electrode fracture and the probability of a research participant having no electrodes break? and (2) What adverse physiological reactions have occurred in association with percutaneous intramuscular electrodes?

METHODS

Studies and Subjects

This study reviews the occurrences of electrode fracture and incidents of infection and granuloma associated with percutaneous intramuscular electrodes that were implanted in the upper-limb muscles of 62 research participants between October 1978 and July 1998. During that time, the research participants were enrolled under one of four protocols.

Subjects enrolled in these studies had upper-limb muscle paralysis resulting from stroke, traumatic brain injury, or cervical-level spinal cord injury. The first protocol included subjects with tetraplegia caused by neural damage at the C5 or C6 levels of the spinal cord [8,9,22]. The objective of the study was to restore hand grasp and release function by

activating finger and thumb muscles located in the hand and forearm. The second protocol included chronic stroke survivors with weak shoulder-stabilizing muscles, resulting in excessive separation of the humeral head from the glenoid fossa and associated pain [23]. Shoulder muscles were activated with electrical stimulation to stabilize the humeral head and reduce shoulder subluxation. Research participants in the third protocol had varying degrees of hand paralysis caused by stroke or traumatic brain injury [24]. Finger and thumb muscles, wrist extensors, and arm extensors were stimulated primarily to restore hand grasp and release. The fourth protocol included individuals with injuries at the C4 and C5 level of the spinal cord [25]. The feasibility of restoring upper-limb function by activating arm, shoulder, chest, and upper trunk muscles was investigated. The specific muscles that were implanted in each of the four protocols are listed in **Table 1**.

Electrode Design and Implantation Procedure

The electrodes used in these studies (**Figure 1**) were manufactured from multifilament (7 or 10 strand), fluorinated ethylene propylene (FEP) Teflon®-insulated, type-316L stainless steel wire, with a diameter of approximately 200 μm. The wire was wound around an arbor into a coil, forming an electrode lead with a diameter of approximately 580 μm. At the end of the electrode lead, 10 mm was deinsulated, exposing a conducting surface area of at least 10 mm^2. A hook at the tip of the electrode was formed by folding back the final 2 mm of the deinsulated segment. The electrode was loaded into a 19-gauge hypodermic needle, and the assembly was packaged for sterilization with ethylene oxide.

Implantation of percutaneous intramuscular electrodes in upper-limb muscles was performed as a clinical laboratory procedure. Preparation for implantation entailed locating the approximate motor points of target muscles by palpation and surface stimulation; choosing an appropriate electrode insertion site; cleaning the skin with alcohol and Betadine™; and for those subjects who retained sensation in the implantation area, administering lidocaine subcutaneously between the motor point and electrode insertion site. An electrode-loaded needle was then inserted through the skin and tunneled subcutaneously toward the motor point of the target muscle. Low-frequency electrical stimulation was delivered through the needle as it was advanced, and the contractile response was observed to help optimally place the electrode. Once

Table 1.
Muscles implanted in upper-limb percutaneous electrode protocols.

Protocol	Muscles Implanted*
1	***Thumb adductors, abductors, flexors, and extensors*** (adductor pollicis, abductor pollicis brevis and longus, flexor pollicis brevis and longus, extensor pollicis brevis and longus, opponens pollicis) ***Finger flexors and extensors*** (flexor digitorum profundus and superficialis; first, second, and third dorsal interossei; extensor digiti minimi; extensor digitorum communis; extensor indicis proprius) ***Wrist flexors, extensors, pronators, and supinators*** (brachioradialis, brachialis, extensor carpi radialis brevis and longus, extensor carpi ulnaris, flexor carpi ulnaris, flexor carpi radialis, pronator quadratus) ***Other:*** triceps, median nerve, ulnar nerve, sensory
2	***Shoulder muscles*** (deltoid, supraspinatus, trapezius) ***Arm muscles*** (biceps, triceps)
3	***Thumb adductors, abductors, and extensors*** (adductor pollicis, abductor pollicis, extensor pollicis longus) ***Finger flexors and extensors*** (second and third dorsal interossei, extensor digitorum communis, extensor indicis proprius, flexor digitorum profundus and superficialis) ***Wrist extensors*** (extensor carpi radialis) ***Arm extensors*** (triceps)
4	***Arm*** (triceps, biceps, brachialis) ***Shoulder*** (deltoid, supraspinatus, infraspinatus) ***Trunk*** (latissimus dorsi, pectoralis major)

*Not every muscle listed was implanted for each subject enrolled in a particular study.

Figure 1.
Percutaneous intramuscular electrode used in upper-limb FES applications at Cleveland FES Center. A 19-gauge needle was used to implant electrodes. (Top) Magnified to approximately 8× actual size. (Bottom) Approximately actual size.

satisfactorily placed, the needle was withdrawn while external pressure was applied to the skin overlying the tip of the electrode, leaving the electrode in the muscle.

Implant Sites and Connector Description

Electrodes were implanted so that their insertion sites were localized to an area of skin approximately 1.5 cm^2 in size. One or more of these implant sites may be required for implementation of a complete FES system, depending on the number and location of muscles to be implanted. Implant sites for the hand-function studies (protocols 1 and 3) were located on the dorsal and volar aspects of the middle forearm. The posterior shoulder area was the implant site for the shoulder subluxation study (protocol 2), and the lateral trunk and upper-arm regions were additional sites for the proximal arm function study (protocol 4).

The electrode leads exiting from the skin surface were trimmed and crimped to connector pins that inserted into a plastic connector block (**Figure 2**). The connector block was mounted to a spunlace bandage taped to the skin adjacent to an implant site. The output cable from a stimulator plugged into the connector block. A bandage was used to cover the connector block-stimulation cable interface and implant site. Research participants and their family members or attendants were instructed to remove the bandage and clean the site with alcohol once or twice a week and to check for signs of irritation.

Electrode Usage, Assessment, and Extraction

The stimulus used in these studies was a train of current-regulated charge-balanced biphasic pulses. The primary pulse was cathodic and elicited an action potential in nearby axons. The secondary pulse was anodic and is intended to minimize potential tissue damage by reversing the electrochemical processes that occur at the electrode-tissue interface during the cathodic pulse [3]. The cathodic pulse had a fixed amplitude of 20 mA and a pulse width that varied between 0 μs and 200 μs. Trains of biphasic pulses were delivered at frequencies of 10 to 20 pulses per second, with the most common settings being 12.5 and 16.0 pulses per second. This stimulus waveform, when delivered through an electrode having an active surface area greater than 10 mm^2, resulted in a charge density of less than 0.4 $\mu C/mm^2$/pulse, a charge density within the range reported to avoid iron dissolution at the interface between stainless steel electrodes and living tissue [3].

Usage of the stimulation system varied across research protocols and from subject to subject. The stimulators were programmed to deliver patterns of stimulation that produced the desired hand motion or muscle contractions

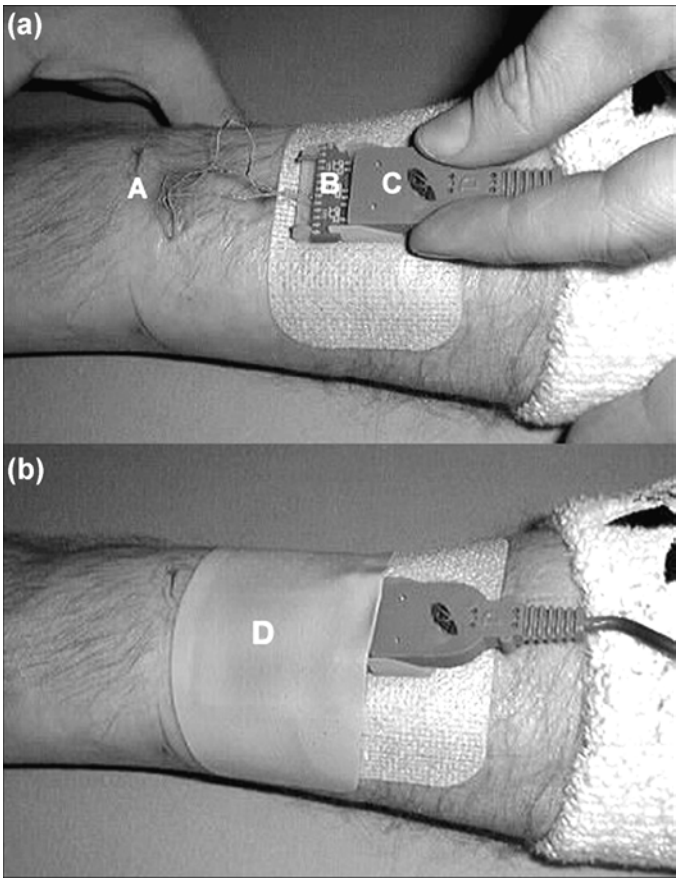

Figure 2.
Skin surface connector used with upper-limb percutaneous FES systems. **(a)** Electrode leads exiting from skin surface A, connector block B, and stimulator cable C. **(b)** Bandage D covering implant site and connector block-stimulation cable interface.

needed to meet the objectives of the study. Typically, with the stimulators set to exercise mode, the muscles were repeatedly activated for 10 s to 20 s, followed by a relaxation period of approximately 10 s. The participants in the hand function studies (protocols 1 and 3) also could switch their systems to a functional mode, in which they controlled the degree of hand opening and closing using an external sensor or switch. Some subjects used their stimulation systems 8 hours or more per day.

The physical status of an electrode was occasionally checked during regularly scheduled visits to the clinical laboratory. Laboratory personnel measured the stimulus threshold, electrode impedance, and force recruitment characteristics [19]. A progressive rise in stimulus threshold coupled with reduced force output for selected stimulation levels over time was interpreted to be due to electrode movement with respect to the muscle motor point or increased encapsulation around the electrode. A large increase in electrode impedance was interpreted to be due to electrode fracture. The presence of adverse physiological reaction was checked by inspecting the implant sites for signs of infection or granuloma. The frequency of visits to the clinical laboratory was variable from study to study but generally occurred at less than 6-month intervals.

Electrodes were extracted if they were found to be fractured or nonfunctional according to the previous assessments. If signs of infection or granuloma formation were present, the physician on the study judged whether to extract associated electrodes or to attempt alternative treatments first. The electrodes that remained functional until the end of the study were extracted before the subject exited the FES program. Electrode extraction was performed by the application of a slow steady tension to the external lead wire. The individual performing the procedure often could feel whether the lead fractured during extraction. The tip of the extracted electrode was visually inspected to judge whether it had indeed been extracted intact. No attempt was made to remove electrode fragments that remained in the body. Research participants were instructed to notify laboratory personnel or the physician if any complications arose during the study or after exiting the study.

Data Collection

Data were recorded in notebooks maintained for each subject. The notebook contained demographic information about the subject, traveler sheets for each electrode implanted, technical information about the FES system implemented for the subject, and progress notes accounting for every appointment the subject had in the laboratory. The electrode traveler sheets included information about the manufacture of the electrode and blanks for entering data regarding its implantation and extraction. The date the electrode was implanted and extracted, the reason for extraction, and whether the electrode was intact after extraction are among the key data that were transferred from the traveler sheets to a computerized database that was used in the fracture analysis (described next). Progress notes, operative reports, surgical pathology reports, culture result reports, and clinical notes kept by laboratory personnel are the sources from which incidents of infection and granuloma were compiled.

Analysis of Electrode Fracture

This analysis was designed to answer the question, "What is the probability that a research participant will have no electrodes fracture?" Based on previous studies of electrode fracture [6,15,19–21], we expect that the answer to this question, as it relates to the electrodes reviewed in these four specific upper-limb studies, depends on at least two factors: (1) the amount of time an electrode is in the body and (2) the number of electrodes implanted. Accounting for these two factors, the analysis of electrode fracture was conducted in two steps.

Our first step was to calculate the probability of a *single* electrode surviving as a function of the time it is in the body, $P_S(t)$. A percutaneous intramuscular electrode may fracture while it is in the body during the course of the study and/or when it is extracted from the body. The probability of an electrode surviving both events, $P_S(t)$, is the product of the probability of an electrode surviving in the body for a specified duration of time, $P_1(t)$, and the probability of an electrode that has survived without fracture for a specified time surviving the extraction procedure, $P_2(t)$,

$$P_S(t) = P_1(t) \times P_2(t) \quad . \tag{1}$$

We performed survival analyses to calculate $P_1(t)$ and $P_2(t)$ using the Kaplan-Meier estimate provided in the SPLUS™ statistical software package [26]. The terminal event for $P_1(t)$ was fracture before extraction (fracture occurred sometime during the study). $P_1(t)$ was estimated by survival analysis of data from electrodes that were extracted before the end of the study because of fracture indicated by high impedance and from electrodes that remained intact until extraction. The terminal event for $P_2(t)$ was fracture during the extraction procedure (intact before, but not after, extraction). $P_2(t)$ was estimated by survival analysis of data from only the electrodes known to be intact before extraction. $P_S(t)$ was then calculated with the use of equation 1.

This calculation assumes that occurrences of electrode fracture are independent of one another (e.g., an electrode breaking during the study is not more or less likely to break during extraction). Our data neither refute nor support this assumption. No single electrode was ever counted to have fractured more than once in this analysis. In cases where an electrode was found to be broken before extraction (detected by a high impedance measure), a second breakage (if one actually did occur during extraction) could not be determined with the inspection of the broken tip; therefore, the electrode was counted to have broken during the study. This analysis focuses on whether or not a fracture occurred for each electrode implanted, rather than whether multiple fractures occurred in a single lead.

The second step in this analysis builds upon the first step. Using the probability of a *single* electrode surviving, $P_S(t)$, we estimated the probability of *all* electrodes in a system of electrodes surviving for specified durations of time in the body. The probability of a research subject having no electrodes fracture (i.e., all electrodes in the system survive) is the probability of a single electrode surviving that amount of time raised to the power of the number of electrodes implanted, n,

$$P_{NF}(t, n) = P_S(t)^n \quad . \tag{2}$$

This calculation assumes that the failure of one electrode has no influence on the failure of another electrode (i.e., each electrode is independent) and that each of the *n* electrodes remains implanted in the body for the same duration of time, *t*.

Analysis of Adverse Physiological Reactions

This analysis was designed to answer the question, "What adverse physiological reactions have occurred in association with percutaneous intramuscular electrodes used in the four upper-limb protocols reviewed?" Incidents of infection and granuloma were identified by reviewing the subject notebooks, the electrode database, operative reports, surgical pathology reports, culture result reports, clinical notes written by laboratory personnel, and patient medical charts.

Medical incidents that occurred in association with percutaneous intramuscular electrodes were classified as either granulomas, infections, or suspected infections. A foreign body granuloma is a mass of nodular granulation tissue resulting from a special form of chronic inflammation response to a foreign object that is not destroyed by the unmodified chronic inflammatory response [27]. A medical incident was judged to be a granuloma if it was identified as a granuloma in either the progress notes, operative reports, surgical pathology reports, or other documentation written or dictated by the attending physician, or if the reason for electrode extraction was indicated to be granuloma in the computer database.

A medical incident was judged to be an infection when any of the following evidence was found:

1. Positive culture report.
2. "Infection" was written in the progress notes.
3. The electrode data sheet indicated infection as the reason for electrode extraction and no other documentation was found to suggest otherwise.

In addition, incidents occurred in which none of the above criteria was met, but either of the following was found:

1. The progress notes stated that an infection was suspected and antibiotics were administered, but there was no purulent discharge.
2. Electrodes were removed because of infection-like signs (inflammation, redness, swelling), but the incident was not called an infection in the progress notes, even if the electrode data sheets indicated "infection" as the reason for electrode extraction.

These incidents were judged to be suspected infections.

RESULTS

Electrodes and Subjects Per Study

Nine hundred forty percutaneous intramuscular electrodes were implanted in the upper-limb muscles of 62 subjects participating in various FES studies conducted at the Cleveland FES Center between October 1978 and July 1998. The majority of the subjects (66 percent) were involved in protocol 1, as shown in **Table 2**. This study also was associated with the majority (84 percent) of the 940 electrodes implanted. The number of electrodes implanted per subject was the least for protocol 2, with a median of three electrodes per subject, and was the greatest for protocol 4, with a median of 19 electrodes per subject. The amount of time the electrodes were in the body was the least for protocol 2, with a median of 62 days, and was the greatest for protocol 1, with a median of 363 days.

Fracture Rates

Number of Intact and Fractured Electrodes

Of the electrodes implanted, 45 of the 940 were functional and remained implanted at the time of this analysis; 895 electrodes were extracted. Data regarding the status of electrode integrity were not recorded on the traveler sheet for 37 of the 895 extracted electrodes, leaving 858 electrodes with data available for analysis (**Table 3**). Of these 858 electrodes, 85 percent (731) remained intact through the duration of the study in which they were used; 15 percent (127 electrodes) fractured during the study. The group of 731 electrodes that remained intact for the duration of the study comprised 215 (25 percent) that survived extraction, 243 (28 percent) that fractured during extraction, and 273 (32 percent) that had no data recorded on the traveler sheet regarding the status of their integrity after extraction.

Probability of Electrode Survival

The results of the survival analyses (**Figure 3**) showed that an electrode was less likely to fracture during the study than during the extraction procedure, $P_1(t) > P_2(t)$ ($p < 0.001$, Cox-Mantel log-rank test). At 6 months postimplant, an electrode had a 95 percent chance ($P_1(t)$) of still being intact in the body, an 82 percent chance ($P_2(t)$) of surviving extraction, and a 78 percent chance ($P_S(t)$) of surviving both the 6-month study and the extraction procedure (**Figure 3**). After 1 year, these survival rates decrease to 91, 63, and 57 percent, respectively.

To examine the individual contributions of each study to the combined survival characteristics, we computed separate survival curves for each study. As expected, the survival curves computed from all studies combined, $P_1(t)$ and $P_2(t)$, largely reflected the survival characteristics of protocol 1 alone. No significant difference was found between the $P_1(t)$ curves individually computed for all four studies ($p = 0.540$). However, the

Table 2.
Research participants and electrodes per protocol.

Variable	Protocol				All Studies
	1	2	3	4	
No. of Subjects	41	13	6	2	62
No. of Electrodes Implanted	787	48	67	38	940
Median No. of Electrodes Implanted Per Subject	16	3	10	19	12
Median No. of Days Electrodes Were in Body	363	62	203	140	313

Table 3.
Electrodes used in analysis of electrode fracture.

Category	Electrodes
Intact Prior to Extraction	731* (85%)
Survived Extraction	215† (25%)
Fractured During Extraction	243† (28%)
Outcome After Extraction Was Not Recorded	273 (32%)
Fractured Prior to Extraction	127* (15%)
Total	**858**

*Used in estimating $P_1(t)$.
†Used in estimating $P_2(t)$.

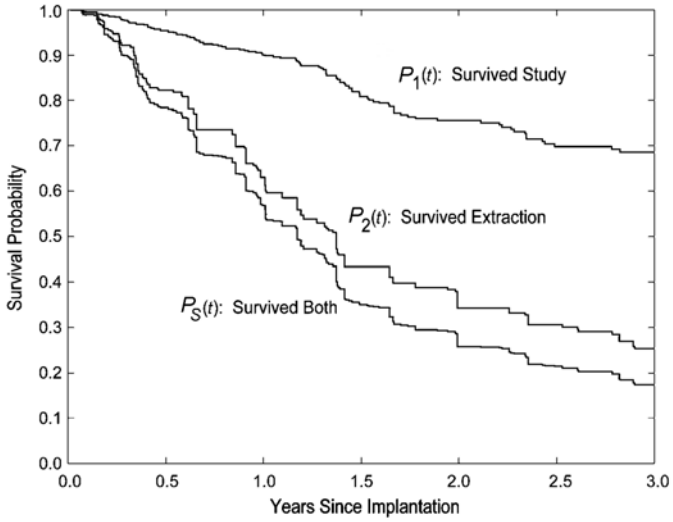

Figure 3.
Probability of a single electrode surviving as a function of length of time it remains in body. $P_1(t)$ (probability that an electrode will not fracture during study) was determined by survival analysis of 858 electrodes. $P_2(t)$ (probability that an electrode will not fracture during extraction procedure) was determined by survival analysis of 458 electrodes known to have been intact before extraction. $P_S(t)$ (probability than an electrode will fracture neither during study nor during its extraction) was calculated as product of $P_1(t)$ and $P_2(t)$.

$P_2(t)$ curve calculated for protocol 4 was significantly lower than the $P_2(t)$ curves of the other three studies ($p < 0.001$). This suggests that a greater probability of electrode fracture existed during extraction in protocol 4 than in the other studies. Nevertheless, the combined survival characteristics of the other three studies were not significantly different from the results of all four studies combined ($p = 0.347$). Therefore, all the survival characteristics in this paper were calculated with electrode data from all four studies combined. Data from more electrodes are required before precise estimates of survival can be calculated for the individual protocols.

The survival curves for systems of 2, 4, 8, and 16 electrodes are shown in **Figure 4**. The greater the number of electrodes implanted, the lower the likelihood of a research participant not having an electrode fracture. This figure can be used as a guide for predicting electrode fracture rates for a specific upper-limb study. For example, a person participating in a 3-month study that requires four electrodes, may reasonably expect to have a 75 percent chance of completing the study and exiting the program without retaining any electrode fragments in his or her body, assuming the presence of no additional extraordinary factors that would affect the fracture rate.

Adverse Physiological Reactions

Infection and Suspected Infection

There were 14 reported incidents of infection or suspected infection that occurred in 9 of the 62 subjects: 13 were associated with functioning intact electrodes and 1 was associated with electrode fragments (**Figure 5**). The one incident associated with electrode fragments (subject 5, **Figure 5**) was resolved by excising three fragments from the inflamed area during an outpatient surgical procedure under local anesthesia. One of the incidents involving functioning intact electrodes required surgical resection under local

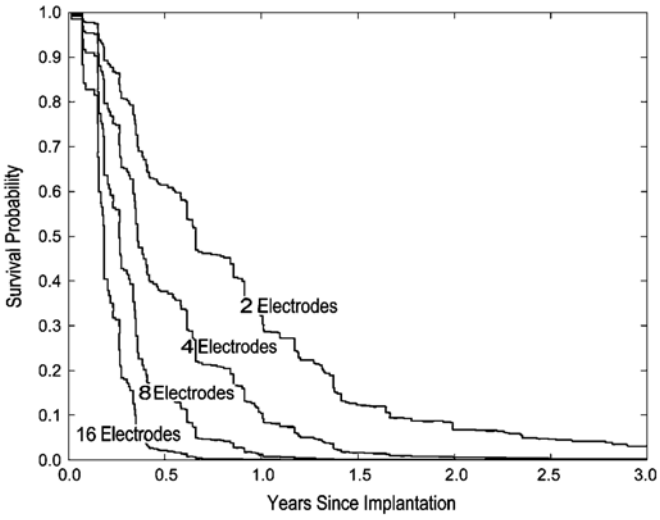

Figure 4.
Probability of no electrode fracturing in a system of electrodes. Equation 2 of current paper was used to calculate each curve.

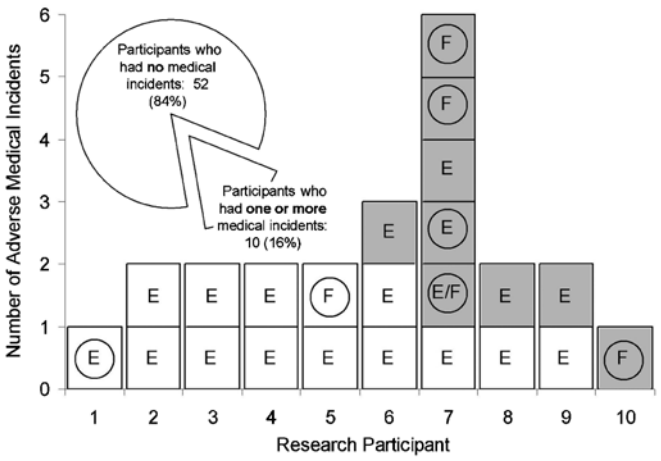

Figure 5.
Summary of adverse physiological reactions. A total of 23 occurrences of infection/suspected infection (□) or granuloma (■) occurred in 10 of 62 participants. Four incidents were associated with electrode fragments (F), eighteen were associated with functioning intact electrodes (E), and one involved both (E/F). Outpatient surgical treatment (○) was required for seven of these incidents.

anesthesia. In this case (subject 1, **Figure 5**), a reaction developed below the skin line and may have been consistent with either an inclusion cyst or a true pyogenic infection. All the other events associated with functioning intact electrodes were resolved by treatment with antibiotics, cleaning the area with antibacterial solution, and/or extracting functioning electrodes from the area.

Granuloma

Nine reported incidents of granuloma occurred in 5 of the 62 subjects: 5 were associated with functioning intact electrodes, 3 were associated with electrode fragments, and 1 was associated with both intact electrodes and electrode fragments (**Figure 5**). The granulomas associated with electrode fragments occurred in two subjects (subjects 7 and 10). The incident involving subject 10 was described in the operative report as a small skin tag and wire fragment that were excised during an outpatient surgical procedure under local anesthesia. Subject 7 had five of the nine incidents of granuloma (**Figure 5**), each of which developed in different places on the forearm and wrist. Two of these incidents involved only electrode fragments, two involved only intact electrodes, and one involved both intact and fractured electrodes. One of the incidents involving only intact electrodes cleared up after cleaning the area and allowing it to be exposed to air. The other four incidents involving subject 7 were treated by administering antibiotics, cauterizing with silver nitrate, or extracting electrodes. Each of these four incidents was finally resolved by excising the granuloma and removing fragments or intact electrodes from the area during an outpatient surgical procedure under local anesthesia. The operative report described the final surgical procedure in subject 7 as a radical resection of the flexor tenosynovectomy under regional anesthesia. The arm was not grossly infected internally; mainly it had foreign body granulomas. The other incidents of granuloma involved only functioning electrodes (subjects 6, 8, and 9, **Figure 5**) and were resolved by cauterizing the granuloma with silver nitrate and/or extracting functioning electrodes from the area.

Fragment-Related Infections and Granulomas

Combining the findings of infection, suspected infection, and granuloma associated with electrode fragments, a total of five medical incidents related to electrode fragments occurred in 3 of 62 subjects (one infection and four granulomas). All of these incidents resolved after the fragments were excised during an outpatient surgical procedure under local anesthesia. Ninety-five percent of the subjects participating in the four upper-limb percutaneous protocols have never had a medical incident associated with electrode fragments while enrolled in the FES program. In addition, these subjects to our knowledge have had no fragment-related infections or granulomas since exiting the program.

Summary of Adverse Physiological Reactions Analysis

A total of 23 incidents of infection, suspected infection, or granuloma have occurred in 10 of 62 of the research participants (**Figure 5**). Eight of these ten subjects experienced more than one incident, and four of the ten subjects experienced both infection and granuloma. All incidents were localized; there were no systemic complications. Outpatient surgical procedures were performed for seven of these incidents in four subjects. Eighty-four percent of the subjects participating in the four upper-limb protocols using percutaneous intramuscular electrodes never had an incident of granuloma, infection, or suspected infection while they were enrolled in the FES program. In addition, these subjects to our knowledge have had no electrode-related infections or granulomas since exiting the program.

Update of Previously Published Results

This analysis of electrode fracture and occurrences of infection and granuloma associated with percutaneous intramuscular electrodes in four upper-limb protocols expands upon our previous report of electrode reliability [19]. In that report, 710 of these percutaneous electrodes were studied and of the 636 electrodes that had been extracted, 113 (17.8 percent) had fractured in the body during the study, 56 (8.8 percent) were extracted because they produced an altered response over time, 16 (2.5 percent) produced adverse sensation, 3 (0.5 percent) were extracted because of suspected infection, and 8 (1.3 percent) were extracted because of the presence of a granuloma. The updated percentages are similar. With an additional 222 electrodes extracted (for a total of 858), 127 (14.8 percent) fractured during the study, 75 (8.7 percent) produced an altered response, 26 (3.0 percent) caused adverse sensation, 5 (0.6 percent) were extracted because of infection, and 23 (2.7 percent) were extracted because of granuloma. The previous work reported that the probability of an electrode remaining functional for 6 months was 88 percent and for 1 year was 80 percent [19]. These are compared to the results of the present analysis, where the probability of an electrode remaining intact at 6 and 12 months is 95 and 91 percent, respectively. The survival rates were higher in the present analysis because electrode fracture (the focus of this study) was the only failure mode used to define survival, whereas the previous report defined survival as the absence of fracture, altered response over time, or adverse sensation.

DISCUSSION

The fracture analysis presented in this paper distinguishes the likelihood of an electrode fracturing sometime during the study from the likelihood of it fracturing as a result of the extraction procedure. **Figure 3** shows that the chance of an electrode surviving for a certain period of time, $P_S(t)$, is due predominantly to its chance of enduring the extraction procedure, $P_2(t)$, and does not depend as much on the survival characteristics before extraction, $P_1(t)$. Indeed, the electrodes serve their purpose well of reliably delivering electrical stimulation in studies that may continue only a few weeks or as long as 2 years. The low rates of adverse sensation and altered response further suggest that the anchoring properties and methods for positioning the electrodes are quite adequate. However, because of extraction, the probability of an electrode fracturing is a steep function of the amount of time it remains in the body. Therefore, unless the study is quite short, an electrode is likely to fracture upon extraction and leave a segment of its lead in the body. Therefore, our evaluation of the consequences of retaining electrode fragments in the body is of paramount importance.

The review of adverse physiological reactions revealed that few incidents of infection, suspected infection, and granuloma occurred in association with functioning intact electrodes and even fewer occurred in association with electrode fragments. Although this finding does not exclude the possibility of the occurrence of fragment-related medical incidents of a more severe nature than have been experienced by the subjects in these studies, in our experience, no basis exists for expecting incidents of a more severe nature to occur when these electrodes are implemented as described in this paper.

Our analysis of adverse physiological reactions suggests that some individuals tend to experience infection and/or granuloma more than others do. All the medical incidents occurred in only 16 percent (10/62) of the research participants, 80 percent of whom had more than one medical incident. In contrast to subjects who seemed to have a predisposition to complications, others did not experience medical incidents. For example, 80 percent of subjects who retained more than 10 electrode fragments have never had a fragment-related medical incident even as long as 13 years since exiting the program. We could not establish a correlation between the number of retained fragments and incidents. We conclude that the occurrence of medical incidents is likely to depend on subject-specific factors, such as the sensitivity of the immune system, the presence of allergies, attentiveness to adverse signs, degree of hygiene, and other factors.

Many of the subjects experienced the normal sequela that often accompanies spinal cord injury and stroke, including the occurrences of pressure sores and urinary tract and bladder infections. Additionally, these subjects may have been receiving medical and dental care that sometimes would require antibiotic coverage. As expected, subjects demonstrated varying levels of attention to their skin management and cleanliness as well as their attention and protection of the electrode site. Given these many factors that are virtually impossible to control across a large subject population, we are unable to extract

any single factor that would predispose an individual to an enhanced likelihood of a granuloma or infection. Nevertheless, in one subject (subject 7, **Figure 5**) who was an exemplary individual regarding his hygiene, care, and overall management of his disability, we observed an extensive number of incidents that we are unable to explain with the available data. Possibly, this subject had developed a state of immunocompromise or had become particularly susceptible to skin infections, which would make the development of granulomas more likely. This supposition is supported by the fact that the subject had been admitted to the hospital for a lower-limb skin infection, unrelated to the electrodes. This subject has had no fragment-related complications since exiting the FES program.

We relied on research participants' self-referral if electrode-related complications arose during or after exiting the FES program. Therefore, we have assumed that fragment-related infections or granulomas did not occur after exiting the FES program if the former research participant did not notify FES laboratory personnel or the physician who implanted the electrodes. Although it is possible that former participants may not inform laboratory staff or physicians of adverse physiological reactions that resolved without medical intervention, we believe it is unlikely that the investigators would not be notified if a former participant had developed a reaction that required medical attention.

The length of time an electrode is in the body is a major factor that affects the probability of an electrode fracturing either during the study or at extraction. Other factors that may be related include the biological or lifestyle characteristics of the research participants, such as their skin characteristics (thickness, toughness), the presence and severity of spasticity, and their degree of physical activity. Additional factors that may affect electrode fracture rates are related to the muscle that is implanted, its depth beneath the skin, the length change of the muscle during contraction (excursion), and how the electrode leads were routed under the skin to the muscle. Our previous study compared electrodes implanted in volar muscles to those in dorsal muscles and compared electrodes crossing the wrist in C6-injured subjects (who have voluntary wrist control) to those crossing the wrist in C5-injured subjects (who often wear a wrist-hand orthosis to brace the wrist) [19]. No statistically significant differences were found. Those comparisons were not repeated in this analysis. Insufficient numbers of electrodes from the shoulder region precluded attempts to compare electrodes implanted in shoulder muscles to electrodes implanted in the forearm.

The survival and fracture rates and analysis of adverse physiological reactions presented in this paper cannot be generalized to different designs of percutaneous electrodes or to the same design used in applications that require different implantation and lead-routing techniques. For example, an indirect approach has been described for implanting lower-limb muscles with motor points that are a long distance from the implant sites [15]. With this method, an electrode lead is tunneled subcutaneously toward the eventual exit site incrementally, resulting in a lead route that crosses several fascial planes. This implantation is likely to result in different stress on the electrode than those that are directly routed, as is possible in the upper limb. In addition, the probability of electrode fracture is also likely to be related to factors such as muscle size and excursion, which are different in the upper limb than in the lower limb.

We cannot definitively predict the fracture rate or the likelihood of the occurrence of an adverse physiological reaction associated with percutaneous electrodes used in future studies given the myriad of factors that come into play. But our analysis of percutaneous intramuscular electrodes used in the four upper-limb electrical stimulation protocols described herein leads us to conclude that unless the study is short and requires few electrodes, a subject participating in an upper-limb study that uses the design of electrodes described in this paper should expect to retain one or more electrode fragments in his or her body. We further conclude that subjects may experience an infection or granuloma because of a retained electrode fragment, but that if such an incident does occur (and it is reported or diagnosed promptly), it is likely to be effectively treated by medication or a minor outpatient surgical procedure to remove the electrode fragment.

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