Award Number:

W81XWH-12-1-0550

TITLE:

Early ICU Standardized Rehabilitation Therapy for the Critically Injured Burn Patient

PRINCIPAL INVESTIGATOR:

Peter E. Morris, MD

ORIGINAL CONTRACTING ORGANIZATION:
University of Kentucky

REPORT DATE:
Dec 2019

TYPE OF REPORT:
Final Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
Dec 2019	Final	**09/20/2012 - 09/19/2019**

4. TITLE AND SUBTITLE
Early ICU Standardized Rehabilitation Therapy for the Critically Injured Burn Patient

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-12-1-0550

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Peter E. Morris, M.D.

E-Mail:peter.morris@uky.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Kentucky

500 S LIMESTONE 109 KINKEAD HALL
LEXINGTON KY 40536-0001

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This project was originally funded in order to conduct a multicenter, randomized controlled trial to determine whether early ICU rehabilitation, for Burn Intensive Care Unit (BICU) patients, would decrease hospital length of stay. The original protocol specified fifty subjects to be randomized at each of three sites for a total of 150 subjects. After twenty-three study subjects had been enrolled and the outpatient phase of testing was instituted, new data from a similar study was published in a medical ICU population that caused great discussion across the investigators. The results of that study in combination with the patient care delivery pattern within the original design of this study caused a shift in focus of this study. The original study was deemed phase I and closed. The second phase proposed to examine medical records within a large national hospital database to identify optimal care delivery patters. Minimizing the duration of immobilization of patients and developing strategies to lessen its impact are the goals of the second phase.

15. SUBJECT TERMS

Burn Injury, Critical Care, Intensive Care, Standardized Rehabilitation Therapy

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
					USAMRMC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**	Unclassified	18	**19b. TELEPHONE NUMBER** *(include area code)*
Unclassified	Unclassified	Unclassified			

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

Table of Contents

1. Introduction

This project was originally funded to conduct a multicenter, randomized controlled trial. The trial was designed to determine whether early ICU rehabilitation compared to usual care, for Burn Intensive Care Unit (BICU) patients, would decrease hospital length of stay. The original protocol specified fifty subjects to be randomized at each of three sites for a total of 150 subjects. Study start-up was initiated in Year #1 and all sites began to enroll patients. Twenty-three study subjects were enrolled. Out-patient visits during the post-enrollment, post-hospital discharge phase of the study were also initiated and the outpatient phase of testing was instituted. When this grant award clinical trial was initiated by the investigators, we were aware of two similar ongoing studies in early ICU rehabilitation care. Each of these studies was actively enrolling and had passed interim DSMB review with approvals to continue to enroll. Hence, the investigators of this grant award began this clinical trial, Early ICU Standardized Rehabilitation Therapy for the Critically Injured Burn Patient, in 2013. Then in 2015, those two very similar trials were published. Their findings had a profound effect on this grant award's clinical trial as both trials, conducted at two separate Universities, were negative. These trials indicated that the mechanism of early ICU rehabilitation planned for this Burn Patient clinical trial, was unsuccessful in both of these other studies conducted in critically ill medical ICU patients. Thus, the fate of this study received intense discussion from the investigators following these publications. It was significant in these studies' implication in that each of these studies showed no efficacy in early rehabilitation for medical patients. Based on these findings, the investigators believed that the potential for futility in the original Burn Early ICU Rehab clinical trial was quite legitimate. The Burn Early ICU Rehab study was then necessarily halted, due to a worry about lack of ever being able to achieve efficacy, given the negative results of the two large clinical trials of similar design. This grant award's clinical trial did enroll 23 patients. The findings of 23 Burn Patients enrolled are described below. Importantly, the investigators did focus efforts of the remainder of this grant award to continue to answer important questions remaining in the field regarding Burn patient rehabilitation in the ICU setting. The second phase of the grant undertook a large national database examination to aid in the future design of clinical trial in burn patients to optimize rehabilitation. The results of the second phase of this grant award are also described below.

2. Keywords

Burn Injury, Critical Care, Intensive Care, Standardized Rehabilitation Therapy

3. Accomplishments

What were the major goals of the project?

- To develop, design, approve, and administer a multicenter, randomized, controlled (usual care) clinical trial to examine the effect of early ICU rehabilitation strategies vs usual care in critically ill Burn ICU patients.
- To develop and conduct an analysis of a national hospital robust, administrative database (Vizient) in order to examine the national practice of frequency of operative procedures for index hospital admission burn patients. As well, the analysis was to determine whether there might be an inverse relationship in burn patients between the increasing number of operative procedures required and a decrement in the number of physical therapy days delivered.

Grant Award Milestones and Achievements

- All IRB and HRPO obligations were met
- All subcontract sites had working relationships with Wake Forest to receive study payments
- All payments on this grant mechanism have been put on hold and have been on hold
- since April 29th, 2015, when Dr. Morris moved from Wake Forest to the University of Kentucky (see below for subsequent plans to continue with this award).
- Monthly study conferences were conducted with discussion across PI's and coordinators. These conferences led to recommendations addressing enrollment volume within the study. These conversations were detailed and examined possibilities at each site to identify improvements in process.
- Electronic secure remote entry database was functioning
- Award transferred to the University of Kentucky- completed May 2016
- All IRB and HRPO obligations were met- completed November 2016
- All subcontract sites had working relationship with the University of Kentucky- completed May 2017
- Data refinement and analysis of Phase I was not feasible due to the early ending of the clinical trial due to futility.
- Research protocol for Phase II prepared and refined- June 2017
- Evaluate retrospective data and report findings-completed

Summary of the Burn Patient Early ICU Rehabilitation Clinical Trial Patient Data

Twenty-three patients were randomized between 8/2013 and 3/2015: 12 patients were from Wake Forest, 6 from Washington University, and 5 from Chapel Hill. Patient characteristics are summarized in **Table 1 and Table 2**. Eighteen of the 23 patients (78%) were in the BICU and 5 (22%) were in the SICU (all from Washington). Fifteen (65%) were males and 8 (35%) had inhalation injuries. Ages ranged from 20 to 79 with a median of 52 years; BMI ranged from 20.1 to 51.3 with a median of 26.3 kg/m^2; Baux Score ranged from 43 to 108 with a median of 71.0.

Table 1. Patient Characteristics by Treatment Assignment			
Characteristic	Control	Mobility	Overall
Total N	11	12	23
Clinical Site			
Wake Forest	6 (55)	6 (50)	12 (52)
Washington	2 (18)	4 (33)	6 (26)
Chapel Hill	3 (27)	2 (17)	5 (22)
Males # (%)	7 (64)	8 (67)	15 (65)
ICU setting of enrolled subject			
Burn ICU # (%)	9 (82)	9 (75)	18 (78)
Surg ICU # (%)	2 (18)	3 (25)	5 (22)
Inhalation Injury # (%)	5 (45)	3 (25)	8 (35)
	Median (Range)	Median (Range)	Median (Range)
Age	49 (20 -79)	53 (33 – 70)	52 (20 – 79)
BMI	26.5 (20.1 – 51.3)	26.3 (23.0 – 42.6)	26.3 (20.1 – 51.3)
Baux Score	70.0 (43 – 108)	75.5 (58 – 103)	71.0 (43 – 108)

Table 2

Co-morbidity	ALL n = 14	Control n = 6	Mobility n = 8
Neurologic	1	0	1
Chronic pulmonary disease	2	1	1
Asthma	2	2	0
Emphysema	1	0	1
Prior ARDS/ALI	1	0	1
Single lung transplant	0	0	0
Double lung transplant	0	0	0
Upper gastrointestinal disease	3	1	2
Visual impairment	1	0	1
Drug use in past month	2	1	1
Past drug use	1	0	1
Psychiatric Dx and/or Tx	4	2	2
Depression	4	2	2
Anxiety	2	0	2
Myocardial infarction	1	0	1
Angina	1	0	1
Peripheral vascular	1	0	1
Arthritis	2	0	2
Degenerative disc disease, chronic back pain, spinal stenosis	1	0	1
Leukemia	0	0	0
Lymphoma	0	0	0
Diabetes	3	0	3
Pregnancy at hospital admission	0	0	0
Formal disability	1	0	1
Current Smoker	4	2	2
None	7	4	3

Enrollment proceeded and both study arms were engaged with study subjects allowing the investigative "early ICU Rehabilatation" strategy to be administered. The study's "Standardized rehabilitation therapy" and usual care were delivered to study subjects. The delivery of multiple intervention arm rehabilitation sessions including delivery of resistance training exercise with Therabands occurred in each of the three enrolling sites. As well, within the design of the protocol, the study mandated that the strength and functional assessments for both arms be completed by a series of "Blinded exercise physiologists" at each of the study's sites. These blinded exercise physiologists were able to conduct the strength and functional assessments according to protocol.

Study Outcomes:
Given that the study enrollment was halted at 23 subjects of a planned 150, the investigators found no outcome differences that were demonstrated between the two arms of the study in planned outcome measurements.

Summary of changes within this grant award from the original "phase 1" of the award's clinical trial to the "phase 2" of the award

Two observations led the Principle Investigators to reconsider the design and execution of the original study, "Early ICU Rehabilitation Therapy for the Critically Injured Burn Patient". The original study set out to examine the effect of early intensive rehabilitation compared with usual care in severely burned patients.

The first observation was prompted by the results of the recently concluded Medical ICU Early Rehab studies[1,2]. These studies failed to demonstrate an effect of early and intensive rehabilitation and reconditioning on pre-specified in-hospital study endpoints. The investigators of this Burn Patient Early ICU Rehabilitation Study seriously weighed their responsibility as chaperones of study administration (i.e., ongoing assessment of the medical literature for any information that would affect outcome or safety of the trial) to consider the Medical ICU trials' data. These two trials were significant in their lack of efficacy and therefore greatly influenced this Burn Study's Investigators in their decision to halt further enrollment in the Burn Trial. The Burn Patient Rehabilitation Trial investigators held that it was unlikely that a treatment effect would have been observed if the Burn Rehab study continued. That consideration was made even if a full complement of the Trial's burn patient enrollment numbers were achieved (i.e. 150 total study subjects had been planned). Thus, an argument for halting the study for reasons of futility was developed and carried out in discussions with our program officer and the HRPO.

The second observation, one that arose directly from the Burn Rehab study itself, dealt with the challenges encountered by the investigators with an occasional observation within the "intervention" arm of the study, of not being able to deliver as many of the the prescribed early rehabilitation sessions as indicated by the protocol. The team meeting discussions postulated that given the number of operative procedures the study subjects underwent, these occasional missed sessions might need an alternate protocol approach for "making up the rehab session". It was not clear at the time of the ongoing study enrollment if the occasional missed sessions would have eventually blocked the study from showing a difference between the two arms.

It was considered an important aspect however. The investigators postulated that if a larger trial were to be considered such a pattern might be sufficient to possibly affect overall outcome. The Burn Rehab study's observation that indeed, Burn ICU patients undergo many operative procedures. Whether a national pattern of an occasional missed physical therapy session due to frequent operative procedures was in existence was unclear from the Burn literature or Physical Therapy literature. There is a necessity of frequent planned operative interventions for the purposes of burn wound debridement, soft tissue coverage or related procedures often precluded delivery of the rehabilitation protocol. These multiple planned surgeries were on occasion sited by the physical therapists involved with the protocol's delivery for study subjects to affect the scheduled rehabilitation sessions for patients randomized to the early, aggressive intervention arm of the Burn Rehab study. What was occasionally reported by the Physical Therapists in these instances was that because of an operative procedure, patients would often be too sedated as they were recovering from surgery to participate in prescribed rehabilitation therapy. As well, it was observed that study subject's delivery of early rehabilitation sessions would be might rarely be held if the patient was about to go to the operating room or would be unavailable for participation because the scheduled rehabilitation session conflicted with the patient's operation.

The suspicion that there would be a disruptive effect of multiple operative interventions was a concern of the investigators over the study was being conducted. Such frequent operative interventions were not previously encountered when the rehabilitation intervention was studied in medical ICU patients (which served as the prototype for the study structure conducted in burn patients). Ultimately, this feature of standard burn care became a significant obstacle to the delivery of the study intervention in this population.

Collectively, the two observations, as stated above (two similar studies being published with a negative outcome; possible effect of operative procedures associating with an inverse number of physical therapy sessions) resulted in the original study being placed on administrative hold and subsequently closed. Enrollment in the "Early ICU Rehabilitation Therapy for the Critically Injured Burn Patient" was terminated by the Principle Investigators. This step was undertaken to allow for reconfiguration and refocus of the investigative effort and resources of this grant award. The investigators wished to maximize the impact of remaining resources to build an improved clinical trial design for future investigations in this area.

Therefore, a new set of tasks was designed within the original Scope of Work addressing the frequent operative needs of Burn patients.

In the latter phase of this grant award, the investigators designed the framework for a future Burn population Rehab study structure, by carefully examining a national hospital administrative database for the frequency of operative procedures among burn ICU patients. We proposed to examine medical records within a large national hospital database (Vizient's database) to identify standard care delivery patterns reflected by outcome analysis. As noted, a suspicion of investigators to the rehabilitation efforts within the original Burn patient Early ICU Rehabilitation study's intervention arm was the unavailability of the critically ill patient to participate in reconditioning sessions, whether due to the injury or as a consequence of supportive care. Developing strategies to mitigate the impact of this unavailability was the goal of the second phase of this grant award. To the extent that periods of unavailability are due partly as a consequence of variability in standard burn practice, understanding and minimizing such variability has the potential to translate into more timely recovery of the severely injured and burned patient.

Thus, critical to the effort of revising our investigative protocol, was the proposal of the 2nd Phase of this grant award. This 2nd Phase of the Study was designed to develop a deeper understanding of clinical factors surrounding the "repetitive and re-look" procedures within the Critically Ill Burn Patient Population. In this final phase of this grant award, the Vizient

database review study sought to increase the medical literature's understanding of what contributes to variability in practice surrounding the care of burn patients with conditions necessitating multiple planned operations. This insight will be essential to the future design and execution of a revised Burn ICU Rehabilitation study (a future grant application). The optimal future design will more effectively coordinate interventions among and across critical care, surgical, nursing, physical therapy, respiratory therapy and related disciplines.

Accordingly, the investigators proposed that the second phase of the grant award's continuation plan fell within the scope of work of the original proposal and would be essential to developing future clinical trial intervention arm strategies to optimize the care of the severely burned patient.

One model system for studying the phenomenon of variability in practice in the setting of multiple planned operations was to query the Vizient administrative database to determine regional frequency patterns that require critically ill burn patients to return to the operating room during their initial hospitalization. The concept of return to the operating room for burn surgical therapies was developed as a management strategy for patients in which the constellation of injuries precludes definitive repair at the time of ICU admission or index operation, when the patient is not sufficiently stable to tolerate a definitive operation, when there is concern that all injuries may not be accurately identified at the index operation, or in an effort to stage the needed surgical therapy.

Subsequently, use of this strategy has become more commonplace and applied along local practice rather than national standards. As a result, the investigators held concern that the use of return procedures to the operating room for burn patients had variability at the institution level and possibly at the practitioner level within institutions. The more extensive the burn injury, the suspicion was that there would be a greater volume of operating room visits but with variability. These needs for multiple operating room visits were suspected alternatively to simply correlate with longer duration of mechanical ventilation, greater intensive care unit (ICU) and hospital lengths of stay (LOS), and higher utilization of operating room resources. In turn, because of this prolongation of hospitalization, these patients also were suspected to appear at increased risk of complications. Adding to and confounding variability in the return to the operating room, is potential lack of availability of operating room resources to accommodate multiple operations and inconsistency in patient management between operating rooms sessions (such as approaches to ventilator weaning, sedation, and mobilization). Cumulatively, this variability translates not only into increased resource expenditure but potentially poses a barrier to early rehabilitation and restoration of function.

One aspect of the previous randomized-controlled early ICU rehabilitation intervention study in burn patients that prompted the investigators to terminate the overall study was the variability across trial enrolling centers in the practice of either returning to the operating room for various procedures or an operative procedure at bedside. The scheduling of the operative procedure was then listed as a reason for study patients, particularly on the intervention arm, not to receive ICU mobility therapy. In order to build a future clinical trial, that may best address these operative needs of burn patients accommodating frequent operative procedures, but also structure in rehabilitation sessions, we sought to examine the frequency of operative procedures for burn patients within the Vizient clinical administrative database.

The hypothesis of the 2nd Phase of this grant award was that variation in practice among patients requiring repetitive operative therapy, when appropriately controlled for severity of burn and comorbid illness, would be shone to negatively impact physical therapy days. If such a pattern were established by examination of hospital data within the Vizient database, future efforts in the design of a new clinical trial, might need to require a standardization of these aspects of care, in order to have potential to more effectively delivery rehabilitative interventions.

Phase 2 of Grant Award's Specific Aims:

The Phase 2 of the Grant Award's proposal consisted of three highly interrelated specific aims:

In Specific Aim 1, we will utilize highly granular administrative databases to demonstrate and quantify inter-institutional variability in a model system - use of return to operating room procedures in critically ill burn patients.

In Specific Aim 2, we will utilize the information obtained in SA1 as a foundation for developing a standardized approach to planned return operating room procedures for critically ill burn patients.

In Specific Aim 3, we will adapt and synthesize a written pilot approach developed in SA2 to optimizing rehabilitative care in patients sustaining significant burn injuries and who require multiple planned operative interventions.

METHODS: We developed analytic models employing the Vizient (Oakbrook, Illinois) database. Administrative coding data (MS-DRGs) were used to identify patients with the principal diagnosis of burn injury **(Table 3**). Data were examined from patients discharged between the beginning of Q4 2015 and end of Q1 2018. Codes also were identified for procedures, complications, post-discharge destination, and survival. Mean resource intensity of participating academic medical centers was determined using risk-adjusted estimates of outcomes. Mortality risk was determined using a multivariable approach that incorporated patient-level demographic and clinical variables and institution-level resource intensity.

From investigator observations within the clinical trial portion of this grant award, we observed that the delivery of the intervention's arm sessions were often not completed due to the report of: (1) patient about to go to the operating room, (2) was in the operating room or (3) had just returned from the operating room.

Therefore, the purpose of this phase of the grant award was to produce a more complete picture of national practice on this aspect of care by examining the Vizient database. With this work now completed, the results will allow the investigators to guide, more effectively, the design of a future trial with realistic expectations for early ICU rehabilitation care delivery.

In this latter phase of the grant's study, the Vizient database was queried to define a population of patients receiving care for a burn injury. Within this population, we explored administrative codes to determine whether an inverse relationship existed between the delivery of physical and occupational therapy sessions and the frequency of operative interventions. Additionally, due to the Vizient data's organization by US national regions, we were able to determine whether an association existed between operative interventions and the lack of delivery regular physical therapy sessions with regional comparisons. By controlling for other factors, we were able to query whether some health care environments were more effective at minimizing these interruptions than others.

By analyzing potential differences in outcomes, nationally and by US region, it became possible to determine whether (1) a relationship between numbers of operative procedures and numbers of physical therapy sessions existed. Possibly more importantly, these regional comparisons allowed for an exploration between frequency of operative procedures, frequency of physical therapy sessions, and outcome.

Within the Vizient organization, there are approximately 160 separate institutions which now participate in mapping of charge codes. Ancillary services such as Physical Therapy within these hospitals' Vizient records, are captured which allowed for exploration of relationships of physical therapy days and outcomes.

For this aspect of the grant, the overall purpose was to evaluate the address whether a pattern of high operative procedures associated with smaller numbers of physical therapy days (an inverse relationship).

Patients receiving care for a burn-related injury for this analysis were limited to adults as defined by age equal to or greater than 18 at the time of admission for the burn injury.

Table 3

MS-DRG	MS-DRG Description
927	Extensive burns or full thickness burns w MV 96+ hrs w skin graft
928	Full thickness burn w skin graft or inhal inj w CC/MCC
929	Full thickness burn w skin graft or inhal inj w/o CC/MCC
933	Extensive burns or full thickness burns w MV 96+ hrs w/o skin graft
934	Full thickness burn w/o skin grft or inhal inj
935	Non-extensive burns

Within the confines of the design of the data captured by the Vizient administrative database, we were not able to assess Trauma Injury Scores for patients identified as receiving care for a burn injury from this database. However, data accounted for burn severity and co-morbidities.

Outcome parameters extracted, per patient, included in-hospital mortality, ICU days, total hospital days, continuous renal replacement therapy and hemodialysis days as well as ventilator days. Operative procedures were determined by specific codes (see list of operative procedures the APPENDIX).

RESULTS:

We analyzed data from 27,207 subjects; 15,358 (56.44%) of whom received at least one in-patient physical therapy day. Race and gender distribution is in **Table 4**.

The average or mean value of general outcomes are contained in **Table 5.**

From this cohort of US Burn patients we were able to establish those patients who received care at any time point of their hospitalization within an ICU setting. **Figure 2** depicts the distribution of the adapted total body surface score for patients identified in the Vizient database by the MS-DRGs above. **Figure 3** demonstrates the relationship between the patients' adapted TBSA score and their mortality.

There were 3,196 distinct procedure codes captured within these 27,207 hospitalizations. Of the 15,358 patients who received at least one inpatient PT day, there were 94,531 total procedures done. Of the 15,358 patients who received at least one inpatient physical therapy day, there were 12,440 who received at least one procedure. Data demonstrated prior to adjustments for burn severity or co-mobidities, that the majority of the patient population that were captured demonstrated a low adapted TBSA score and a low overall mortality risk.

At the national level there was no inverse relationship between number of procedures performed and the number of physical therapy sessions received.

There were regional differences observed in both the mean number of daily physical therapy sessions and the mean number of procedures ($p<0.0001$ for both PT sessions and procedures). There was an association between the number of physical therapy days and ventilator days (β coefficient = 0.0534, p-value <0.0001, positive relationship), ICU days (β coefficient = 0.0201, p-value <0.0001, positive relationship), overall hospital days (β coefficient = 0.0753, p-value <0.0001, positive relationship), and mortality (OR = 0.876, p-value <0.0001, negative relationship). Lastly, within the region to region comparisons, within the Vizient data was a positive (not inverse) relationship (β coefficient = 0.0426, p-value <0.0001) between the number of procedures and the number of physical therapy days. At the regional level there was no inverse relationship between number of procedures performed and the number of physical therapy sessions received.

Table 4 Race/Sex by region

	Hosp Region Desc						
Race Desc	Mid-Atl..	Mid-Co..	Midwes..	New England	Southe..	Western	Grand Total
Asian	3.60%	1.98%	1.81%	2.51%	0.89%	4.76%	2.46%
Black	27.78%	19.03%	21.74%	10.96%	24.17%	7.77%	20.09%
Other	15.95%	16.87%	7.97%	15.65%	14.32%	19.38%	15.02%
White	52.68%	62.12%	68.49%	70.88%	60.62%	68.09%	62.43%
Grand Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

% of Total Number of Records broken down by Hosp Region Desc vs. Race Desc. The data is filtered on Sex Code, which excludes No Information. The view is filtered on Race Desc, which excludes Declined, Unavailable and Unknown.

Table 5 Average Outcomes by Region

	Hosp Region Desc					
	Mid-Atl..	Mid-Co..	Midwes..	New England	Southe..	Western
Number of Records	5,540	4,157	4,034	1,282	7,397	4,797
Avg. Age 90 plus truncated	36	39	37	40	36	37
Avg. Chemotherapy Flag	0.00%	0.00%	0.05%	0.00%	0.00%	0.00%
Avg. Days To Readmit	9	7	10	9	10	9
Avg. Dialysis Flag	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Avg. Expected Direct Cost	11,786	17,502	14,440	15,044	14,641	15,846
Avg. Death Flag	1.57%	3.27%	2.83%	2.34%	2.87%	2.56%
Avg. Expecteddead	2.11%	3.23%	2.63%	2.34%	3.05%	2.77%
Avg. LOS	7.05	9.04	7.67	7.85	7.77	10.17
Avg. Expectedlos	7.24	9.14	8.28	8.82	8.47	8.67
Avg. ICU Days	3.61	4.36	2.49	2.39	2.52	3.78
Avg. Msdrg Weight	3.10	3.98	3.51	3.44	3.55	3.57
Avg. Otdays2	1.71	2.86	3.47	2.54	3.42	2.31
Avg. Planned Admissionfl..	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Avg. Ptdays2	1.95	2.56	3.08	2.00	3.18	2.66
Avg. Rrtdays2	0.66	1.49	1.42	0.73	1.25	1.66
Avg. Ventdays2	0.35	0.65	0.49	0.55	0.47	0.83
Avg. SUM of DirectCost	12,677	14,669	11,652	9,977	13,381	18,214

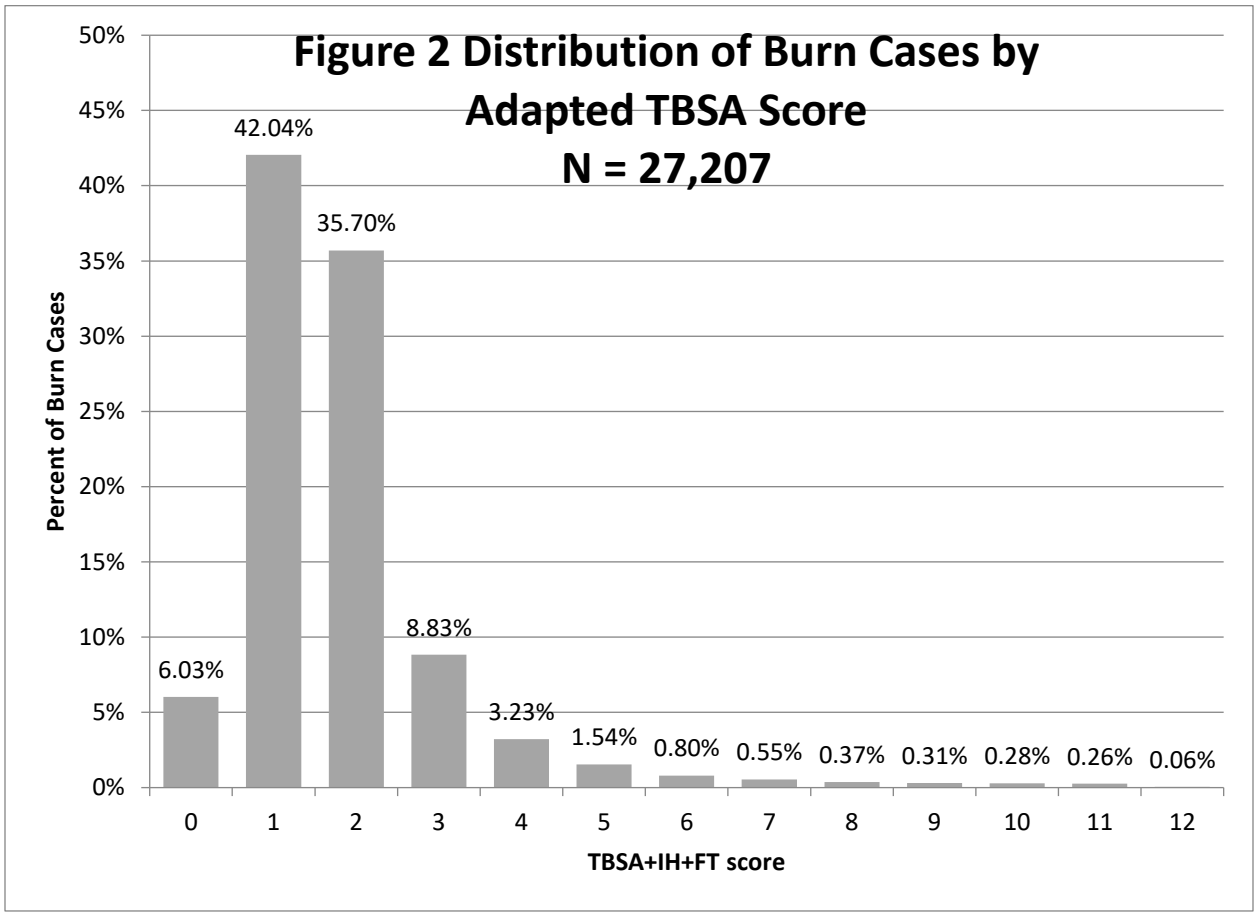
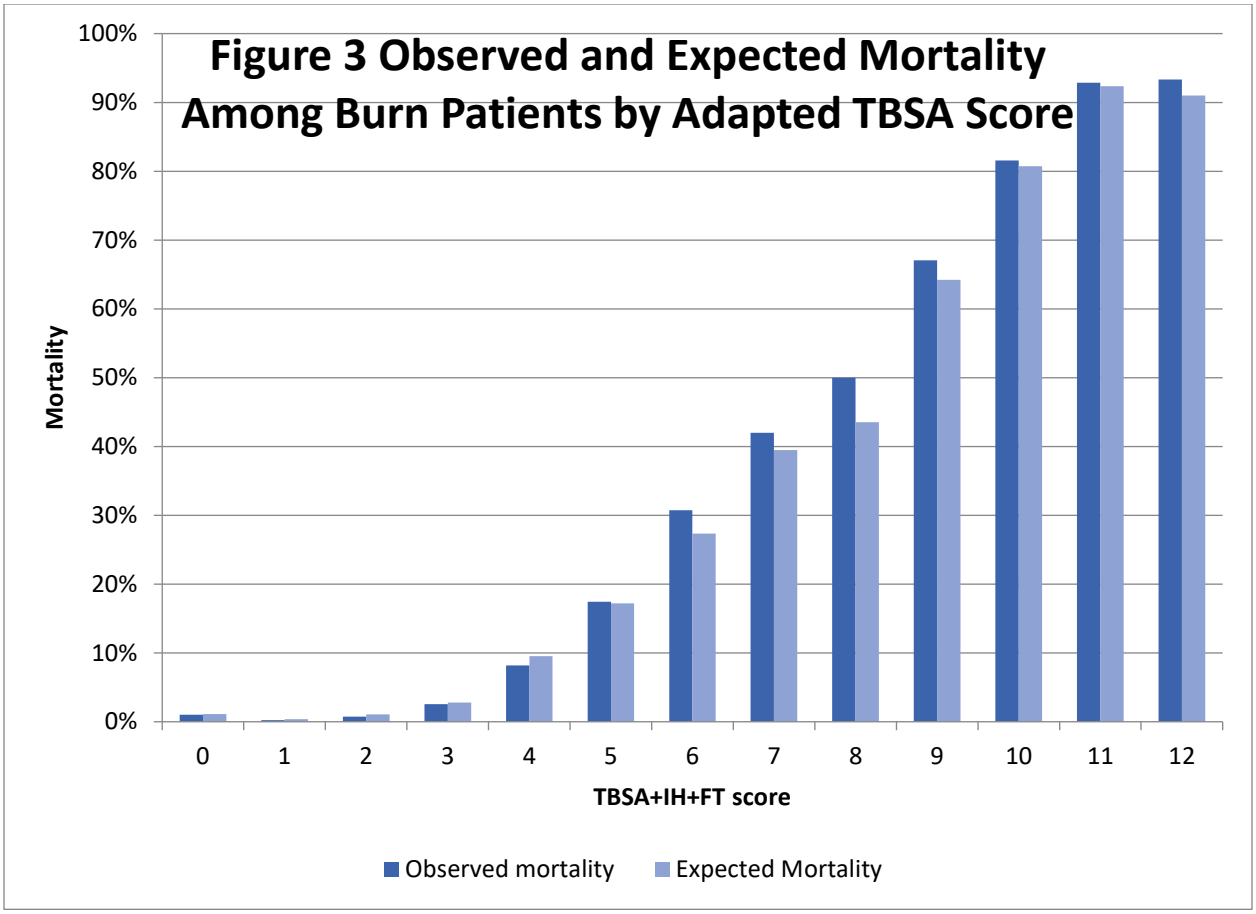


Figure 2 Distribution of Burn Cases by Adapted TBSA Score
N = 27,207
Percent of Burn Cases
50%
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
42.04%
35.70%
8.83%
6.03%
3.23%
1.54%
0.80%
0.55%
0.37%
0.31%
0.28%
0.26%
0.06%
0
1
2
3
4
5
6
7
8
9
10
11
12
TBSA+IH+FT score



The Vizient Database was not able to allow us to determine whether a calendar effect existed for the pattern of physical therapy delivery (whether or not weekend delivery of OT/PT was associated with better or worse outcomes).

Overall database limitations included:

1. Although the Vizient database provided an opportunity to estimate the number of patients with burn injuries receiving care within the Vizient Hospitals, the data fields within the database did not capture the mechanism of injury of the burn, specifically the nature of any thermal injuries.

2. The Vizient database provides de-identified patient demographic information. There is a possibility that within the Vizient Hospitals, a single patient received care in more than one hospital for the same episode of burn-injury.

CONCLUSIONS:

We were unable to demonstrate a relationship between a higher of procedures over the course of a burn patient's hospitalization and a decrement in physical therapy days.

Therefore, for future study structure, an increased consideration of flexibility for early ICU rehabilitation may be considered in arranging for procedures, but an early delivery of rehabilitation is potentially feasible since higher numbers of procedures did not negatively affect the administration of physical therapy sessions to a large population of burn patients.

As this field of early ICU Burn patient rehabilitation grows, along with its related field of early ICU rehabilitation in general, an emerging theme is that a linked approach to rehabilitation throughout the inpatient and outpatient stay might be the optimal delivery.
Success however for such an approach may be best measured at the six and twelve month post-index hospitalization discharge.

For medical ICU survivors, the floor level rehabilitation and outpatient rehabilitation are not tightly linked in the United States. For Burn patients however, the continuum appears to be more tightly linked.

The initial clinical trial design for this grant award did not contain a provision for a strong link of aggressively structured, homogeneously designed rehabilitation regimens to continue into the outpatient arena for the Burn ICU patient survivors. Such future design inclusions may be necessary to track patients specifically with capture of the emotional positivity, cognition and memory as these factors may be emerging from the literature as independent predictors of optimal post-ICU recovery.

The investigators are deeply and sincerely grateful to our patients and families to be able to work with them in such horrifically difficult time of crises as is a severe burn injury. We are also grateful to the members of our research teams, our local IRB members and institutional research administrators. Lastly and importantly, we are grateful for the opportunity with this grant award to contribute knowledge for the care of our injured military personnel and wish to specifically thank our colleagues within the Department of Defense, US Army, the Congressionally Directed Medical Research Program (CDMRP), and its Program Managers and Science Officers.

◦ **What opportunities for training and professional development has the project provided?**

The findings of the first and second phase of this grant will serve to purposefully guide future trial design in the investigation of early ICU rehabilitation therapy.

◦ **How were the results disseminated to communities of interest?**

Much of the related work from this grant award contributed to a number of publications regarding the approach to early ICU rehabilitation care for the critically ill and injured patient. As well, Dr. Morris presented to the Society of Critical Care Medicine's yearly meeting on the state of early ICU rehabilitation specifically for Burn ICU patients.

4. Impact

◦ **What was the impact on the development of the principal discipline(s) of the project?**

Possibly the most impactful aspect of this grant award's work was the establishment of the relationship by work with the Vizient national database, between the numbers of procedures experienced by a critically ill burn patient during the index hospitalization and their receipt of physical therapy. By the work completed by this research team examining the Vizient database's information on burn admissions, an inverse relationship was not demonstrated by the national data. Therefore, this positively affects future clinical trial design in that, if there were to be a future trial, it may proceed with intervention therapies not having to worry that overall impact of procedures on delivery of physical therapy, may occur if the number of procedures is high per patient.

What was the impact on other disciplines?

Although certainly there are nuances to the care of the injured burn patient, there is much overlap to the care of the general ICU patient's rehabilitation needs as gleaned from work with critically ill burn patients.
Therefore, the work of this award is not only applicable to the population of critically ill and injured burn ICU patients but rather to all ICU patients.

◦ **What was the impact on technology transfer?**

Nothing to Report."

What was the impact on society beyond science and technology?

Information based upon the design of the grant award's clinical trial protocol and the Vizient database analysis will lend directly to and contribute to the development and design of any future

trial undertaking an intervention of early ICU Rehabilitation strategies within the critically ill or injured ICU Burn patient population.

5. Changes/Problems

◦ **Changes in approach and reasons for change**

There were changes to the original grant award that arose. The original trial was halted, as per usual clinical trial conduct, if other medical literature arises after the start of a trial that lends the investigators to believe the any further patient enrollment will lead to a futile attempt to achieve the primary outcome of the clinical trial. Such a situation arose here, with two other similar trials demonstrated no effect based on a similar design. Therefore, the investigators reinvested their efforts through help with the HRPO, local IRBs, program officers and science officers to redirect the grant award support to a national database analysis of critically ill burn patients.

◦ **Actual or anticipated problems or delays and actions or plans to resolve them**

Nothing further to report.

◦ **Changes that had a significant impact on expenditures**

The grant award's budget was reformulated to direct effort to the completion of the Phase 2 of the grant award.

◦ **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

Nothing to report other than the early end of the clinical trial and the shift of the investigators' efforts to the national database examination.

6. Products

Publications, Abstracts, and Presentations:

a. Manuscripts:

1. Lay Press:

   Nothing to report

2. Peer-Reviewed Scientific Journals:

   Nothing to report

3. Abstracts:

   Nothing to report

b. Presentations: by Peter Morris, MD (PI)

1. February, 2018. Society of Critical Care Medicine, International Meeting, "Managing Critical Burns Rehabilitation"

Reportable Outcomes

Please see above for discussion regarding analysis of Vizient's national database and the potential analysis' effect to guide future clinical trial design.

Other Achievements

Nothing to report

References

1. Morris PE, Berry MJ, Files DC, et al. Standardized Rehabilitation and Hospital Length of Stay Among Patients With Acute Respiratory Failure: A Randomized Clinical Trial. *Jama.* 2016;315(24):2694-2702.
2. Moss M, Nordon-Craft A, Malone D, et al. A Randomized Trial of an Intensive Physical Therapy Program for Patients with Acute Respiratory Failure. *American journal of respiratory and critical care medicine.* 2016;193(10):1101-1110.

Appendices

Appendix #1
Clinical Trial Protocol

Appendix #2
List of Procedures used in the Vizient Database query

Study Title:

Early ICU Standardized Rehabilitation Therapy for the Critically Injured Burn Patient

Principal Investigator:

Peter E. Morris, M.D., Wake Forest University School of Medicine

Co-Investigators:

James Holmes, M.D., Wake Forest University School of Medicine
Michael Berry, Ph.D., Wake Forest University H&ES (Reynolda Campus)
L. Douglas Case, Ph.D., Wake Forest University PHS
Bradley Freeman, M.D., Washington University, St. Louis
Bruce Cairns, M.D., University of North Carolina, Chapel Hill

Funding Source: Department of Defense - Army

Background and Significance:

During the last several years research groups including ours have published data which demonstrates the feasibility and safety of initiating aggressive rehabilitation in critically ill patients while they require mechanical ventilation. The unique rehab team of critical care nurse, physical therapist and nursing assistant provide the daily sessions interacting with the bedside team. The development of these data provided the background for this grant which will initiate early ICU exercise with passive range of motion, physical therapy and strength training sessions for mechanically ventilated burn patients. The Mobility Team provides the unique capability to safely and regularly administer sessions which will be shown to halt the deterioration of muscle size, architecture and function, typically experienced by critically ill severe burn patients who require mechanical ventilation. The standardized approach to strength assessments during hospitalization and post-hospital follow-up (dynamometer, hand grip, Short Performance Physical Battery (SPPB)), will provide specific details linking the intervention with direct, object evidence of alteration of muscle pathophysiology. Our group has published an association between the receipt of early ICU rehab and decreased hospital readmissions over the first year for survivors of critical illness. This study will draw on these experiences and establish data to support the safety and efficacy of early ICU delivery of rehab therapy including strength training, to mechanically ventilated severe burn patients.

Acute Respiratory Failure survivors experience difficulties in function and quality of life for months following hospital discharge

Most outcomes research regarding acute respiratory failure has examined short-term endpoints such as in-hospital mortality and morbidities, yet the human cost of these illnesses extends well beyond the period of hospitalization. In a large prospective cohort study of 1,075 survivors of acute respiratory failure, at five months post-discharge 48 percent needed help with at least one activity of daily living, and 27 percent reported their quality of life as fair or poor [15]. Twenty-four percent of patients reported needing assistance with more activities of daily living five months post-discharge as compared to pre-hospitalization [4] . Several investigators have reported on the decrease in health-related quality of life in survivors of the acute respiratory distress syndrome (a subset of ARF), [5;6] but the reasons for this impairment seemed disproportionate to the improvements in objective pulmonary function tests. In one of the most complete follow-up study of survivors of the acute respiratory distress syndrome to date (86 percent with follow-up data at one year), there was a high prevalence of persistent muscle weakness and fatigue[1]. These data illustrate the deleterious effects that acute respiratory failure has on post-hospital patient function and quality of life. They also signal the importance of including measurements of function and quality of life in the study design of an intervention study such as Standardized Rehabilitation Therapy, in order to capture not only the immediate hospital endpoints of LOS, but to more importantly to capture the intervention's effect on post-hospital patient status.

ICU Care imposes immobility which contributes to weakness

Deconditioning may be described as the multiple changes in organ system physiology that are induced by inactivity and reversed by activity [7] . In the clinical setting, acute deconditioning refers to changes that occur within days to a few weeks of a sudden decrease in activity [8;9]. Concern regarding bedrest in hospitalized patients is not new [10 11 12] . In current

practice, admission to an ICU implies almost certain imposed immobility, particularly with mechanical ventilation. In numerous reports from zero gravity (NASA) research, the immobilization of healthy subjects, i.e. without an acute illness, induces muscle atrophy mechanisms with resultant weakness in otherwise normal muscles. However, in addition to immobility, in a new ICU weakness paradigm, the weakness seen in patients with ARF results from multiple potential injuries [8;9;13;14]. Another potential injury is the exposure to systemic inflammation. Injury caused by immobility and acute inflammation may be accentuated by ICU medications such as corticosteroids and neuromuscular blockers[15], as well as hyperglycemia [16]. For those patients with ARF who survive mechanical ventilation, there are reports of substantial difficulties with deconditioning, muscle weakness, joint contractures and dyspnea [1;17;18] , and the most severe forms have become known as critical illness polymyoneuropathies (CIP) [19] .

Evidence for direct role of inflammation in muscle-wasting and inhibition of muscle function

Studies suggest that inflammatory mediators inhibit muscle function, although the mechanisms by which this occurs are not fully known [20-22]. Cytokine effects on muscle have been studied in conditions such as aging, HIV, uremia, and cancer demonstrating loss of muscle mass [23-25]. Skeletal muscles express tumor necrosis factor (TNF) receptors and binding of TNF to these receptors adversely alters muscle fibers. In animals, TNF overexpression causes skeletal myopathy and endothelial dysfunction, leading to myocyte apoptosis and decreases in skeletal muscle mass with subsequent weakness [26] . In animal models, TNF decreases force of contraction [27] as well as producing a catabolic effect, disrupting myogenesis with this protein loss [28]. A recent study showed that TNF gene transfer resulted in muscle atrophy as well as inhibition of muscle regeneration following injury[29]. In humans, *in vivo* myosin heavy chain protein synthesis rates correlate negatively with muscle protein expression of TNF[30], and with plasma concentrations of c-reactive protein (CRP), interleukin-6 (IL-6) and soluble TNF-Receptor II[31]. These results strongly suggest that elevated cytokine levels via immune system activation induce muscle proteolysis and also may inhibit muscle protein synthesis.

Exercise may be an anti-inflammatory intervention:

In chronic disease such as chronic heart failure (CHF) [2] and frailty of aging [3;32], exercise has been associated with a reduction in cytokine concentration and improvement in function compared to non-exercised controls. As well, there are clinical data which may link exercise to an attenuating effect on acute inflammation [33;34]. The pattern of cytokine responses to exercise looks like the "resolution" phase of acute inflammation in that in exercise the classic proinflammatory cytokines, TNF and IL-1, do not increase and typically, IL-6 is the first cytokine present in the circulation during exercise. Other cytokines, described as anti-inflammatory in nature are also found to rise in response to exercise, such as IL-10, Interleukin 1 receptor antagonist (IL-1ra) and soluble TNF-Receptor (sTNF-R). With the similarities seen between the cytokine pattern of exercise with the "resolution" phase of acute inflammation, many have speculated on exercise's therapeutic potential in acute inflammatory conditions [35] . The proposed study will pursue whether Standardized Rehabilitation Therapy alters biomarkers of inflammation and whether these alterations will associate with functional improvements.

Significance:

Early ICU Rehabilitation, optimizing principles of physical therapy and exercise training, has great potential to restore lost function in critically ill burn patients. Traditionally, however, aggressive rehab efforts have not started until after weaning from mechanical ventilation, inevitably prolonging and enhancing deconditioning. Skeletal muscle dysfunction in Burn ICU (BICU) patients with ARF suggest that participating in organized rehabilitation therapy program, while still on mechanical ventilation will be safe and improve outcomes. Our preliminary data suggest that rehabilitation initiated while on mechanical ventilation in critically ill medical patients shortened hospital length of stay. Therefore, standardized rehabilitation therapy, started early in the BICU could provide the optimal preventative, as well as therapeutic effect, to counter the deleterious effects of immobility, neuromyopathic drugs, and systemic inflammation for Burn patients with ARF. Our unique team combines the care and safety provided by Burn/Trauma Surgeons (Holmes, Cairns, Freeman) with Critical Care Trials experience (Morris, Case) and innovative therapy combining physical therapy and exercise physiology strength training principles (Berry) and long-term functional outcome follow-up (Duncan). We designed a mechanism to realize the potential of rehabilitation therapy by daily delivery of safe amounts of rehabilitation therapy. If this study's aims are met and rehabilitation therapy with BICU initiation is successful in reducing hospital length of stay and long-term outcomes, this new knowledge will significantly impact how BICU services will be delivered to future Burn patients with ARF.

Objectives/Specific Aims:

1) Standardized Rehabilitation Therapy (SRT) will shorten hospital stay in burn patients with ARF. 2) SRT will prevent loss in muscle size and loss of architecture during critical illness of severe burns. 3) SRT will improve objective functional measures and quality of life at 3, 6, 12, 24, and 36 months post-enrollment. ICU care imposes immobility which contributes to weakness. Deconditioning may be described as the multiple changes in organ system physiology that are induced by inactivity and reversed by activity. In the clinical setting, acute deconditioning refers to changes that occur within days to a few weeks of a sudden decrease in activity. Concern regarding bedrest in hospitalized patients is not new. In current practice, admission to an ICU implies almost certain imposed immobility, particularly if mechanical ventilation is required. In numerous reports from zero gravity (NASA) research, the immobilization of healthy subjects, i.e. without an acute illness, induces muscle atrophy mechanisms with resultant weakness in otherwise normal muscles. However, in addition to immobility, a theory within a new ICU weakness paradigm, is that the weakness seen in Burn ICU patients with ARF results from multiple potential mechanisms other than immobility. Another potential injury to the neuromuscular system is the systemic inflammation experienced by severe burn patients. For those patients with ARF who survive mechanical ventilation, there are reports of substantial difficulties with deconditioning, muscle weakness, joint contractures and dyspnea and the most severe forms have become known as critical illness polymyoneuropathies (CIP). There is evidence for a direct role of inflammation in muscle-wasting and inhibition of muscle function. Studies suggest that during systemic inflammation, inflammatory mediators inhibit muscle function, though the mechanisms by which they cause protein degradation are not fully elucidated. Cytokine effects on muscle have been studied in conditions such as aging, HIV, uremia, and cancer demonstrating loss of muscle mass. Skeletal muscles express TNF receptors and binding of TNF to these receptors adversely alters muscle fibers. In animals, TNF overexpression causes skeletal myopathy and endothelial dysfunction, leading to myocyte apoptosis and decreases in skeletal muscle mass with subsequent weakness. In animal models, TNF decreases force of contraction as well as producing a catabolic effect, disrupting myogenesis with this protein loss. A recent study showed that TNFα gene transfer resulted in muscle atrophy as well as inhibition of muscle regeneration following injury. In humans, in vivo myosin heavy chain protein synthesis rates correlate negatively with muscle protein expression of TNFα48, and with plasma concentrations of CRP, IL-6 and sTNFRII. These results strongly suggest that elevated cytokine levels via immune system activation induce muscle proteolysis and also may inhibit muscle protein synthesis. In contrast to the negative muscle effects of cytokines such TNF, “exercise” has been considered as an anti-inflammatory intervention. In chronic disease such as CHF and frailty of aging, exercise has been associated with a reduction in cytokine concentration and improvement in function compared to non-exercised controls. As well, there are clinical data which may link exercise to an attenuating effect on acute inflammation. The pattern of cytokine responses to exercise looks like the "resolution" phase of acute inflammation in that in exercise the classic proinflammatory cytokines, TNF and IL-1, do not increase and typically, IL-6 is the first cytokine present in the circulation during exercise. Other cytokines, described as anti-inflammatory in nature are also found to rise in response to exercise, such as IL-10, IL-1ra and sTNF-R. With the similarities seen between the cytokine pattern of exercise with the "resolution" phase of acute inflammation, many have speculated on exercise's therapeutic potential in acute inflammatory conditions. The proposed study will pursue whether Standardized Rehabilitation Therapy alters effects of inflammation (muscle size, muscle architecture by ultrasound, and serial strength measurements in the burn patient) and whether these alterations will associate with functional improvements. For patients with ARF there is variability of administration of in-hospital rehabilitation strategies, and there is a lack of guidelines for an organized ICU rehabilitative approach. Despite a general notion by many groups that mobility and exercise may play a strong role in facilitating a return to pre-hospital functional status for Burn patients with ARF, the exact manner in which to administer mobility and the appreciation of the safety of mobility maneuvers administered to these critically ill patients are not clear. Overall, rehabilitation research for BICU patients has not received much attention, particularly in the area of applying systematic strength training. To date reports of early ICU rehab strategies have reported feasibility, safety and improvements in hospital outcomes. Discharge Activity of Daily Living Scores, walking distance and one year readmission rates have been reported to improve with such early administration of these techniques. No current consensus statements exist for the timing or content of BICU or hospital rehabilitative strategies for burn patients with ARF. In this setting, burn centers have a varied approach to these patients’ rehabilitative needs. The proposed work has the potential to serve as the standard for practice, to prioritize the in-hospital rehabilitation of burn patients with ARF, and produce improvements in these patients’ functional status and quality of life.

Setting:

Study participants will consist of 150 severe burn patients with ARF admitted to the Burn Intensive Care Units of Wake Forest University Baptist Medical Center, Washington University at St. Louis Medical Center, and University of North

Carolina at Chapel Hill Medical Center.

Methods/Measures:

Design: The proposed study will be a patient-randomized, multi-centered, with blinded assessment analysts, Phase III investigation with two arms: 1. Intervention (Standardized Rehabilitative Therapy initiated in the BICU, administered throughout hospitalization) and 2. Control (Usual Care). Patients will remain in the study from enrollment, through their hospital discharge and through a 36-month follow-up period. Study subjects randomized to the standardized rehabilitative therapy arm will receive Standardized Rehabilitation Therapy within the hospital only, from the time of enrollment through hospital discharge, including days spent in a regular floor bed. There will be no delivery of Standardized Rehabilitation Therapy from hospital discharge through the 36-month follow-up period, although both arms will undergo functional testing, HRQoL assessments and muscle ultrasounds at hospital discharge, 3, 6 and 12-months post-enrollment, performed by research analysts blinded to the arm of the study.

Subjects: Study participants will consist of 150 severe burn patients with ARF admitted to the Intensive Care Units of Wake Forest University Baptist Medical Center, Washington University at St. Louis Medical Center, and University of North Carolina at Chapel Hill Medical Center. A study nurse will screen newly admitted BICU patients for acceptability into the study. Patients who meet the entry criteria will be invited to participate. Inclusion and exclusion criteria are listed in Table 1. These criteria were designed to target a population in which a rehabilitation program would have reasonable chances of success of achieving the patient's pre-acute illness ambulatory status.

Feasibility:

Randomization: Patients will be stratified by center and Baux Score (≤ 60, >60) and assigned within strata using variably sized permuted block randomization to balance burn severity and organ dysfunction between the two study arms. The generated file will be stored in an area of the study's server that is only accessible by the study programmer. An application will be written to allow on-line randomization via the study website.

Study Arms:

Standardized Rehabilitation Therapy (SRT):

Participants randomized to the Standardized Rehabilitation Therapy arm will receive three types of interventions - Passive Range of Motion (PROM), Physical Therapy (PT) and Progressive Resistance Exercise (PRE). The SRT protocol will be administered by the BICU Mobility Team within 80 hours of ventilation and contains four levels of activity therapy. This Protocol will be delivered 7 days a week. Patients will be assessed daily and if appropriate will receive 3 separate sessions of activity each day. When patients are unconscious, they will receive level I of the protocol which will consist of three sessions of only PROM. When the patient regains consciousness, the three sessions per day will consist of one PROM, one physical therapy session and one PRE strength training session depending on the subject's level of consciousness. Once the patient gains consciousness, level II of the protocol will be initiated. Consciousness will be determined by the responses to the following commands: "Open (close) your eyes", "Look at me", "Open your mouth

Table 1.

Inclusion Criteria

Age ≥ 18 years
Mechanically ventilated via an endotracheal tube or mask (via tracheostomy is acceptable if performed emergently due to burn injury)
Burn injury requiring ICU admission

Exclusion Criteria

Inability to walk without assistance prior to burn injury (use of a cane or walkers not exclusions)
Cognitive impairment prior to burn injury (non-verbal)
Acute stroke
Body mass index (BMI) >50
Neuromuscular disease that could impair ventilator weaning (myasthenia gravis, ALS, Guillian-Barre)
Hospitalization within 30 days prior to burn injury
Re-admission to ICU/BICU within current hospitalization
Hip fracture, unstable cervical spine or pathological fracture
Mechanically Ventilated > 80 hours prior to study enrollment
Current hospitalization or transferring hospital stay > 7 days prior to study enrollment
DNR/DNI on admission
Ineligible cancer treatment within the last 6 months
Investigator judgment/determination that patient is unable to participate in intervention (SRT)
Moribund
Participation in another research study within the past 30 days

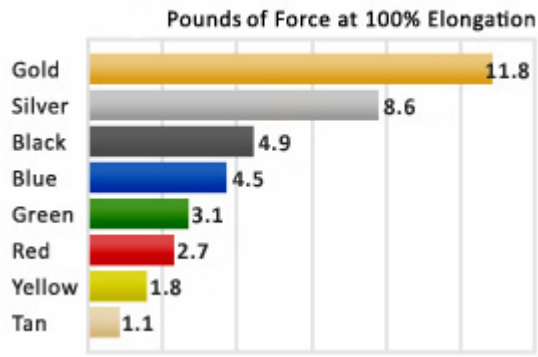
and put out your tongue", "Nod your head", and "Raise your eyebrows when I have counted up to 5"[15].

The patient will have to respond correctly to three of the five commands to be considered sufficiently alert to participate in level II, which consists of Physical Therapy and PRE training. Patients will be advanced through levels II-IV as they become more alert and able. Advancement from level II to level III will be based on the patient achieving a "level 3 arm strength", specifically that the patient can move the limb through a full range of motion against gravity. Advancement from level III to level IV will be based on the patient achieving "level 3 leg strength", specifically meaning that the patient can move the limb through a full range of motion against gravity.

Passive Range of Motion (PROM)-PROM therapy will be administered to all upper and lower extremity joints by one of the Mobility Team nursing assistants. Five repetitions of PROM will be provided for each joint. For the upper extremities PROM includes finger flexion and extension; wrist flexion, extension and ulnar and radial deviation; elbow flexion, extension, supination, and pronation; shoulder flexion, abduction, and internal and external rotation. Shoulder extension will be deferred due to positioning in bed. Lower extremity PROM includes toe flexion and extension; ankle dorsi flexion, plantar flexion, inversion, and eversion; knee flexion and extension; and hip flexion, abduction, adduction, internal and external rotation. Hip extension will be deferred due to positioning in bed.

Physical Therapy-Patients randomized to the rehabilitation therapy arm will receive a function-based physical therapy intervention targeted toward identified functional deficits. This intervention is based on the protocol described in section 4 and includes bed mobility, transfer training and balance training. As patients progress, the Physical Therapy will increasingly focus on the functional activities such as transfer to edge of bed; safe transfers to and from bed, chair, or commode; seated balance activities; pre-gait standing activities (forward and lateral weight shifting, marching in place), and ambulation. Bridging will also be started to improve functional strength for bed mobility. The bridging maneuver asks the patients to plant both feet firmly on the surface of the bed and raise their pelvis vertically with the goal to have the pelvis completely off the surface of the bed. If the subject can do double leg bridges, single leg bridges with opposite leg held in hip flexion with slight elevation off bed will be started. Being free from mechanical ventilation is not a pre-requisite for any these activities.

Progressive Resistance Exercise (PRE) Training- Once the patient is alert and can complete Physical Therapy active range of motion exercises unassisted, PRE training will be added to the mobility training. The PRE for each subject will consist of a separate Physical Therapist-directed second daily session with a focus only on PRE. The subjects will be progressed from bed level exercise, to exercises done while sitting on the edge of the bed (EOB) as detailed below. Patients will participate in PRE every day while in the BICU and hospital. The goal is for patients to complete 3 sets of 8 repetitions for each exercise. Resistance will be applied using Thera-Band elastic resistance bands. Patients will begin using the tan colored Thera-Bands which exert 1.1 pounds of force at 100% elongation. Once the patient can complete 3 sets of 8 repetitions, the resistance will be increased using the next-highest resistance band. Exercise intensity will be monitored by recording the color of the band used, and the number of repetitions and sets completed.



Bed-Level Supine PRE: If a participant cannot move from supine to sitting positions with at least moderate assistance and can hold their sitting balance for >5 minutes with only standby assistance from the Physical Therapist, they will be deemed suitable for bed-level supine exercise. If the subject is on a bed that converts to a chair position, the PRE session will be held with the bed in the chair position. If there is a vascular access device in place (eg. femoral vascular catheter or femoral arterial line) compromised by the sitting position, the subject will be seen with the head of the bed no greater than a 60 degree angle.

The subject will first engage in PRE maneuvers that are actively-assisted exercises (performing the maneuver without a TheraBand) and then progress to active maneuvers using good form with a goal of 8 repetitions per exercise. PRE will include dorsiflexion, knee flexion, knee extension, and hip flexion (straight leg raise). Exercises for the upper extremities will include elbow flexion and extension, shoulder flexion in scaption plane (halfway between flexion and abduction in order to maximize working in a functional plane), DI and D2 PNF patterns for shoulder internal and external rotation. (Shoulder PNF-Proprioceptive Neuromuscular Facilitation; Direction 1 = up, Direction 2=down). When subjects can

achieve 8 repetitions of each exercise independently without loss of form, Thera-Bands® will be introduced using progressively more resistance: yellow (light), red (medium), green (heavy), and if applicable, blue for extra heavy and black for special heavy.

Sitting Position PRE: Subjects will be progressed to this level when they can transfer to a sitting position at the edge of the bed with only moderate assistance and can sit > 5 minutes without loss of balance (standby assistance level only). Patients will participate in similar lower and upper extremity exercises as above.

Control- Patients randomized to the control arm will receive the standard of care for patients requiring mechanical ventilation in the BICU. These patients will not receive the standardized rehabilitative therapy per protocol. Participants in the control group will receive Physical Therapy evaluations as dictated by the patient's attending physician. Follow-up physical therapy sessions for the control group participants will occur as per initial physical therapy consultation recommends.

Data Collection - In this section, we describe the instruments and measures that will be used as dependent variables, covariates, demographic and screening variables, and timetable for collection Table 2.

Table 2. Schedule of Data Collection Events

	BICU Admit	Hosp Day 3, 7, 14	BICU D/C	Hosp D/C	3-mo	6-mo	12-mo	24-mo	36-mo
Consent	X								
Randomization	X								
Baseline co-morbidities	X								
Baseline Acuity	X								
Standardized Rehabilitation Therapy vs. Usual Care	X (Daily while in hosp)	X	X	X					
Charlson Index				X					
Dynamometer-Strength			X	X	X	X	X		
SPPB			X	X	X	X	X		
SF-36 v2				X	X	X	X	X	X
BSHS-B				X	X	X	X	X	X
Readmission					X	X	X	X	X
Muscle Ultrasound	X	X	X	X	X	X	X		
Handgrip Strength			X	X	X	X	X		
Telephone Follow-Up								X	X

Data Collection for Demographic, Baseline and On-Study Variables- Demographic information will be obtained on all patients. Additionally, Acute Physiology and Chronic Health Evaluation (APACHE) III scores will be calculated based on values from the initiation of BICU admission [38]. The baseline status of patients will be evaluated by two separate co-morbidity assessments, the Charlson index and the Co-morbidity index[39-41]. Other variables to be collected, such as medications, fluid administration, dialysis and other therapies are described in detail in the Human Subjects section. The volume of information to be collected is complex and is often not directly available in an electronic download format. The ability to accurately analyze outcomes in relation to covariates, depends on the detail, organization and completeness of these efforts, necessitating the structure of the research team described (Project Manager, Research Nurse, Exercise Physiologist-Analyst, Mobility Team Nurses).

Description of Primary Outcome - The primary endpoint for this study will be hospital length of stay and is defined as the hospital calendar days (or any portion of a calendar day) at the enrolling hospital and at any long term acute care facility to which the subject is directly transferred. We will include days at the transferring hospital, if a participant was transferred to our facility. If a subject is subsequently transferred from enrolling hospital to a rehab hospital or skilled nursing facility, the discharge calendar date from the enrolling hospital will end the in-patient hospitalization for the

purposes of this study. Of note, none of the research team members will be involved in the decision for hospital discharge, the primary endpoint.

Description of Secondary and Tertiary Outcome - Studies reporting follow-up for patients after ARF suggest that functional status improves markedly between 3 and 6 months post-hospital discharge [4;1] . Our approach will be to optimize evaluation of the pattern and timing of recovery with post-hospital in-person evaluations scheduled at 3, 6, and 12 months *post-enrollment*, as opposed to post-discharge. The first functional status testing and health related quality of life testing will occur at hospital discharge (unless hospital discharge is within one week of the 2 month follow-up visit). If a patient's hospital discharge is within one week of the 3, 6, or 12 month follow-up evaluation, the results will be used for both the discharge and follow-up analyses.

We chose to use the enrollment date for the timing of the outpatient follow-up visits rather than hospital discharge date to demonstrate functional outcomes at set points with relation to having received rehabilitation therapy. Using the hospital discharge date to base the scheduling of follow-up appointments runs the risk of examining patients at variable time points post-BICU care, since the number of days from study enrollment to hospital discharge is highly variable for this patient population. Using the enrollment date instead means that there is an expected, but low, percentage of the population within each arm that will still be hospitalized at the 3, 6, and even 12-month follow-ups. This approach also allows for a definite end-of-study date, i.e. 36 months post-enrollment for patient number 150 will signify the end of this study.

Blinding of Functional Status and Health Related Quality of Life Measurements

There is great difficulty in the design of blinding for non-pharmacologic Critical Care studies. Interventions such as ventilator or fluid administration and in the case of this study, standardized rehabilitation therapy, are difficult to blind to the patient, the bedside practitioners and the research team. However, in the design of this study two separate design aspects address this concern. First, the subject's hospital discharge is not the responsibility of the research team, but is the responsibility of the general medical floor team. Secondly, the research analyst will be blinded to the patient's randomization so that the outcome measurements of strength testing, functional testing and health related quality of life testing will be obtained in a blinded fashion. Prior to any testing, the patients and family members will be cautioned by the research nurses to refrain from comments concerning in-patient rehabilitation therapy.

Selection of assessment tools

The electronic dynamometer, the short physical performance battery (SPPB), the Medical Outcomes Study 36 Item Short Form (SF-36), and the Burn Specific Health Scale (BSHS-B) were selected to address the issue of preventing missing data during a longitudinal follow-up design. These tools will allow research team members not only to conduct the assessments in clinic, but also perform these tests in a patient's home and some of the tools (SF-36 and BSHS-B) perform well in phone administrations. For these reasons, we believe the study's tools allow for a minimum of missing data points in the follow-up portion of the study.

Schedule of Follow-up visits

Prior to discharge, subjects will be approached for re-consent if initial consent was by proxy. They will be invited to continue with this study as outpatients at 3, 6, and 12-months post-enrollment (scheduled for +/- 2 weeks of the 3, 6, and 12-month dates). If the subject does not wish to or cannot physically make the outpatient visit, we will ask if our study team personnel may visit the subject at home to conduct the assessments. If neither option is acceptable to the subject, we will request that the HRQoL assessments be performed by phone call. This strategy will help insure the most complete capture of data in this longitudinal follow-up study. Contact information will be obtained for the subject, his/her legal representative, and (if possible) at least 1 other contact person during hospitalization. All phone calls will be administered by a member of the research team. For consistent administration, the same person will administer the tools if at all possible. All data collected will be stored in a secure password-protected database, with limited access. These data will be stored utilizing a subject-specific identifier to protect confidentiality. Follow-up assessments will start with assessing the subject as alive, at home, and recording employment status.

Functional Status Assessments-Patients from both arms of the study will undergo functional status assessments at ICU discharge and then at hospital discharge and during in-person follow-up visits scheduled at 3, 6, and 12 months from the date of enrollment. A few patients will still be in the hospital or a medical facility at these time points. The in-person evaluations are structured so that they may be accomplished not only at the medical center clinic but also in the home or

other medical facility if the subject cannot return to the enrolling hospital for their in-person follow-up visit. Functional status will be evaluated using measures of skeletal muscle strength and the SPPB as surrogates for functional capacity.

Specific Muscle Group Strength Determinations: Hand grip strength is a commonly used measure of upper body skeletal muscle function and has been widely used as a general indicator of frailty. Grip strength in both hands will be measured using a Jamar hand held grip strength dynamometer. Additionally, an electronic strength dynamometer (MicroFET 2MT Dynamometer, Hoggan Health Industries, Salt Lake City, UT) will be used to collect strength measures of the biceps, triceps, ankle dorsiflexion, knee extension and hip extension, bilaterally. Three trials with brief pauses will be performed for each muscle group. The best performance of three trials will be selected for each side. Examiners will be trained with a standardized method and sequence of data collection.

Short Physical Performance Battery (SPPB): Physical functioning will be assessed using the SPPB [36;37]. Briefly, the SPPB score is based on timed measures of standing balance, walking speed, and ability to rise from a chair. Each performance measure is assigned a score ranging from 0 to 4, with 4 indicating the highest level of performance and 0 inability to complete the test. A summary score (range 0-12) will be calculated by adding the three scores. Few studies have looked at functional outcomes post-hospital discharge for burn patients with ARF. Although the "best" instrument to employ to measure functional outcome in burn patients after ARF, or any critical illness, is not known, we have explored the SPPB standardized functional assessment tool that was developed for evaluations in the geriatric population. The target population in this study will be comprised of very low-functioning individuals, due to their severe burn and requiring BICU care. Although the SPPB has been validated in the geriatric population, not the post-BICU population, we specifically chose the SPPB tool for its low function discriminatory capabilities. There is no tool validated in the post-BICU population in regards to function assessment. The SPPB is easily conducted, may be conducted in a patient's home or hospital room, and has been shown to be sufficiently discriminatory to be used in several geriatric intervention studies[37].

Health Related Quality of Life Assessments- It has been noted previously that patients with ARF may suffer with significant impairment in their health related quality of life for months following hospital discharge. The long term outcome measurements for this project will be conducted at hospital discharge and at 3, 6, and 12 months post-enrollment, as well as phone follow-up at 24 and 36 months post-enrollment. The two tools selected to assess health related quality of life are the SF-36 [43;44] , and the BSHS-B. The SF-36 is a generic measure of health related quality of life that examines the domains of physical and mental functioning. Given ARF in burn patients is an extremely variable and heterogeneous syndrome that does not encompass a single disease, we will not be using a disease specific measure of health related quality of life. These tools were selected both for their specific scope and to assess the survivor population as uniformly as possible, given that some follow-up time points may be conducted by phone and others in person. Phone follow-up at 24 and 36 months post-enrollment will include survival and employment status if applicable. Copies of questionnaires are attached in Appendix.

Muscle Ultrasound - Each study subject will undergo an ultrasound to examine the size and echogenicity of their muscles. This involves gel applied to the skin and then the ultrasound probe will be placed on the gel, and the entire process takes less than 20 minutes. The muscles studied will include the biceps brachii, rectus femoris, abductor digiti minimi, brachialis complex, diaphragm, and tibialis anterior.

Exercise Adherence – Adherence to and progress through the PROM, Physical Therapy, and PRE interventions will be monitored daily. The PROM intervention will be recorded as the number of repetitions of PROM exercises, the number of times performed per day and the number of days performed. Similar data will be collected for Physical Therapy sessions. If the patient cannot complete the task, the reason why will also be recorded. The strength training program will be monitored by recording the color of the Thera-Band® used by the patient for a given exercise, number of repetitions and number of sets completed for each exercise performed. Inability to complete the exercise or the required number of sets, and why, will also be recorded. The reasons why a patient would be discontinued appear in the Case Report Form as standardized answers; the research nurse will pick the most appropriate corresponding reason to keep free-text answers to an absolute minimum. We will calculate the number of sessions each participant exercised at the prescribed resistance.

Assessment of Delirium during Physical Therapy and PRE sessions using the CAM-ICU

Standardized physical exam can detect focal weakness in a conscious, cooperative patient. For BICU care, unconsciousness and delirium certainly hamper efforts to evaluate onset and severity of weakness in BICU patients. As well compliance to an exercise regimen may be less complete for those individuals demonstrating signs of delirium (eg, decreased ability to concentrate on repetitions). Assessment for the presence of delirium will be conducted before each BICU Standardized Rehabilitation Therapy session by applying the Confusion Assessment Method for the ICU (CAM-ICU) [49] . The recording of the CAM-ICU prior to each Physical Therapy session and PRE session will facilitate the interpretation of the effect of delirium on the number and quality of the tasks performed.

Statistical Considerations

The primary objective of this study is to assess the effect of the overall Standardized Rehabilitation Therapy (SRT) intervention on the length of hospital stay in burn patients with ARF. Secondary objectives are to assess the effect of SRT on 1) muscle size and architecture, 2) functional status, and 3) quality of life. Hospital LOS will be calculated as the number of days from randomization until hospital discharge. Patients who die before discharge will be censored in the analyses. Adverse events will be quantified by deaths, device removals, re-intubations, and the number of patient falls during "intervention-related" supervised periods.

Patients will be stratified by center and Baux score and assigned within strata to receive Standardized Rehabilitative Therapy or usual care with equal probability using variably sized permuted block randomization. Analysis of primary and secondary outcome measures will be carried out based on an 'intent to treat' approach. That is, all randomized patients will be used in all analyses, whether or not they were actually treated or whether or not they were treated according to protocol.

Power/Sample Size: As discussed below, the primary analysis used to assess the effect of rehabilitative therapy will be an Accelerated Failure Time model where hospital discharge will be the 'event' of interest. A greater hazard represents a greater likelihood of discharge. Assuming an exponential time to discharge distribution, the hazard ratio (HR) or acceleration factor can be interpreted as a percent change in the median LOS. The power for assessing the intervention effect is impacted by the number of deaths (censored observations), which is unknown. However, conservatively assuming an in-hospital death rate of 10%, we need a total sample size of 150 patients to detect a HR of 1.75 between groups (e.g., 2 week median LOS vs 1.14 weeks) with 90% power at the 5% two-sided level of significance. We will also compare the proportion of patients who are successfully discharged within two weeks of randomization. Our sample size will allow us to detect a 27% difference in discharge rates between the groups (e.g., 50% vs 23%) with 90% power.

Data Analysis: Kaplan-Meier methods will be used to estimate the time to hospital discharge and an accelerated failure time will be used to assess the unadjusted and adjusted difference in time to discharge between treatment groups, and to determine which baseline covariates are predictive of the outcome. While not powered to detect interactions, separate exploratory analyses will be done to determine if the effect of the intervention differs by levels of covariates. Logistic regression will be used to determine if the proportion of patients successfully discharged within two weeks differs by intervention. Repeated measures ANOVA and random coefficient mixed models will be used to assess the intervention effect on muscle size and architecture, function, and quality of life.

Regression diagnostics, residual plots, and exploratory analyses will be done to find appropriate transformations for the variables in these analyses. An unstructured covariance matrix will be used to model the within patient correlations. Other covariance patterns will be assessed, and choices will be made based on the Bayesian Information criterion.

Data Management:

We propose a secure web-based data entry system for data collection and participant tracking. It will be adapted from an ICU Mobility data management system already underway and systems that have been successfully used our previous clinical trial (REACT I and II) and in large multi-center clinical trials such as ACCORD, Look AHEAD, and LIFE. The web-based system allows great flexibility in processing data management tasks. As data are entered and submitted, edit checks are immediately applied. Entered data are inserted directly into central database. The infrastructure will be a Windows server, running Internet Information Server, with a middleware product (ColdFusion) to integrate database content within the website. Data will be stored in a SQL server relational database. With this web infrastructure, data entered into the system are immediately available for review and reporting. Advanced data cleaning processes are invoked

automatically on each form submission using a rules engine for form/field level validation rules and initiation of SAS programs for more extensive reviews and analyses. All systems are backed up nightly to disk or tape and tapes are rotated off site several times a month. In addition, changes to the database are always "inserts" and never "updates" so that inadvertent overwriting of valid data cannot occur and a complete record of database activity is maintained. The web-based system will provide the ability to enter and verify eligibility criteria prior to randomization.

Distributed data entry network**:** Using the proposed web-based system, research personnel will be able to interact with data through a secure website using web forms that mimic paper forms. We will provide a state-of-the-art query resolution system for forms data. The web-based system is more efficient for research staff to manage data edits than older, paper-based edit query systems. It provides an immediate correction to databases, creates a reliable audit trail, and minimizes redundancies. In prior studies, we have developed and deployed models that incorporate complete sets of validation rules (e.g. range and consistency checks) and display invalid data and potential queries on the data entry screen as the form is submitted. Research staff can resolve many queries immediately, comparing the screen to the form, often cleaning the entire database record on the spot. For queries not immediately resolvable, warnings are displayed whenever the data entry screen is recalled.

Data integrity and security**:** All study data will be stored centrally in our relational database management system. All systems are securely controlled in the Wake Forest University Medical Center Department of Public Health Sciences data center, which has limited access through badge access (with direct reporting to the Security office). The data center has environmental controls to monitor power, temperature, humidity and sound levels and triggers for notifying staff and engineering, who are on-call 24x7.

Human Subjects Protection:

Subjects will be enrolled from the patients who present to the BICU service at Wake Forest University Medical Center, Washington University at St. Louis Medical Center, or University of North Carolina at Chapel Hill Medical Center. No children will be enrolled in this trial.

Surrogate consent will be obtained from the legally authorized representative when the subject is unable to consent on their own behalf. They will have the protocol explained to them, be given the opportunity to ask questions and have all of their questions answered to their satisfaction. Appropriate time will be allowed for them to review the consent form and talk with other family members or friends as needed. No study procedures will take place prior to informed consent being obtained. There will be an ongoing dialog between the study team and the family to allow for withdrawal of the subject at any time if they so choose. At the point that the subject is conscious and coherent, the consent procedure will be repeated and the subject will be given the opportunity to sign themselves

Subjects if able will be the primary source of consent. Whenever possible a family member or person of their choice will be included in the discussion and consent process. If the subject is not able to participate in the consent process due to critical illness or sedation the following procedure will be followed.

The legally authorized representative will be identified and approached for consent. Members of the research team will be introduced. It will be made clear that the research is separate from the potential study subjects' routine clinical care. The Legally Authorized Representative will be invited to a private conference room in the critical care area. If subjects become alert, coherent, and oriented and able to sign consent at some point after surrogate consent was obtained, consent will be re-obtained from them and the same documentation process will occur.

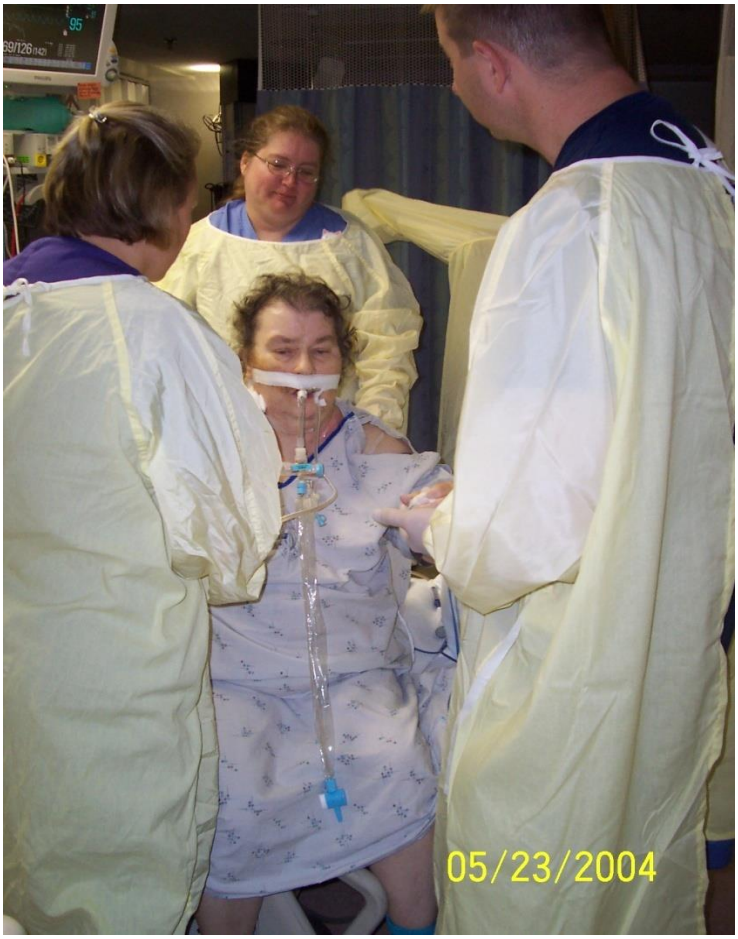
A brief overview of the subject's current condition will be given, the protocol will be reviewed in detail, and the legally authorized representative will be given an opportunity to ask questions. All questions will be answered. The legally authorized representative will be given an opportunity to read the consent form in full; if unable to read, the consent form will be read to them, or another family member or friend who can read will be identified and asked to read it to the legally authorized representative. The legally authorized representative will be offered a period of time to consider the protocol if they so desire prior to signing the consent. A copy of the consent will be given to the legal representative as well as information as to how they can contact the research team with any questions or if they should change their mind about continuing participation.

A written statement will be placed in the subject's research file noting the individuals present during the consent conversation, and the date and time that consent was obtained. It will be signed by the person obtaining consent as well as co-signed by the PI or Co-Investigator.

Protection Against Risk

The specific attributes of the Mobility Team (namely a critical care nurse, a nursing assistant and a physical therapist) allow for this intervention to be applied safely. The Mobility Team's structure with these three members, allows the Team to provide the Standard Rehabilitation Therapy and at the same time continuously assess the subject for signs of hemodynamic or respiratory decline, Figures 4 and 5.

Figure 4. Orally intubated patient with Mobility Team monitoring session at beside (Mobility Team: left to right, Physical Therapist, Nurses Aid (behind patient), Critical Care Nurse)



The unique design of the ICU Mobility Team with its components of different medical professionals (Physical Therapist, Critical Care Nurse and Nurses Aid) optimizes the safety of the delivery of this intervention.

Global subject protection: Universal precautions are practiced throughout the facilities. In the event of an adverse event, medical management will be provided at no expense to the subject by the principal investigator, in accordance with the enrolling medical center's institutional policy for research related injury.

Subject safety is of the utmost concern. In the event of a serious adverse event, subjects will receive state-of-the-art emergency medical care at a level consistent with the Emergency Department or BICU at the enrolling medical center. All serious adverse events will be reported to the appropriate IRB, clinical coordinating center, and DOD within a 24 hour time period of notification of the event. All clinical coordinators, physician investigators and research personnel involved in clinical trials at these enrolling sites will be expected to attend educational programs on the protection of human subjects as required by their institutions and local IRBs.

These subjects are critically ill and require mechanical ventilation. They often have underlying serious illnesses. Complications of underlying diseases, complications from the admitting diagnosis as well as complications from general BICU exposure are unfortunately common in this population, aside from any participation in a clinical trial. Those conditions present at baseline, or in the opinion of the investigator not felt to be directly study procedure related will be considered a clinical outcome and not a serious adverse event. Therefore, risks felt to be possibly associated with this study would be hypoxemia during the delivery of the protocol, cardiac arrhythmias during the delivery of the protocol, or the loss of a management device such as an endotracheal tube or vascular access. Study subjects, while receiving mechanical ventilation and the Standardized Rehabilitation Therapy, will be monitored in the BICU. Study subjects will be monitored continuously, while in the BICU setting. If dysrhythmias, or increasing ventilatory demands are noted, the protocol will be stopped and the subject re-assessed to determine whether the patient's condition warrants return to the protocol. Confidentiality is maintained by limiting access to study related records, and maintaining password protection on all databases.

Confidentiality:
All clinical trial data reviewed by the DSM will be held in strict confidence. The data will not be shared with any person involved in the conduct of the study until all patient enrollment in the study has ceased, all enrolled patients have completed the study, and final data lock has occurred. It is of utmost importance that study personnel performing the functional and HRQoL queries remain blinded until the data lock has occurred.

Figure 5. Mobility Team monitoring session at beside

Data and Safety Monitoring Plan

a. Data Safety / Medical Monitor

Study Data Safety/Medical Monitor: Jason Hoth, MD, Wake Forest University School of Medicine

Dr. Hoth will serve as the Study's Data Safety/Medical Monitor (DS/MM). Responsibilities of the DS/MM with regards to this study will include:

- Review of serious, unexpected adverse events, whether or not thought to be related to the protocol's intervention or study procedures.

- Review of clinical data and other related data at unplanned intervals when appropriate or when safety issues occur.

- Ensure that analyses performed by or provided to the DS/MM are recorded, handled and stored in a way that allows accurate interpretation, verification and reporting of the data.

- Maintain records of all DS/MM reviews including a summary of the information, recommendations and the rationale for recommendations.

- Make recommendations to the Study's Co-PI's, IRB and DOD representatives including the following: suspend study enrollment due to safety concerns, recommend changes to the protocol, procedures and/or informed consent document or continue the current study.

- Authority to stop research protocol in progress, remove individual human subjects from research

protocol, and take whatever steps are necessary to protect the safety and well-being of human subjects until the IRB can assess the monitor's report.

In this study, individual reports of adverse events will be reviewed in an unblinded fashion. Aggregate reports are not planned for review until the end of the study unless they are requested on an ad hoc basis by the DS/MM.

b. Data Safety Plan Procedures

1) Study safety monitoring schedule

The study will be monitored quarterly by the DS/MM.

The Study's Project Manager will initiate review of 2 study subjects per quarter, randomly chosen who have completed hospitalization. The case report forms and subject file will be reviewed for:

Compliance with IRB requirements
Conformance with informed consent requirements
Verification of source documents
Investigator compliance
Missed adverse events

Institutional IRB will provide additional oversight if needed. The results of the Project Manager's review will be presented at the next monthly phone conference staff meeting. At monthly phone conference meetings, opportunity will be provided to discuss new human safety concerns by any of our team. Additionally, the study team will review each of the new subjects enrolled since the last staff meeting in regards to consent form signature and other compliance concerns (such as when the subject was approached to discuss re-consent).

We will have ongoing weekly review from Public Health Sciences with queries regarding any incomplete data within the case report form.

2) Minimizing research-associated risk

The protocol gives specific information about patient safety during research study participation. All study patients are monitored electronically during the BICU stay and by a critical care nurse presence as well as the continuation of the critical care nurse's presence during the stay in the hospital during exercise sessions. If patient's status decreases during session, the session is ended and the critical care nurse communicates verbally with the patient's assigned bedside nurse, as well as written documentation within the patient's electronic medical record.

3) Protecting the confidentiality of participant data

The protocol gives guidelines which we follow to protect the confidentiality of patient data. Confidentiality is maintained by limiting access to study related records and maintaining password protection on the database. Also, all records are kept secure in locked offices and are identified by subject study ID.

c. Procedures for identifying, reviewing, and reporting adverse events and unanticipated problems to the IRB, DOD.

The intervention is considered a low risk intervention. The identification, review and reporting process would begin with the Study's Critical Care Nurse notifying a study physician of a potential safety event. The physician and nurse will review the potential safety event together. Patient records will be reviewed for evidence of risk to the patient. The Physician and Nurse will follow the local IRB and NIH guidelines in adverse event reporting and if the potential event is deemed to have met the criteria, the event will be reported. The reporting of adverse events will be the primary responsibility of the Study physicians in conjunction with the research nurse who will notify the IRB, the clinical coordinating center and representatives of the DOD.

If applicable, the type and number of events that would halt accrual and it would then generate a review of eligibility, monitoring, assessments, intervention, and how the resumption of accrual would occur.

Appendix

Cancer Exclusions

Types of Cancer	Exclude if:
Bladder Cancer	Stage III and IV
Colorectal Cancer	State III and IV
	Dukes Stage C
	MAC Stage C1, C2, C3, D
Lung: Non small cell	Stage III and IV (Stage I and II acceptable if "curative resection done")
Lung: Small Cell	Extensive stage (Limited stage evaluated by case basis)
Prostate	AJCC (TNM) stage 3 and 4
	Jewett Staging System Stage C and D
Breast Cancer	Stage IIIB, IIIC, and IV
Hepatic Cancer	Exclude
Lymphoma Non-Hodgkin's Indolent	Noncontiguous stage 2, 3, and 4
Lymphoma Non-Hodgkin's Aggressive	Stage 3 and 4
Lymphoma Hodgkin's	BMT Planned
Renal	Any cancer is not confined to capsule
Cervical	Stage III and IV
Leukemia – Acute Myelocytic Leukemia (AML)	Unless in remission
	BMT Planned
	Unless receiving Gleevec
Multiple Myeloma	ISS Stage 2 and 3
Skin	Melanoma if Metastasis
CNS Cancer	Evaluated case by case basis
Leukemia – Chronic Myelocytic Leukemia (CML)	Blast or Accelerated Phase
Leukemia – Chronic Lymphocytic Leukemia (CLL)	All
Pancreatic	Exclude
Stomach	Stage III and IV (Stage I and II acceptable if "curative resection done")

ProcedureCode	Description	COUNT_of_RecordId
0HBHXZZ	0HBHXZZ - Excision of Right Upper Leg Skin, External Approach	5231
0HBJXZZ	0HBJXZZ - Excision of Left Upper Leg Skin, External Approach	4744
0HRKX74	0HRKX74 - Replace R Low Leg Skin w Autol Sub, Part Thick, Extern	1840
0HRFX74	0HRFX74 - Replace R Hand Skin w Autol Sub, Part Thick, Extern	1750
0HRLX74	0HRLX74 - Replace L Low Leg Skin w Autol Sub, Part Thick, Extern	1737
0HDFXZZ	0HDFXZZ - Extraction of Right Hand Skin, External Approach	1545
0HRDX74	0HRDX74 - Replace R Low Arm Skin w Autol Sub, Part Thick, Extern	1482
0HRGX74	0HRGX74 - Replace L Hand Skin w Autol Sub, Part Thick, Extern	1465
0HRBX74	0HRBX74 - Replace R Up Arm Skin w Autol Sub, Part Thick, Extern	1463
0HD1XZZ	0HD1XZZ - Extraction of Face Skin, External Approach	1415
0HRHX74	0HRHX74 - Replace R Up Leg Skin w Autol Sub, Part Thick, Extern	1393
0HDGXZZ	0HDGXZZ - Extraction of Left Hand Skin, External Approach	1371
0HRJX74	0HRJX74 - Replace L Up Leg Skin w Autol Sub, Part Thick, Extern	1340
0HRCX74	0HRCX74 - Replace L Up Arm Skin w Autol Sub, Part Thick, Extern	1304
0HREX74	0HREX74 - Replace L Low Arm Skin w Autol Sub, Part Thick, Extern	1292
0HRMX74	0HRMX74 - Replace R Foot Skin w Autol Sub, Part Thick, Extern	1288
0HDDXZZ	0HDDXZZ - Extraction of Right Lower Arm Skin, External Approach	1166
0HR5X74	0HR5X74 - Replace Chest Skin w Autol Sub, Part Thick, Extern	1160
0HRNX74	0HRNX74 - Replace L Foot Skin w Autol Sub, Part Thick, Extern	1138
0HR7X74	0HR7X74 - Replace Abd Skin w Autol Sub, Part Thick, Extern	1134
0HD5XZZ	0HD5XZZ - Extraction of Chest Skin, External Approach	1125
0HDEXZZ	0HDEXZZ - Extraction of Left Lower Arm Skin, External Approach	1051
0HR6X74	0HR6X74 - Replace Back Skin w Autol Sub, Part Thick, Extern	1022
0HDBXZZ	0HDBXZZ - Extraction of Right Upper Arm Skin, External Approach	1008
0HB6XZZ	0HB6XZZ - Excision of Back Skin, External Approach	941
0HDKXZZ	0HDKXZZ - Extraction of Right Lower Leg Skin, External Approach	921
0HBKXZZ	0HBKXZZ - Excision of Right Lower Leg Skin, External Approach	918
0HDCXZZ	0HDCXZZ - Extraction of Left Upper Arm Skin, External Approach	897
0HBLXZZ	0HBLXZZ - Excision of Left Lower Leg Skin, External Approach	893
0HDLXZZ	0HDLXZZ - Extraction of Left Lower Leg Skin, External Approach	881
0HD7XZZ	0HD7XZZ - Extraction of Abdomen Skin, External Approach	870
0HDHXZZ	0HDHXZZ - Extraction of Right Upper Leg Skin, External Approach	796
0HRHXK4	0HRHXK4 - Replace R Up Leg Skin w Nonaut Sub, Part Thick, Extern	755

0HDJXZZ	0HDJXZZ - Extraction of Left Upper Leg Skin, External Approach	739
0HRKXK3	0HRKXK3 - Replace R Low Leg Skin w Nonaut Sub, Full Thick, Extern	735
0HB7XZZ	0HB7XZZ - Excision of Abdomen Skin, External Approach	733
0JBN0ZZ	0JBN0ZZ - Excision of R Low Leg Subcu/Fascia, Open Approach	686
0HBFXZZ	0HBFXZZ - Excision of Right Hand Skin, External Approach	672
0JBL0ZZ	0JBL0ZZ - Excision of R Up Leg Subcu/Fascia, Open Approach	671
0HRLXK3	0HRLXK3 - Replace L Low Leg Skin w Nonaut Sub, Full Thick, Extern	669
0HRHXK3	0HRHXK3 - Replace R Up Leg Skin w Nonaut Sub, Full Thick, Extern	661
0HRJXK4	0HRJXK4 - Replace L Up Leg Skin w Nonaut Sub, Part Thick, Extern	658
0JBP0ZZ	0JBP0ZZ - Excision of L Low Leg Subcu/Fascia, Open Approach	655
0HRFXK4	0HRFXK4 - Replace R Hand Skin w Nonaut Sub, Part Thick, Extern	653
0HD6XZZ	0HD6XZZ - Extraction of Back Skin, External Approach	652
0HRDXK4	0HRDXK4 - Replace R Low Arm Skin w Nonaut Sub, Part Thick, Extern	652
0HDMXZZ	0HDMXZZ - Extraction of Right Foot Skin, External Approach	637
0HD4XZZ	0HD4XZZ - Extraction of Neck Skin, External Approach	623
0HRBXK3	0HRBXK3 - Replace R Up Arm Skin w Nonaut Sub, Full Thick, Extern	615
0HDNXZZ	0HDNXZZ - Extraction of Left Foot Skin, External Approach	605
0HREXK4	0HREXK4 - Replace L Low Arm Skin w Nonaut Sub, Part Thick, Extern	602
0HRBXK4	0HRBXK4 - Replace R Up Arm Skin w Nonaut Sub, Part Thick, Extern	594
0JBM0ZZ	0JBM0ZZ - Excision of L Up Leg Subcu/Fascia, Open Approach	594
0HRJXK3	0HRJXK3 - Replace L Up Leg Skin w Nonaut Sub, Full Thick, Extern	592
0HRGXK4	0HRGXK4 - Replace L Hand Skin w Nonaut Sub, Part Thick, Extern	590
0HRKXK4	0HRKXK4 - Replace R Low Leg Skin w Nonaut Sub, Part Thick, Extern	589
0HBGXZZ	0HBGXZZ - Excision of Left Hand Skin, External Approach	587
0HRFXK3	0HRFXK3 - Replace R Hand Skin w Nonaut Sub, Full Thick, Extern	581
0HRDXK3	0HRDXK3 - Replace R Low Arm Skin w Nonaut Sub, Full Thick, Extern	573
0HR5XK4	0HR5XK4 - Replace Chest Skin w Nonaut Sub, Part Thick, Extern	569
0HR7XK3	0HR7XK3 - Replace Abd Skin w Nonaut Sub, Full Thick, Extern	566
0HRLXK4	0HRLXK4 - Replace L Low Leg Skin w Nonaut Sub, Part Thick, Extern	562
0HBBXZZ	0HBBXZZ - Excision of Right Upper Arm Skin, External Approach	560
0HRCXK3	0HRCXK3 - Replace L Up Arm Skin w Nonaut Sub, Full Thick, Extern	554
0HRGXK3	0HRGXK3 - Replace L Hand Skin w Nonaut Sub, Full Thick, Extern	554
0HR5XK3	0HR5XK3 - Replace Chest Skin w Nonaut Sub, Full Thick, Extern	531
0JBQ0ZZ	0JBQ0ZZ - Excision of R Foot Subcu/Fascia, Open Approach	530

0HBDXZZ	0HBDXZZ - Excision of Right Lower Arm Skin, External Approach	518
0HREXK3	0HREXK3 - Replace L Low Arm Skin w Nonaut Sub, Full Thick, Extern	509
0HR7XK4	0HR7XK4 - Replace Abd Skin w Nonaut Sub, Part Thick, Extern	504
0HRCXK4	0HRCXK4 - Replace L Up Arm Skin w Nonaut Sub, Part Thick, Extern	500
0HB8XZZ	0HB8XZZ - Excision of Buttock Skin, External Approach	498
0HBCXZZ	0HBCXZZ - Excision of Left Upper Arm Skin, External Approach	497
0HR8X74	0HR8X74 - Replace Buttock Skin w Autol Sub, Part Thick, Extern	492
0JBD0ZZ	0JBD0ZZ - Excision of R Up Arm Subcu/Fascia, Open Approach	489
0JB80ZZ	0JB80ZZ - Excision of Abd Subcu/Fascia, Open Approach	488
0HB5XZZ	0HB5XZZ - Excision of Chest Skin, External Approach	486
0JBJ0ZZ	0JBJ0ZZ - Excision of R Hand Subcu/Fascia, Open Approach	481
0JBR0ZZ	0JBR0ZZ - Excision of L Foot Subcu/Fascia, Open Approach	480
0JBK0ZZ	0JBK0ZZ - Excision of L Hand Subcu/Fascia, Open Approach	469
0JBF0ZZ	0JBF0ZZ - Excision of L Up Arm Subcu/Fascia, Open Approach	462
0JB60ZZ	0JB60ZZ - Excision of Chest Subcu/Fascia, Open Approach	447
0HR6XK3	0HR6XK3 - Replace Back Skin w Nonaut Sub, Full Thick, Extern	442
0HR4X74	0HR4X74 - Replace Neck Skin w Autol Sub, Part Thick, Extern	437
0HBMXZZ	0HBMXZZ - Excision of Right Foot Skin, External Approach	434
0JBG0ZZ	0JBG0ZZ - Excision of R Low Arm Subcu/Fascia, Open Approach	433
0HBEXZZ	0HBEXZZ - Excision of Left Lower Arm Skin, External Approach	422
0HRMXK3	0HRMXK3 - Replace R Foot Skin w Nonaut Sub, Full Thick, Extern	422
0JBH0ZZ	0JBH0ZZ - Excision of L Low Arm Subcu/Fascia, Open Approach	422
0HBNXZZ	0HBNXZZ - Excision of Left Foot Skin, External Approach	395
0JB70ZZ	0JB70ZZ - Excision of Back Subcu/Fascia, Open Approach	389
0HRNXK3	0HRNXK3 - Replace L Foot Skin w Nonaut Sub, Full Thick, Extern	353
0HD8XZZ	0HD8XZZ - Extraction of Buttock Skin, External Approach	334
0HR6XK4	0HR6XK4 - Replace Back Skin w Nonaut Sub, Part Thick, Extern	325
0HRNXK4	0HRNXK4 - Replace L Foot Skin w Nonaut Sub, Part Thick, Extern	287
0HRMXK4	0HRMXK4 - Replace R Foot Skin w Nonaut Sub, Part Thick, Extern	281
0HR1X74	0HR1X74 - Replace Face Skin w Autol Sub, Part Thick, Extern	235
0HB1XZZ	0HB1XZZ - Excision of Face Skin, External Approach	224
0JB90ZZ	0JB90ZZ - Excision of Buttock Subcu/Fascia, Open Approach	224
0HR8XK3	0HR8XK3 - Replace Buttock Skin w Nonaut Sub, Full Thick, Extern	221
0HB0XZZ	0HB0XZZ - Excision of Scalp Skin, External Approach	193

0HR1XK3	0HR1XK3 - Replace Face Skin w Nonaut Sub, Full Thick, Extern	181
0HR4XK3	0HR4XK3 - Replace Neck Skin w Nonaut Sub, Full Thick, Extern	174
0HRFX73	0HRFX73 - Replace R Hand Skin w Autol Sub, Full Thick, Extern	173
0HB4XZZ	0HB4XZZ - Excision of Neck Skin, External Approach	170
0HD3XZZ	0HD3XZZ - Extraction of Left Ear Skin, External Approach	170
0HD2XZZ	0HD2XZZ - Extraction of Right Ear Skin, External Approach	167
0HR8XK4	0HR8XK4 - Replace Buttock Skin w Nonaut Sub, Part Thick, Extern	161
0HR1XK4	0HR1XK4 - Replace Face Skin w Nonaut Sub, Part Thick, Extern	160
0HRGX73	0HRGX73 - Replace L Hand Skin w Autol Sub, Full Thick, Extern	159
0HDAXZZ	0HDAXZZ - Extraction of Inguinal Skin, External Approach	157
0HD0XZZ	0HD0XZZ - Extraction of Scalp Skin, External Approach	156
0HR4XK4	0HR4XK4 - Replace Neck Skin w Nonaut Sub, Part Thick, Extern	156
0JB10ZZ	0JB10ZZ - Excision of Face Subcu/Fascia, Open Approach	134
0HNLXZZ	0HNLXZZ - Release Left Lower Leg Skin, External Approach	124
0HRLX73	0HRLX73 - Replace L Low Leg Skin w Autol Sub, Full Thick, Extern	121
0HNKXZZ	0HNKXZZ - Release Right Lower Leg Skin, External Approach	120
0HRKX73	0HRKX73 - Replace R Low Leg Skin w Autol Sub, Full Thick, Extern	119
XHRPXL2	XHRPXL2 - Replace Skin w Porc Livr Sub, Extern, New Tech 2	112
0HNGXZZ	0HNGXZZ - Release Left Hand Skin, External Approach	111
0HPPXKZ	0HPPXKZ - Removal of Nonaut Sub from Skin, Extern Approach	105
0JB40ZZ	0JB40ZZ - Excision of Rt Neck Subcu/Fascia, Open Approach	105
0HNEXZZ	0HNEXZZ - Release Left Lower Arm Skin, External Approach	104
3E0T3CZ	3E0T3CZ - Introduce Regional Anesth in Periph Nrv, Plexi, Perc	104
0HRCX73	0HRCX73 - Replace L Up Arm Skin w Autol Sub, Full Thick, Extern	98
0HRDX73	0HRDX73 - Replace R Low Arm Skin w Autol Sub, Full Thick, Extern	97
0HRBX73	0HRBX73 - Replace R Up Arm Skin w Autol Sub, Full Thick, Extern	96
0HRJX73	0HRJX73 - Replace L Up Leg Skin w Autol Sub, Full Thick, Extern	93
0HRMX73	0HRMX73 - Replace R Foot Skin w Autol Sub, Full Thick, Extern	90
0HREX73	0HREX73 - Replace L Low Arm Skin w Autol Sub, Full Thick, Extern	89
0HRNX73	0HRNX73 - Replace L Foot Skin w Autol Sub, Full Thick, Extern	89
0HNBXZZ	0HNBXZZ - Release Right Upper Arm Skin, External Approach	85
0HRHX73	0HRHX73 - Replace R Up Leg Skin w Autol Sub, Full Thick, Extern	83
0JDJ0ZZ	0JDJ0ZZ - Extraction of R Hand Subcu/Fascia, Open Approach	83
0HR7X73	0HR7X73 - Replace Abd Skin w Autol Sub, Full Thick, Extern	82

0JDK0ZZ	0JDK0ZZ - Extraction of L Hand Subcu/Fascia, Open Approach	82
0HNCXZZ	0HNCXZZ - Release Left Upper Arm Skin, External Approach	81
0HR0X74	0HR0X74 - Replace Scalp Skin w Autol Sub, Part Thick, Extern	81
0HNDXZZ	0HNDXZZ - Release Right Lower Arm Skin, External Approach	80
0HNFXZZ	0HNFXZZ - Release Right Hand Skin, External Approach	78
01N50ZZ	01N50ZZ - Release Median Nerve, Open Approach	75
0HR6X73	0HR6X73 - Replace Back Skin w Autol Sub, Full Thick, Extern	74
0HD9XZZ	0HD9XZZ - Extraction of Perineum Skin, External Approach	72
0HR5X73	0HR5X73 - Replace Chest Skin w Autol Sub, Full Thick, Extern	71
F08F5BZ	F08F5BZ - Wound Mgmt Trmt Integu Up Back/UE w Physical Agent	70
0KB90ZZ	0KB90ZZ - Excision of Right Lower Arm and Wrist Muscle, Open Approach	69
0KBT0ZZ	0KBT0ZZ - Excision of Left Lower Leg Muscle, Open Approach	68
0JDG0ZZ	0JDG0ZZ - Extraction of R Low Arm Subcu/Fascia, Open Approach	67
0JDN0ZZ	0JDN0ZZ - Extraction of R Low Leg Subcu/Fascia, Open Approach	66
F08G5BZ	F08G5BZ - Wound Mgmt Trmt Integu Low Back/LE w Physical Agent	64
0JDP0ZZ	0JDP0ZZ - Extraction of L Low Leg Subcu/Fascia, Open Approach	63
0KBS0ZZ	0KBS0ZZ - Excision of Right Lower Leg Muscle, Open Approach	63
0HNJXZZ	0HNJXZZ - Release Left Upper Leg Skin, External Approach	61
0HQ1XZZ	0HQ1XZZ - Repair Face Skin, External Approach	61
0JDR0ZZ	0JDR0ZZ - Extraction of L Foot Subcu/Fascia, Open Approach	61
0HR0XK3	0HR0XK3 - Replace Scalp Skin w Nonaut Sub, Full Thick, Extern	60
0HRHXJZ	0HRHXJZ - Replacement of R Up Leg Skin with Synth Sub, Extern Approach	60
0HRJXJZ	0HRJXJZ - Replacement of L Up Leg Skin with Synth Sub, Extern Approach	59
3E0T3BZ	3E0T3BZ - Introduce Anesthetic in Periph Nrv, Plexi, Perc	59
0JDM0ZZ	0JDM0ZZ - Extraction of L Up Leg Subcu/Fascia, Open Approach	58
0HB3XZZ	0HB3XZZ - Excision of Left Ear Skin, External Approach	56
0HNHXZZ	0HNHXZZ - Release Right Upper Leg Skin, External Approach	56
0JDL0ZZ	0JDL0ZZ - Extraction of R Up Leg Subcu/Fascia, Open Approach	56
0JB50ZZ	0JB50ZZ - Excision of Lt Neck Subcu/Fascia, Open Approach	55
0KBB0ZZ	0KBB0ZZ - Excision of Left Lower Arm and Wrist Muscle, Open Approach	55
0HN5XZZ	0HN5XZZ - Release Chest Skin, External Approach	54
0JDH0ZZ	0JDH0ZZ - Extraction of L Low Arm Subcu/Fascia, Open Approach	54
0JDQ0ZZ	0JDQ0ZZ - Extraction of R Foot Subcu/Fascia, Open Approach	54
0JNN0ZZ	0JNN0ZZ - Release R Low Leg Subcu/Fascia, Open Approach	53

0JNP0ZZ	0JNP0ZZ - Release L Low Leg Subcu/Fascia, Open Approach	53
5A1D70Z	5A1D70Z - Performance of Urinary Filtration, <6 hrs/day	52
0HRAX74	0HRAX74 - Replace Inguin Skn w Autol Sub, Part Thick, Extern	51
0JD60ZZ	0JD60ZZ - Extraction of Chest Subcu/Fascia, Open Approach	50
0JD80ZZ	0JD80ZZ - Extraction of Abd Subcu/Fascia, Open Approach	50
0JDD0ZZ	0JDD0ZZ - Extraction of R Up Arm Subcu/Fascia, Open Approach	50
0JNG0ZZ	0JNG0ZZ - Release R Low Arm Subcu/Fascia, Open Approach	50
0HBAXZZ	0HBAXZZ - Excision of Inguinal Skin, External Approach	49
0KNC0ZZ	0KNC0ZZ - Release Right Hand Muscle, Open Approach	49
0HB2XZZ	0HB2XZZ - Excision of Right Ear Skin, External Approach	47
0HQ0XZZ	0HQ0XZZ - Repair Scalp Skin, External Approach	46
0HR2X74	0HR2X74 - Replace R Ear Skin w Autol Sub, Part Thick, Extern	46
0JB00ZZ	0JB00ZZ - Excision of Scalp Subcu/Fascia, Open Approach	46
0JNK0ZZ	0JNK0ZZ - Release L Hand Subcu/Fascia, Open Approach	46
0KBV0ZZ	0KBV0ZZ - Excision of Right Foot Muscle, Open Approach	46
0JNJ0ZZ	0JNJ0ZZ - Release R Hand Subcu/Fascia, Open Approach	45
0HR5XJZ	0HR5XJZ - Replacement of Chest Skin with Synth Sub, Extern Approach	44
0HRLXJZ	0HRLXJZ - Replace of L Low Leg Skin with Synth Sub, Extern Approach	44
0JNH0ZZ	0JNH0ZZ - Release L Low Arm Subcu/Fascia, Open Approach	44
0QBG0ZZ	0QBG0ZZ - Excision of Right Tibia, Open Approach	44
3E013GC	3E013GC - Introduction of Oth Therap Subst into Subcu, Perc Approach	44
0HN7XZZ	0HN7XZZ - Release Abdomen Skin, External Approach	43
0HR3X74	0HR3X74 - Replace L Ear Skin w Autol Sub, Part Thick, Extern	43
02PYX3Z	02PYX3Z - Removal of Infusion Dev from Great Vessel, Extern Approach	42
0HBRXZZ	0HBRXZZ - Excision of Toe Nail, External Approach	42
0HRCXJZ	0HRCXJZ - Replacement of L Up Arm Skin with Synth Sub, Extern Approach	42
0JNF0ZZ	0JNF0ZZ - Release L Up Arm Subcu/Fascia, Open Approach	42
0KBW0ZZ	0KBW0ZZ - Excision of Left Foot Muscle, Open Approach	42
0JND0ZZ	0JND0ZZ - Release R Up Arm Subcu/Fascia, Open Approach	41
0W9G3ZZ	0W9G3ZZ - Drainage of Peritoneal Cavity, Percutaneous Approach	39
0JNM0ZZ	0JNM0ZZ - Release L Up Leg Subcu/Fascia, Open Approach	38
0HRKXJZ	0HRKXJZ - Replace of R Low Leg Skin with Synth Sub, Extern Approach	37
0JDF0ZZ	0JDF0ZZ - Extraction of L Up Arm Subcu/Fascia, Open Approach	37
0KB70ZZ	0KB70ZZ - Excision of Right Upper Arm Muscle, Open Approach	37

0KBD0ZZ	0KBD0ZZ - Excision of Left Hand Muscle, Open Approach	37
0H8DXZZ	0H8DXZZ - Division of Right Lower Arm Skin, External Approach	36
0HR6XJZ	0HR6XJZ - Replacement of Back Skin with Synth Sub, Extern Approach	36
0HRDXJZ	0HRDXJZ - Replace of R Low Arm Skin with Synth Sub, Extern Approach	36
0JD10ZZ	0JD10ZZ - Extraction of Face Subcu/Fascia, Open Approach	36
0H8BXZZ	0H8BXZZ - Division of Right Upper Arm Skin, External Approach	35
0JD70ZZ	0JD70ZZ - Extraction of Back Subcu/Fascia, Open Approach	35
0JNL0ZZ	0JNL0ZZ - Release R Up Leg Subcu/Fascia, Open Approach	35
0KBQ0ZZ	0KBQ0ZZ - Excision of Right Upper Leg Muscle, Open Approach	35
0H8FXZZ	0H8FXZZ - Division of Right Hand Skin, External Approach	34
0HR0XK4	0HR0XK4 - Replace Scalp Skin w Nonaut Sub, Part Thick, Extern	34
0HR1X73	0HR1X73 - Replace Face Skin w Autol Sub, Full Thick, Extern	34
0J8K0ZZ	0J8K0ZZ - Division of L Hand Subcu/Fascia, Open Approach	34
0KBC0ZZ	0KBC0ZZ - Excision of Right Hand Muscle, Open Approach	34
0HNNXZZ	0HNNXZZ - Release Left Foot Skin, External Approach	33
0HR9X74	0HR9X74 - Replace Perineum Skin w Autol Sub, Part Thick, Extern	33
0HRBXJZ	0HRBXJZ - Replacement of R Up Arm Skin with Synth Sub, Extern Approach	33
0HR8X73	0HR8X73 - Replace Buttock Skin w Autol Sub, Full Thick, Extern	32
0QBH0ZZ	0QBH0ZZ - Excision of Left Tibia, Open Approach	32
0HRFXJZ	0HRFXJZ - Replacement of R Hand Skin with Synth Sub, Extern Approach	31
0JN60ZZ	0JN60ZZ - Release Chest Subcutaneous Tissue and Fascia, Open Approach	31
0JRK07Z	0JRK07Z - Replace of L Hand Subcu/Fascia with Autol Sub, Open Approach	31
F00ZJWZ	F00ZJWZ - Instru Swal/Oral Funct Assessment using Swallow Equipment	31
0KB80ZZ	0KB80ZZ - Excision of Left Upper Arm Muscle, Open Approach	30
0KN90ZZ	0KN90ZZ - Release Right Lower Arm and Wrist Muscle, Open Approach	30
0LB70ZZ	0LB70ZZ - Excision of Right Hand Tendon, Open Approach	30
2W0LX6Z	2W0LX6Z - Change Pressure Dressing on Right Lower Extremity	30
0HPPXJZ	0HPPXJZ - Removal of Synthetic Substitute from Skin, External Approach	29
0JRJ07Z	0JRJ07Z - Replace of R Hand Subcu/Fascia with Autol Sub, Open Approach	29
0KBR0ZZ	0KBR0ZZ - Excision of Left Upper Leg Muscle, Open Approach	29
0LBV0ZZ	0LBV0ZZ - Excision of Right Foot Tendon, Open Approach	29
0HR7XJZ	0HR7XJZ - Replacement of Abdomen Skin with Synth Sub, Extern Approach	28
0HRGXJZ	0HRGXJZ - Replacement of L Hand Skin with Synth Sub, Extern Approach	28
0KBG0ZZ	0KBG0ZZ - Excision of Left Trunk Muscle, Open Approach	28

0KNT0ZZ	0KNT0ZZ - Release Left Lower Leg Muscle, Open Approach	28
0LB80ZZ	0LB80ZZ - Excision of Left Hand Tendon, Open Approach	28
2W1LX6Z	2W1LX6Z - Compression of Right Lower Extremity using Pressure Dressing	28
30233M1	30233M1 - Transfuse Nonaut Plasma Cryoprecip in Periph Vein, Perc	28
0H8EXZZ	0H8EXZZ - Division of Left Lower Arm Skin, External Approach	27
0HQDXZZ	0HQDXZZ - Repair Right Lower Arm Skin, External Approach	27
0HREXJZ	0HREXJZ - Replace of L Low Arm Skin with Synth Sub, Extern Approach	27
0JN80ZZ	0JN80ZZ - Release Abd Subcu/Fascia, Open Approach	27
2W1TX6Z	2W1TX6Z - Compression of Left Foot using Pressure Dressing	27
4A033R1	4A033R1 - Measure of Arterial Saturation, Peripheral, Perc Approach	27
0H9FXZZ	0H9FXZZ - Drainage of Right Hand Skin, External Approach	26
0HNMXZZ	0HNMXZZ - Release Right Foot Skin, External Approach	26
0HRAXK3	0HRAXK3 - Replace Inguin Skn w Nonaut Sub, Full Thick, Extern	26
0JBB0ZZ	0JBB0ZZ - Excision of Perineum Subcu/Fascia, Open Approach	26
0JDJ3ZZ	0JDJ3ZZ - Extraction of R Hand Subcu/Fascia, Perc Approach	26
0KNB0ZZ	0KNB0ZZ - Release Left Lower Arm and Wrist Muscle, Open Approach	26
2W1MX6Z	2W1MX6Z - Compression of Left Lower Extremity using Pressure Dressing	26
0HB9XZZ	0HB9XZZ - Excision of Perineum Skin, External Approach	25
0J8J0ZZ	0J8J0ZZ - Division of R Hand Subcu/Fascia, Open Approach	25
0LBN0ZZ	0LBN0ZZ - Excision of Right Lower Leg Tendon, Open Approach	25
08QNXZZ	08QNXZZ - Repair Right Upper Eyelid, External Approach	24
0HQFXZZ	0HQFXZZ - Repair Right Hand Skin, External Approach	24
0HRTXKZ	0HRTXKZ - Replacement of Right Breast with Nonaut Sub, Extern Approach	24
0HRVXKZ	0HRVXKZ - Replacement of Bi Breast with Nonaut Sub, Extern Approach	24
0LBP0ZZ	0LBP0ZZ - Excision of Left Lower Leg Tendon, Open Approach	24
0Y6Y0Z0	0Y6Y0Z0 - Detachment at Left 5th Toe, Complete, Open Approach	24
2W13X6Z	2W13X6Z - Compression of Abdominal Wall using Pressure Dressing	24
0H8CXZZ	0H8CXZZ - Division of Left Upper Arm Skin, External Approach	23
0HRTX7Z	0HRTX7Z - Replacement of Right Breast with Autol Sub, Extern Approach	23
0HRUXKZ	0HRUXKZ - Replacement of Left Breast with Nonaut Sub, Extern Approach	23
0JDN3ZZ	0JDN3ZZ - Extraction of R Low Leg Subcu/Fascia, Perc Approach	23
0JDP3ZZ	0JDP3ZZ - Extraction of L Low Leg Subcu/Fascia, Perc Approach	23
0JRQ07Z	0JRQ07Z - Replace of R Foot Subcu/Fascia with Autol Sub, Open Approach	23
0LBW0ZZ	0LBW0ZZ - Excision of Left Foot Tendon, Open Approach	23

2W1RX6Z	2W1RX6Z - Compression of Left Lower Leg using Pressure Dressing	23
08QRXZZ	08QRXZZ - Repair Left Lower Eyelid, External Approach	22
0H8GXZZ	0H8GXZZ - Division of Left Hand Skin, External Approach	22
0H8LXZZ	0H8LXZZ - Division of Left Lower Leg Skin, External Approach	22
0HR4X73	0HR4X73 - Replace Neck Skin w Autol Sub, Full Thick, Extern	22
0HR9XK4	0HR9XK4 - Replace Perineum Skin w Nonaut Sub, Part Thick, Extern	22
0HRVX7Z	0HRVX7Z - Replacement of Bi Breast with Autol Sub, Extern Approach	22
0JD13ZZ	0JD13ZZ - Extraction of Face Subcu/Fascia, Perc Approach	22
0JRP07Z	0JRP07Z - Replace L Low Leg Subcu/Fascia w Autol Sub, Open	22
0JRR07Z	0JRR07Z - Replace of L Foot Subcu/Fascia with Autol Sub, Open Approach	22
0KND0ZZ	0KND0ZZ - Release Left Hand Muscle, Open Approach	22
0KNS0ZZ	0KNS0ZZ - Release Right Lower Leg Muscle, Open Approach	22
08QPXZZ	08QPXZZ - Repair Left Upper Eyelid, External Approach	21
0HXFXZZ	0HXFXZZ - Transfer Right Hand Skin, External Approach	21
0J8H0ZZ	0J8H0ZZ - Division of L Low Arm Subcu/Fascia, Open Approach	21
0JD40ZZ	0JD40ZZ - Extraction of Rt Neck Subcu/Fascia, Open Approach	21
0JD90ZZ	0JD90ZZ - Extraction of Buttock Subcu/Fascia, Open Approach	21
0JRD07Z	0JRD07Z - Replace R Up Arm Subcu/Fascia w Autol Sub, Open	21
0Y6H0Z1	0Y6H0Z1 - Detachment at Right Lower Leg, High, Open Approach	21
5A05121	5A05121 - Extracorporeal Hyperbaric Oxygenation, Intermittent	21
0HQGXZZ	0HQGXZZ - Repair Left Hand Skin, External Approach	20
0HRUX7Z	0HRUX7Z - Replacement of Left Breast with Autol Sub, Extern Approach	20
0HXGXZZ	0HXGXZZ - Transfer Left Hand Skin, External Approach	20
0J8G0ZZ	0J8G0ZZ - Division of R Low Arm Subcu/Fascia, Open Approach	20
0JD73ZZ	0JD73ZZ - Extraction of Back Subcu/Fascia, Perc Approach	20
0JDM3ZZ	0JDM3ZZ - Extraction of L Up Leg Subcu/Fascia, Perc Approach	20
0JRF07Z	0JRF07Z - Replace L Up Arm Subcu/Fascia w Autol Sub, Open	20
0JRG07Z	0JRG07Z - Replace R Low Arm Subcu/Fascia w Autol Sub, Open	20
0PBV0ZZ	0PBV0ZZ - Excision of Left Finger Phalanx, Open Approach	20
08QQXZZ	08QQXZZ - Repair Right Lower Eyelid, External Approach	19
0H8KXZZ	0H8KXZZ - Division of Right Lower Leg Skin, External Approach	19
0HBUXZZ	0HBUXZZ - Excision of Left Breast, External Approach	19
0JR807Z	0JR807Z - Replace of Abd Subcu/Fascia with Autol Sub, Open Approach	19
0W9G3ZX	0W9G3ZX - Drainage of Peritoneal Cavity, Percutaneous Approach, Diagn	19

0X6N0Z3	0X6N0Z3 - Detachment at Right Index Finger, Low, Open Approach	19
0Y6N0ZD	0Y6N0ZD - Detachment at Left Foot, Partial 4th Ray, Open Approach	19
0Y6N0ZF	0Y6N0ZF - Detachment at Left Foot, Partial 5th Ray, Open Approach	19
0Y6R0Z0	0Y6R0Z0 - Detachment at Right 2nd Toe, Complete, Open Approach	19
0Y6X0Z0	0Y6X0Z0 - Detachment at Right 5th Toe, Complete, Open Approach	19
2W1NX6Z	2W1NX6Z - Compression of Right Upper Leg using Pressure Dressing	19
01N40ZZ	01N40ZZ - Release Ulnar Nerve, Open Approach	18
0HPPX7Z	0HPPX7Z - Removal of Autol Sub from Skin, Extern Approach	18
0HXEXZZ	0HXEXZZ - Transfer Left Lower Arm Skin, External Approach	18
0JDL3ZZ	0JDL3ZZ - Extraction of R Up Leg Subcu/Fascia, Perc Approach	18
0JR607Z	0JR607Z - Replace of Chest Subcu/Fascia with Autol Sub, Open Approach	18
0JR707Z	0JR707Z - Replace of Back Subcu/Fascia with Autol Sub, Open Approach	18
0JRM07Z	0JRM07Z - Replace L Up Leg Subcu/Fascia w Autol Sub, Open	18
0JRN07Z	0JRN07Z - Replace R Low Leg Subcu/Fascia w Autol Sub, Open	18
0X6P0Z3	0X6P0Z3 - Detachment at Left Index Finger, Low, Open Approach	18
0X6Q0Z3	0X6Q0Z3 - Detachment at Right Middle Finger, Low, Open Approach	18
2W03X6Z	2W03X6Z - Change Pressure Dressing on Abdominal Wall	18
2W0CX6Z	2W0CX6Z - Change Pressure Dressing on Right Lower Arm	18
2W1EX6Z	2W1EX6Z - Compression of Right Hand using Pressure Dressing	18
0H85XZZ	0H85XZZ - Division of Chest Skin, External Approach	17
0HBVXZZ	0HBVXZZ - Excision of Bilateral Breast, External Approach	17
0W993ZZ	0W993ZZ - Drainage of Right Pleural Cavity, Percutaneous Approach	17
0Y6M0Z9	0Y6M0Z9 - Detachment at Right Foot, Partial 1st Ray, Open Approach	17
0Y6M0ZF	0Y6M0ZF - Detachment at Right Foot, Partial 5th Ray, Open Approach	17
2W1BX6Z	2W1BX6Z - Compression of Left Upper Arm using Pressure Dressing	17
2W1QX6Z	2W1QX6Z - Compression of Right Lower Leg using Pressure Dressing	17
2W1SX6Z	2W1SX6Z - Compression of Right Foot using Pressure Dressing	17
0HBTXZZ	0HBTXZZ - Excision of Right Breast, External Approach	16
0HQEXZZ	0HQEXZZ - Repair Left Lower Arm Skin, External Approach	16
0HRAXK4	0HRAXK4 - Replace Inguin Skn w Nonaut Sub, Part Thick, Extern	16
0JDG3ZZ	0JDG3ZZ - Extraction of R Low Arm Subcu/Fascia, Perc Approach	16
0KB10ZZ	0KB10ZZ - Excision of Facial Muscle, Open Approach	16
0QBP0ZZ	0QBP0ZZ - Excision of Left Metatarsal, Open Approach	16
0RHX34Z	0RHX34Z - Insertion of Int Fix into L Finger Phalanx Jt, Perc Approach	16

0Y6M0ZC	0Y6M0ZC - Detachment at Right Foot, Partial 3rd Ray, Open Approach	16
0Y6M0ZD	0Y6M0ZD - Detachment at Right Foot, Partial 4th Ray, Open Approach	16
0Y6N0ZB	0Y6N0ZB - Detachment at Left Foot, Partial 2nd Ray, Open Approach	16
0Y6N0ZC	0Y6N0ZC - Detachment at Left Foot, Partial 3rd Ray, Open Approach	16
0HB7XZX	0HB7XZX - Excision of Abdomen Skin, External Approach, Diagnostic	15
0HR4XJZ	0HR4XJZ - Replacement of Neck Skin with Synth Sub, Extern Approach	15
0HRKXJ3	0HRKXJ3 - Replace R Low Leg Skin w Synth Sub, Full Thick, Extern	15
0HRMXJ3	0HRMXJ3 - Replace R Foot Skin w Synth Sub, Full Thick, Extern	15
0JBC0ZZ	0JBC0ZZ - Excision of Pelvic Subcu/Fascia, Open Approach	15
0JDQ3ZZ	0JDQ3ZZ - Extraction of R Foot Subcu/Fascia, Perc Approach	15
0PBT0ZZ	0PBT0ZZ - Excision of Right Finger Phalanx, Open Approach	15
0X6M0Z3	0X6M0Z3 - Detachment at Left Thumb, Low, Open Approach	15
0X6R0Z3	0X6R0Z3 - Detachment at Left Middle Finger, Low, Open Approach	15
0Y6M0ZB	0Y6M0ZB - Detachment at Right Foot, Partial 2nd Ray, Open Approach	15
0Y6N0Z9	0Y6N0Z9 - Detachment at Left Foot, Partial 1st Ray, Open Approach	15
0Y6V0Z0	0Y6V0Z0 - Detachment at Right 4th Toe, Complete, Open Approach	15
2W04X6Z	2W04X6Z - Change Pressure Dressing on Chest Wall	15
2W1PX6Z	2W1PX6Z - Compression of Left Upper Leg using Pressure Dressing	15
0HQKXZZ	0HQKXZZ - Repair Right Lower Leg Skin, External Approach	14
0HR2XK3	0HR2XK3 - Replace R Ear Skin w Nonaut Sub, Full Thick, Extern	14
0HR8XJZ	0HR8XJZ - Replacement of Buttock Skin with Synth Sub, Extern Approach	14
0HRMXJZ	0HRMXJZ - Replacement of R Foot Skin with Synth Sub, Extern Approach	14
0HXHXZZ	0HXHXZZ - Transfer Right Upper Leg Skin, External Approach	14
0JDF3ZZ	0JDF3ZZ - Extraction of L Up Arm Subcu/Fascia, Perc Approach	14
0JDR3ZZ	0JDR3ZZ - Extraction of L Foot Subcu/Fascia, Perc Approach	14
0JNR0ZZ	0JNR0ZZ - Release L Foot Subcu/Fascia, Open Approach	14
0JRH07Z	0JRH07Z - Replace L Low Arm Subcu/Fascia w Autol Sub, Open	14
0JRL07Z	0JRL07Z - Replace R Up Leg Subcu/Fascia w Autol Sub, Open	14
0KBF0ZZ	0KBF0ZZ - Excision of Right Trunk Muscle, Open Approach	14
0KBP0ZZ	0KBP0ZZ - Excision of Left Hip Muscle, Open Approach	14
0QBL0ZZ	0QBL0ZZ - Excision of Right Tarsal, Open Approach	14
0QBQ0ZZ	0QBQ0ZZ - Excision of Right Toe Phalanx, Open Approach	14
0X6S0Z3	0X6S0Z3 - Detachment at Right Ring Finger, Low, Open Approach	14
0Y6D0Z3	0Y6D0Z3 - Detachment at Left Upper Leg, Low, Open Approach	14

0Y6H0Z3	0Y6H0Z3 - Detachment at Right Lower Leg, Low, Open Approach	14
0Y6S0Z0	0Y6S0Z0 - Detachment at Left 2nd Toe, Complete, Open Approach	14
2W08X6Z	2W08X6Z - Change Pressure Dressing on Right Upper Extremity	14
2W0EX6Z	2W0EX6Z - Change Pressure Dressing on Right Hand	14
2W0RX6Z	2W0RX6Z - Change Pressure Dressing on Left Lower Leg	14
0H9GXZZ	0H9GXZZ - Drainage of Left Hand Skin, External Approach	13
0HN4XZZ	0HN4XZZ - Release Neck Skin, External Approach	13
0HQLXZZ	0HQLXZZ - Repair Left Lower Leg Skin, External Approach	13
0HR1XJZ	0HR1XJZ - Replacement of Face Skin with Synth Sub, Extern Approach	13
0HR2XK4	0HR2XK4 - Replace R Ear Skin w Nonaut Sub, Part Thick, Extern	13
0HRNXJZ	0HRNXJZ - Replacement of L Foot Skin with Synth Sub, Extern Approach	13
0HXJXZZ	0HXJXZZ - Transfer Left Upper Leg Skin, External Approach	13
0JD50ZZ	0JD50ZZ - Extraction of Lt Neck Subcu/Fascia, Open Approach	13
0JD93ZZ	0JD93ZZ - Extraction of Buttock Subcu/Fascia, Perc Approach	13
0JDD3ZZ	0JDD3ZZ - Extraction of R Up Arm Subcu/Fascia, Perc Approach	13
0KBK0ZZ	0KBK0ZZ - Excision of Right Abdomen Muscle, Open Approach	13
0NB00ZZ	0NB00ZZ - Excision of Skull, Open Approach	13
0WJG0ZZ	0WJG0ZZ - Inspection of Peritoneal Cavity, Open Approach	13
0X6L0Z3	0X6L0Z3 - Detachment at Right Thumb, Low, Open Approach	13
2W05X6Z	2W05X6Z - Change Pressure Dressing on Back	13
2W0AX6Z	2W0AX6Z - Change Pressure Dressing on Right Upper Arm	13
2W1FX6Z	2W1FX6Z - Compression of Left Hand using Pressure Dressing	13
0H9KXZZ	0H9KXZZ - Drainage of Right Lower Leg Skin, External Approach	12
0HBHXZX	0HBHXZX - Excision of Right Upper Leg Skin, External Approach, Diagn	12
0HRGXJ4	0HRGXJ4 - Replace L Hand Skin w Synth Sub, Part Thick, Extern	12
0HX7XZZ	0HX7XZZ - Transfer Abdomen Skin, External Approach	12
0JD63ZZ	0JD63ZZ - Extraction of Chest Subcu/Fascia, Perc Approach	12
0JDH3ZZ	0JDH3ZZ - Extraction of L Low Arm Subcu/Fascia, Perc Approach	12
0JDK3ZZ	0JDK3ZZ - Extraction of L Hand Subcu/Fascia, Perc Approach	12
0JNQ0ZZ	0JNQ0ZZ - Release R Foot Subcu/Fascia, Open Approach	12
0QBK0ZZ	0QBK0ZZ - Excision of Left Fibula, Open Approach	12
0QBN0ZZ	0QBN0ZZ - Excision of Right Metatarsal, Open Approach	12
0RHW34Z	0RHW34Z - Insertion of Int Fix into R Finger Phalanx Jt, Perc Approach	12
0Y6C0Z3	0Y6C0Z3 - Detachment at Right Upper Leg, Low, Open Approach	12

0Y6Q0Z0	0Y6Q0Z0 - Detachment at Left 1st Toe, Complete, Open Approach	12
0Y6T0Z0	0Y6T0Z0 - Detachment at Right 3rd Toe, Complete, Open Approach	12
2W14X6Z	2W14X6Z - Compression of Chest Wall using Pressure Dressing	12
2W15X6Z	2W15X6Z - Compression of Back using Pressure Dressing	12
0HR0X73	0HR0X73 - Replace Scalp Skin w Autol Sub, Full Thick, Extern	11
0HR3XK3	0HR3XK3 - Replace L Ear Skin w Nonaut Sub, Full Thick, Extern	11
0HR9XK3	0HR9XK3 - Replace Perineum Skin w Nonaut Sub, Full Thick, Extern	11
0HRHXJ4	0HRHXJ4 - Replace R Up Leg Skin w Synth Sub, Part Thick, Extern	11
0HRJXJ4	0HRJXJ4 - Replace L Up Leg Skin w Synth Sub, Part Thick, Extern	11
0HRKXJ4	0HRKXJ4 - Replace R Low Leg Skin w Synth Sub, Part Thick, Extern	11
0HXCXZZ	0HXCXZZ - Transfer Left Upper Arm Skin, External Approach	11
0J8N0ZZ	0J8N0ZZ - Division of R Low Leg Subcu/Fascia, Open Approach	11
0J8P0ZZ	0J8P0ZZ - Division of L Low Leg Subcu/Fascia, Open Approach	11
0JD83ZZ	0JD83ZZ - Extraction of Abd Subcu/Fascia, Perc Approach	11
0JR70KZ	0JR70KZ - Replace of Back Subcu/Fascia with Nonaut Sub, Open Approach	11
0JRP0KZ	0JRP0KZ - Replace L Low Leg Subcu/Fascia w Nonaut Sub, Open	11
0KB60ZZ	0KB60ZZ - Excision of Left Shoulder Muscle, Open Approach	11
0KN70ZZ	0KN70ZZ - Release Right Upper Arm Muscle, Open Approach	11
0KXS0ZZ	0KXS0ZZ - Transfer Right Lower Leg Muscle, Open Approach	11
0LBS0ZZ	0LBS0ZZ - Excision of Right Ankle Tendon, Open Approach	11
0QSG04Z	0QSG04Z - Reposition Right Tibia with Int Fix, Open Approach	11
0X6D0Z2	0X6D0Z2 - Detachment at Right Lower Arm, Mid, Open Approach	11
0X6T0Z3	0X6T0Z3 - Detachment at Left Ring Finger, Low, Open Approach	11
0XBJ0ZZ	0XBJ0ZZ - Excision of Right Hand, Open Approach	11
0Y6H0Z2	0Y6H0Z2 - Detachment at Right Lower Leg, Mid, Open Approach	11
0Y6J0Z1	0Y6J0Z1 - Detachment at Left Lower Leg, High, Open Approach	11
0Y6P0Z0	0Y6P0Z0 - Detachment at Right 1st Toe, Complete, Open Approach	11
0Y6R0Z1	0Y6R0Z1 - Detachment at Right 2nd Toe, High, Open Approach	11
0Y6R0Z3	0Y6R0Z3 - Detachment at Right 2nd Toe, Low, Open Approach	11
0Y6W0Z0	0Y6W0Z0 - Detachment at Left 4th Toe, Complete, Open Approach	11
2W3DX1Z	2W3DX1Z - Immobilization of Left Lower Arm using Splint	11
F08F5ZZ	F08F5ZZ - Wound Management Treatment of Integu Up Back/UE	11
08NPXZZ	08NPXZZ - Release Left Upper Eyelid, External Approach	10
0BP1XDZ	0BP1XDZ - Removal of Intraluminal Device from Trachea, Extern Approach	10

0DB68ZX	0DB68ZX - Excision of Stomach, Endo, Diagn	10
0H8HXZZ	0H8HXZZ - Division of Right Upper Leg Skin, External Approach	10
0H9EXZZ	0H9EXZZ - Drainage of Left Lower Arm Skin, External Approach	10
0HQ7XZZ	0HQ7XZZ - Repair Abdomen Skin, External Approach	10
0HQBXZZ	0HQBXZZ - Repair Right Upper Arm Skin, External Approach	10
0HQJXZZ	0HQJXZZ - Repair Left Upper Leg Skin, External Approach	10
0HR3XK4	0HR3XK4 - Replace L Ear Skin w Nonaut Sub, Part Thick, Extern	10
0HRCXJ4	0HRCXJ4 - Replace L Up Arm Skin w Synth Sub, Part Thick, Extern	10
0HRJXJ3	0HRJXJ3 - Replace L Up Leg Skin w Synth Sub, Full Thick, Extern	10
0HRLXJ4	0HRLXJ4 - Replace L Low Leg Skin w Synth Sub, Part Thick, Extern	10
0HX5XZZ	0HX5XZZ - Transfer Chest Skin, External Approach	10
0HXBXZZ	0HXBXZZ - Transfer Right Upper Arm Skin, External Approach	10
0HXKXZZ	0HXKXZZ - Transfer Right Lower Leg Skin, External Approach	10
0JD00ZZ	0JD00ZZ - Extraction of Scalp Subcu/Fascia, Open Approach	10
0JR60KZ	0JR60KZ - Replace of Chest Subcu/Fascia with Nonaut Sub, Open Approach	10
0JRD0KZ	0JRD0KZ - Replace R Up Arm Subcu/Fascia w Nonaut Sub, Open	10
0KBL0ZZ	0KBL0ZZ - Excision of Left Abdomen Muscle, Open Approach	10
0KBN0ZZ	0KBN0ZZ - Excision of Right Hip Muscle, Open Approach	10
0PHV34Z	0PHV34Z - Insertion of Int Fix into L Finger Phalanx, Perc Approach	10
0QSH04Z	0QSH04Z - Reposition Left Tibia with Int Fix, Open Approach	10
0T2BX0Z	0T2BX0Z - Change Drainage Device in Bladder, External Approach	10
0X6N0Z0	0X6N0Z0 - Detachment at Right Index Finger, Complete, Open Approach	10
0X6P0Z0	0X6P0Z0 - Detachment at Left Index Finger, Complete, Open Approach	10
0X6T0Z1	0X6T0Z1 - Detachment at Left Ring Finger, High, Open Approach	10
0X6W0Z3	0X6W0Z3 - Detachment at Left Little Finger, Low, Open Approach	10
0Y6T0Z3	0Y6T0Z3 - Detachment at Right 3rd Toe, Low, Open Approach	10
0YBJ0ZZ	0YBJ0ZZ - Excision of Left Lower Leg, Open Approach	10
0YPBXKZ	0YPBXKZ - Removal of Nonaut Sub from L Low Extrem, Extern Approach	10
2W0SX6Z	2W0SX6Z - Change Pressure Dressing on Right Foot	10
2W18X6Z	2W18X6Z - Compression of Right Upper Extremity using Pressure Dressing	10