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Expansion of the Biodynamics Data Resource (BDR): Non-Human Primate Impact Acceleration Research Data in the BDR

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Human Use

Human subjects were also involved in the legacy studies conducted at the NBDL. The participation of the human subjects (1974-1995) was in accordance with procedures specified in the Secretary of the Navy Instruction 3900.39 series and the Bureau of Medicine and Surgery Instruction 3900.6 series. These instructions are based upon free and informed voluntary consent, and met (or exceeded) the provisions of national and international guidelines at the time of research.

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14. ABSTRACT

The Biodynamics Data Resource (BDR) was established by the U.S. Army Aeromedical Research Laboratory (USAARL) and the U.S. Naval Air Systems Command (NAVAIR) Human Systems Department to restore, preserve, organize, and provide a functional relational database for the materials of the legacy collection recovered from the Naval Biodynamics Laboratory (NBDL) Impact Acceleration Program. Initially, the BDR was established with a focus on the human research volunteer (HRV) data within the NBDL collection, which includes data for over 3000 HRV non-contact inertial loading exposures. The BDR project has since expanded to include the non-human primate (NHP) data within the NBDL collection. This report reflects the efforts that expanded the BDR to incorporate the recovered NHP data and provides an overview of the NHP impact acceleration work conducted at the NBDL.

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impact acceleration, NBDL, inertial loading, injury biomechanics, sled test, legacy collection, non-human primate, IBPG

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Summary

The impact acceleration program at the Naval Biodynamics Laboratory (NBDL) used non-human primates (NHPs) as living human surrogates to investigate the dynamic response (head and neck kinematics, injury, and physiological effects) to controlled whole-body impact acceleration exposures. These NHP exposures were conducted as a complement to the non-injurious exposures performed by the NBDL with human research volunteers (HRV). Much of the data collected as a part of these experiments remains unpublished and inaccessible to the scientific community.

The Biodynamics Data Resource (BDR) project exists, in part, to catalog, organize, digitize, and modernize the NBDL collection and to make it available for research. The initial stages of the BDR project focused on the HRV data from the NBDL collection and making these HRV data accessible via the BDR relational database. The BDR project has since expanded to include the NHP data also within the NBDL collection. These NHP data within the NBDL collection are referred to collectively as the "NHP collection."

A multifaceted effort was initiated to discern what NHP data exist, in what amount, and to what degree of usefulness. The NHP collection, complex with a variety of physical and digital materials, was organized and inventoried. Usability of physical material as a diagnostic tool was reviewed. Physical materials of the collection were digitized into archival formats. Documentation was reviewed to characterize the collection and its potential for use in future research. Through this multifaceted effort, the overview of the NHP collection was reconstructed.

The NHP collection from the NBDL impact acceleration program includes three different species of NHPs and data for 400 impact exposures of varying direction and acceleration. The impact acceleration program at the NBDL used both a horizontal and vertical accelerator for studying the dynamic response to whole-body, non-contact, inertial loading. The majority of impact acceleration research at the NBDL was conducted on a horizontal accelerator, including 366 NHP runs. Frontal impacts were the most numerous and had the highest peak accelerations (up to 193 G). Rear, lateral, and axial runs were also conducted. On the vertical accelerator, 34 NHP axial runs were completed (up to 70 G). Types of time series data acquired during impact included sensor, photo (i.e., high-speed film), and electrophysiological data. Additional data were collected from anthropometry and diagnostic tests (e.g., X-rays). Evaluation of NHPs was documented immediately post-run and at regular intervals until sacrifice, analgesic medications were logged, and necropsies and tissue samples taken were recorded. These samples, in the form of slides and embedded-tissue blocks, remain in usable condition. Thus, the NHP data constitute a robust collection of exposure and response data.

The collection of NHP data from the impact acceleration program is represented in digital form within the BDR relational database and will be accessible to researchers by use of metadata terms applied to each item. The BDR relational database will provide the data from the impact acceleration program to researchers in a way that will allow it to be used to address research gaps, supported by a firm understanding of what the NBDL accomplished in the 25 years of its operation. This work is especially important because the experiments done by the NBDL impact acceleration program will likely never be repeated, largely due to the current regulations surrounding both human and animal research. Therefore, the NBDL NHP collection must be

provided to the scientific community and leveraged to expand the understanding of injuries evident in whole-body acceleration events. This technical report reflects the expansion of the BDR project to incorporate the valuable NHP collection and provides an overview of the NHP impact acceleration work conducted at the NBDL.

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Introduction

In 1971, the impact acceleration program at the Naval Biodynamics Laboratory (NBDL) was established to systematically investigate dynamic human response (i.e., head and neck kinematics, injury, and physiological effects) to controlled whole-body impact acceleration exposures. The program used two unique platforms to impart non-contact inertial loading to the head-neck: both a horizontal and vertical accelerator. The subject of the inertial loading was positioned and restrained in a chair atop a carriage (Appendix A), which attached to either the horizontal or vertical accelerator track. A controlled impact acceleration pulse was applied to the resting carriage to simulate various types of impacts (e.g., rear, frontal, lateral). The carriage and subject were instrumented with arrays of accelerometers and phototargets, and high-speed cameras were used to capture the kinematic response to impact (Appendix A). Additional data before, during, and following the inertial loading, including radiological and physiological data, were collected for most subjects.

Data were collected from over 7000 non-contact inertial loading exposures, referred to as "runs." The majority of these runs were conducted with human research volunteers (HRVs); the remainder were conducted with human surrogates, including anthropomorphic test devices (ATDs) and both chimpanzee and macaque non-human primates (NHPs). NHP runs, which began in 1973, were conducted jointly with HRV runs. Schmidt et al. (2009) previously provided an overview of the impact acceleration program at the NBDL with an emphasis on the HRV portion of the program. The NHPs were used as a human surrogate in the impact acceleration program for higher acceleration levels that could be potentially injurious and, therefore, could not be safely tested with HRVs. The NHP runs account for 400 of the total number of exposures conducted at the NBDL, including runs in multiple impact directions (single vector) and with both the horizontal and vertical accelerators.

In 1989, NHP testing for the impact acceleration program concluded. The NBDL continued to collect impact acceleration data from HRVs and ATDs until 1996, when the NBDL was closed following recommendations by the Base Realignment and Closure (BRAC) Commission (Naval Biodynamics Laboratory, 1996). Schmidt et al. (2009) provide more detail on the history of the legacy collection following 1996. Briefly, following the BRAC the materials and equipment remained at the NBDL but were largely left untouched and inaccessible for research. In 2007, through collaboration with the U.S. Naval Air Systems Command (NAVAIR) Human Systems Department, the U.S. Army Aeromedical Research Laboratory (USAARL) recovered the NBDL collection with the broad goals of making the data accessible for research and performing new analysis with the data. Much of the material had become disorganized since the BRAC closed the NBDL. Some material had deteriorated, and a portion of the material included formats that became obsolete.

The USAARL Biodynamics Data Resource (BDR) was established by USAARL and NAVAIR to restore, preserve, and organize the materials of the NBDL collection and construct a functional, accessible relational database for housing and sharing these materials digitally.

This BDR relational database was designed as a data repository with fidelity, usability, and standardization to facilitate research with the NBDL collection as well as biodynamics data from other sources. Though additional biodynamics datasets will be contained in the BDR, the NBDL impact acceleration collection was the first to be scrutinized and prepared for inclusion

into the database. More specifically, the BDR relational database was established with a focus on the invaluable HRV collection, the HRV data within the NBDL collection (Schmidt et al., 2009). Since then, efforts have been underway to expand the BDR to include the equally invaluable NHP collection, the NHP data within the NBDL collection. While both the NHP and HRV collections include similar data, films, photographs, and equipment, the NHP collection also includes some data unique to animal testing. These unique NHP data are diverse and extensive, including detailed subject records, data from surgically implanted somatosensory evoked potential recordings, modified test setups and data processing algorithms, diagnostic radiology, necropsy photos, pathology records, and preserved tissue samples in the form of prepared microscope slides and embedded-tissue blocks.

This report reflects information gained during the intermediary stages of the BDR expansion, during which time the NHP materials were organized and inventoried to account for content within the collection, digitized to provide effective access for researchers, and reviewed for research potential within the field of biomechanics. Concurrent with the in-depth review that was necessary to establish a comprehensive understanding of the collection, additional efforts into analysis with the NHP collection were undertaken. These efforts towards expanding the BDR relational database provide researchers a wealth of NHP experimental data, much of which is unpublished and cannot be reproduced. When expansion is complete, the result will be a thorough, searchable database that will allow researchers to access the data and advance the fields of research in injury biomechanics, military operations, crashworthiness and automotive safety, and medical trauma.

Methods

The establishment of the BDR and the requisite broad organizational efforts for the NBDL datasets focusing on the HRV collection are elucidated at length in USAARL Report No. 2010-01, “Establishing the Biodynamics Data Resource (BDR): Human Volunteer Impact Acceleration Research Data in the BDR” (Schmidt et al., 2009). The previously established methods for organizing and categorizing material were extended to incorporate the NHP collection into the BDR. The major efforts towards accomplishing this broad goal are described in this report, including developing inventories, digitizing materials, applying metadata, and ensuring the usability of the data itself.

Developing Inventories

In the post-establishment era of the BDR, expanding comprehension of the NHP dataset within the NBDL collection became a priority. These data had largely been untouched during the initial organization of the NBDL collection. As such, a multifaceted effort was initiated to determine what NHP data existed and in what amount. Thus, inventories were developed for the various materials contained in the NHP collection. Each inventory was developed to include similar fields that could be used to organize and link related data. For example, subject numbers and run numbers, any handwritten notes on the material, material appearance and location, and, in some instances, the presence or absence of expected materials were captured whenever applicable. These materials are described in the Results section. Comprehensive records detailing the NHP subject identifiers and any inconsistencies of these identifiers throughout the impact acceleration program were included in these inventories.

Digitizing Materials

Concurrent with the development of the NHP inventories, the NHP materials were transformed into accessible, non-proprietary, digital formats (PDF/A, TIFF, etc.). In general, the NHP collection and HRV collection are comprised of similar materials such as data, film, photographs, radiology, and equipment. Therefore, proven methods, developed for the HRV collection and documented in the BDR Best Practices and Standard Operating Procedures (SOPs; Biodynamics Data Resource, 2019a, 2019b), were applied to the materials in the NHP collection. The applied methods ensured appropriate handling of materials to protect and preserve the often delicate resources.

Unique to the NHP collection are the available pathology samples. The pathology collection contains embedded and slide-mounted tissue samples that were collected from the NHP during necropsy. The prepared microscope slides were digitized by the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID). A Leica Biosystems Aperio slide scanner microscope at 40x power magnification was used by USAMRIID to create a digital image (i.e., scan) of each slide. Conversely, the embedded tissue samples exist in block form (e.g., paraffin blocks) and cannot be effectively digitized in their current state. To accommodate the obvious difficulties of including a three-dimensional object in the database, the embedded-tissue block inventory, which includes the information for each block (subject, tissue, etc.), was developed in a format compatible with the database table structures. In doing so, both the prepared microscope slides and embedded-tissue block information were translated into a representative digital format that is useable within the BDR relational database.

While this report focuses on the NHP collection, additional expansion efforts not described in the previous report by Schmidt et al. (2009) were undertaken for the NBDL collection at large. Notable efforts include the digitization of obsolete media (e.g., magnetic tapes) and the development and application of metadata. Obsolete media are storage media that were used throughout the 25-year span of work at the NBDL but, in a modern setting, are unreadable without special equipment. Using the inventory developed for the obsolete media, pieces of media were prioritized and selected for digitization. Prioritization was dependent on the likelihood of the media containing the critical time series data collected during each run. Viable data were recovered from these media through contracted work with a subject matter expert. The other effort, the development and application of metadata, was necessary to facilitate searching and retrieving the NBDL collection within the BDR relational database. Metadata were developed and applied to all digitized material. A separate report is in progress and will describe these efforts in more detail.

Using the Data

Additional efforts were essential to ensure the usability of the data for research. These efforts focused on regulatory compliance, viability of the pathology collection, and characterization of the NHP collection.

Regulatory compliance was guided by the intent to use both the HRV and NHP collections together for research. Respective regulatory bodies provided guidance for research involving human and animal subjects. The BDR was initially established with the focus on performing research with the HRV collection. Thus, to guide research with the HRV collection, a

research repository protocol was developed and approved by the U.S. Army Medical Research and Development Command (USAMRDC) Institutional Review Board (IRB; Chancey & Vasquez, 2009). As a companion to the protocol, the BDR SOP was developed to establish the physical and electronic archive, digitizing guidelines, protections, and operations of the BDR data research repository. Later, when the focus of the BDR expanded to include research with the NHP collection, the USAMRDC Animal Care and Use Review Office (ACURO) was contacted for guidance on appropriate handling, use, and dissemination of the existing animal data generated by the NBDL. The BDR SOP was then updated to be inclusive of handling and protecting the NHP collection.

Due to the age of the tissue samples in the pathology collection, their viability for research was evaluated. Samples from both the slide collection and embedded-tissue block collection were reviewed by pathology experts. The Joint Pathology Center (JPC) applied immunohistochemical stains on tissue samples from a selection of the embedded-tissue blocks. Also, a selection of the slides was reviewed by a JPC pathologist.

Finally, to characterize the NHP collection, documents (publications, protocols, reports, subject records, etc.) were reviewed for NHP-related information and available data were summarized. Specifically, the documents and data were used to characterize the experimental methodologies, data, and research outcomes of the NBDL impact acceleration program.

Results

Incorporating the NHP collection into the BDR yielded a considerable understanding of the NHP portion of the impact acceleration program at the NBDL. Following an introduction of the physical items contained in the overall NHP collection, the complex program is described according to several major topics, including the NHP subjects, experimentation (instrumentation and data collection procedures), and research outcomes.

Overall Collection

Impact acceleration research with the NHPs occurred jointly with similar research involving HRVs and ATDs. Though comparable data were acquired for each of these three subject types, the NHP data include unique information that were unable to be collected from the other subject types. The variations in data gathered between these three subject types led to the creation of multiple collections, some specific to the subject type, that capture all available sources of data. The NHP collection consists of several forms of physical materials, including, but not limited to:

- subject records (documentation on care, maintenance, etc., and necropsy reports),
- radiological films (pre-/post-run and pre-/post-surgery X-rays),
- photographs (facility, equipment, subject, run, etc.),
- 35-millimeter (mm) slides (presentations),
- 16-mm high-speed film (on-board and off-board film),
- run summaries (engineering parameters for each run),
- run records (medical information recorded post-run for a subject),
- obsolete media (9-tracks, 4-mm data tapes, quarter-inch cartridge tapes, etc.),
- laboratory notebooks,

- strip charts (electrophysiology, including electrocardiographs [ECGs]),
- microfiche (plots, run summaries),
- pathology (prepared microscope slides and embedded-tissue blocks), and
- publications.

The relationships between these items and the effort put into preserving these relationships in a manner that is most useful to other researchers are the foundation of the overview provided in the subsequent sections.

Impact Acceleration Program

The NHPs were used as living human surrogates in the impact acceleration program for studying higher, potentially injurious accelerations to which human volunteers could not be safely exposed. Thus, an injurious threshold and fatal limit could be characterized according to the observed physiologic and kinematic responses of the NHPs and scaled to the human. In order to define these same injurious thresholds in humans, the size difference between the species required a scaling model. The impact acceleration program's planned scaling effort included a comparison of the electrophysiological and kinematic data that were collected from both NHPs and HRVs. This plan to develop a scaling model using the kinematic response required at least two species of NHPs, meeting the criteria of (1) a large difference in size and (2) a morphological similarity to humans (Naval Biodynamics Laboratory, 1985a).

The NBDL began NHP impact acceleration experimentation in 1973 and concluded these experiments with NHPs in 1989; all NHPs were relocated from the NBDL by February 1991 (Naval Biodynamics Laboratory, 1993). Based on discussions with the USAMRDC ACURO and a review of NBDL documentation, compliance of NBDL with all regulatory guidance available at the time of the original research period was determined. All Department of Defense (DoD) and Federal regulations were adhered to by the NBDL even as legislation regarding animal use in research evolved over the decades the lab operated. The NBDL maintained an Institutional Animal Care and Use Committee (IACUC) that met regularly to review, approve/disapprove all animal protocols, and inspect the animal care facilities to ensure that ethical quality care was provided to the NHPs. The laboratory was also an accredited organization with the American Association for the Accreditation of Laboratory Animal Care (AAALAC)[*] from February 1984 through May 1991 (K. Bayne, personal communication, September 17, 2015). An example of adherence to these animal use regulations is included in a publication by Thomas and Jessop (1986). In this published work, which focuses on a large portion of initial NHP testing conducted between 1974 and 1983, Thomas and Jessop (1986) included the following:

> The animals used in this study were handled in accordance with the "Guide for the Care of Laboratory Animals", prepared by the Committee on Care and Use of Laboratory

[*] The American Association for Accreditation of Laboratory Animal Care (AAALAC) was established in 1965. The organization subsequently changed its name to the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International) in 1996 and then revised its name again in 2016 to AAALAC International ("History [Long Version]", n.d.).

Animals of the Institute of Laboratory Animal Resources, National Research Council (Thomas & Jessop, 1986, p. 393).

Non-Human Primate Subjects

The researchers at the NBDL indexed the NHP subjects used in their programs with a variety of techniques. These indexing techniques included: subject number (dependent on the project[s] the NHP was involved in, both in and out of the NBDL), identification tattoo (should match the subject number and was located on the chest or inner thigh), species of the NHP, vivarium colony the NHP resided in, and name of the NHP, if named. Indexing was critical because these NHPs were life-long research subjects and were transferred between laboratories as subjects in various experiments. During their tenure at the NBDL, several of the NHPs were subjects in research studies apart from those of the impact acceleration program, such as the NBDL vibration studies. The space available at the NBDL for NHP care was limited; therefore, NHP subjects also resided at facilities near the NBDL such as the Delta Regional Primate Research Center. Also, a selection of the NHPs was sent temporarily to the Medical College of Wisconsin (MCW) for permanent electrode placement for somatosensory evoked potential (SEP) experiments as part of the impact acceleration program. These NHPs resided at the MCW for the duration of their surgical and recovery period.

An original, comprehensive inventory for the NHP collection was not among the items recovered from the NBDL. To organize and incorporate these data within the BDR, this lack of inventory created the potential for confusion in identifying the NHPs, particularly considering the vast scope of experiments that the NHPs were subjects of as well as the many forms of materials on which the NHP data were stored. Multiple inventories were created within the NHP data for each collection (e.g., subject records, radiological films, pathology). These inventories catalog the known information about each NHP subject, such as research project(s), sex, subject number(s), dates of activities, and lab accession numbers. Through cross-referencing these inventories, confusion and possible errors were eliminated and a thorough and accurate view into the specific details of the program's NHP subjects is provided. While these inventories are not included in this report due to the level of detail they encompass, an overview of the NHPs and their involvement in the impact acceleration program is provided.

Demographics.

The NHP subjects involved in the impact acceleration program comprised three different species: chimpanzee (*Pan troglodytes*), rhesus macaque (*Macaca mulatta*), and the Assam macaque (*Macaca assamensis*). These species were represented in the program by 3 male chimpanzees, 17 male Assam macaques, and 105 male and 3 female rhesus macaques (Table 1). All NHP subjects were mature adults. Therefore, the size and weight of each NHP throughout the duration of the program remained consistent (Thomas & Jessop, 1983).

Care and maintenance.

To oversee all procedures and experiments involving animals, the NBDL established a team of trained personnel. The team, which comprised the Veterinarian Resources Division, included an on-site veterinarian, the supervisor biological laboratory technician, and an animal care specialist. The team oversaw the day-to-day activities of the NHP subjects, including all

procurement, housing, and maintenance of the NHPs. They were also responsible for providing and handling the NHPs for experiments. After experiments, the team was responsible for monitoring the NHPs in addition to documenting and evaluating clinical and pathological results. Lastly, this team was charged with ensuring compliance with any federal and DoD regulations regarding experiments with the NHPs (Naval Biodynamics Laboratory, 1991).

Table 1. Overview of Non-Human Primate Demographics

	NHP Type	Number of NHPs	Species Average Weight at Run (pounds [lb])	Number of Runs	Years of Runs
	Chimpanzee	3	132	34	1974 –1976
	Assam macaque	17	24	20	1980 – 1987
	Rhesus macaque	108	19	346	1973 – 1989
Total:	3	128		400	1973 – 1989

Note. The Species Average Weight at Run were calculated from NHP weights recorded on the run day (if weight was not recorded on the run day, the weight on the nearest day to the run was used). A single average weight for a given NHP was calculated from all the run day weights that were available for that NHP. The majority (95%) of the subjects have recorded weights available.

A regimen of routine procedures was used to maintain the NHPs. These maintenance procedures included observation of eating and physical activity behaviors, overall physical appearance, and demeanor as well as performance of teeth cleaning and blood tests to monitor for disease and to establish baseline chemical measurements. Each subject record was annotated with these procedures as they occurred, providing the foundation for understanding the daily activities involving the NHPs.

During routine and experimental procedures, additional efforts were made to ensure the safety and well-being of both the NHPs and research personnel. The safety of the NHPs during the experimental procedures was ensured by constant monitoring of each NHP's vital signs. To protect research personnel, procedures were established, such as those for using personal protective equipment and only handling anesthetized NHPs. Personal protective equipment was critical when handling the NHPs because of the threat of zoonotic diseases. Zoonotic diseases that were closely monitored include shigellosis and Herpes B, which can produce severe and even life-threatening illness in an infected human (Burgos-Rodriguez, 2011). Proper procedures, such as using anesthesia, were also required when handling the NHPs both during routine and experimental procedures because of the physical threat that the NHPs posed. The chimpanzees posed the greatest physical threat to personnel due to their large size and strength; the impact acceleration program chimpanzees weighed as much as 137 pounds according to the subject records. Overall, the NBDL committed extensive effort into caring for the NHPs and keeping research personnel safe throughout the period of experimental testing.

Although the NBDL established procedures to allow them to work safely with the NHPs, other factors surrounding the use of the NHPs were also considered. The use of chimpanzees as experimental subjects was further complicated by the addition of the chimpanzee species to the threatened species list in 1976 (41 FR 45990), and later the endangered species list in 1990 (55 FR 9129). However, for the NBDL, use of the chimpanzees remained desirable because the species could be run with a test setup very similar to that of the HRVs. In comparison, though the test setup required to run the macaques required extensive modification, the macaques were generally more available, less dangerous, and less expensive to work with than chimpanzees.

Experimentation

During an operational period of more than 20 years, the NBDL used a variety of data collection techniques and data storage materials, as permitted by the technology of the time. The various types of materials used include magnetic tapes, strip charts, microfiche, and 16-mm film; each of which is a source of data once digitized. Much of the knowledge presented hereafter pertaining to the instrumentation used and data collected was assembled by reviewing these materials and the information related to each run in published and unpublished documents.

In general, the instrumentation used for impact acceleration research with NHPs was designed to be similar to that of the HRV experiments, such that similar data could be collected and scaled between species. The time-series data acquired during impact was of three types: 1) sensor, 2) photo, and 3) electrophysiology. Sensor and photo (i.e., high-speed film) data were used to capture motion of both the subject and sled. The redundant sensor and photo data were used to validate the critical motion of key anatomical segments throughout the exposure. Additional data, including anthropometry measurements and diagnostic tests, were collected to both define the injurious threshold as well as to scale the response to humans. While the test setup for the chimpanzee was similar to that used for the HRV (Appendix A), more modifications to the test setup were required to run macaque subjects (Thomas & Jessop, 1983; Unterharnscheidt, 1986), but the technology to do so was well-developed by the NBDL (Ewing et al., 1976).

Head and neck instrumentation.

The chimpanzees, closer in size than the macaque to the average human, had nearly identical head and neck instrumentation to that of the HRVs. This instrumentation included the mouth mount (customized to the subject via a stainless steel casting) and first thoracic vertebrae (T1) mount, both of which incorporated the use of the T-plate (Figure 1). The T-plate was used for mounting sensor and phototargets at both the mouth and T1. Though the instrumentation was similar to that of the HRVs, certain modifications were imposed throughout the development of the instrumentation mounting system. Ewing et al. (1976) report on the mounting systems used during the chimpanzee runs: after a failed attempt to chronically implant the T1 mounting system for directly measuring the input at T1, the mount was instead secured directly to the exposed posterior spinous process (Ewing et al., 1976; Unterharnscheidt & Ewing, 1978).

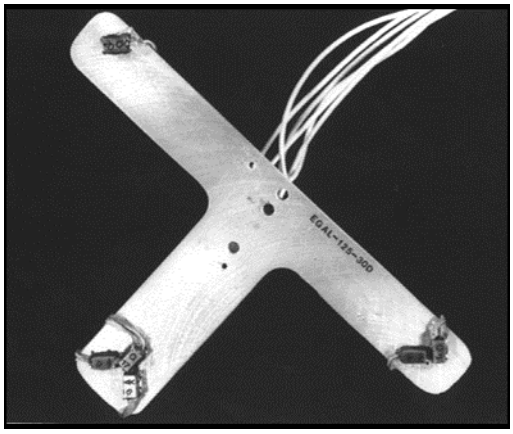

Figure 1. Instrumentation used to collect kinematic data for the chimpanzee. The T-plate includes an array of six linear accelerometers for determining acceleration, velocity, and displacement at the mouth and the first thoracic vertebrae (T1). The T-plate instrumentation was also used in the HRV runs (Ewing et al., 1976).

The rhesus and Assam macaques, which were smaller, could not use the same instrumentation setup as the chimpanzees and HRVs, so more significant modifications to the instrumentation were necessary. In order to obtain comparable sensor and photo data, instrumentation was mounted directly to the macaque head via a surgically implanted cranial pedestal made of dental acrylic. Attached to the calvarium, via the implanted cranial pedestal, was the A-plate (Figure 2), developed specifically to mount the sensors and phototargets. Therefore, head kinematic data were collected for the macaque subjects, but neck (i.e., T1) kinematic data were not (Matson, 1990; Thomas & Jessop, 1983; Unterharnscheidt & Ewing, 1978).

Sensor data.

Subject- and sled-mounted sensors were used to collect acceleration data. For each run, sled acceleration was captured by sled-mounted linear accelerometers (2000 samples per second). For runs with the chimpanzees, subject acceleration data were collected using accelerometers attached to a T-plate at both the mouth and T1. Each T-plate was configured with an array of six linear accelerometers, also with a sampling rate of 2000 samples per second (Becker & Willems, 1975; Ewing et al., 1976).

For the smaller macaques, the subject-mounted sensor setup was modified. Mounted on the A-plate were six linear accelerometers that measured acceleration of the head. Generally, sensor data were collected at 2000 samples per second. In one analysis, Matson (1990) reports a sample rate of 4000 samples per second collected for a set of 14 runs. Overall, the calibration and signal conditioning of the sensor data for all NHP runs were the same as that used for the HRV (Thomas & Jessop, 1983), but because the setup differed on the A-plate used for the macaques, additional efforts for analysis were required (Ewing et al., 1976; Unterharnscheidt & Ewing, 1978). Thus, the use of the A-plate supported the collection of valuable head kinematics, similar to the T-plate, which was used for HRVs and chimpanzee subjects.

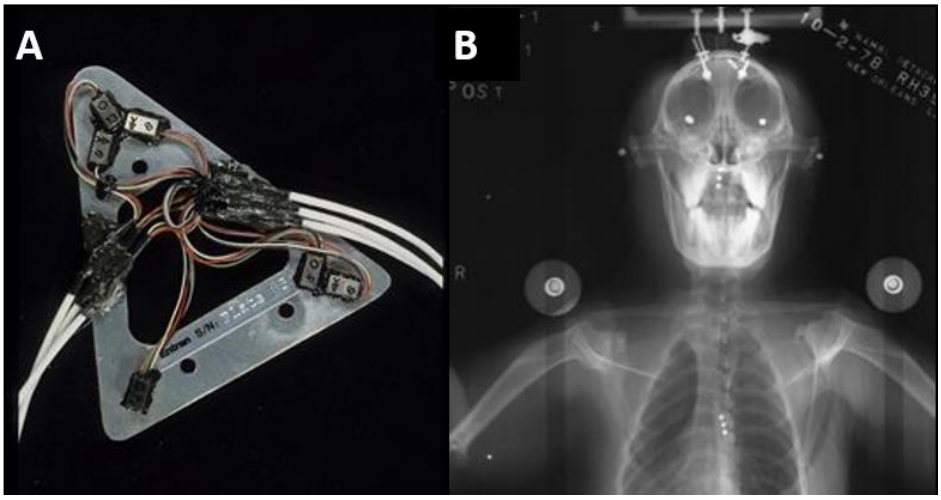

Figure 2. Instrumentation used to collect kinematic data for the macaque non-human primates. (A) The A-plate with an array of six linear accelerometers for determining acceleration, velocity, and displacement of the head. (B) An X-ray of a rhesus macaque with an implanted cranial pedestal. X-ray was used to measure the location of accelerometers relative to the NHP anthropometry (Thomas & Jessop, 1983).

Photo data.

Photo data, used to validate the sensor data, were obtained by tracking the displacement of subject- and sled-mounted phototargets (Figure 3). Each run was captured by multiple high-speed film cameras. After the run, the high-speed film from these cameras was processed; the phototargets attached to the sled and subject instrumentation were tracked frame-by-frame to measure displacement of the head and neck. For the chimpanzees, displacement data were collected using a custom-developed set of up to 14 phototargets at each anatomical site of interest, which is similar to the setup used for the HRVs (Ewing et al., 1976; Willems et al., 1981). For the smaller macaques, fewer phototargets were used (Thomas & Jessop, 1986; Unterharnscheidt, 1986).

The majority of the NHP runs were filmed with on-board cameras, but the earliest NHP runs (36 runs) were only filmed with off-board cameras. Initially, all NHP runs were conducted with a different sled than the sled used for HRV runs, and this NHP sled did not have on-board cameras. Instead, off-board cameras operating at 500 frames per second were used to capture the acceleration event. However, these off-board cameras did not provide the visual accuracy necessary to track the subject response kinematics. Therefore, on-board cameras were used in subsequent NHP runs.

The type of on-board camera used in the subsequent NHP runs depended on the size of NHP being tested. The NHP sled continued to be used for the smaller macaque subjects, and the HRV sled was used for the larger chimpanzee subjects (Ewing et al., 1976). Therefore, the chimpanzee runs were filmed using the same cameras used to film the HRV runs: on-board, pin-registered cameras that captured the critical kinematics at 500 frames per second. The macaque runs were captured with on-board, rotary-prism cameras that operated at 1000 frames per second. For most NHP runs, a minimum of two cameras were used in order to capture a frontal and lateral view of the subject. To improve calculations in runs with any out-of-plane motion, additional on-board cameras may have been mounted overhead (Thomas & Jessop, 1986).

Figure 3. T-plate phototarget setup used to collect kinematic data from the high-speed film. The phototargets used for the T-plate and A-plate setups were similar, but, due to limitations of the subject size and test setup, the array configurations differed. The T-plate instrumentation was used for the chimpanzee subjects. See Appendix A for an example of the T-plate instrumentation on an HRV subject.

Electrophysiology data.

Electrophysiology types collected prior to, during, and/or after the runs include electrocardiography (ECG), vectorcardiography (VCG), SEP, and electroencephalography (EEG; Matson, 1990; Thomas & Jessop, 1986, 1983). The type of electrophysiology collected varied depending on the instrumentation technology available at the time as well as the specific test plan. Some of these types of electrophysiology were also collected from the HRVs, including ECG, VCG, and EEG (Ewing et al., 1976; Schmidt et al., 2009). Although electromyography (EMG) and electrooculography (EOG) were collected from the HRVs, collecting both EMG and EOG from the NHP during the run was planned but never completed.

ECG was collected from both rhesus and chimpanzee subjects. The ECG electrodes were sutured (Thomas & Jessop, 1983) or pasted to the skin (Ewing et al., 1976). In order to obtain VCG (to measure respiration), the ECG electrodes were positioned according to a Frank lead system (Ewing et al., 1976).

SEP was only collected from macaque subjects (both anesthetized and unanesthetized). SEP was not collected from the more-protected chimpanzee subjects since the methodology required invasive surgery to implant the electrodes. In the work by Matson (1990), the electrodes implanted for SEP included an array of three electrodes in the epidural space of the first or second lumbar vertebra (stimulating electrodes) as well as an array of three cervical electrodes in the epidural space of the atlanto-occipital area and two arrays of five cortical electrodes each in

the epidural space over the primary somatosensory cortex (recording electrodes; Figure 4). The exact placement of the electrodes was determined during the surgical procedure, such that the electrodes captured the largest evoked response (Walsh et al., 1978). The electrode leads continued to the data acquisition system through the implanted cranial pedestal (Ewing et al., 1976; Matson, 1990; Saltzberg et al., 1982a; Thomas & Jessop, 1983; Unterharnscheidt & Ewing, 1978; Walsh et al., 1978; Weiss & Berger, 1982).

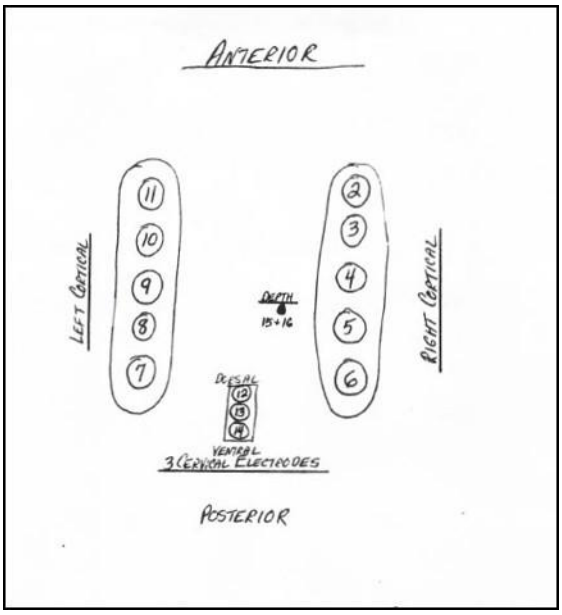

Figure 4. Original drawing of recording electrodes implanted for somatosensory evoked potential. To collect SEP data, three arrays of recording electrodes were used, represented at cortical and cervical locations in the drawing, in addition to a single array of stimulating electrodes.

EEG collection was not possible at the beginning of research with the NHPs because the required EEG electrodes were not yet available (Ewing et al., 1976). Once the EEG electrodes were made available, experiments were conducted with the electrodes non-invasively pasted onto the NHP. Later experiments used EEG in conjunction with SEP. The SEP stimulation occurred in intervals; during periods free of stimulation, uninterrupted EEG data collection was permitted (Weiss & Berger, 1978).

Radiography.

X-rays (radiographs) of the NHP head and neck were taken before and after instrumentation/surgery and pre- and post-run (or set of runs; Figure 5). The X-ray methodology used simultaneous X-rays of the head and neck in the anterior-posterior and lateral planes so that three-dimensional anatomical measurements could be obtained. Radiopaque lead markers were located in the X-ray cassette holders and on the NHP in each external auditory meadus and infraorbital notch (Thomas & Jessop, 1983). This general method of three-dimensional X-ray was also used for the HRVs (Becker, 1977; Ewing et al., 1976). For the macaques, a radiolucent Plexiglas® structure was used to position the NHP. This structure allowed for accurate, repeatable positioning of the NHP. Because of the methodology used, these X-rays could be used to obtain three-dimensional anthropometry, critical for transforming the kinematic data appropriately from the instrumentation coordinate system(s) to the desired anatomical coordinate

system(s), as well as assess the NHP for injury (Ewing et al., 1976; Thomas & Jessop, 1983).

Restraint system.

Because the NHP species involved in the impact acceleration program varied in size among each other as well as compared with their HRV and ATD counterparts, the NHP restraint systems were modified with custom designs to accommodate them. The chimpanzees, being of similar size and shape to humans, were able to use the HRV sled for their runs. A restraining system, similar to that employed with the HRVs, was adapted for the chimpanzee experiments (Appendix A). The chimpanzee subjects were held in place by a lap belt that threaded though the shoulder and crotch straps, keeping the body immobile while allowing free movement of the head and neck. The chimpanzee's torso was further restrained against lateral motion with a nylon strap. Additionally, the chimpanzee's arms and hands were restrained to the chair to deter the subject from pulling at any of the instrumentation or being injured by arm flail during the run (Ewing et al., 1976).

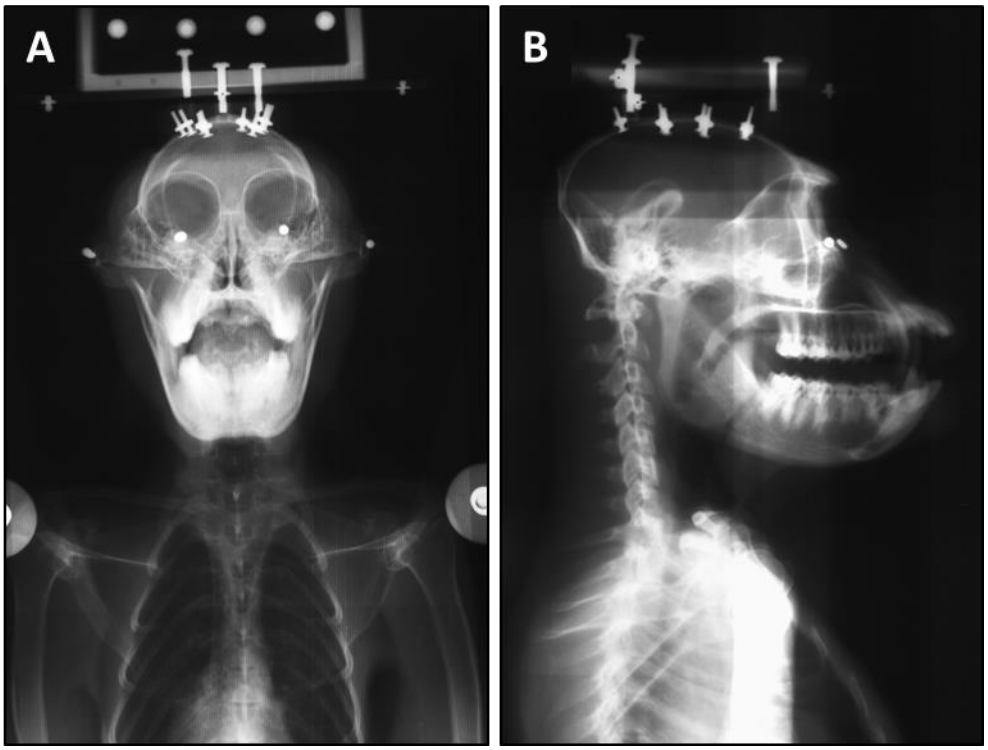

Figure 5. Pre-run X-rays for a non-human primate subject. The (A) anterior-posterior and (B) lateral X-rays were taken simultaneously. Simultaneous anterior-posterior and lateral X-rays were also captured post-run. Lead markers were placed in each external auditory meatus and infraorbital notch to assist in anatomical examination.

For the macaques, two different restraint systems were used (Figure 6). Because the macaques could be exposed to high accelerations, both of the restraint system designs avoided straps that could contribute to extraneous severe tissue injury or fatality. One restraint system designed for the macaques was a hard, fiberglass shell. To achieve the exact shape of the NHP, a mold was taken of the subject's full-body (clavicle to toes). For the run, the mold was contained within a box structure, which (in two halves, securing the NHP inside, and held together by metal fasteners) would completely enclose the NHP, leaving only its head and neck free. The

box was then affixed to the sled on the track in preparation for the anticipated run. The other restraint system used for the macaques consisted of a fabric bodysuit that covered the subject from thorax to thighs. The subject was then, by a series of straps and belts, secured to a chair (or "couch," as it is referred to in the literature) specifically formed for the size and shape of the macaques. The hard restraint was only useable with the subject it was crafted for and, therefore, was a labor-intensive device. Conversely, the soft restraint system was useable with multiple NHPs of similar size and proportion. Of the two restraint systems employed for the macaques, the soft restraint was used more frequently than the fiberglass mold. Notably, the NBDL found no significant difference in head dynamic response due to the restraint system used (Thomas & Jessop, 1983).

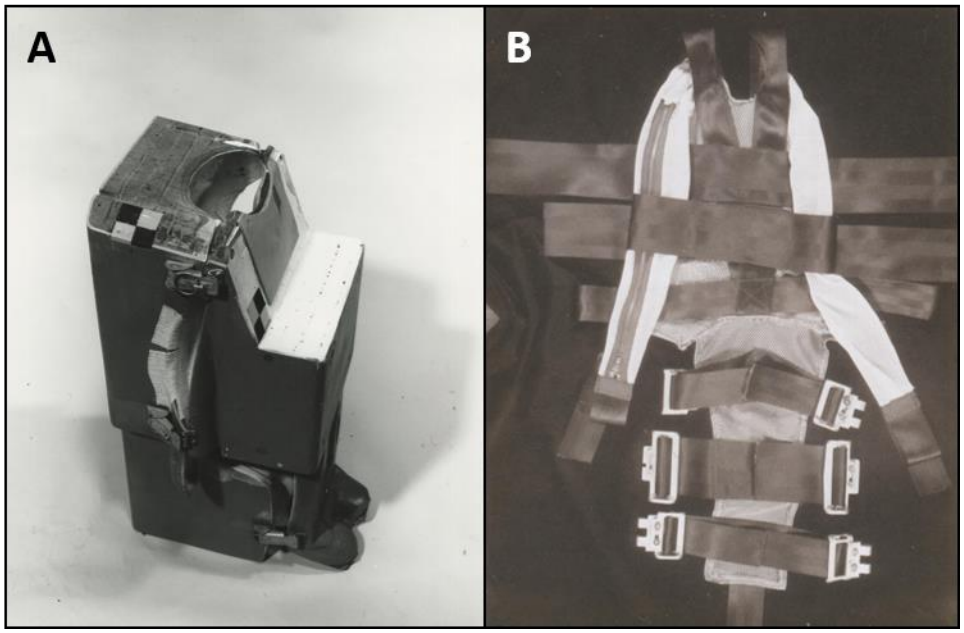

Figure 6. Restraint systems used for the macaque non-human primates. (A) Hard-shell restraint system. (B) Soft fabric restraint.

For some runs, the head of the NHP was also restrained in order to control its initial position. Runs were conducted with both anesthetized and unanesthetized NHPs. While the anesthesia procedure is discussed in more detail in the following section, "Run Procedures," the use of anesthesia is relevant to how the head was restrained. For runs with anesthetized NHPs, measures were taken to restrain the initial position of the head. The chimpanzee runs, all of which were conducted with the NHP under anesthesia, used straps suspending the head pre-run in a repeatable initial condition. The straps were then released approximately 80 milliseconds before the start of acceleration (Ewing et al., 1976). For impact test procedures utilizing anesthetized macaques described by Matson and Weiss (1987), the initial head conditions were "controlled by quick release connectors and thread" (p. 2). Otherwise, the initial rotation of the head was estimated from photography immediately prior to first motion and applied to analysis (Thomas & Jessop, 1983).

The macaque NHPs were conditioned to being restrained prior to ever being tested in an acceleration run. To condition the NHP, the NHP was placed in a Plexiglas® restraint chair for gradually increasing durations of time until the subject became comfortable and displayed no signs of distress. This allowed for more accurate electrophysiological testing of the NHPs as they

would not experience abnormal heart and respiratory rates during the experiment itself (Thomas & Jessop, 1983). The chimpanzees were not similarly conditioned since they were anesthetized throughout handling and experimentation procedures.

Run procedures.

To prepare the NHP for the run, the NHP was anesthetized. The macaque NHPs were anesthetized using an anesthetic box. The NHP was placed within the box and gaseous halothane was administered. The NHP was then intubated, and anesthesia was maintained via the airway while the subject was instrumented (with electrodes, an indwelling catheter, a rectal thermocouple, and the A-plate), outfitted in the restraint system, and placed on the sled (Thomas & Jessop, 1983; Unterharnscheidt, 1986). A blood sample was also collected at this time. The macaque NHP runs were conducted with both anesthetized and unanesthetized NHPs. For unanesthetized runs, the NHP would then be extubated one to two hours prior to the run or collection of run-related data, which could include pre-run electrophysiology recordings (Thomas & Jessop, 1983). Conversely, intravenous and intramuscular anesthesia was administered to chimpanzee subjects in order to maintain a sedated state throughout the entire experimental period.

Constant monitoring of the NHP continued throughout the process of run preparation, from initial contact through execution of the run and the subsequent recovery period. This monitoring included heartrate, respiration, and body temperature. Body temperature was especially important once the subject was secured on the sled and, therefore, under the high-intensity lights that were necessary to facilitate good quality photographs and film. A chronological run diary was kept for the NHP runs to detail the time each activity occurred, such as: the amount of pharmaceuticals given, vital signs, the subject's activity, visible signs of stress or lack thereof, any electrophysiological testing done prior, during, or after the run, any anomalies, the run itself, and finally, the condition of the subject post-run. The veterinarian was present for the run and had full authority to stop a run at any point. If a subject displayed great distress or alarming and/or inexplicable changes in their vital signs, immediate intervention was initiated.

Exposures.

The NBDL studied the effects of non-contact inertial loading using both a horizontal accelerator (HA) and a vertical accelerator (VA). The NHP runs on the HA and VA encompassed impacts of the frontal, rear, lateral, and axial directions (Figure 7). The impact direction (thrust vector) was described in terms of a right-hand coordinate system applied to the head-neck complex. In this system, "+X" was to the subject's front, "+Y" was to the subject's left, and "+Z" was in the subject's superior direction. Variables characterizing the exposure pulse, including peak sled acceleration (PSA) and rate of sled acceleration onset, were calculated by the NBDL from the sled acceleration profiles. The exposure direction and PSA used in this report were documented in the run summary that was generated by the NBDL following each run (Schmidt et al., 2010). The majority of NHPs were involved in multiple runs (Figure 8). Most frequently, an individual NHP was tested in two total runs, which typically included a low-level, "control" run followed by a high-level run. Eight individual NHPs were run in more than one impact direction.

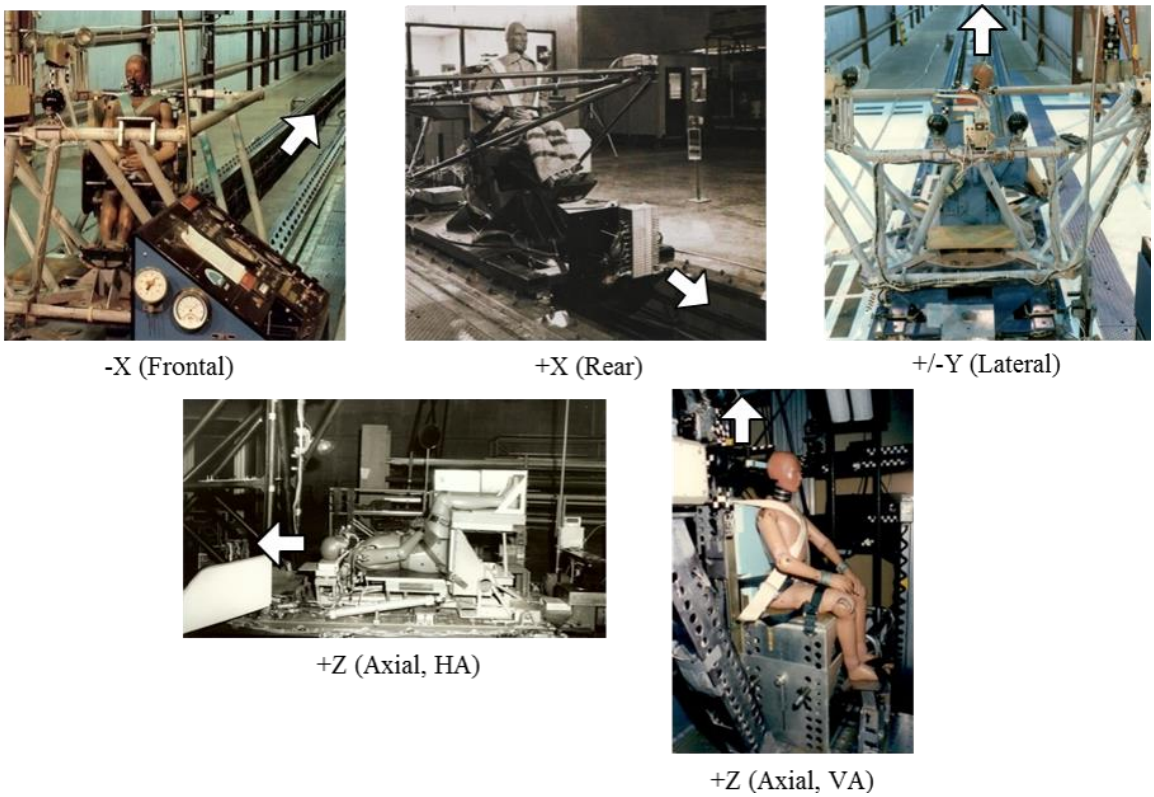

Figure 7. Non-human primate subject orientations illustrated by anthropomorphic test devices. -X (Frontal): Subject is positioned facing the accelerator, simulating frontal impact. +X (Rear): Subject is positioned facing away from the accelerator, simulating rear impact. +/-Y (Lateral): Subject is positioned perpendicular to the accelerator, simulating lateral impact. +Z (Axial): Subject is positioned supine (horizontal accelerator; HA) or upright (vertical accelerator; VA) with the accelerator impacting from the bottom (caudocephalad), simulating aircraft ejection and ship shock. The HRVs and ATDs were tested using the same sled, but, for the majority of NHP runs, a different sled than the sled that is pictured was used.

Exposures on the horizontal accelerator.

The majority of impact acceleration research at the NBDL was conducted on the HA. Beginning in 1972 and ending in 1994, researchers logged 6,600 total horizontal runs, including 366 NHP runs. The HA was powered by a 12-inch diameter, nitrogen-pressurized HYGE™ system, which propelled the sled carriage and its occupant with a thrust of up to 225,000 pounds of force. After the controlled acceleration pulse, the sled was gently decelerated by friction at a rate of 7 to 13 feet per second squared over the 700-foot enclosed track (Naval Biodynamics Laboratory, 1996). ATDs were used to develop and verify the test equipment and perform daily safety checks.

Of the 366 NHP runs conducted on the HA, sensor data were successfully recorded for 354 runs. Sensor data were not captured for the remaining 12 runs due to instrumentation/data acquisition system failures and aborted runs. Impact exposures on the HA are categorized by run direction in Table 2. Tests in the -X (frontal impact) direction were the most numerous and were conducted at the highest peak accelerations. The next most frequent test direction was the +X (rear impact) direction, followed by tests in the +Y and -Y (lateral impact) directions. On the

HA, axial accelerations (+Z) were applied to subjects seated in the supine position. The horizontal impact tests are broken down by acceleration level in Figure 9. The 12 runs without sensor data are not captured in Table 2 or Figure 9.

Exposures on the vertical accelerator.

In 1986, the vertical accelerator construction was completed by the NBDL and testing commenced. This nitrogen-powered HYGE™ system supplied a +Z acceleration pulse, propelling the instrumented test carriage up a 42-foot vertical track with 40,000 pounds of thrust (Naval Biodynamics Laboratory, 1985b). In all runs on the VA, axial accelerations were applied to the subjects seated upright. The vertical testing provided a more authentic ejection seat simulation than was achievable using axial accelerations on the horizontal accelerator. Similar to testing done with the horizontal accelerator, ATDs were used for system verification, safety checks, etc.

A total of 1,184 runs, including 34 NHP runs, were conducted at the NBDL on the vertical accelerator. NHP testing began on the vertical tower prior to the equipment being man-rated in February 1990 (Naval Biodynamics Laboratory, 1991). Within the span of a few months in 1989, all 34 NHP runs were completed. Sensor data were successfully collected for each NHP run. Details of the NHP vertical accelerator dataset are shown in Table 3, and the vertical impact tests are categorized by acceleration level in Figure 10. Worthwhile to note is that a single NHP was run on both the HA and VA. (All seven runs with this NHP were +Z accelerations).

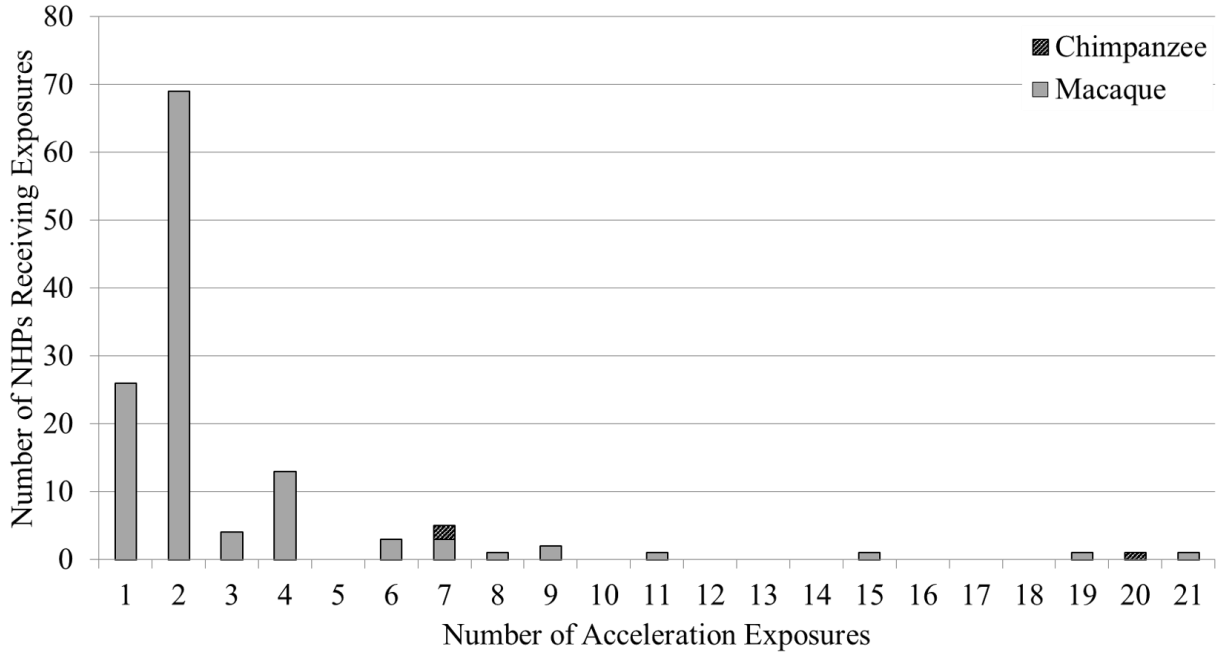

Figure 8. Number of non-human primate subjects receiving a given number of total acceleration exposures. A total of 393 runs are represented; runs where the sled did not fire (aborted runs, n = 7) are excluded. The majority of NHP subjects received one or two exposures.

Table 2. Non-Human Primate Runs Conducted on the Horizontal Accelerator According to Impact Direction

Direction	Accelerations (G)	Runs	NHPs	Species	Years
- X (Frontal)	5.16 - 192.84	206	60	Assam, Rhesus	1973 – 1987
+ X (Rear)	4.16 - 148.54	69	36	Assam, Rhesus	1983 – 1987
+ Y (Lateral)	4.01 - 20.77	25	3	Chimpanzee	1974 – 1976
- Y (Lateral)	5.21 - 98.42	26	8	Chimpanzee, Rhesus	1976 – 1979
+ Z (Axial)	6.13 - 85.72	28	13	Rhesus	1989
Summary:	4.01 - 192.84	354	114*		1973 - 1989

Note. Only runs with sensor data are included. The acceleration reported is the PSA. Chimpanzees only ran in the lateral directions: +Y (n = 25) and -Y (n = 8). The remainder of the runs were conducted with macaques.
*This total represents the number of unique NHPs involved in the HA impact exposures; eight NHPs were exposed to accelerations in more than one direction.

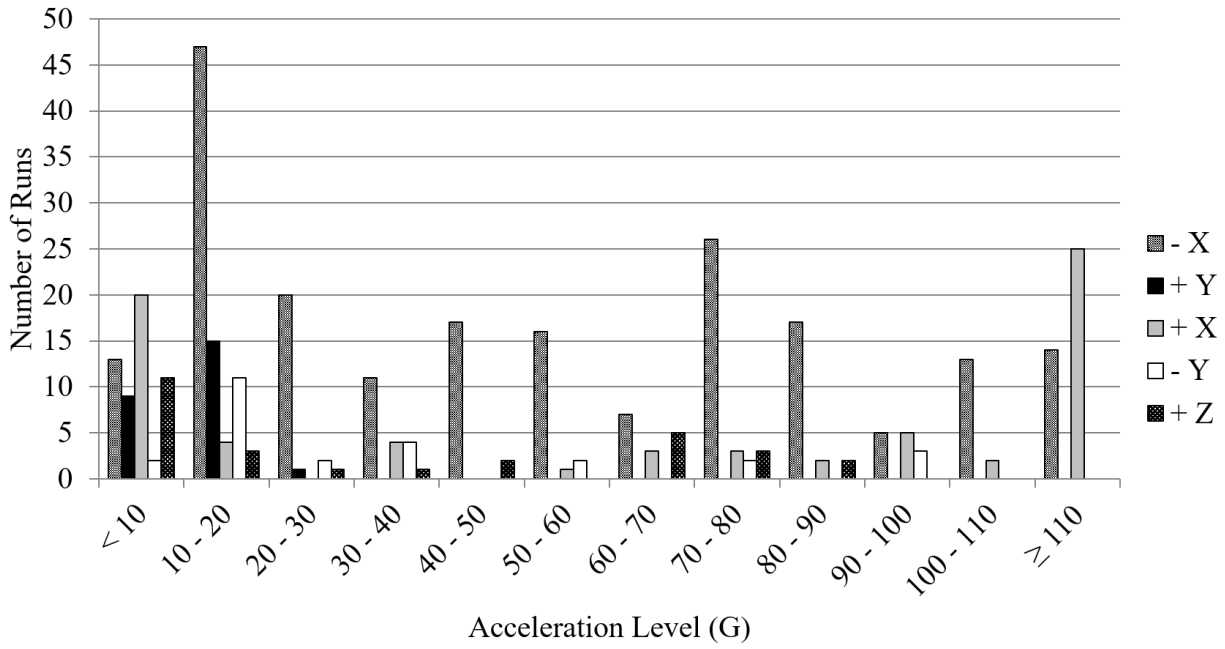

Figure 9. Distribution of impact acceleration levels for non-human primate runs conducted on the horizontal accelerator. Most NHP runs on the HA had a PSA greater than 20 G. Only 2 chimpanzee runs had a PSA greater than 20 G; these runs, of 21 G and 28 G PSA, were conducted with the same subject.

Table 3. Non-Human Primate Runs Conducted on the Vertical Accelerator

Direction	Accelerations (G)	Runs	NHPs	Species	Year(s)
+ Z (Axial)	8.11 - 69.50	34	16	Rhesus	1989

Note. Sensor data were collected for all runs. The acceleration reported is the PSA. Notably, NHP runs on the VA were only conducted with the macaques, not the chimpanzees.

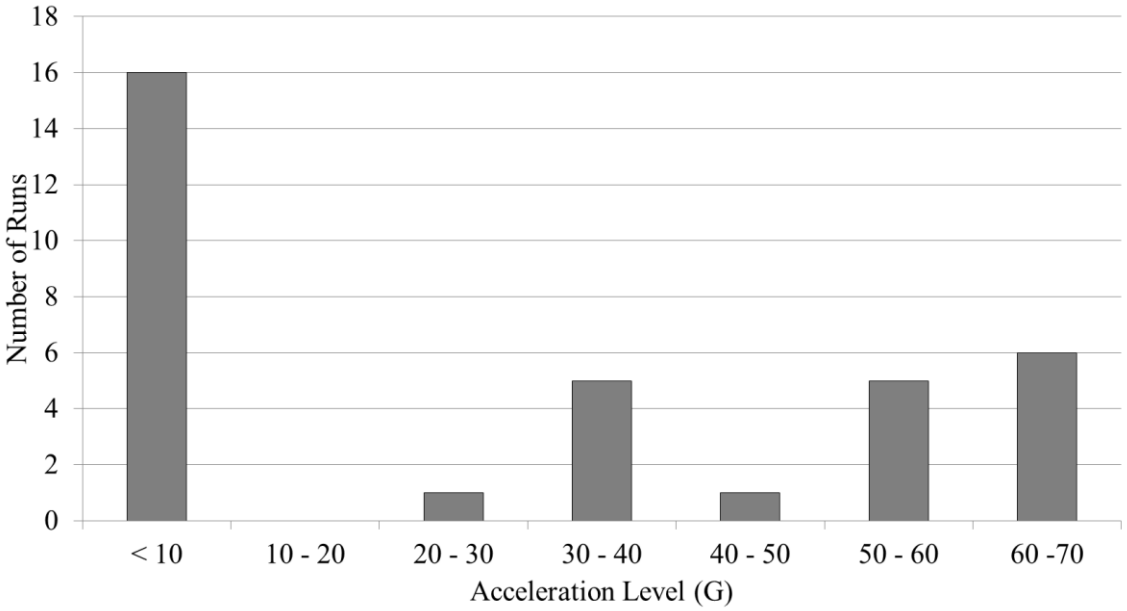

Figure 10. Distribution of impact acceleration levels for non-human primate runs conducted on the vertical accelerator. NHP runs on the VA were only conducted with the macaques, not the chimpanzees.

Post-Run.

Following the impact exposure, all NHPs were evaluated by a veterinarian through a series of medical examinations and laboratory tests to ascertain the condition of the subject. The most immediate evaluation was the medical examination, a general visual and physical observation conducted while the NHP was still restrained on the sled. For runs with electrophysiology data collected during the event, post-run electrophysiology data were also collected while the NHP was still restrained on the sled. Prior to being removed from the sled, the NHP was anesthetized appropriately to maintain the necessary level of sedation for safe handling. Additional anesthesia was administered as needed throughout the remaining procedures.

Once the NHP was removed from the sled, post-run X-rays were obtained. Following these immediate post-run evaluations, medical examination and laboratory tests continued at regular intervals (e.g., 12, 24, 35, and 48 hours post-run, or longer if indicated; Lustick, 1984). Laboratory tests could include additional electrophysiological examinations and clinical pathology evaluations, such as the Complete Blood Count test and tests used for other designated blood chemistries and isoenzyme determinations. This regular monitoring continued as indicated.

For the macaques, which could be run with the intent to sacrifice post-run, monitoring continued until the time of sacrifice (Lustick, 1984; Thomas & Jessop, 1983). Regular monitoring of the chimpanzees continued as indicated, but the chimpanzees, a more-protected species, were not run with the intent to sacrifice. While these post-run procedures were generally adhered to, the procedure did vary depending on the results of the medical examination that was conducted immediately post-run.

Based on the immediate post-run evaluation of the NHP, the NHP was categorized into one of three groups:

- unaffected,
- non-fatal injury, or
- fatal injury.

Subjects in the unaffected group were not treated, as there was no discernable injury. Subjects in the non-fatal injury group were treated medicinally based on the veterinarian's determination. In the event that a subject sustained an injury that appeared painful, a full battery of analgesic medication was available for use at the discretion of the attending veterinarian, and painful injuries were treated expeditiously (Lustick, 1984). Subjects in the fatal injury group required no treatment.

The time to sacrifice (i.e., time to necropsy) following a non-fatal run could vary. Subjects in the fatal injury group were necropsied almost immediately following the run. These subjects from fatal runs were scheduled for sacrifice with the intent of performing the necropsy immediately to avoid any deterioration of the tissues. Subjects that were unaffected or had non-fatal injuries might be sacrificed immediately (within the hour), at a later time (within hours or days), or could be run again and be sacrificed thereafter. The time to sacrifice could vary depending on the research question of interest. Time to necropsy was reported in the subject record for 113 of the 128 NHP subjects and ranged from immediate to 40 days.

Sacrifice was typically achieved through the injection of an anesthetic (Ketamine) and a barbiturate (Surital) and necropsy of the subjects was initiated by perfusion through the subject's carotid arteries. Then, the tissues were fixed in 10% neutral buffered formalin (McLeod, 1991; Unterharnscheidt & Ewing, 1978; Unterharnscheidt, 1983). Specimens were embedded in paraffin or, occasionally, celloidin. Celloidin was the preferred medium for larger hemorrhages to avoid breaks and folds that can appear in paraffin (Unterharnscheidt, 1983). According to Unterharnscheidt (1983) and McLeod (1991), hematoxylin and eosin was the standard technique used for prepared slides. For brain tissue specimens with suspected lesions, examinations were conducted with other specific stains such as Cresyl Violet (Nissl), Luxol Fast Blue, and Glees' method (Unterharnscheidt & Ewing, 1978). According to the NBDL records, other stains, such as van Gieson's stain, were also applied to central nervous system (CNS) tissue for examination.

The tissues removed for microscopic study could vary. However, the CNS comprised the majority of tissues sampled. Typical tissue samples that were collected from the CNS include regions of the brain (e.g., medulla, pons, frontal lobe, parietal lobe, occipital lobe, temporal lobe, cerebellum, midbrain, vermis cerebelli, and pituitary; Figure 11) and spinal cord. Other organs were examined as well, such as the heart, lungs, liver, spleen, digestive organs, and kidneys. Horizontal, coronal, and longitudinal tissue sections were produced. These pathology samples

taken during the necropsies provided a microscopic evaluation of the effects of the acceleration event on the body.

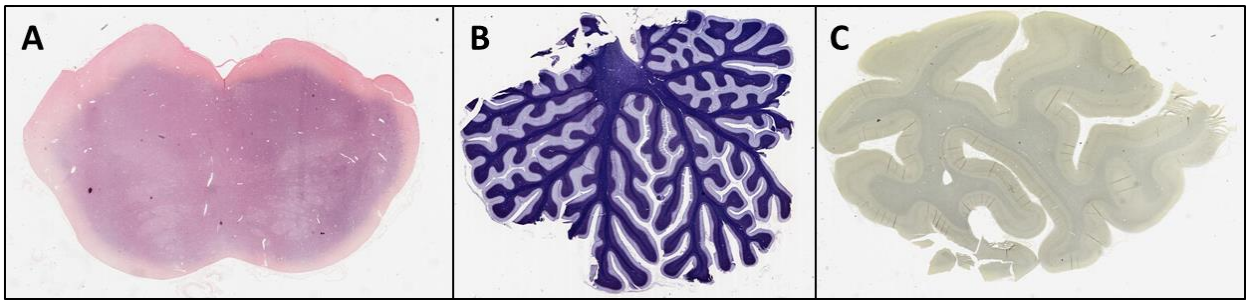

Figure 11. Microscope slide-mounted tissue samples from the non-human primate pathology collection. A Leica Biosystems Aperio slide scanner microscope at 40x power magnification was used by USAMRIID to create a digital image (i.e., scan) of each slide. (A) Hematoxylin and eosin stain on a pons sample. (B) Luxol Fast Blue (Kluver-Barrera) stain on a vermis cerebelli sample. (C) Van Gieson's stain on an occipital lobe sample.

A variety of these samples, in the form of microscope slides and embedded-tissue blocks, remain within the NHP collection in the BDR (Table 4 and Appendix B). Slides and/or embedded-tissue blocks have been identified for the majority (95%) of the 128 NHP subjects. Because these pathology samples were prepared well over 20 years ago, ascertaining their viability for research was a necessary task. Pathology experts found the slides and blocks to be in useable condition. The Joint Pathology Center (JPC) successfully applied several immunohistochemical stains on tissue samples from one subject's embedded-tissue blocks. Also, a random sampling of the slides was found to be in a usable condition. Overall, the existing tissue specimen collection (embedded tissue blocks and microscope slides) appear viable for future use and analysis.

Table 4. Pathology Samples within the Non-Human Primate Collection

	CNS Region Specified	**CNS Region Unspecified**	**Non-CNS Organ Specified**	**Organ Unspecified**	**Total**
Unique NHPs (*n* = 128)	61	16	2	103	121
Slide-Mounted Tissue Samples	1155	215	3	2758	4131
Embedded-Tissue Blocks	1270	372	0	1877	3519

Note. Samples were identified by labels on the samples themselves or matched identifiers within the NBDL pathology record book. The majority (95%) of NHP subjects have pathology samples identified ("Total").

Research Outcomes

The BRAC of the NBDL in 1996 resulted in a paucity of NHP data being published. Though data were collected for nearly 400 NHP runs, encompassing different species and several vectors, few publications extend past the -X rhesus macaque runs. The runs of the -X direction make up a majority of the NHP collection since these early experiments were critical in devising a working methodology and elucidating the relationships necessary for both defining injury and developing a scaling model. Additional results have been published on the analysis of both +X and -Y rhesus macaque runs as well as the +Y chimpanzee runs (Ewing et al., 1976; Saltzberg et al., 1982b; Thomas & Jessop, 1983). An overview of these results and the results of the -X experiments are provided in the following sections in terms of electrophysiology, pathology, and kinematics and modeling efforts.

Electrophysiology.

Electrophysiology was used to monitor the NHP throughout the experimental procedures and provide experimental data that could help establish impact injury thresholds. ECG and VCG were used to monitor the heartrate and respiration of the NHP throughout the experimental procedures. SEP and EEG data were used to measure the neurophysiological effects of head acceleration. Research at the time suggested that the somatosensory system was considered representative of CNS function (Sances et al., 1978). In order to develop the methodology necessary to collect the physiological measurements related to the effects of acceleration on the somatosensory system, the NBDL collaborated with the MCW. Their work on evaluating spinal cord injury with SEP is well-documented in several publications (Berger et al., 1979; Berger, 1982; Berger & Weiss, 1982, 1983; Matson, 1990; Saltzberg et al., 1982b; Saltzberg et al., 1983; Sances et al., 1978, 1980, 1981; Walsh et al., 1978; Weiss & Berger, 1979). In particular, Sances (1989) summarized much of the work done by the MCW to evaluate the neurophysiological effects of -X impact acceleration in the rhesus NHP.

Walsh et al. (1978) described the feasibility of using implanted electrodes during impact acceleration tests with rhesus macaques. Sances et al. (1980, 1981, 1983) reported SEPs in the rhesus macaque as a diagnostic for measuring spinal injury resulting from axial loading. The development of data analysis techniques for SEPs was documented in detail by Berger (1982) and Berger and Weiss (1982). Unanesthetized -X rhesus runs with SEP collected were analyzed by Berger et al. (1979) in an attempt to discover the neurophysiological mechanisms underlying concussion. Decreased amplitude and increased latency of these potentials were exhibited after acceleration (Berger et al., 1979). Saltzberg et al. (1983) described similar results.

In additional analyses, Berger (1982) examined both cortical and cervical SEPs as a function of PSA and found that changes in cervical average evoked potentials were substantial for accelerations greater than approximately 74 G. At lower accelerations, the increased latency of the cortical evoked response was considered a possible indicator of pre-pathological injury (Berger & Weiss, 1983; Weiss & Berger, 1982). Many of these SEP results were obtained using unanesthetized NHPs; it was not until later that Matson (1990) demonstrated that the injury threshold defined by SEPs obtained from anesthetized rhesus macaques exposed to -X accelerations was comparable to those obtained from unanesthetized rhesus macaques.

Using SEP, Saltzberg et al. (1982b) showed that recovery to pre-impact latency and amplitude measures took longer for impacts at higher accelerations. Additionally, asymmetrical changes in cortical SEP at high impact levels were observed for lateral +Y impact accelerations (Saltzberg et al., 1982b). Matson (1989) reported on the cervical SEPs recorded from humans undergoing +Z acceleration; the human runs, being non-injurious, did not show the same changes in latency that were demonstrated in rhesus macaque +Z runs. Conversely, Weiss et al. (1983) determined that EEG at that time was not useful in measuring neurological effects of impact in the NHPs.

Pathology.

Through pathological evaluation of the NHPs, exposure outcomes were characterized as non-injurious, injurious, and fatal. Several publications report exposure outcomes (and, occasionally, time to necropsy is reported): Ewing et al. (1976), Guccione (1990), Matson (1990), Mauro et al. (1986), Smith and Peterson (1979), Smith and Aarons (1982), Unterharnscheidt (1982, 1983, 1986), and Unterharnscheidt and Ewing (1978). Outcomes, compiled by USAARL researchers using NBDL publications available within the BDR, vary according to PSA and direction (Figure 12). Time to necropsy, compiled with few exceptions by USAARL researchers using subject records, varies for non-injurious and injurious outcomes, but NHP subjects of fatal outcomes were necropsied immediately (Figure 13).

Pathological evaluation of the NHPs exposed to frontal (-X) and rear (+X) impact accelerations demonstrated that whole-body acceleration of a particular direction produced potentially repeatable and predictable injuries to the head-neck junction. Unterharnscheidt and Ewing (1978) compared the pathology of 11 rhesus NHPs exposed to -X non-contact acceleration to previous findings from NHPs exposed to direct impacts of the head (translational and rotational acceleration). Unterharnscheidt and Ewing (1978) found that each type of input acceleration produced a different, predictable type of injury; for -X acceleration, this included damage at the atlanto-occipital junction. This was expanded on by Thomas and Jessop (1983). Thomas and Jessop (1983) reported on the results of 28 -X rhesus macaque runs, specifically conducted to identify the parameters of fatal injury. The most frequent fatal injury was atlanto-occipital separation without fracture. This injury was dependent on several parameters, including head rotation. Due to this dependence, various levels of sled acceleration were observed to produce this injury (Thomas & Jessop, 1983). In a later analysis, Unterharnscheidt (1983) reviewed the neuropathology for these runs. Unterharnscheidt (1983) observed that other injuries, secondary to injuries produced by this tension of the neck, may be caused by additional shearing, stretch, and spinal cord compression. Furthermore, Unterharnscheidt (1983) reported that PSAs above approximately 110 G in the -X direction were acutely fatal and the injurious threshold was between 105 G and 110 G. Additional series of the -X rhesus macaque experiments involved determining residual neurophysiological effects from a run, thus demonstrating the effects of multiple runs in a single day (Thomas & Jessop, 1986).

Pathological evaluation of NHPs exposed to rear (+X) impact accelerations produced comparable injuries that differed in frequency and threshold from the frontal (-X) impact accelerations. In an analysis of 15 NHP exposed to rear impact, Thomas and Jessop (1983) found that the acceleration required to cause the same anatomical injury, atlanto-occipital dislocation (AOD) and transection of the spinal cord, in the rear direction is possibly higher than

the acceleration required in the frontal direction. The mechanics of and threshold for major anatomical failure was discussed in a comparison of the -X and +X rhesus runs by Thomas and Jessop (1986). The importance of initial head position was emphasized; the threshold for disruption of the head/neck junction was lower if the initial head position deviated 60 degrees or more (of yaw) from straight ahead (Thomas & Jessop, 1986). Further comparison of the pathological and neuropathological findings between the -X and +X vectors was provided by Unterharnscheidt (1986). Unterharnscheidt (1986) indicated that tissue damage occurred at accelerations as low as 78 G for the -X experiments, while damage was not evident until an acceleration of 97 G for the +X experiments. Overall, the difference in thresholds for atlanto-occiptial separations and traumatic transections of the spinal cord for the -X and +X impact directions was described as "disparate and sometimes very surprising" (Unterharnscheidt, 1986, p. 643).

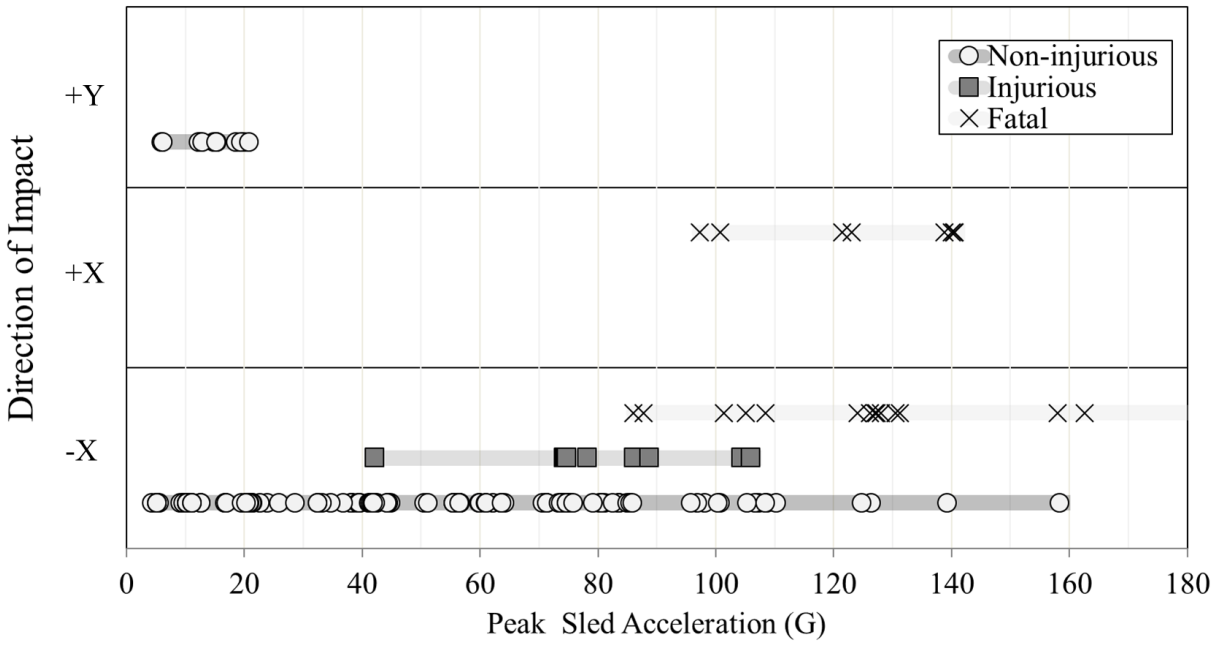

Figure 12. Outcome-by-exposure data compiled from Naval Biodynamic Laboratory publications. Outcome data were obtained from Ewing et al. (1976), Guccione (1990), Matson (1990), Mauro et al. (1986), Smith and Peterson (1979), Smith and Aarons (1982), Unterharnscheidt (1982, 1983, 1986), and Unterharnscheidt and Ewing (1978). Only runs with published outcome data are included. Injurious outcomes were classified based on the definition of injury used in the original NBDL publications. PSA values were obtained from the run summaries with the exception of one data point obtained from published data. One run was excluded because outcome varied across multiple sources. A total of 197 runs are represented in the figure; a single subject can have more than one run represented. All runs included in the lateral (+Y) impact direction were conducted with chimpanzee subjects; the remaining runs were conducted with macaque subjects. A total of 19 run outcomes (7 -X, frontal; 12 +X, rear) were reported as nonfatal and are not included here because they could not be classified as non-injurious or injurious.

Kinematics and modeling.

Ewing et al. (1976) detailed the development of the test setup and software programs necessary for testing with the chimpanzee and the results of those computed kinematics relative to the human dynamic response. The results emphasized the complexity of the chimpanzee head dynamic response as compared to what was observed in +Y HRV runs and the implications of head initial position for developing an accurate model (Ewing et al., 1976).

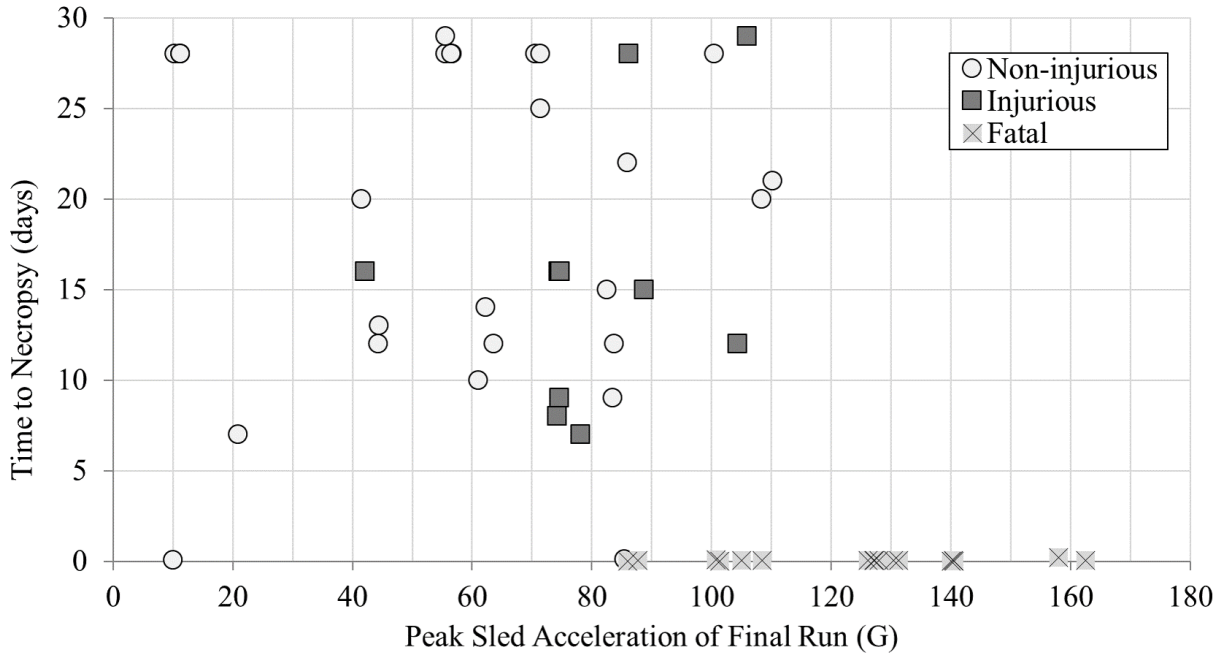

Figure 13. Relationship between time to necropsy, exposure, and outcome. Time to necropsy was obtained from the subject records with the exception of six data points that were obtained from published data. Outcome data (and six time to necropsy data points) were obtained from Ewing et al. (1976), Guccione (1990), Matson (1990), Mauro et al. (1986), Smith and Peterson (1979), Smith and Aarons (1982), Unterharnscheidt (1982, 1983, 1986), and Unterharnscheidt and Ewing (1978). Only runs with published outcome data are included. Injurious outcomes were classified based on the definition of injury used in the original NBDL publications. A total of 54 final runs (with 54 unique subjects) are represented in the figure. All runs included were conducted with macaque subjects. PSA values were obtained from the run summaries with the exception of one data point obtained from published data. One run was excluded because outcome varied across multiple sources. A total of 11 run outcomes (4 -X, 7 +X) were reported as nonfatal and are not included here because they could not be classified as non-injurious or injurious.

Models of the rhesus macaque head kinematics have been derived using the -X runs, taking into account a series of statistical relationships, including those derived to assess the effect of initial head condition (Guccione, 1990; Mauro et al., 1986; Smith & Aarons, 1982; Smith & Peterson, 1979). Several versions of statistical models resulted from the NBDL collection. Smith and Aarons (1982) of Desmatics, Inc., contracted by the NBDL, used the head dynamic response and sled acceleration of runs with the rhesus NHP in the -X direction to develop fatality prediction models. Mauro et al. (1986) showed how fatality prediction models are improved by including initial head yaw as a variable. Burns (1984) highlighted the importance of including

other primate species in developing an injury prediction model and presents a model for rhesus macaques and baboons based on PSA and initial head position for -X impact acceleration. Using the -X rhesus macaque dataset, Guccione (1990) provided statistical findings supporting that the effect of anesthesia on the head kinematics is not significant. Lastly, the preliminary results of statistical analysis by Weiss et al. (1989) demonstrated the similarity between the rhesus response and human response to -X acceleration.

Discussion

The impact acceleration program of the NBDL was established to study the injurious effects of acceleration on the human body. However, the NBDL was abruptly closed under the BRAC of 1996, leaving much of the data that was collected inaccessible and not analyzed. Aware of the value and potential of this non-repeatable research, the available equipment, material, and data was recovered by USAARL in 2007. USAARL established the BDR to make the impact acceleration collection accessible and searchable to researchers. As part of this effort, the NHP collection was inventoried and digitized, and usability of the data itself was established. This process provided details on what data exist and are accessible in the collection, while also emphasizing future research directions.

Non-Human Primates

The NHP collection recovered from the NBDL includes 400 runs by 128 unique NHPs (rhesus, Assam, and chimpanzee). Data for these experiments, including time-series data (both kinematic and electrophysiological) and injury outcomes in the form of X-rays, pathology, and subject records, are being made digitally accessible in the BDR relational database. These data can be used to define the exposures and outcomes required for predicting the human head and neck response to whole-body impact acceleration.

The NHP is more representative of the human than other animal surrogates (Morganti-Kossmann, 2010; Shultz et al., 2017). While differences between primates and humans do exist, other historical NHP datasets (Kanda et al., 1981; Kikuchi et al., 1982; Ommaya et al., 1967; Ono et al., 1980; Sakai et al., 1982) as well as datasets collected from other surrogates, including both animal and post-mortem human subjects, have been used to define injury criteria. A review of historical tests and injury criteria, with a focus on head kinematics that cause brain injury, was provided by Antona-Makoshi et al. (2016).

For example, the BrIC, or brain injury criteria, was defined by the National Highway Transportation Safety Administration (NHTSA) using scaled rhesus, baboon, and miniature pig test data (Takhounts et al., 2013), but, potentially due in part to the scaling methodology, it was found to over-predict injury when validated with human data (Sanchez et al., 2016). The Nij, the criteria used by NHTSA to define allowable neck kinematics in automotive crashes, was developed based on a series of piglet tests that were scaled to other sized occupants (Kleinberger et al., 1998; Mertz et al., 1982; Prasad & Daniel, 1984). Nusholtz et al. (2003) described several challenges in using the Nij, including the use of anesthesia during the piglet tests and the modification required in order to apply the criteria, developed for frontal impacts, to other impact directions.

The data from the NBDL NHP tests have not yet been used to develop injury criteria. These standardized laboratory data, in addition to other historical animal data, can be leveraged in lieu of data collected from humans during potentially injurious exposures. Accurate, real-world data from complex exposures involving humans remain a challenge to collect (Bartsch et al., 2014; Kutilek et al., 2017; Rooks et al., 2018; Shaw et al., 2004; Wu et al., 2016). And, though tests with post-mortem human subjects (PMHSs) are anatomically more accurate, animal test subjects, like NHPs, offer significant insight into physiological responses that PMHSs cannot, including both electrophysiological measurements and clinical observations (Crandall et al., 2011; Eichberger et al., 2000; Yoganandan et al., 2000, 2002).

Pathology

The pathology from the NHP collection has potential to elucidate modern issues regarding brain injury. Specifically, the embedded-tissue blocks can be analyzed with modern techniques and novel approaches, such as those involving biomarkers that have more recently been studied as possible indicators of brain injury in humans (Chandran et al., 2017; Johnson et al., 2016; Kondo et al., 2015). Previous analyses with the NHP collection were limited by the knowledge of brain injury at the time that the research was conducted and did not consider microscopic injury past the level of hemorrhage (Unterharnscheidt, 1982). Because the pathology collection is not limited to brain tissue of a single region, but includes tissue from several brain regions (e.g., medulla, pons, and pituitary), it can provide a comprehensive platform for studying the physiological effects of acceleration in the brain. Some models based on specific brain regions (e.g., the corpus callosum) that associate quantified stresses and strains to brain injury have been developed (Ng et al., 2017; Patton et al., 2015), but brain injury may also affect other regions (Wallace et al., 2018). The difference in time to sacrifice among the NHP subjects may offer additional insight into the development and healing processes of brain injury. This insight can be applied to understanding the effects of repeated or cumulative exposures and the time between exposures. Given the current regulations on animal research (Bronsted et al., 2016; Goodman et al., 2015), potentially lethal experimentation on primates is unlikely to be repeated in the United States; thus, the NHP collection is unique and poised to support investigation into a variety of research questions that may not be supported with data otherwise.

Whole-Body Non-Contact Acceleration Exposure

The standardized setup used for the NHP tests (as well as the HRV and ATD tests) provides a realistic representation of a well-restrained subject under whole-body linear acceleration and allowed for studying the unencumbered head and neck response. Other historical research on primates investigated acceleration injuries due to forces applied to the head-neck complex. In a series of NHP studies completed in the 1960s, cerebral concussion was produced from rotational acceleration by impacting the base of the chair upon which the NHP was seated (Ommaya et al., 1967). Gennarelli et al. (1972) also studied head acceleration using a primate model, comparing brain pathology following rotational or translational head accelerations. Abel et al. (1978) and Gennarelli et al. (1982) expanded on this work. Between 1976 and 1978, experiments were conducted where the head of the NHP was impacted in different locations (Kanda et al., 1981; Kikuchi et al., 1982; Ono et al., 1980; Sakai et al., 1982). This research on primate response to acceleration and head impacts ended in the 1980s due to the controversial nature of large-animal testing. Recent reviews of these historical tests are available

(Antona-Makoshi, 2016; Melvin & Yoganandan, 2015).

While the aforementioned isolated head-neck experiments have demonstrated implications in brain injury and been used in head injury models, considering the effects of acceleration on the whole body may be beneficial. Doing so will provide analytical results that are more representative of the human response in actual scenarios, like those experienced by restrained occupants of vehicles, aircraft, and mishaps or crashes (Bernstock et al., 2015; Chen et al., 2016; Labun, 2014; Yoganandan et al., 2015, 2013). Additionally, the NBDL dataset includes multidirectional exposures with a range of accelerations, onsets, and durations. The incorporation of these variables would strengthen the predictive capabilities of any single model applied to the complex impacts that occupants experience.

Lastly, the whole-body acceleration tests performed at the NBDL provide data on injuries other than those of the head and neck. For example, upper torso injuries are common in the well-restrained occupants of military aircraft and vehicles (Barth & Balcena, 2007; Vasquez et al., 2018). Because pathological, histological, and electrophysiological data were collected from organs of the thoracic regions for the NHP subjects, the NBDL collection can support research to study blunt trauma. Myocardial contusion, for example, continues to go undiagnosed following trauma, and no gold standard for its identification exists (Plautz et al., 2005).

Anesthesia and Initial Head Position

The NHP collection contains both anesthetized and non-anesthetized runs. The effects of anesthesia (or, more specifically, the lack thereof) can be extended to study the role of muscle tension in injury prevention during impacts. By relating the events in electrophysiology with the head-neck kinematics and injury outcomes of runs in these conditions with or without anesthesia, the significance of anesthesia may be examined. This understanding of anesthesia effects can provide insight into head-neck behavior during instances of loss-of-consciousness as well as in comparisons of PMHS tests to the actual human response. Similarly, the initial head position could vary among runs. Initial head position is a valuable metric when predicting the outcome of impact, and its role in anatomical failure must be considered. Both the effect of anesthesia and initial head position have been examined in a subset of runs previously (Burns, 1984; Guccione, 1990; Mauro et al., 1986; Thomas & Jessop, 1983) but should be examined for significance using a more comprehensive dataset and modern analysis and computations.

Repetitive Exposure

The effect of repetitive exposures is a concern in both the military and civilian world. Research has shown that both concussive and subconcussive impacts to the head can cause accumulation of tau, a protein biomarker thought to be linked to brain injury (Baugh et al., 2012; McKee et al., 2010). Within the NHP collection, the number of exposures per subject ranges from 1 to 21 total runs, with 2 runs being the most common (usually a run of low acceleration, followed by a run at higher, potentially injurious acceleration). Not only can comparisons be made between subjects with low-level versus high-level exposures, but comparisons can also be made between tissue samples from NHP with varying numbers of exposures. In theory, measures of the tissue response as it evolves throughout additional exposures can be obtained. Covariates, such as the level of previous exposures and time between exposures, can be analyzed, which, when translated to the human, may provide relevant data for clinical guidance as well as form a

basis for updated tolerances and injury criteria.

Human Research Volunteer Counterpart

One major benefit of this NHP collection is the similarity and standardization in the data collected between the NHPs and HRVs. Not only were tests with each subject type conducted to collect similar pre-, post-, and during-run data, but they were also conducted using the same equipment (HA and VA; Schmidt et al., 2010). In traditional scaling, the predicted response is often validated with dissimilar data from other test series. Considering the NBDL collection, which includes NHP, ATD, and HRV subjects, an opportunity exists to make more direct comparisons across these groups and their subsets (e.g., different sex, anthropometry, and/or, for NHP, species). To the authors' knowledge, no other dataset such as this is known to exist, and the existence of this substantial subject base may alleviate some of the assumptions made when using animal models, particularly those required in today's stand-alone studies (Panzer et al., 2014). While traditional scaling can be used to show preliminary comparisons to the human response, more modern methods of translating the response at the neuronal level may make inter-species comparisons more accurate (Antona-Makoshi et al., 2016; Ng et al., 2017).

Biodynamics Data Resource Relational Database

Access to the database is driven by current research guidelines and regulations. The NHP collection and its counterparts can be shared according to an approved research SOP and a partnership with USAARL. These access conditions ensure that the NHP data are used appropriately for research as they were originally intended.

Challenges and Limitations

Several challenges of working with the legacy collections exist (Chancey et al., 2016; McGhee et al., 2016; Olszko et al., 2016; Schmidt et al., 2009; Vasquez et al., 2016a; Vasquez et al., 2016b). Some challenges are especially applicable to the unique NHP collection. First, the data were not collected as data would be collected in modern research. For example, much of the NHP clinical record is handwritten, making it time-consuming to extract relevant information. Also, the high-speed film for the NHP runs was captured at 1000 frames per second (or less), whereas similar accelerative injury research today uses a sampling rate 1000 times greater than that (McEntire et al., 2018).

Further, X-rays, while useful for determining fractures and dislocations, are limited compared to imaging techniques (e.g., magnetic resonance imaging [MRI], computed tomography [CT]) that are more commonly used to examine brain injury today (Brody et al., 2015). Second, any retrospective studies must rely on the data that are available, which may not necessarily be complete or in the most useful form. The physical collection became scattered and disorganized in the decade following the closure of the lab. Based on the inventories that were developed thereafter, it is evident that some expected pieces of the collection are missing. Depending on the level of detail desired by a researcher, other pieces of the collection may appear to have incomplete information (e.g., a general description of an injury in a pathology report where a more detailed description might be expected). Lastly, the pathology collection includes materials that can be used only once. In particular, the embedded-tissue blocks have the potential to be used for determining brain injury on a modern scale according to the presence of

biomarkers (Simon et al., 2017). The prominence of brain-related research in the last decade offers several methods to do so that must be compared and prioritized given a specific research question because the blocks are a finite resource. Though these limitations exist, they are not insurmountable, and the benefits of using the collection are numerous.

Current and Future Work

Using the data that are currently accessible from the NHP collection, modern analysis techniques have been applied to a substantial portion of the NHP collection (Abraczinskas et al., 2018a; Olszko et al., 2018). A survival analysis based on PSA compared the injury and fatality risk for frontal and rear impacts, showing that risk is higher in rear impact (Olszko et al., 2018). This supports previous analyses on subsets of these data (Thomas & Jessop, 1983, 1986; Unterharnscheidt et al., 1986). The injuries documented in the frontal and rear impact cases were compared to those documented in automobile accidents, including those with pediatric occupants and dynamic exposures like rollovers (Olszko et al., 2018). A subsequent analysis compared the injury risk for axial loading on both the horizontal and vertical accelerators. According to this analysis, axial loading on the VA produced significantly different injuries than those of frontal and rear loading. Frontal and rear loading produced predominantly neck injury (AODs, etc.), while under axial loading, cardiovascular injuries (e.g., hemorrhage or tearing of the aorta) and thoracic injuries (e.g., spinal fracture or hemorrhage) were most documented (Abraczinskas et al., 2018a). Furthermore, axial loading on the VA produced injury at a lower threshold (40 G) than the same axial loading to the occupant on the HA (70 G). However, the injuries documented following axial loading on both the HA and VA were comparable to those reported in aviation (Abraczinskas et al., 2018b).

While some potential future work has been alluded to previously within this report, the ultimate research goal of BDR project at this time is to define injury criteria and develop improved human biofidelic corridors, which can then be used to define standards for test and equipment development. To do this, an in-depth analysis of the multidirectional NHP exposures will be performed. This analysis will utilize all relevant and accessible data, including the appropriate version of sensor data, tracked photo data for kinematic validation, and potential covariates, such as anesthesia, initial head position, and restraint system, as well as the outcomes in terms of physiological response. By following a similar analysis for the human collection, these datasets may be used in combination such that the NHP response can be translated to the human response, and the data from the human volunteers can be used as a set of data for validation. Thus, a set of improved human biofidelity corridors based on a large set of exposures applied to live subjects in a controlled setting will be developed and validated. These research efforts have application in military and automotive environments; however, the robust collection may be extended to other investigations, even outside the biodynamics community.

Conclusions

The NHP collection contained in the BDR represents 400 impact acceleration experiments conducted with 128 unique NHP subjects. The current regulations surrounding both human volunteer and animal subject research renders these historical experiments unlikely to be repeated. The materials in this NHP collection were previously inaccessible for modern research; however, these materials offer potential for supporting research efforts spanning several research disciplines. In particular, this body of work continues to be vital to furthering the understanding

of how the human body responds in impact scenarios. The goal of the BDR is to make these data accessible to the Department of Defense and the scientific community at large and to incorporate the research results back into the BDR relational database, thus, maintaining the cohesiveness of the collection. Towards this goal, the materials have been broadly organized and cataloged, and efforts to digitize and preserve the legacy collection, and the connections within the collection, have been established. The NHP collection has also been reviewed from a biomechanics perspective and is viable for current and future research. With the expansion to incorporate the NHP collection complete, the living, searchable BDR database will allow researchers to access the data and advance the fields of research in injury biomechanics, military operations, crashworthiness and automotive safety, and medical trauma.

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Appendix A. Naval Biodynamics Laboratory Human Research Volunteer Run Setup

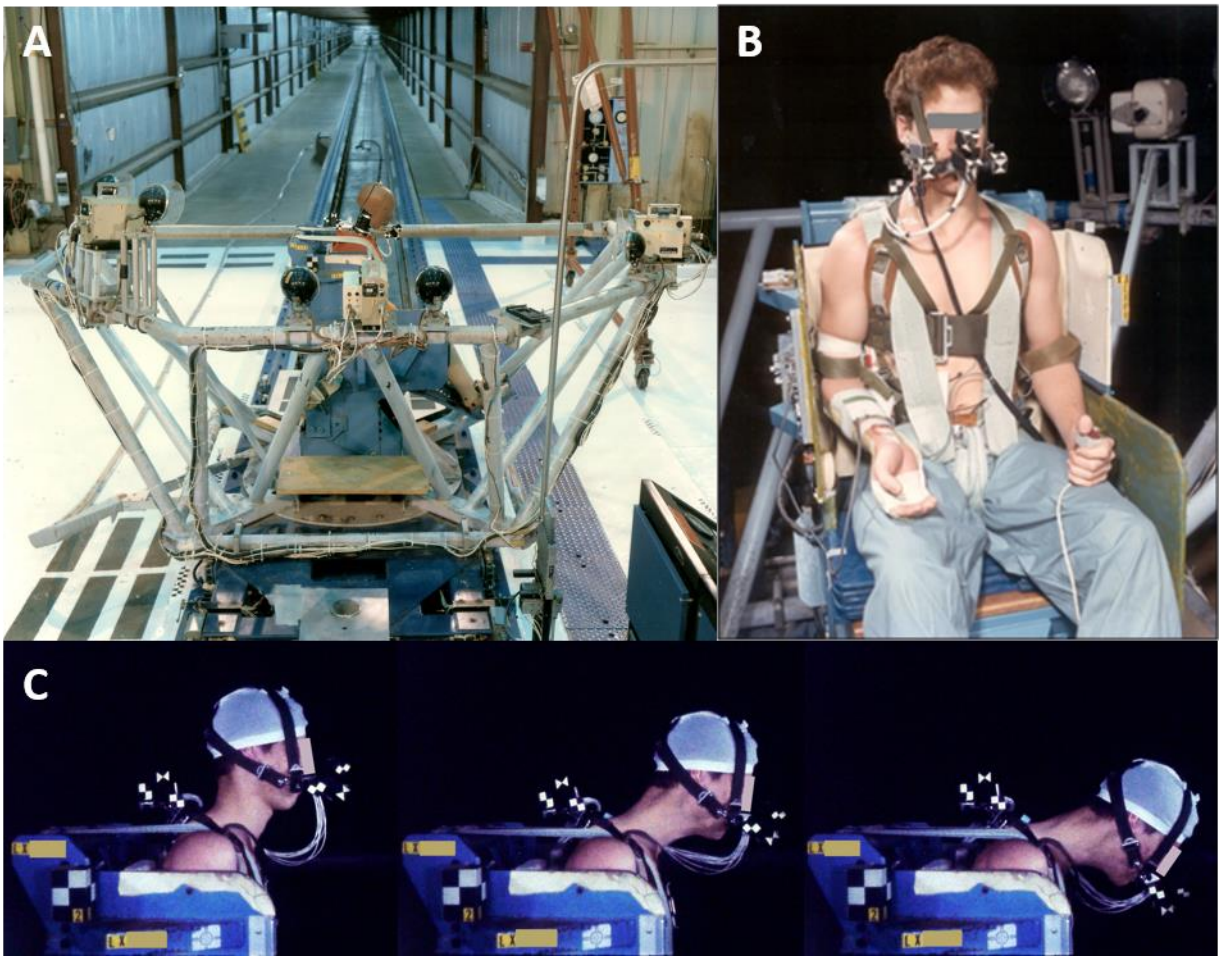

Figure A1. Human research volunteer run setup. (A) anthropomorphic test device (ATD) positioned for +Y impact acceleration run on the horizontal accelerator. The human research volunteer (HRV) runs were conducted using the same setup as the ATDs. Three high-speed cameras and an array of high-intensity lamps are rigidly mounted on the carriage to capture motion throughout the impact event. Phototarget/accelerometer clusters are affixed to the ATD's mouth and base of neck. (B) HRV fully instrumented for a run to collect sensor, photo, and electrophysiology data. (C) Three (non-consecutive) frames from one of the high-speed films of an HRV run, with phototargets on the mouth mount, first thoracic vertebrae (T1) mount, and carriage.

Appendix B. Non-Human Primate Pathology Collection

Table B1. Detailed Overview of the Samples within the Non-Human Primate Pathology Collection

Organ	Slide-Mounted Tissue Samples	Embedded-Tissue Blocks	Total Pathology Samples	Total Unique NHP
Brain	1086	1083	2169	74
basal ganglia	0	1	1	1
cerebellum	111	88	199	56
cerebrum	51	0	51	15
dura	0	6	6	6
fourth ventricle	98	31	129	27
frontal lobe	54	43	97	44
hippocampus	1	3	4	4
medulla	105	100	205	58
midbrain	60	52	112	44
occipital lobe	54	45	99	46
parietal lobe	54	37	91	36
pituitary	45	52	97	53
pons	78	73	151	46
temporal lobe	99	63	162	37
thalamus	7	0	7	4
vermis cerebelli	54	41	95	42
unspecified	215	448	663	11
Spinal Cord	384	643	1027	60
Digestive Organs	0	16	16	1
Unspecified	2761	1809	4570	118
Summary:	4231	3551	7782	121

Note. Samples were identified by labels on the samples themselves or matched identifiers within the NBDL pathology record book. All samples are classified “as-recorded.” No re-classification of samples was attempted and only organs and regions that are explicitly labeled (or matched to labels) on the sample are captured in this table. For any sample labeled with multiple organ and/or organ region locations, the sample is captured in each location. Therefore, the total samples reported in this table may be greater than the total number of physical items in the pathology collection. If the organ and/or organ region of the tissue sample was not identified, the sample is classified as "unspecified."

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